Night Sleep Duration and Risk of Incident Anemia in a Chinese Population: A Prospective Cohort Study

Xiaoxue Liu1, Qiaofeng Song1, Wanning Hu2,3, Xiaochen Han3, Jianhui Gan4, Xiang Zheng5, Xizhu Wang1 & Shouling Wu6

The purpose was to study the association between sleep duration and the prevalence of anemia in Chinese people. There were 84,791 participants (men: 79.1%; women: 20.9%) aged 18–98 years in the prospective study. We divided the participants into five categories based on the individual sleep duration: ≤5 h, 6 h, 7 h (reference), 8 h, and ≥9 h. Anemia was defined based on hemoglobin <12 g/dL for men and <11 g/dL for women. The Cox proportional hazards model was used to assess the association between sleep duration and anemia. During median follow-up of 7.9 years, 2698 cases of anemia had occurred. The HR and (95% CI) of anemia (7 h as the reference group) for individuals reporting ≤5 h, 6 h, 8 h, and ≥9 h were 1.23 (1.04–1.45), 1.26 (1.11–1.44), 1.04 (0.92–1.16) and 1.42 (1.08–1.86), respectively. It showed that there was a significant interaction on the risk of anemia between sleep duration and sex in the secondary analysis (p < 0.001). The significant association between long sleep duration and anemia was found in women (HR, 2.29; 95% CI, 1.56–3.37), not in men (HR, 0.90; 95% CI, 0.60–1.34). Both short and long night sleep duration were associated with increased risk of anemia.

Anemia has been linked to cardiovascular disease and mortality1–4. Similar with the common cardiovascular risk factors, such as smoking, diabetes, hypertension and hypercholesterolemia, anemia can also increase the risk of mortality, morbidity and hospitalization1–6. Consequently, anemia has lately been characterized as another cardiovascular risk factor7–9. Thus, it is necessary to identify anemia-related risk factors so that we can take effective prevention and management strategies as early as possible. In addition to the traditional risk factors including age10, malnutrition, chronic kidney disease11, and poor glycemic control12,13, we have found some new risk factors for anemia, such as sleep14,15.

Recently, many epidemiological studies have reported that either a long or a short sleep duration is independently associated with cardiovascular disease16–22. Both sleep duration and anemia are recognized as strong, independent risk factors for ischemia and mortality events23,24. However, only a few studies to date have examined the association between sleep alterations and risk of iron deficiency anemia in infancy14,15. Another study evaluated the association between self-reported sleep duration and anemia on British people over 50 years old. The result showed that short sleep time could lead to low hemoglobin concentration, and disturbed sleep also increased the risk of anemia25. It is limited on the association between night sleep duration and risk for anemia in the general population. Alternatively, considering that a women-specific associations of short sleep duration with hypertension were reported in British population26,27, we further conducted a longitudinal analysis focusing primarily on the association between sleep duration and anemia, using the comprehensive data from the Kailuan Study28 stratified by age and sex.
Table 1. Baseline characteristics according to sleep duration.

