Short and long sleep duration are associated with prevalent cardiovascular disease in Australian adults

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Short and long sleep duration are associated with prevalent cardiovascular disease in Australian adults

Abstract
A growing number of studies from a range of different countries have observed an association between sleep duration and cardiovascular disease. The objective of this paper was to examine the associations between sleep duration and prevalent cardiovascular disease in a large sample of Australian adults, and identify the sociodemographic and health-related factors moderating these associations. Participants included 218 155 Australian adults aged 45 years and over. The results indicated that 6 h versus 7 h sleep was associated with increased odds of heart disease [odds ratio (OR) = 1.11 (1.06–1.17)], diabetes [OR = 1.15 (1.09–1.22)], stroke [OR = 1.25 (1.14–1.38)] and high blood pressure [OR = 1.08 (1.04–1.11)]. Long sleep (≥9 h sleep) was also related to elevated odds of heart disease [OR = 1.14 (1.09–1.19)], diabetes [OR = 1.25 (1.19–1.31)], stroke [OR = 1.50 (1.38–1.62)] and high blood pressure [OR = 1.04 (1.01–1.08)] compared to 7 h sleep. Some of these relationships varied by age, and were not evident in adults aged 75 years and over. The magnitude of some associations varied significantly by body mass index, smoking and physical activity. These findings provide further insight into the nature of the relationship between sleep and cardiovascular health.

Keywords
sleep, adults, long, disease, short, australian, cardiovascular, prevalent, associated, duration

Disciplines
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Short Title: Sleep duration and cardiovascular disease

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Summary

A growing number of studies from a range of different countries have observed an association between sleep duration and cardiovascular disease. The objective of this paper was to examine the associations between sleep duration and prevalent cardiovascular disease in a large sample of Australian adults, and identify the sociodemographic and health-related factors moderating these associations. Participants included 218,155 Australian adults aged 45 years and over. The results indicated that 6 h versus 7 h sleep was associated with increased odds of heart disease [odds ratio (OR) = 1.11 (1.06–1.17)], diabetes [OR = 1.15 (1.09–1.22)], stroke [OR = 1.25 (1.14–1.38)] and high blood pressure [OR = 1.08 (1.04–1.11)]. Long sleep (≥9 h sleep) was also related to elevated odds of heart disease [OR = 1.14 (1.09–1.19)], diabetes [OR = 1.25 (1.19–1.31)], stroke [OR = 1.50 (1.38–1.62)] and high blood pressure [OR = 1.04 (1.01–1.08)] compared to 7 h sleep. Some of these relationships varied by age, and were not evident in adults aged 75 years and over. The magnitude of some associations varied significantly by body mass index, smoking and physical activity. These findings provide further insight into the nature of the relationship between sleep and cardiovascular health.

Keywords: sleep duration, cardiovascular disease, epidemiology, short sleep, long sleep, diabetes, high blood pressure.
INTRODUCTION

Cardiovascular disease (CVD) is one of the leading causes of morbidity and mortality in developed countries, and is expected to become increasingly common (WHO, 2000). Smoking, obesity, high-fat diets and physical inactivity are established behavioural risk factors for CVD (WHO, 2000). Recent research has also identified relationships between sleep duration and CVD, which may have implications for further understanding behavioural contributors to CVD. Short sleep (i.e. ≤ 6 h sleep a night) has been associated with hypertension (Gangwisch et al., 2006; Gottlieb et al., 2006), stroke (Sabanayagam and Shankar, 2010), myocardial infarction (Ayas et al., 2003; Sabanayagam and Shankar, 2010), diabetes (Spiegel et al., 2005) and mortality from coronary heart disease (Ikehara et al., 2009; Shankar et al., 2008). Long sleep (≥ 9 h sleep a night) has also been linked with a variety of cardiovascular outcomes including hypertension (Gangwisch et al., 2006), stroke (Sabanayagam and Shankar, 2010) and cardiovascular mortality (Cappuccio et al., 2011).

