Sleep is an important modulator of cardiovascular, metabolic, and immune function, and sleep disorders are associated with vascular outcomes such as myocardial infarction (MI), stroke, and vascular death. Suboptimal sleep disrupts both circadian rhythms and many physiological systems while also inducing deleterious behavioral compensation including overeating and decreased exercise.1–5 It is also hypothesized that sleep disordered breathing (SDB), a condition characterized by repetitive apneas and hypopneas, causes a temporary spike in blood pressure associated with blood oxygen desaturation, arousal, and sympathetic activation causing cardiovascular disease (CVD) and stroke. An emerging literature on sleep suggests that sleep disorders may be highly problematic and linked to many health problems. The prospective literature on sleep and vascular disease typically measures sleep abnormalities in 1 of 3 ways: (1) engagement in shift work; (2) presence of SDB; and (3) sleep length. Investigations of shift work are equivocal with some investigators finding associations with CVD, 6–9 some not, 10,11 and some others finding an association with ischemic stroke11,12 and others not.13 The 4 prospective studies of the association between SDB and vascular end points have found an increased risk of a cardiovascular end point among individuals with severe apnea–hypopnea compared with individuals with either no or mild apnea–hypopnea suggesting an association between the two.14–17 Research on sleep length and vascular disease has documented positive relationships between short or long sleep compared with normal sleep length (7–8 hours per night) and CVD, 18–20 but only one has assessed stroke risk.19 One study found an association...
WHAT IS KNOWN

- Sleep problems are prevalent in adults in the United States.
- Poor quality and quantity of sleep may be independently associated with vascular events.

WHAT THIS ARTICLE ADDS

- People with significant daytime dozing had a significantly increased risk of vascular events including stroke, heart attack, and vascular death.
- The risk of vascular events associated with daytime dozing did not vary by race–ethnicity.

between daytime somnolence and an increased risk of CVD but not stroke. The Northern Manhattan Study (NOMAS) is a prospective population-based cohort study documenting incidence, risk factors, and prognosis of stroke in a multiethnic urban community. Based in northern Manhattan, an area of 63% Hispanic, 20% black, and 15% white and is strongly representative of the underlying ethnic mix in this community. The methodology for the NOMAS study has been described previously and will be summarized briefly below.

Selection of Prospective Cohort

A total of 3298 subjects were recruited and enrolled in NOMAS between 1993 and 2001. Individuals were eligible if they (1) had never been diagnosed with an ischemic stroke, (2) were ≥40 years of age, and (3) had resided for at least 3 months in a household with a telephone in northern Manhattan. Subjects were identified by random digit dialing, and interviews were conducted using trained bilingual interviewers. The telephone response rate was 91% (9% refused to be screened). This study was approved by the Columbia University IRB.

Baseline Evaluation

Subjects were recruited from the telephone sample to have an in-person baseline interview and assessment. The enrollment response rate was 75%, giving an overall response rate of 68% (Telephone Response Enrollment Response). Standardized questions focused on vascular risk factors were adapted from the validated Centers for Disease Control and Prevention Behavioral Risk Factor Surveillance System.

Definition of the Sleep Cohort

As part of NOMAS, the Epworth Sleepiness Scale (ESS) was administered during the 2004 annual follow-up. We collected the ESS on 2153 participants. Individuals did not have data on the ESS for these reasons: the participant died before January 1, 2004; was unable to be contacted during the year 2004 follow-up; had an incomplete follow-up interview; or the survey was completed by a proxy respondent. Of the 2153 who were administered the ESS, 124 individuals had a prevalent stroke or MI. Accordingly, each analysis uses individuals free of the clinical CVD event in question in 2004.