| Variable                        | Sleep duration(hours) | ≤5 (n = 5998) | 6.0 (n = 14697) | 7 (n = 15103) | 8.0 (n = 47481) | ≥9 (n = 1512) | p value |
|---------------------------------|-----------------------|---------------|-----------------|---------------|----------------|--------------|---------|
| Age, years                      | 54.67 ± 11.36         | 52.24 ± 11.60 | 50.34 ± 12.17   | 49.58 ± 11.88 | 49.62 ± 13.87  | <0.01       |
| Sex male, n (%)                 | 4946 (82.46)          | 12377 (84.21) | 12169 (80.57)   | 36398 (76.66) | 1153 (76.26)   | <0.01       |
| High school or above, n (%)     | 1105 (18.42)          | 3527 (24.00)  | 4765 (31.55)    | 7939 (16.72)  | 468 (30.95)    | <0.01       |
| Current smoker, n (%)           | 3402 (56.72)          | 8636 (58.76)  | 8445 (55.92)    | 13173 (27.74) | 842 (55.69)    | <0.01       |
| Current alcohol, n (%)          | 3474 (57.92)          | 8974 (61.06)  | 8870 (58.73)    | 13458 (28.34) | 835 (55.22)    | <0.01       |
| Active physical-activity level, n (%) | 1535 (25.59)      | 3456 (23.52)  | 3523 (23.33)    | 4475 (9.42)   | 290 (19.18)    | <0.01       |
| Hypertension, n (%)             | 2951 (49.20)          | 6438 (43.80)  | 5992 (39.67)    | 20347 (42.85) | 602 (39.81)    | <0.01       |
| Systolic blood pressure, mmHg   | 132.89 ± 11.36        | 130.90 ± 20.39| 129.23 ± 20.47 | 130.04 ± 20.64| 128.44 ± 21.87| <0.01       |
| Diastolic blood pressure, mmHg  | 84.09 ± 11.76         | 83.38 ± 11.38 | 82.60 ± 11.37   | 83.61 ± 11.83 | 82.08 ± 12.22  | <0.01       |
| Diabetes mellitus, n (%)        | 698 (11.64)           | 1418 (9.65)   | 1333 (8.83)     | 3920 (8.26)   | 154 (10.19)    | <0.01       |
| Fasting blood glucose, mmol/L   | 5.51 ± 1.74           | 5.46 ± 1.62   | 5.43 ± 1.51     | 5.45 ± 1.63   | 5.48 ± 1.74    | 0.22        |
| Dyslipidemia, n (%)             | 2481 (41.36)          | 5699 (38.78)  | 5610 (37.14)    | 15749 (33.17) | 566 (37.43)    | <0.01       |
| Total cholesterol, mmol/L       | 5.02 ± 1.17           | 4.99 ± 1.21   | 4.96 ± 1.21     | 4.94 ± 1.11   | 4.89 ± 1.16    | <0.01       |
| Triglycerides, mmol/L           | 1.68 ± 1.31           | 1.71 ± 1.42   | 1.68 ± 1.36     | 1.67 ± 1.37   | 1.68 ± 1.37    | 0.35        |
| Low-density lipoprotein, mmol/L | 2.46 ± 0.87           | 2.46 ± 0.87   | 2.46 ± 0.87     | 2.31 ± 0.85   | 2.36 ± 0.87    | <0.01       |
| High-density lipoprotein, mmol/L| 1.55 ± 0.42           | 1.55 ± 0.40   | 1.52 ± 0.39     | 1.55 ± 0.40   | 1.53 ± 0.39    | <0.01       |
| Body mass index, kg/m²          | 25.04 ± 3.44          | 25.13 ± 3.41  | 25.09 ± 3.42    | 25.05 ± 3.50  | 25.09 ± 3.60   | <0.05       |
| High sensitivity C-reactive protein, mg/L | 0.80 (0.31–2.00) | 0.78 (0.30–1.89) | 0.80 (0.30–1.90) | 0.73 (0.28–2.00) | 0.88 (0.30–2.10) | <0.01      |

Results

The percent of participants who reported sleeping for ≤5 h, 6 h, 7 h, 8 h, and ≥9 h per night were 7.1%, 17.3%, 17.8%, 60.0%, and 1.8%, respectively. The baseline characteristics by sleep duration was shown in Table 1. There were significant associations between sleep duration and age, sex, education level, smoking status, drinking status, physical activity, body mass index, blood pressure level, fasting blood glucose, total cholesterol, hypertension, diabetes mellitus, dyslipidemia, snoring status, and high sensitive C-reactive protein. The similar result was also found in our previous paper.

Age, the percentage of women, education level, and the level of sensitivity C-reactive protein among participants with anemia were higher than those without anemia. In contrast, the prevalence of hypertension, the prevalence of obesity and snoring prevalence were lower among participants with anemia than without anemia (all p < 0.001).