Existing studies have examined the associations between sleep duration and CVD in a range of countries including the United States, Germany, the Netherlands, Singapore, Japan, and the United Kingdom (Cappuccio et al., 2011). However, there have been some inconsistencies in the results of these studies, perhaps reflecting lack of statistical power (especially for outcomes such as stroke) or differences in the types of confounding variables controlled. Furthermore, few studies have examined in detail whether the associations between sleep duration and cardiovascular conditions vary according to sociodemographic factors such as age and sex, obesity or health behaviours which are associated with sleep duration and CVD risk (Sabanayagam and Shankar, 2010). Thus, the objective of the present study was to investigate whether sleep duration was related to a range of cardiovascular conditions including stroke,
heart disease, diabetes and high blood pressure in a large sample of middle-aged and older Australian adults. This involved examining whether these associations varied by key sociodemographic variables, health behaviours (i.e. physical activity and smoking), and body mass index (BMI).

METHOD

This paper utilized data collected through the 45 and Up Study, a large cohort study of 266 848 adults aged 45 years and over who reside in the state of New South Wales in Australia. Participants for this study were recruited through the Medicare Australia enrolment database, which provides virtually complete enumeration of the general population, and were mailed a self-report questionnaire assessing a variety of sociodemographic and health-related factors. The primary objective of the 45 and Up Study was to collect information from a large, heterogeneous sample of adults and allow for meaningful comparisons of outcomes between subgroups (Banks et al., 2009). Informed consent was obtained from all participants and the 45 and Up Study received ethics approval from the University of NSW Human Research Ethics Committee. Ethics approval to use the 45 and Up Study data in this paper was obtained from the NSW Population and Health Services Ethics Committee.

Measures

The self-report questionnaire included the following question on sleep duration: ‘About how many hours in each 24-h day do you usually spend sleeping (including at night and naps)’?’. Consistent with existing research, sleep duration was recoded into five categories: <6 h sleep, 6 h sleep (i.e. ≥6 h and <7 h), 7 h (i.e. ≥7 h and <8 h), 8 h (i.e. ≥8 h and <9 h) and ≥9 h
(Cappuccio et al., 2011; Magee et al., 2009). The reference category was 7 h a night, which has the lowest rate of morbidity and all-cause mortality (Cappuccio et al., 2011; Kripke et al., 2002). Participants were also asked to indicate whether they had ever been diagnosed by a doctor as having heart disease, high blood pressure, stroke and diabetes.

Relevant sociodemographic and health-related variables were included in this paper as covariates. These included sex, age (categorized into 5-year age groups), country of birth (coded as Australia and Other country), education level (coded as <high school, high school, trade/apprenticeship/diploma, university), employment status (coded as not in paid work, retired, employed in part-time work, employed in full-time work) and marital status (coded as divorced/separated, widowed, single, married/partner). Participant postcodes were derived from the Medicare Australia enrolment database and were used to assess remoteness (i.e. whether individuals lived in a major city, rural or remote area). This was achieved using the Accessibility/Remoteness Index of Australia (ARIA) (Australian Bureau of Statistics, 2008), whereby participants were categorized as living in a major city (ARIA between 0 and 0.2), an inner regional area (ARIA > 0.2 and ≤2.4), an outer regional area (ARIA > 2.4 and ≤5.92) or a remote/very remote area (ARIA > 5.92).