Assessment of Daytime Sleepiness

We used the ESS to measure daytime sleepiness as a measure of disrupted sleep. In light of apparent race–ethnic heterogeneity in the amount of sleep needed, we believe reports of daytime sleepiness will most accurately reflect the construct of disrupted/poor sleep across racial groups. We adapted the ESS for use in our community. Participants were asked, on a scale of 0 to 3, “How often would you say you doze while (1) sitting and reading, (2) watching TV, (3) sitting inactive in a public place, (4) as a passenger in a car, train, or bus, (5) sitting and talking to someone, (6) sitting quietly after lunch without alcohol, and (7) as a driver in a car while stopped for a few minutes in traffic?” The question “Lying down to rest in the afternoon when circumstances permit” was removed because there were differences in the interpretation of this question between Hispanic, black, and white populations. Additionally, after we began administering the survey, it quickly became apparent that the question “How often would you say you doze as a driver in a car while stopped for a few minutes in traffic?” was not applicable to most of a population-based cohort in Manhattan. We, therefore, adapted the scoring in 2 ways: instead of using 24 as the maximum score, we used 21. To account for the nonapplicability of the driving question, we calculated proportions of ESS (sum of scores/3×[the number of applicable and nonmissing question(s)]), and then the proportions were multiplied by 21 to make scores comparable across our participants. In order to make our scores comparable to other populations, we used threshold values from the literature to approximate categories of no, mild/moderate, and significant daytime dozing.

Methods

Study Population

The Northern Manhattan Study (NOMAS) is a prospective population-based cohort study documenting incidence, risk factors, and prognosis of stroke in a multiethnic urban community. Based in northern Manhattan, an area of ≤200,000 people, with 104,000±39 years of age, this study has a unique race–ethnic distribution of ≤63% Hispanic, 20% black, and 15% white and is strongly representative of...
Annual Prospective Follow-Up
Subjects were screened annually by telephone to determine change in vital status, detect neurological and cardiac symptoms and events, and review interval hospitalizations. Subjects and family are continually reminded to notify us in the event of ischemic stroke, MI, or death. Positive screens were scheduled for in-person assessment including chart review and examination by the study neurologists. Ongoing hospital surveillance of admission and discharge International Classification of Diseases-9 codes provided current data on morbidity and mortality.

Outcome Classifications—Stroke, MI, and Vascular Death
We classified incidence of ischemic stroke, MI, other vascular events, and all deaths (vascular and nonvascular). Ischemic stroke was defined by World Health Organization criteria. Ischemic stroke subjects underwent standard diagnostic tests, including brain imaging, to confirm ischemic stroke subtype, when possible. Over 70% of the ischemic stroke cases were hospitalized at the Columbia University Medical Center. Two neurologists classified the ischemic strokes independently after review of all of the data. MI was defined by criteria adapted from the Lipid Research Clinics Coronary Primary Prevention Trial and required at least 2 of the 3 criteria listed here: (1) ischemic cardiac pain determined to be typical angina; (2) cardiac enzyme abnormalities defined as abnormal creatine phosphokinase-MB fraction or troponin values; and (3) EKG abnormalities. For subjects who died, the date of death was recorded along with the cause of death. Deaths were classified as vascular or nonvascular based on information obtained from families, physicians, medical records, and death certificates. Causes of vascular death included ischemic stroke, MI, heart failure, pulmonary embolus, cardiac arrhythmia, and other vascular causes. All deaths were reviewed and validated by our team of study cardiologists and neurologists. The primary outcome of interest in this analysis was ischemic stroke. We also investigated these groups of outcomes: all stroke, MI, vascular death, nonvascular death, all deaths, and all vascular events (stroke, MI, vascular death). If an individual experienced multiple events (eg, 2 strokes), only the first event was included. However, if an individual experienced multiple but different events (eg, a stroke and an MI), each event was included in models with only 1 outcome, but only the first event was included in the aggregated outcomes. Thirty-six individuals had multiple events (3 stroke and MI; 14 stroke and vascular death; 13 MI and vascular death; 2 MI, stroke, and vascular death).

Definition of Race–Ethnicity
Race and ethnicity were defined by self-identification based on a series of interview questions modeled after the US census. Race was mutually exclusive and defined by 6 categories: white, black, Indian (American), Eskimo, Asian or Pacific Islander, and other. Ethnicity was subdivided as Hispanic or non-Hispanic based on the answer to the question “Are you of Spanish/Hispanic origin?” Race–ethnic groupings were mutually exclusive. All participants responding affirmatively to being of Spanish origin or identifying as Hispanic were classified as Hispanic in these analyses.