As shown in Table 3, we can observe the hazard ratios for anemia according to sleep duration in total population and stratified by sex. Out of all the 84791 individuals, 2,698 participants developed anemia (men: 1,770; women: 928). The incidence per 1000 person years of anemia was 3.8 in men, and 7.2 in women. In the COX regression analysis, with adjustment for all variables (model 3), the multivariable adjusted hazard ratios of anemia among the participants were 1.23 (95% CI, 1.04–1.45) for ≤5 h sleep duration, 1.26 (95% CI, 1.11–1.44) for 6 h, 1.04 (95% CI, 0.92–1.16) for 8 h and 1.42 (95% CI, 1.08–1.86) for ≥9 h compared with the participants with 7 h of sleep. The risk of anemia in women who had more than 8 hours of sleep (HR, 2.29; 95% CI, 1.56–3.37) was higher, but not in men (HR, 0.90; 95% CI, 0.60–1.34), a formal test for difference by sex also found statistical significance (p-interaction for long sleep duration <0.001; P-interaction for short sleep duration >0.05). In addition, the association between sleep duration and anemia was still significant in participants excluding the individuals who have myocardial infarction, stroke and cancer.

Further study stratified by different age groups was analysed in Table 4. Participants aged <60 years and who slept ≤5 hours (HR, 1.24; 95% CI, 1.01–1.53) or ≥9 hours (HR, 1.40; 95% CI, 1.04–1.90) were found likely to develop anemia. The older participants (ages ≥60) who slept ≤5 h (HR, 1.16; 95% CI, 0.86–1.56) or ≥9 hours (HR, 1.04; 95% CI, 0.57–1.89) were less likely to develop anemia. The interaction of sleep duration with age on the incident anemia is not significant (p > 0.05).

Discussion

In the present study, both long and short sleep durations independently predicted an increased risk for incident anemia, after a follow-up of median 7.9 years, as shown during a median 7.9 years of follow-up. These relationships persist even after adjusting other known major risk factors, such as smoking, drinking, diabetes, hypertension, dyslipidemia, obesity, and high-sensitivity C-reactive protein. Sensitivity analyses further confirmed these findings. The English Longitudinal Study of Ageing (ELSA), with participants of 6465 men and women aged 50–99 years, found that there was significant influence of short and disturbed sleep on low hemoglobin concentrations. Results of this study further found that the disturbed sleep was a risk factor of anemia.
partly consistent with this study. But the difference is that we also demonstrated that a long sleep duration was an independent predictor for incident anemia. Additionally, in the previous studies, traditional predictors for anemia had no significant difference between men and women. However, we found that the risk of anemia in women with long sleep duration was higher. But the difference was not significant among men. We have not found the exact cause of the result yet. The reason for the gender difference in the relationship between the sleep time and the anemia may be due to the differences in hormonal secretion and psychological factors in gender. Unfortunately, we did not collect sufficient data on the pre- or post-menopause status of women participants, which appeared to be an important determinant of anemia risk in women. In addition, considering that this connection might be affected by different sleep behaviors in different age groups, we performed a stratified analysis based on age. Participants aged < 60 years and sleeping ≥ 9 hours were found to be more likely to develop anemia. However, there was no interaction between sleep duration and age in the risk of anemia (p-interaction > 0.05). The above results stratified by age and sex further endorsed the possibility that the associations observed may be driven entirely by younger women. However, the lack of information on biological differences among different groups limits us to further investigate whether the association could be modified or mediated by these factors.

Previous studies found that sleep apnea might be another pathway mediating long sleep duration with chronic diseases. Evidence also have showed that sleep apnea may be an important anemia predictor. A cohort study conducted in children also showed that children with sickle cell anemia had a high prevalence of sleep apnea with typical symptoms. Unfortunately, sleep apnea was not measured in our study, but snoring status was used as an alternative confounder instead of sleep apnea. After adjusting snoring status, sleep duration in our study was persistently associated with incident anemia.