Body mass index was used to provide an indication of body composition (WHO, 2000), and was coded into nine categories to allow fine-grained analyses (<18.5 kg m$^{-2}$, 18.5–19.9 kg m$^{-2}$, 20–22.49 kg m$^{-2}$, 22.5–24.9 kg m$^{-2}$, 25–27.49 kg m$^{-2}$, 27.5–29.9 kg m$^{-2}$, 30–32.49 kg m$^{-2}$, 32.5–34.9 kg m$^{-2}$, ≥35 kg m$^{-2}$). Alcohol consumption was assessed in terms of number of drinks consumed each week, with responses coded as no drinks, one to seven drinks, eight to 14 drinks and ≥15 drinks (Magee et al., 2009; National Health and Medical Research Council,
Cigarette smoking was assessed on the basis of three questions; this information was used to classify individuals as ‘current smokers’, ‘former smokers’ and ‘never-smokers’. Each participant was asked to indicate the amount of time spent in each of the following activities in the previous 1 week: walking continuously for at least 10 min; moderate physical activities (e.g. gentle swimming, vigorous gardening); and vigorous physical activities (e.g. jogging, cycling) (Department of Health and Ageing, 2005). Total physical activity each week was calculated by adding the time spent walking, engaged in moderate physical activity and engaged in vigorous physical activity (multiplied by a factor of 2). Participants were then categorized as engaging in insufficient (<150 min week$^{-1}$) or sufficient (≥150 min week$^{-1}$) physical activity. Screen time was assessed by the following question: ‘About how many hours in each 24-h day do you usually spend watching television or using a computer?’. Responses were coded as 0–1 h, 2–3 h, 4–5 h, 6–7 h and ≥8 h.

Participants were excluded from the analyses if they had missing data for sleep duration, high blood pressure, heart disease, stroke or diabetes. For the remaining variables, a separate category was added for missing values where appropriate.

Statistical Analysis

All data analysis was performed using sas Enterprise version 4.2. The associations between sleep duration and each cardiovascular outcome were assessed separately using logistic regression. For each cardiovascular outcome, three regression models were tested. In model 1, sleep duration was included as an independent variable with age, sex, country of birth, education, employment status, marital status and remoteness included as covariates. In model 2, BMI (categories) was included as an additional covariate. In model 3, physical activity,
smoking, screen time and alcohol consumption were added to test whether the associations between sleep duration and each cardiovascular outcome attenuated in the presence of these variables.

Interaction terms examining whether the associations between sleep duration and each cardiovascular outcome varied by age, sex, country of birth, education level, employment status, physical activity, smoking and BMI were then added separately to model 3. The significance of each interaction term was examined using a likelihood ratio test, which compared the models with and without the interaction terms. All results are presented as odds ratios (OR) with 95% confidence intervals (CI). Statistical significance was determined by a $P$-value <0.05.

Interaction terms examining whether the associations between sleep duration and each cardiovascular outcome varied by age, sex, country of birth, education level, employment status, physical activity, smoking, and BMI were then added separately to model 3. The significance of each interaction term was examined using a likelihood ratio test, which compared the models with and without the interaction terms. All results are presented as odds ratios (OR) with 95% confidence intervals (CI). Statistical significance was determined by a $P$-value <.05.

RESULTS

The 45 and Up Study baseline data set consists of 266 848 adults aged 45 years and over. Approximately 18% of participants had missing data on sleep duration, high blood pressure, diabetes, heart disease and stroke. When these cases were excluded, the sample size consisted of 218 155 participants aged 45–106 years old [mean = 62.4; standard deviation (SD) = 11.0].
The majority of participants reported 7 (23.9%) or 8 (40.7%) h sleep a night, with 3.6% reporting <6 h sleep, 12.1% reporting 6 h sleep and 19.7% reporting ≥ 9 h sleep a night. High blood pressure was the most common cardiovascular condition (35.5% of participants), followed by heart disease (11.8%), diabetes (8.7%) and stroke (3.0%). As shown in Table 1, these conditions were significantly more likely among short and long sleepers. Table 1 also indicates that demographic and behavioural characteristics varied significantly between the sleep categories. In particular, short and long sleepers were more likely to be current smokers and obese, and less likely to have a tertiary qualification and meet current recommendations for sufficient physical activity.

Table 1. Socio-demographic and health characteristics of participants from the 45 and Up Study according to sleep duration (n = 218,155)