Covariates
Age, sex, race–ethnicity, and education were considered sociodemographic factors. Vascular risk factors included waist circumference, alcohol use, smoking, physical activity, fasting glucose, systolic blood pressure, diastolic blood pressure, ratio of total cholesterol to high-density lipoprotein level, peripheral vascular disease, and coronary artery disease. These covariates were found to be critical to the NOMAS Global Vascular Risk Score and are included in our models. Age was modeled continuously, and years of completed formal education were dichotomized into those who had completed high school versus those who had not received a high school diploma. Waist circumference, blood pressure, fasting glucose, and the total cholesterol to high-density lipoprotein index were modeled continuously. Moderate alcohol use was defined as current drinking of >1 drink per month and ≤2 drinks per day. Smoking was categorized as never, former, and current. Physical activity was defined as engaging in any leisure physical activity over the past 10 days prior to enrollment. Cardiac disease was defined as a history of angina, coronary artery disease, including surgery, atrial fibrillation, or valvular heart disease. We controlled for depression and use of sedative medications because these may confound the relationship between daytime sleepiness and vascular disease. Depression was measured using the Hamilton Depression Index and modeled continuously. Participants were asked whether they took any of the classes of medications listed here: antidepressants, antipsychotics, and pain medications. If the participant responded a “yes” or “sometimes,” they were judged to take a sedative medication. All covariates were measured at enrollment (baseline examination). Serum glucose, high-density lipoprotein, and triglycerides were measured from fasting plasma samples.

Statistical Analyses
We calculated the distribution of sociodemographics, vascular risk factors, history of sleep, and vascular outcomes across categories of daytime dozing and assessed for differences using the χ² test of independence and ANOVA as appropriate. We calculated the crude incidence for all outcomes in the total sample and by level of daytime dozing. We built a series of Cox proportional hazards regression models to examine the association of daytime dozing and risk of outcome events both before and after adjusting for the potential confounders described above. We dichotomized daytime sleepiness scores using previously reported cut points that reflect groups of individuals that do not doze, doze some, and doze significantly. We ran models adjusting (in turn) for our 3 measures of SDB to assess the effect of daytime sleepiness on our outcomes not mediated through SDB. Interactions between daytime sleepiness and race–ethnicity and between daytime sleepiness and sex were tested to assess whether the association between the level of daytime dozing and our outcomes varies by race–ethnicity or sex. Statistical analyses were performed with SAS (version 9.2, SAS Institute Inc., Cary, NC).

Results
Table 1 describes the distribution of sociodemographics, vascular risk factors, history of sleep, and vascular outcomes overall and across categories of daytime dozing. The mean age of study participants was 73.5 ± 9.3 years; 64% were women; 60% were Hispanic, 20% black, 18% white, and 3% other. Over 44% of the cohort reported no daytime dozing, whereas 47% reported some dozing and 9% significant daytime dozing. Women, Hispanics and blacks (compared with whites), individuals with less than a high school education, a larger waist circumference, nonmoderate drinkers, never smokers, sedentary individuals, and a higher fasting blood glucose were more likely to report severe dozing. Individuals reporting a sleep apnea diagnosis or snoring during the night were more likely to report mild or severe dozing during the day. Table 2 shows the frequency of end points and the incidence (per 100 person-years at risk) in the total cohort and by level of daytime dozing. There was a mean of 5.1 years of follow-up between administration of the ESS and the end of data collection for the sample used in this analysis. We documented 86 strokes, of which 75 were ischemic, as well as 53 MIs. We recorded 316 deaths, of which 124 (39%) were categorized as vascular. There were 219 total vascular outcomes. From the no dozing category to the severe dozing category, the incidence of stroke increased from 0.59 to 1.41, whereas
Table 1. Distribution of Sociodemographics, Vascular Risk Factors, History of Sleep and Vascular Outcomes Across Categories of Daytime Dozing in the NOMAS Sleep Cohort 2004–2010