We have not found the underlying mechanism for sleep duration and incident anemia. Inflammation is one of the most important biological pathways, because the long sleep time can lead to the increasing of inflammatory markers. In addition, the result that sleep deprivation could cause an increase in inflammatory response has been shown by a recent study. And in this study, individuals who reported short (≤ 5 h) or long sleep duration (≥ 9 h) were more likely to be engaged in higher level of sensitivity C-reactive protein group than those who slept 7 h. We also found that the level of sensitivity C-reactive protein in participants with anemia was higher than those without anemia.

**Limitations.** First, we collect the data of sleep duration through self-reported questionnaires. In contrast, the polysomnography is a more valid and reliable measurement of sleep. Information on Chinese midday naps and sleep quality were not collected in current study. Participants with sleep apnea were not excluded, which is associated with high risk of anemia. However, we adjusted for snoring status as an alternative confounder. In addition, the full model in our study was adjusted for corresponding risk factors for sleep apnea, such as body mass index, age, and smoking. Second, anemia in our study was only diagnosed using the hemoglobin content without employing red cell hematocrit, mean cellular volume, and bone marrow iron staining. Therefore, we could not distinguish different types of anemia (including sickle cell anemia, iron deficiency anemia or renal anemia) in this study. Third, we only investigated the sleep duration at the baseline, without taking the sleep

| Variable | Anemia | Without anemia | p value |
|----------|--------|----------------|---------|
| No. | 2698 | 8293 | |
| **Questionnaire-based data** | | | |
| Age, years | 50.55 ± 13.36 | 50.52 ± 11.93 | 0.008 |
| Sex male, n (%) | 1770 (65.60) | 65273 (79.51) | < 0.0001 |
| High school or above, n (%) | 627 (23.24) | 17177 (20.92) | < 0.05 |
| Current smoker, n (%) | 882 (32.69) | 33616 (40.95) | < 0.0001 |
| Current alcohol, n (%) | 970 (35.95) | 34641 (42.20) | < 0.0001 |
| Active physical-activity level, n (%) | 347 (12.86) | 12932 (15.75) | < 0.0001 |
| Snoring, n (%) | 328 (12.16) | 11843 (14.43) | < 0.0001 |
| **Exam-based data** | | | |
| Hypertension, n (%) | 1024 (37.95) | 35306 (43.01) | < 0.0001 |
| Systolic blood pressure, mmHg | 127.64 ± 21.64 | 130.30 ± 20.62 | < 0.0001 |
| Diastolic blood pressure, mmHg | 81.40 ± 11.73 | 83.46 ± 11.68 | < 0.0001 |
| Diabetes mellitus, n (%) | 244 (9.04) | 7279 (8.87) | 0.750 |
| Fasting blood glucose, mmol/L | 5.49 ± 1.93 | 5.45 ± 1.60 | 0.291 |
| Dyslipidemia, n (%) | 912 (33.80) | 29193 (35.56) | 0.060 |
| Total cholesterol, mmol/L | 4.93 ± 1.12 | 4.96 ± 1.15 | < 0.05 |
| Triglycerides, mmol/L | 1.53 ± 1.19 | 1.68 ± 1.38 | < 0.0001 |
| Low-density lipoprotein, mmol/L | 2.23 ± 1.07 | 2.38 ± 0.85 | < 0.0001 |
| High-density lipoprotein, mmol/L | 1.54 ± 0.40 | 1.54 ± 0.40 | 0.142 |
| Body mass index, kg/m² | 21.64 ± 5.90 | 21.64 ± 5.90 | < 0.0001 |
| High sensitivity C-reactive protein, mg/L | 0.94 (0.29–3.10) | 0.76 (0.30–1.90) | < 0.0001 |

Table 2. Comparisons between patients with and without anemia among Kailuan study.
duration changes into consideration. Indeed, any subsequent alterations in sleep may lead to a non-differential misclassification and potentially underestimate the sleep–anemia association. Fourth, there was not a rationale for the analysis in our study using 60 years as a cut-off value. Alternatively, we used the same cut-off value of 60 in our previous publications. Finally, we only investigated employees of the Kailuan Coal Company, which most of them were men. Therefore, the results may not be applicable to the general population.