|                       | < 6 hours (n = 7752) | 6 hours (n = 26,383) | 7 hours (n = 52,088) | 8 hours (n = 88,875) | ≥ 9 hours (n = 43,057) | P value  
|-----------------------|----------------------|----------------------|----------------------|----------------------|-----------------------|---------
| Age, mean (SD)        | 64.5 (11.9)          | 61.8 (10.9)          | 60.3 (10.2)          | 61.9 (10.6)          | 66.3 (11.6)           | < .001  
| Sex, %                |                      |                      |                      |                      |                      |         
| Male                  | 41.8                 | 46.0                 | 48.0                 | 46.1                 | 50.5                 | < .001  
| Female                | 58.2                 | 54.0                 | 52.0                 | 53.9                 | 49.5                 |         
| Born in Australia, %  | 70.1                 | 72.4                 | 73.2                 | 76.1                 | 77.6                 | < .001  
| Tertiary Education, % | 13.3                 | 22.5                 | 29.9                 | 24.4                 | 17.6                 | < .001  
| Urban Resident, %     | 47.4                 | 49.7                 | 49.7                 | 43.5                 | 39.1                 | < .001  
| Married, %            | 61.7                 | 70.4                 | 77.3                 | 78.0                 | 74.6                 | < .001  
| Employed Full         | 25.2                 | 40.3                 | 45.6                 | 35.1                 | 18.2                 | < .001  

<table>
<thead>
<tr>
<th>Time, %</th>
<th></th>
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<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>High Blood Pressure, %</td>
<td>39.1</td>
<td>36.5</td>
<td>32.2</td>
<td>34.2</td>
<td>41.1</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Diabetes, %</td>
<td>12.5</td>
<td>9.1</td>
<td>6.8</td>
<td>7.9</td>
<td>11.7</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Stroke, %</td>
<td>5.0</td>
<td>2.9</td>
<td>1.9</td>
<td>2.5</td>
<td>5.1</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Heart Disease, %</td>
<td>14.9</td>
<td>11.4</td>
<td>9.3</td>
<td>10.8</td>
<td>7076</td>
<td>&lt; .001</td>
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<td>Sufficient physical activity, %</td>
<td>65.2</td>
<td>73.7</td>
<td>79.2</td>
<td>77.4</td>
<td>70.2</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Current Smoker, %</td>
<td>11.0</td>
<td>9.2</td>
<td>6.8</td>
<td>6.3</td>
<td>6.8</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Obese, %</td>
<td>27.5</td>
<td>24.8</td>
<td>20.7</td>
<td>21.3</td>
<td>23.5</td>
<td>&lt; .001</td>
</tr>
</tbody>
</table>

* P value based on chi-square tests of independence, with the exception of age where the differences between sleep categories were examined using ANOVA.

**Stroke**

The results for model 1 (see Table 2 and Fig. 1a) indicated a U-shaped association between sleep duration and stroke. Compared to 7 h sleep, <6 h [odds ratio (OR) = 1.70 (1.50–1.92)], 6 h [OR = 1.31 (1.19–1.45)], 8 h [OR = 1.09 (1.01–1.18)] and ≥9 h sleep [OR = 1.58 (1.46–1.71)] were associated significantly with elevated odds of stroke. These effects were similar when BMI was added (model 2), but attenuated slightly when the behavioural factors were added (model 3). In the fully adjusted model (model 3), <6 h [OR = 1.54 (1.36–1.75)], 6 h [OR = 1.25 (1.14–1.38)], 8 h [OR = 1.08 (1.00–1.17)] and ≥9 h sleep [OR = 1.50 (1.38–1.62)] were associated with increased odds of stroke.
Table 2. Association between sleep duration and CVD in the 45 and Up Study cohort (n = 218,155).