<table>
<thead>
<tr>
<th></th>
<th>Overall*</th>
<th>No Dozing†</th>
<th>Some Dozing†</th>
<th>Severe Dozing†</th>
<th>P Value‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sociodemographics</td>
<td>n=2088</td>
<td>n=921</td>
<td>n=981</td>
<td></td>
<td>n=186</td>
</tr>
<tr>
<td>Age, y</td>
<td>73.5 ± 9.3</td>
<td>73.0 ± 9.3</td>
<td>74.0 ± 9.0</td>
<td>73.6 ± 10.2</td>
<td>0.07</td>
</tr>
<tr>
<td>Sex</td>
<td>751 (36.0)</td>
<td>307 (40.9)</td>
<td>383 (51.0)</td>
<td>61 (8.1)</td>
<td>0.02</td>
</tr>
<tr>
<td>Women</td>
<td>1337 (64.0)</td>
<td>614 (45.9)</td>
<td>598 (44.7)</td>
<td>125 (9.4)</td>
<td></td>
</tr>
<tr>
<td>Race–ethnicity</td>
<td>372 (17.8)</td>
<td>183 (49.2)</td>
<td>175 (47.0)</td>
<td>14 (3.8)</td>
<td>0.0003</td>
</tr>
<tr>
<td>Non-Hispanic white</td>
<td>413 (19.8)</td>
<td>177 (42.9)</td>
<td>209 (50.6)</td>
<td>27 (6.5)</td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>1252 (60.0)</td>
<td>539 (43.1)</td>
<td>574 (45.9)</td>
<td>139 (11.1)</td>
<td></td>
</tr>
<tr>
<td>Education</td>
<td>1128 (54.0)</td>
<td>460 (40.8)</td>
<td>555 (49.2)</td>
<td>113 (10.0)</td>
<td>0.002</td>
</tr>
<tr>
<td>≥High school</td>
<td>960 (46.0)</td>
<td>461 (48.0)</td>
<td>426 (44.4)</td>
<td>73 (7.6)</td>
<td></td>
</tr>
<tr>
<td>Other vascular risk factors</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Waist circumference</td>
<td>36.8 ± 4.8</td>
<td>36.4 ± 4.8</td>
<td>37.0 ± 4.9</td>
<td>37.1 ± 4.6</td>
<td>0.02</td>
</tr>
<tr>
<td>Systolic blood pressure</td>
<td>142.7 ± 20.6</td>
<td>142.2 ± 20.8</td>
<td>143.5 ± 20.6</td>
<td>141.0 ± 19.1</td>
<td>0.2</td>
</tr>
<tr>
<td>Diastolic blood pressure</td>
<td>83.5 ± 10.9</td>
<td>83.3 ± 11.1</td>
<td>83.6 ± 10.9</td>
<td>84.2 ± 10.1</td>
<td>0.57</td>
</tr>
<tr>
<td>Fasting glucose</td>
<td>103.3 ± 43.6</td>
<td>99.7 ± 38.5</td>
<td>105.5 ± 45.3</td>
<td>110.1 ± 55.2</td>
<td>0.002</td>
</tr>
<tr>
<td>HDL</td>
<td>46.2 ± 13.8</td>
<td>46.7 ± 14.0</td>
<td>45.9 ± 13.7</td>
<td>45.0 ± 13.7</td>
<td>0.2</td>
</tr>
<tr>
<td>Alcohol consumption</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate (X no. of drinks)</td>
<td>747 (35.8)</td>
<td>348 (46.6)</td>
<td>345 (46.2)</td>
<td>54 (7.2)</td>
<td>0.07</td>
</tr>
<tr>
<td>Not moderate</td>
<td>1341 (64.2)</td>
<td>573 (43.5)</td>
<td>566 (47.8)</td>
<td>132 (9.8)</td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>1035 (49.6)</td>
<td>446 (43.1)</td>
<td>476 (46.0)</td>
<td>113 (10.9)</td>
<td>0.01</td>
</tr>
<tr>
<td>Former</td>
<td>725 (34.7)</td>
<td>315 (43.5)</td>
<td>359 (49.5)</td>
<td>51 (7.0)</td>
<td></td>
</tr>
<tr>
<td>Current</td>
<td>327 (15.7)</td>
<td>160 (48.9)</td>
<td>145 (44.3)</td>
<td>22 (6.7)</td>
<td></td>
</tr>
<tr>
<td>Physical activity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>876 (42.0)</td>
<td>360 (41.1)</td>
<td>414 (47.3)</td>
<td>102 (11.6)</td>
<td>0.0004</td>
</tr>
<tr>
<td>Any</td>
<td>1212 (58.0)</td>
<td>561 (46.3)</td>
<td>567 (46.8)</td>
<td>84 (6.9)</td>
<td></td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>313 (15.0)</td>
<td>120 (38.3)</td>
<td>161 (51.4)</td>
<td>32 (10.2)</td>
<td>0.08</td>
</tr>
<tr>
<td>No</td>
<td>1775 (85.0)</td>
<td>801 (45.1)</td>
<td>820 (46.2)</td>
<td>154 (8.7)</td>
<td></td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>337 (16.1)</td>
<td>140 (41.5)</td>
<td>162 (48.1)</td>
<td>32 (10.4)</td>
<td>0.43</td>
</tr>
<tr>
<td>No</td>
<td>1751 (83.9)</td>
<td>781 (44.6)</td>
<td>819 (46.8)</td>
<td>151 (8.6)</td>
<td></td>
</tr>
<tr>
<td>Hamilton Depression Index</td>
<td>3.19 ± 3.98</td>
<td>3.10 ± 4.03</td>
<td>3.19 ± 3.84</td>
<td>3.61 ± 4.41</td>
<td>0.29</td>
</tr>
<tr>
<td>Sedative medication</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>542 (26.0)</td>
<td>228 (42.1)</td>
<td>253 (46.7)</td>
<td>61 (11.3)</td>
<td>0.07</td>
</tr>
<tr>
<td>No</td>
<td>1546 (74.0)</td>
<td>693 (44.8)</td>
<td>728 (47.1)</td>
<td>125 (8.1)</td>
<td></td>
</tr>
<tr>
<td>Sleep history</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dx sleep apnea (n=2004)</td>
<td>56 (2.9)</td>
<td>15 (23.2)</td>
<td>35 (62.5)</td>
<td>8 (14.29)</td>
<td>0.004</td>
</tr>
<tr>
<td>Reported snoring</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>737 (35.3)</td>
<td>387 (52.5)</td>
<td>303 (41.1)</td>
<td>47 (6.4)</td>
<td>&lt;0.0001‡</td>
</tr>
<tr>
<td>Some</td>
<td>1038 (49.7)</td>
<td>394 (38.0)</td>
<td>524 (50.5)</td>
<td>120 (11.6)</td>
<td></td>
</tr>
<tr>
<td>Don’t know</td>
<td>312 (15.0)</td>
<td>139 (44.6)</td>
<td>154 (49.4)</td>
<td>19 (6.1)</td>
<td></td>
</tr>
</tbody>
</table>