In conclusion, our study suggests that both long and short sleep durations may cause an increased risk of anemia in a Chinese population. In addition to nutritional deficiencies, malignant tumor or other chronic illnesses, inappropriate sleep might be taken in this condition.

**Methods**

**Ethics statement.** The protocol for the present study was approved by the Ethics Committee of Kailuan General Hospital in compliance with the Declaration of Helsinki, and all participants provided written informed consent.

**Study design and participants.** The Kailuan study was a prospective cohort study involving 101510 participants (men: 81110; women: 20400, aged 18–98 years) in Kailuan community from June 2006 to October 2007. This study enrolled 84791 participants, excluding someone who had history of anemia (3703), incomplete sleep data (3986), and incomplete hemoglobin data (9030). We carried out questionnaire surveys and investigated clinical and laboratory indicators among all the participants. Before the study, all doctors and nurses received rigorous unified training.

**Assessment of sleep duration.** Sleep duration data was collected through a self-reported answer to the question “How many hours of sleep have you had on an average night in the preceding 3 months?” We divided sleep durations into five groups according to the responses: ≤ 5 hours, 6 hours, 7 hours, 8 hours, and ≥ 9 hours. Additionally, participants were asked to answer “yes” or “no” to the question “Do you generally snore when you sleep?”

**Assessment of potential covariates.** We collected the data of demographic and clinical characteristics self-reported questionnaires, including age, sex, alcohol use, education, and disease history. Educational status was divided into “illiterate or primary school”, “middle school”, or “high school or above”. Physical activity was divided into “≥ 80 minutes every week (active)”, “1 to 79 minutes every week (intermediate)”, or “none”. Smoking status and drinking status were divided into “never”, “former”, or “current”. Body mass index (BMI) was

| Total | Sleep duration(hours) | ≤ 5 | 6 | 7 | 8 | ≥ 9 |
|-------|-----------------------|-----|---|---|---|-----|
| Case(incidence per 1000 person years) | 204 (4.93) | 510 (4.94) | 431 (4.01) | 1490 (4.47) | 63 (6.08) |
| Model 1 | 1.22 (1.03–1.44) | 1.26 (1.10–1.43) | reference | 1.08 (0.97–1.20) | 1.45 (1.11–1.89) |
| Model 2 | 1.24 (1.04–1.46) | 1.26 (1.11–1.44) | reference | 1.03 (0.92–1.15) | 1.45 (1.11–1.88) |
| Model 3 | 1.23 (1.04–1.45) | 1.26 (1.11–1.44) | reference | 1.04 (0.92–1.16) | 1.42 (1.08–1.86) |

**Table 3.** Hazard ratios (95% CI) for anemia according to sleep duration in the Kailuan Study. Model 1: Adjusted for age and sex. Model 2: Adjusted for age, sex, level of education, smoking, alcohol, physical activity, and snoring. Model 3: Adjusted for variables in Model 2 plus hypertension, diabetes mellitus, dyslipidemia, body mass index, and high-sensitivity C-reactive protein. *Adjusted for Model 3 and further excluded individuals with myocardial infarction, stroke and cancer. †Adjusted for above confounding factors without sex. §Adjusted for Model 3 and used 8 hours/night as the reference group.

P for interaction < 0.001

Table 3. Hazard ratios (95% CI) for anemia according to sleep duration in the Kailuan Study. Model 1: Adjusted for age and sex. Model 2: Adjusted for age, sex, level of education, smoking, alcohol, physical activity, and snoring. Model 3: Adjusted for variables in Model 2 plus hypertension, diabetes mellitus, dyslipidemia, body mass index, and high-sensitivity C-reactive protein. *Adjusted for Model 3 and further excluded individuals with myocardial infarction, stroke and cancer. †Adjusted for above confounding factors without sex. §Adjusted for Model 3 and used 8 hours/night as the reference group.
2-year routine medical examination until December 31, 2015, or until the event of interest or death29. Person-years
dyslipidemia, body mass index, and high-sensitivity C-reactive protein. Physical activity, and snoring. Model 3: Adjusted for variables in Model 2 plus hypertension, diabetes mellitus, dyslipidemia, body mass index, and high-sensitivity C-reactive protein.