<table>
<thead>
<tr>
<th>No. Cases</th>
<th>Model 1&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Model 2&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Model 3&lt;sup&gt;c&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Stroke</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 6 hours</td>
<td>6,541 (3.00)</td>
<td>1.70* [1.50 – 1.92]</td>
<td>1.66* [1.47 – 1.88]</td>
</tr>
<tr>
<td>6 hours</td>
<td>Ref</td>
<td>1.31* [1.19 – 1.45]</td>
<td>1.30* [1.18 – 1.43]</td>
</tr>
<tr>
<td>7 hours</td>
<td>Ref</td>
<td>Ref</td>
<td>Ref</td>
</tr>
<tr>
<td>8 hours</td>
<td>1.09* [1.01 – 1.18]</td>
<td>1.09* [1.01 – 1.18]</td>
<td>1.08* [1.00 – 1.17]</td>
</tr>
<tr>
<td>≥ 9 hours</td>
<td>1.58* [1.46 – 1.71]</td>
<td>1.56* [1.44 – 1.69]</td>
<td>1.50* [1.38 – 1.62]</td>
</tr>
<tr>
<td><strong>Heart Disease</strong></td>
<td>25,669 (11.77)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 6 hours</td>
<td>1.28* [1.19 – 1.38]</td>
<td>1.25* [1.16 – 1.35]</td>
<td>1.23* [1.15 – 1.33]</td>
</tr>
<tr>
<td>6 hours</td>
<td>1.14* [1.08 – 1.20]</td>
<td>1.13* [1.07 – 1.18]</td>
<td>1.11* [1.06 – 1.17]</td>
</tr>
<tr>
<td>7 hours</td>
<td>Ref</td>
<td>Ref</td>
<td>Ref</td>
</tr>
<tr>
<td>8 hours</td>
<td>1.01 [0.97 – 1.05]</td>
<td>1.01 [0.97 – 1.05]</td>
<td>1.01 [0.97 – 1.05]</td>
</tr>
<tr>
<td>≥ 9 hours</td>
<td>1.16* [1.12 – 1.21]</td>
<td>1.15* [1.10 – 1.20]</td>
<td>1.14* [1.09 – 1.19]</td>
</tr>
<tr>
<td><strong>Diabetes</strong></td>
<td>18,974 (8.70)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 6 hours</td>
<td>1.50* [1.39 – 1.62]</td>
<td>1.37* [1.27 – 1.49]</td>
<td>1.28* [1.18 – 1.39]</td>
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<tr>
<td>6 hours</td>
<td>1.26* [1.19 – 1.33]</td>
<td>1.19* [1.13 – 1.26]</td>
<td>1.15* [1.09 – 1.22]</td>
</tr>
<tr>
<td>7 hours</td>
<td>Ref</td>
<td>Ref</td>
<td>Ref</td>
</tr>
<tr>
<td>8 hours</td>
<td>1.07* [1.03 – 1.12]</td>
<td>1.06* [1.02 – 1.11]</td>
<td>1.07* [1.02 – 1.12]</td>
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<tr>
<td>≥ 9 hours</td>
<td>1.33* [1.27 – 1.39]</td>
<td>1.27* [1.21 – 1.33]</td>
<td>1.25* [1.19 – 1.31]</td>
</tr>
<tr>
<td><strong>High Blood Pressure</strong></td>
<td>77,541 (35.54)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sleep Duration</td>
<td>A. Stroke Odds Ratio</td>
<td>B. Heart Disease Odds Ratio</td>
<td>C. Diabetes Odds Ratio</td>
</tr>
<tr>
<td>----------------</td>
<td>---------------------</td>
<td>-----------------------------</td>
<td>-----------------------</td>
</tr>
<tr>
<td>&lt; 6 hours</td>
<td>1.10* [1.04 – 1.15]</td>
<td>1.02 [0.97 – 1.08]</td>
<td>1.06* [1.03 – 1.09]</td>
</tr>
<tr>
<td>6 hours</td>
<td>1.12* [1.09 – 1.16]</td>
<td>1.07* [1.04 – 1.11]</td>
<td>Ref</td>
</tr>
<tr>
<td>7 hours</td>
<td>Ref</td>
<td>Ref</td>
<td>Ref</td>
</tr>
<tr>
<td>8 hours</td>
<td>1.00 [0.97 – 1.02]</td>
<td>0.99 [0.97 – 1.02]</td>
<td>0.99 [0.96 – 1.01]</td>
</tr>
<tr>
<td>≥ 9 hours</td>
<td>1.10* [1.07 – 1.13]</td>
<td>1.06* [1.03 – 1.09]</td>
<td>Ref</td>
</tr>
</tbody>
</table>

* a: age, sex, country of birth, marital status, education, employment status, and remoteness included as covariates.
  b: obesity added as a covariate.
  c: physical activity, smoking, alcohol and screen time added as covariates.