*Means and standard deviations are reported for continuous variables; frequency and column percentage reported for categorical variables (the percentage of the overall sample in each category).
†Means and standard deviations are reported for continuous variables; frequency and row percentage reported for categorical variables (the percentage of each level of a variable in each sleep category).
‡χ² Test of independence reported for categorical variables; ANOVA F-test reported for continuous variables.
§Excludes the Don’t know category.
In fully adjusted models, compared with those with no daytime dozing, individuals reporting severe daytime dozing had an increased risk of ischemic stroke (hazard ratio, 2.74 [95% confidence interval [CI], 1.38–5.43]); all stroke [3.00 (1.57–5.73)]; the combination of ischemic stroke, MI, and vascular death (2.38 [1.50–3.78]); all vascular events (2.48 [1.57–3.91]) (Table 3). There was also a borderline (P=0.06) association with all vascular deaths (1.91 [0.98–3.73]) compared with individuals reporting no daytime dozing. Mild daytime dozing was not significantly associated with any of our outcomes, though there was a trend toward increased risk for the combination of ischemic stroke, MI, and vascular death (1.22 [0.90–1.67]); all vascular events (1.24 [0.92–1.69]); and all vascular deaths (1.35 [0.89–2.04]). Models including product terms between race–ethnicity and categories of daytime dozing indicated that the associations between daytime dozing and the risk of outcomes do not vary by race–ethnicity (data not shown). There were interactions between sex and severe daytime dozing with all-cause mortality as