Table 4. Hazard ratios (95% CI) for anemia according to sleep duration stratified by age in the Kailuan Study. Model 1: Adjusted for age and sex. Model 2: Adjusted for age, sex, level of education, smoking, alcohol, physical activity, and snoring. Model 3: Adjusted for variables in Model 2 plus hypertension, diabetes mellitus, dyslipidemia, body mass index, and high-sensitivity C-reactive protein. Anemia status (no/yes) was defined based on hemoglobin <12 g/ dL for men and <11 g/dL for women40.

Follow-up and anemia assessment. Participants were followed up by face-to-face interviews at every 2-year routine medical examination until December 31, 2015, or until the event of interest or death29. Person-years were calculated from the date the 2006 interview was conducted to the date when anemia was detected, date of death, or date of the last attended interview in this analysis, whichever came first29. Anemia status (no/yes) was defined based on hemoglobin <12 g/ dL for men and <11 g/dL for women40.

Statistical analyses. The statistical analysis was performed using SAS 9.4. We described continuous variables by their means ± standard deviations, and compared groups using one-way analysis of variance (ANOVA). Categorical variables were described as percentages and compared by the Chi-square test. We used Cox proportional hazards regression to estimate the risk of anemia by HR with 95% confidence intervals (CIs). Model 1 adjusted for age and sex. Model 2 further adjusted for level of education, smoking, alcohol, physical activity, and snoring. Model 3 further adjusted for hypertension, diabetes mellitus, dyslipidemia, body mass index, and high-sensitivity C-reactive protein. We assessed the association between sleep duration and age/sex in the secondary analyses. In addition, the robustness of our findings also be tested by a sensitivity analysis. Because major chronic illnesses including history of myocardial infarction, stroke and cancer can affect sleep behavior and future anemia risk, we repeated our analysis after excluding individuals with these conditions. Because 11 hospitals participated in the study, we used a Cox proportional hazards model with a sandwich covariance matrix as a random effect to account for the potential confounding effect of multiple hospitals participating in the study28. All statistical tests were two-sided, and the significance level was set at 0.05.

References
1. Coresh, J., Astor, B. & Sarnak, M. J. Evidence for increased cardiovascular disease risk in patients with chronic kidney disease. Current opinion in nephrology and hypertension 13, 73–81 (2004).
2. Cullleton, B. F. et al. Impact of anemia on hospitalization and mortality in older adults. Blood 107, 3841–3846, https://doi.org/10.1182/blood-2005-10-4308 (2006).
3. Dong, X. et al. A population-based study of hemoglobin, race, and mortality in elderly persons. The journals of gerontology. Series A, Biological sciences and medical sciences 63, 873–878 (2008).
4. Penninx, B. W., Pahor, M., Woodman, R. C. & Guralnik, J. M. Anemia in old age is associated with increased mortality and hospitalization. The journals of gerontology. Series A, Biological sciences and medical sciences 61, 474–479 (2006).
5. Zakai, N. A. et al. A prospective study of anemia status, hemoglobin concentration, and mortality in an elderly cohort: the Cardiovascular Health Study. Archives of internal medicine 165, 2214–2220, https://doi.org/10.1001/archinte.165.19.2214 (2005).
6. Anand, I. et al. Anemia and its relationship to clinical outcome in heart failure. Circulation 110, 149–154, https://doi.org/10.1161/01.CIR.0000134279.79571.73 (2004).
7. Lee, W. C. et al. Anemia: A significant cardiovascular mortality risk after ST-segment elevation myocardial infarction complicated by the comorbidities of hypertension and kidney disease. PloS one 12, e0180165, https://doi.org/10.1371/journal.pone.0180165 (2017).
8. Spence, R. K. The economic burden of anemia in heart failure. *Heart failure clinics* **6**, 373–383, https://doi.org/10.1016/j.hfc.2010.02.003 (2010).