* p < .05

Figure 1. Associations of sleep duration with stroke (a), heart disease (b), diabetes (c) and high blood pressure (d). Data presented as odds ratios (adjusted for age, sex, country of birth, marital status, education, employment status and remoteness) with 95% confidence interval.
The relationship between sleep duration and stroke did not vary significantly by age, sex, education, country of birth, employment status, smoking status or BMI. However, the association varied significantly by physical activity ($\chi^2$ for interaction = 15.6, $P = 0.004$). In particular, the association between <6 h sleep and stroke was more pronounced in those with <150 min of physical activity per week [OR = 1.72 (1.47–2.02)] compared to those engaging in ≥150 min of physical activity per week [OR = 1.36 (1.12–1.65)].

**Heart Disease**

In model 1, <6 h [OR = 1.28 (1.19–1.38)], 6 h [OR = 1.14 (1.08–1.20)] and ≥9 h sleep [OR = 1.16 (1.12–1.21)] were associated significantly with elevated odds of heart disease (Table 2 and Fig. 1b). The magnitude of the odds ratios remained similar despite the addition of BMI and health behaviours in models 2 and 3. The results for the fully adjusted model (model 3), indicated that <6 h [OR = 1.23 (1.15–1.33)], 6 h [OR = 1.11 (1.06–1.17)] and ≥9 h sleep [OR = 1.14 (1.10–1.19)] were significantly related to heart disease. The relationship between sleep duration and heart disease did not differ significantly by sex, country of birth, employment status, education, physical activity or BMI. However the sleep × age interaction was significant ($\chi^2_{32}$ for interaction = 66.3, $P < 0.001$). The results indicated that short sleep was associated significantly with increased odds of heart disease in adults aged <75 years, but not in those aged 75 years and over. Long sleep was associated with heart disease only in adults aged <65 years. The association between sleep duration and heart disease also varied significantly based on smoking status, with a generally weaker relationship of short sleep duration to heart disease in smokers compared to non-smokers ($\chi^2_{12}$ for interaction = 24.8, $p = .016$).
**Diabetes**

As shown in Table 2 and Fig. 1c, <6 h [OR = 1.50 (1.39–1.62)], 6 h [OR = 1.26 (1.19–1.33)], 8 h [1.07 (1.03–1.12)] and ≥9 h sleep [OR = 1.33 (1.27–1.39)] were associated significantly with diabetes in model 1. The magnitude of the relationships between short sleep and diabetes attenuated but remained significant when BMI and health behaviours were added in models 2 and 3. The relationship between long sleep and diabetes also attenuated slightly in the presence of BMI and the health behaviour variables. In the fully adjusted model, <6 h [OR = 1.28 (1.18–1.39)], 6 h [OR = 1.15 (1.09–1.22)], 8 h [OR = 1.07 (1.02–1.12)] and ≥9 h [OR = 1.25 (1.19–1.31)] remained associated with diabetes. The relationship between short sleep and diabetes did not vary significantly by any of the sociodemographic variables, health behaviours or BMI.

**High Blood Pressure**

In the total sample, <6 h [OR = 1.10 (1.04–1.15)], 6 h [OR = 1.12 (1.09–1.16)] and ≥9 h sleep [OR = 1.10 (1.07–1.13)] were associated with high blood pressure in model 1 (see Table 2 and Fig. 1d). These effects attenuated slightly with the addition of BMI and health behaviours as covariates. The final model (model 3) indicated that 6 h sleep [OR = 1.08 (1.04–1.11)] and ≥9 h sleep [OR = 1.04 (1.01–1.08)] were associated with high blood pressure.

The association between sleep duration and high blood pressure varied significantly by age ($\chi^2_{32}$ for interaction = 59.9, $P = 0.002$). Further analyses indicated that both short and long sleep were associated significantly with high blood pressure in participants aged <70 years, but diminished and was no longer significant in those aged 70 years and over. The relationship between sleep duration and high blood pressure also varied according to an individual’s BMI ($\chi^2_{32}$ for interaction = 74.002, $P < 0.001$). Short and long sleep duration were associated
significantly with high blood pressure across most of the BMI categories. However, the association between short sleep and high blood pressure was attenuated in individuals with a BMI above 32.5 kg m$^{-2}$.