Table 3. Epworth Sleepiness Scale Scores and Hazards of Vascular Outcomes Among 2088 Participants in the Northern Manhattan Study 2004–2010

<table>
<thead>
<tr>
<th>Covariate</th>
<th>Ischemic Stroke*</th>
<th>All Stroke*</th>
<th>MI</th>
<th>Ischemic Stroke, MI, or Vascular Death</th>
<th>All Vascular Events (Stroke, MI, and Vascular Death)</th>
<th>All Deaths</th>
<th>Vascular Death</th>
<th>Nonvascular Death</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HR 95% CI</td>
<td>HR 95% CI</td>
<td>HR 95% CI</td>
<td>HR 95% CI</td>
<td>HR 95% CI</td>
<td>HR 95% CI</td>
<td>HR 95% CI</td>
<td>HR 95% CI</td>
</tr>
<tr>
<td>Model 1</td>
<td>Mild dozing</td>
<td>1.16 0.71–1.92</td>
<td>1.31 0.82–2.10</td>
<td>0.93 0.53–1.62</td>
<td>1.34 1.00–1.80</td>
<td>1.36 1.02–1.82</td>
<td>1.28 1.01–1.62</td>
<td>1.41 0.96–2.07</td>
</tr>
<tr>
<td></td>
<td>Severe dozing</td>
<td>2.41 1.25–4.65</td>
<td>2.60 1.40–4.83</td>
<td>0.86 0.30–2.46</td>
<td>2.12 1.39–3.24</td>
<td>2.18 1.44–3.30</td>
<td>1.35 0.91–2.00</td>
<td>1.81 1.01–3.25</td>
</tr>
<tr>
<td>Model 2</td>
<td>Mild dozing</td>
<td>1.1 0.66–1.85</td>
<td>1.21 0.74–1.97</td>
<td>0.90 0.51–1.60</td>
<td>1.25 0.93–1.69</td>
<td>1.27 0.95–1.71</td>
<td>1.16 0.91–1.47</td>
<td>1.32 0.89–1.95</td>
</tr>
<tr>
<td></td>
<td>Severe dozing</td>
<td>2.41 1.23–4.73</td>
<td>2.62 1.39–4.94</td>
<td>1.06 0.36–3.09</td>
<td>2.36 1.53–3.86</td>
<td>2.42 1.57–3.72</td>
<td>1.34 0.89–2.03</td>
<td>1.90 1.03–3.52</td>
</tr>
<tr>
<td>Model 3</td>
<td>Mild dozing</td>
<td>1.07 0.63–1.82</td>
<td>1.17 0.71–1.93</td>
<td>0.82 0.46–1.47</td>
<td>1.22 0.90–1.67</td>
<td>1.24 0.92–1.69</td>
<td>1.15 0.89–1.48</td>
<td>1.35 0.89–2.04</td>
</tr>
<tr>
<td></td>
<td>Severe dozing</td>
<td>2.74 1.38–5.43</td>
<td>3.00 1.57–5.73</td>
<td>0.83 0.24–2.82</td>
<td>2.38 1.50–3.78</td>
<td>2.48 1.57–3.91</td>
<td>1.36 0.87–2.12</td>
<td>1.91 0.98–3.73</td>
</tr>
</tbody>
</table>