**DISCUSSION**

The present study identified significant relationships between sleep duration and a range of cardiovascular conditions in a large sample of middle aged and elderly Australian adults. Short and long sleeps were associated with heart disease, stroke, diabetes and high blood pressure; the magnitudes of the odds ratios were substantially smaller for high blood pressure possibly reflecting the higher prevalence of this condition. Our results are generally consistent with studies conducted in the United States, Europe and Asia (Ayas *et al.*, 2003; Gangwisch *et al.*, 2006; Gottlieb *et al.*, 2006; Ikehara *et al.*, 2009; Sabanayagam and Shankar, 2010; Shankar *et al.*, 2008).

The key strengths of the present study were the large sample size and the inclusion of multiple sociodemographic and health-related covariates. This provided sufficient statistical power to examine formally whether the associations between sleep duration and cardiovascular conditions varied by a range of sociodemographic factors, BMI, smoking and physical activity, and provides increased precision around the estimates of association. The U-shaped association between sleep duration and cardiovascular health did not vary significantly by most sociodemographic or health-related groups. However, there were some significant interactions. There was a trend towards short sleep being linked with heart disease and high blood pressure in middle-aged and elderly adults, but not in the very elderly. This supports some existing studies demonstrating that associations of certain sleep parameters such as short sleep and
sleep-disordered breathing with poor health (e.g. CVD, obesity, mortality) are sometimes not observed in the elderly (Gangwisch et al., 2006; Punjabi et al., 2009; Suzuki et al., 2009). The lack of significant findings in the elderly could reflect a range of age-related changes associated with health problems, such as cancers, sleep disorders and mental illnesses, which are more common in the elderly and may impact on sleep and cardiovascular health. In addition, individuals with sleep problems and CVD have a reduced likelihood of living as long as their peers. (Gangwisch et al., 2006). Thus, the lack of a significant finding in the elderly could also reflect the higher mortality rates of individuals with poorer health. The associations for sleep duration with stroke and diabetes did not differ by age, suggesting a similar pattern in middle aged, elderly and very elderly adults. The associations between long sleep and cardiovascular health were more consistent with age, perhaps indicating that long sleep is a marker of CVD in the elderly.

Some of the observed relationships varied by health-related factors. For example, the relationship between short sleep and high blood pressure was attenuated in individuals with a very high BMI (i.e. $\geq 32.5$ kg m$^{-2}$). This is in contrast to Sabanayagam and Shankar (2010), who found that short and long sleep were associated with CVD in both lean ($<25$ kg m$^{-2}$) and overweight/obese ($\geq 25$ kg m$^{-2}$) individuals. These discrepancies are likely to reflect the different analytical approaches adopted in these studies, with the present study examining more fine-grained categories of BMI. Our results indicate that high blood pressure was much more common in individuals with a BMI $\geq 32.5$ kg m$^{-2}$ (54.3%) compared to those with a BMI $< 32.5$ kg m$^{-2}$ (33.0%), which may be due to lifestyle and health-related factors (e.g. diet, physical activity, stress, other health conditions). These factors could mask the association between sleep duration and high blood pressure in individuals with a higher BMI.
The association between heart disease and sleep was weaker in current smokers compared with non-smokers and former-smokers. The reason for this is unclear, but could reflect a ‘masking’ effect, i.e. that the effect of smoking on heart disease is so pronounced that it is difficult to discern other influences beyond this. Finally, the association between short sleep and stroke was more pronounced in individuals who engaged in less physical activity. Although there are a number of possible explanations for this finding, individuals with stroke have lower rates of physical activity because of poorer physical functioning (Gordon et al., 2004). As physical activity is associated with improved sleep (Youngstedt, 2005), short sleep and lower physical activity could co-occur in some individuals with stroke.