Model 1: unadjusted.
Model 2: adjusted for age, sex, race, and education.
Model 3: adjusted for model 2 plus waist circumference, alcohol use, smoking, physical activity, fasting glucose, systolic blood pressure, diastolic blood pressure, ratio of total cholesterol to high-density lipoprotein (HDL) level, peripheral vascular disease, coronary artery disease, depression, and medication usage.
*Models did not meet proportional hazards assumption for alcohol use; models stratified by alcohol use produce similar results to models excluding alcohol use; therefore, we report estimates unadjusted for alcohol use for these outcomes.
an outcome \( (P=0.04) \), indicating that compared with no
daytime dozing, severe daytime dozing was associated with
greater risk of all-cause mortality among women but not men
(women: hazard ratio, 1.94 [95% confidence interval, 1.15–
3.27]); men: hazard ratio, 0.67 [95% confidence interval,
0.28–1.60]). When we used models (1) additionally adjusted
(in turn) for self-reported snoring, self-reported breathing or
choking experiences at night, and self-report of physician
diagnosed sleep apnea, (2) substituting diabetes mellitus for
fasting glucose and body mass index for waist circumference,
and (3) models adjusted for the NOMAS Global Vascular
Risk Score as opposed to its individual components, the
associations between daytime dozing and risk of outcomes
were consistent with those from models presented here (data
not shown).

Discussion
In a large, multiethnic, population-based, urban cohort, we
found that daytime sleepiness, as assessed by the ESS, is
associated with an increased risk of ischemic stroke and other
vascular events. Daytime sleepiness was not associated with
MI or nonvascular causes of death. Additionally, we found
no evidence that this association differed by race–ethnicity.
The implication, however, is that sleep is equally problematic
across race–ethnic groups, and our finding that non-Hispanic
blacks and Hispanics have higher levels of suboptimal sleep
than non-Hispanic whites suggests that sleep patterns may
have underlying health disparities in stroke and vascular
disease.33 Research reporting at least one third of Hispanics and
blacks are kept awake by financial, employment, personal
relationships, and/or health-related concerns suggests that
multiple social causes are potentially involved.22 Furthermore,
although much of the significance of sleep lies in the upper
10th percentile, or severe daytime dozing, the high prevalence
of moderate sleep disturbance as well as the high prevalence
of factors such as obesity and hypertension that may mediate
the relationship (see below) between sleep and vascular
outcomes additionally speaks to the public health significance
of sleep disturbance. Our results have important clinical impli-
cations as well. Daytime sleepiness remained a significant
predictor of vascular outcomes despite adjustment for a set of
covariates designed to optimize prediction of vascular events
in our study population.23 Our findings provide an opportunity
for potential intervention in the clinic setting. Asking whether
a patient dozes a lot during the day may greatly improve our
ability to identify individuals at high risk of a vascular event.
Further confirmation of risk could be ascertained through
diagnostic nights.

Although Elwood et al21 did not find an association between
daytime sleepiness and stroke, our results are generally in
agreement with the sleep length and SDB literatures.14–20,23
However, our fully adjusted hazard ratios were much larger
than any reported for the association between sleep length and
vascular events. For example, in extant studies, the strongest
fully adjusted measure of association (outcome of interest
in the study, sleep measure, study population) ranged from
1.4 (ischemic stroke, daytime somnolence, 7844 NHANES
I participants),19 1.41 (ischemic heart disease, daytime sleepi-
ness, 1986 55–69-year-old men in the United Kingdom),21
1.45 (CHD event, ≤5 hours of sleep, 71 617 participants in
the Nurses Health Study), and 1.79 (CHD mortality, ≥9 hours
of sleep, 58 044 Chinese ≥45 years of age).20 This indicates
that there may be substantial measurement error toward the
null when assessing sleep disturbance via self-reported sleep
length. Our findings were generally similar in magnitude to
associations between SDB and vascular events reported in
clinical populations again underscoring the importance of
suboptimal sleep as a significant population health issue.