Although the present paper included a very large sample of middle aged and older Australian adults, it is limited by the cross-sectional nature of the data which means we are unable to determine the direction of causation. This is an important consideration, given that the temporal associations between short sleep and cardiovascular conditions are likely to be bi-directional. For instance, short sleep could be a consequence of an underlying cardiovascular condition. This is because the conditions examined in this study are associated with pain and discomfort which have the potential to disrupt normal sleep and contribute to shorter sleep durations. Furthermore, various medications such as statins and antihypertensives used to treat/prevent cardiovascular-related conditions have the potential to affect the quality and duration of sleep. The use of these medications may also explain the link between short sleep and CVD, but were not examined in this paper.

Prospective data also indicate that short sleep predicts increased risk of CVD over time (Cappuccio et al., 2011), which could reflect a variety of mechanisms. Short sleep may increase CVD risk via obesity (Cappuccio et al., 2008), reflecting alterations in neuroendocrine
hormones such as leptin and ghrelin (Knutson et al., 2007). However, the association between short sleep and CVD in this paper did not attenuate considerably in the presence of BMI; this may indicate that factors additional to the metabolic syndrome and obesity could also link short sleep and CVD. Such mechanisms could include reduced insulin sensitivity (Spiegel et al., 2005), impaired glucose tolerance (Chaput et al., 2007), increased sympathetic nervous system activation (Knutson et al., 2007) or inflammation (Mullington et al., 2009).

Although there are plausible physiological mechanisms for the association between short sleep and CVD, it is less clear how long sleep is associated with CVD morbidity and mortality. It has been suggested that long sleep is a consequence, and not a cause, of health problems such as CVD (Cappuccio et al., 2011; Patel et al., 2006). Another possibility is that the relationship between long sleep and poor health reflects residual confounding, whereby factors relevant to sleep and health are omitted or not controlled adequately (Grandner and Drummond, 2007; Knutson and Turek, 2006; Patel et al., 2006). This is especially relevant in the present context, as we were not able to control adequately for factors such as sleep apnoea, depression and socio-economic status (Grandner and Drummond, 2007; Knutson and Turek, 2006; Patel et al., 2006), which may link long sleep duration to CVD.

As noted above, the main limitation of the present study relates to its cross-sectional nature, which does not allow for inferences regarding causation to be made. Some relevant methodological issues relate to self-report of sleep duration, which are less accurate than actigraphy and polysomnography (van den Berg et al., 2008), may overestimate sleep duration (Lauderdale et al., 2008) and be biased by factors such as age, sex and health status (van den Berg et al., 2008). However, these more objective measures of sleep are not feasible for use in a large cohort study such as the 45 and Up Study. Furthermore, although less accurate, there is
generally reasonable agreement between objectively measured sleep and subjectively assessed sleep, with most adults able to estimate their sleep duration to within 1 h of sleep measured using actigraphs (van den Berg et al., 2008). The use of a single self-reported item to assess sleep duration is therefore an important limitation of this study, but the results are still meaningful given that the direction of bias due to measurement error in the hours of sleep is likely to be towards the null. The inclusion of multiple covariates also allowed for sufficient statistical analyses to examine whether these associations varied by sociodemographic and health-related factors.

The 45 and Up Study is a cohort study, and is not designed to be representative of the general population but rather provide sufficient heterogeneity of exposure to permit appropriate comparisons within the cohort. Although the response rate for the questionnaire was comparable to other studies of this nature (approximately 18%), experience with cohorts such as the British Doctors’ Study (Doll et al., 2004), and empirical and theoretical analyses demonstrate that relative risks derived from internal comparisons, such as those presented here, remain generalizable even if the cohort is not representative of the general population (Mealing et al., 2010).

This study is, to our knowledge, one of the largest cohort studies to report on the associations between sleep duration and indices of cardiovascular health. Evidently, there is a need for more prospective research to clarify ways in which sleep duration and CVD are related. This needs to involve investigation of relevant physiological and behavioural mechanisms, and formal analysis of how these associations vary by important sociodemographic variables. Although cross-sectional, the present results provide further insight into the nature of the association
between sleep duration and a range of cardiovascular conditions in middle-aged and older adults.

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