With regard to the cause of the association between
sleep and CVD, though there may be people with sleep
disturbances caused by a subclinical disease, this does not
appear to be the dominant mechanism linking sleep and
CVD at the population level.20,34 Importantly, we excluded
individuals with prevalent stroke and CVD and controlled for
depression and use of sedative medications minimizing the
potential for reverse causation. Additionally, although daytime
sleepiness is associated with sleep apnea in our population,
models adjusted for measures of SDB were not substantially
different from our final models suggesting that the associa-
tion between daytime sleepiness and CVD is driven by more
than the biological effects of apnea. Our measure of the ESS,
therefore, represents a more general construct of sleepiness
(rather than a specific disorder), and there are various biological
and behavioral responses to poor sleep that may, there-
fore, explain our results. Research has found an association
between poor sleep and the incidence of hypertension and
diabetes mellitus.35–39 Results in Table 1 indicate that higher
levels of fasting glucose are associated with increasing levels
of daytime dozing, and we are planning future analyses of
these associations in NOMAS. Short sleep durations could
lead to these conditions through a combination of biologi-
cal and behavioral responses including increased 24-hour
blood pressure and heart rate, elevated sympathetic nervous
system activity, dysregulated hormonal control of appetite
and the immune system, increased salt retention, increased
exposure to stressors (physical and psychosocial), increased
irritability, impatience, pessimism, and decreased ability
to follow dietary or exercise regimens.1–4 Our final models
were adjusted for a number of biological and behavioral risk
factors, including systolic and diastolic blood pressure, fast-
ing blood glucose, physical activity, smoking and alcohol
consumption, suggesting that poor sleep may have an effect
on vascular disease not mediated through these pathways.
Importantly, in contrast to previous literature, we were able
to investigate the relationship between daytime sleepiness
and MI separate from other vascular outcomes. We found
no effect of daytime sleepiness on the risk of MI, which
suggests that among the elderly, the relationship between
sleep and vascular events is primarily driven by the associa-
tion between sleep and stroke; a relationship may still exist
among middle-age populations.

The results of this study should be considered in light of
its limitations. First, we adapted the ESS for use in our urban
community by removing a question about napping in the
afternoon. It is unclear how well this adaptation coincides
with the validated ESS. However, including a question that was
differentially applicable within the study population likely
would have biased the true level of sleepiness. Furthermore,
using proportions we converted our scores to reflect the same level of sleepiness in our sample as reported in the original validation of the ESS. Second, though the assessment of the ESS preceded each vascular outcome (the sleep cohort was free of prevalent stroke and MI) and we controlled for baseline comorbidities, the true latent period between the onset of sleepiness and the development of vascular disease is unknown. It is, therefore, impossible to rule out reverse causation. Third, evidence suggests blacks may interpret specific questions on the ESS differently than whites, artificially elevating their scores.41 If true, this would imply we have nondifferential (with respect to the outcome) misclassification of the exposure such that blacks are being classified as having more daytime sleepiness than they do. Blacks have higher rates of stroke and CVD than whites suggesting that our results may be upwardly biased. However, the association persisted when controlled for race and a number of important CVD risk factors mitigating this concern. Still, validation of the ESS in multiethnic populations should be a priority. Fourth, the mean age of our population is 75, and therefore, our results may have limited generalizability to younger age groups. Fifth, we were unable to control for psychological characteristics or life stresses. Sixth, we present results for 3 models on 8 outcomes with 8 additional tests or sensitivity analyses for each outcome. Although our outcomes and tests were chosen a priori, it is possible that some results were significant by chance alone. Another limitation lies in our inability to distinguish the type of sleep disturbance in the cohort and a lack of standard overnight sleep studies. Finally, our sample size and follow-up period are limited, but we have a very well-defined cohort with extremely rigorous follow-up and independent assessment of all outcomes by trained study physicians.

As the burden of vascular disease including stroke continues to dominate the public health arena, the need to identify and act on novel risk factors becomes more imperative. Building on our results, future research should attempt to replicate our findings particularly given that we modified the ESS for use in our population. Other work should focus on identifying specific mechanisms leading to sleep disturbance as well as a focus on control of sleep disturbances. This work provides evidence of the clinical significance of sleep disorders and the importance of identifying them, perhaps most effectively in the primary care setting. Indeed, the development of innovative prevention strategies to identify and modify sleep behaviors may positively and significantly decrease vascular disease burden.

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