9. Tanimura, M. et al. Effect of Anemia on Cardiovascular Hemodynamics, Therapeutic Strategy and Clinical Outcomes in Patients With Heart Failure and Hemodynamic Congestion. *Circulation journal: official journal of the Japanese Circulation Society* **81**, 1670–1677, https://doi.org/10.1253/circj.CJ-17-0171 (2017).

10. Stauffer, M. E. & Fan, T. Prevalence of anemia in chronic kidney disease in the United States. *PloS one* **9**, e84943, https://doi.org/10.1371/journal.pone.0084943 (2014).

11. Portoles, J. et al. The development of anemia is associated to poor prognosis in NKF/KDOQI stage 3 chronic kidney disease. *BMC nephrology* **14**, 2, https://doi.org/10.1186/1471-2369-14-2 (2013).

12. Gucci, R., Hunter, M., Bruce, D. G., Davis, W. A. & Davis, T. M. E. Anemia complicating type 2 diabetes: Prevalence, risk factors and prognosis. *Journal of diabetes and its complications* **31**, 1169–174, https://doi.org/10.1016/j.jdc.2017.04.002 (2017).

13. Cui, J., Lou, Q., Wu, H., Ouyang, X. & Bian, R. Lack of association between dementia and renal disease progression in Chinese patients with type 2 diabetes. *Journal of diabetes investigation* **7**, 42–47, https://doi.org/10.1111/jdi.12368 (2016).

14. Peirano, P. D. et al. Sleep alterations and iron deficiency anemia in infancy. *Sleep medicine* **11**, 637–642, https://doi.org/10.1016/j.sleep.2010.03.014 (2010).

15. Peirano, P., Algarin, C., Garrido, M., Algarin, D. & Lozoff, B. Iron-deficiency anemia is associated with altered characteristics of sleep spindles in NREM sleep in infancy. *Neurochemical research* **32**, 1665–1672, https://doi.org/10.1007/s11064-007-9396-8 (2007).

16. Ferrie, J. E. et al. A prospective study of change in sleep duration: associations with mortality in the Whitehall II cohort. *Sleep* **30**, 1659–1666 (2007).

17. Gangwisch, J. E. et al. Short sleep duration as a risk factor for hypertension: analyses of the first National Health and Nutrition Examination Survey. *Hypertension* **47**, 833–839, https://doi.org/10.1161/HYPERTENSIONAHA.108.147728 (2006).

18. Behara, S. et al. Association of sleep duration with mortality from cardiovascular disease and other causes for Japanese men and women: the JACC study. *Sleep* **32**, 295–301 (2009).

19. Patel, S. R. et al. A prospective study of sleep duration and mortality risk in women. *Sleep* **27**, 440–444 (2004).

20. Song, Q. et al. Long Sleep Duration and Risk of Ischemic Stroke and Hemorrhagic Stroke: the Kailuan Prospective Study. *Scientific reports* **6**, 33664, https://doi.org/10.1038/srep33664 (2016).

21. Song, Q., Liu, X., Zhou, W., Wang, X. & Wu, S. Changes in sleep duration and risk of metabolic syndrome: the kailuan prospective study. *Scientific reports* **6**, 36861, https://doi.org/10.1038/srep36861 (2016).

22. Wang, X., Liu, X., Song, Q. & Wu, S. Sleep duration and risk of myocardial infarction and all-cause death in a Chinese population: the Kailuan study. *Sleep medicine* **19**, 13–16, https://doi.org/10.1016/j.sleep.2015.09.027 (2016).

23. Liposc, E. et al. Hemoglobin levels and 30-day mortality in patients after myocardial infarction. *International journal of cardiology* **100**, 289–292, https://doi.org/10.1016/j.ijcard.2004.10.043 (2005).

24. Sabatine, M. S. et al. Association of hemoglobin levels with clinical outcomes in acute coronary syndromes. *Circulation* **111**, 2042–2049, https://doi.org/10.1161/01.CIR.0000164277.70955.5F (2005).

25. Jackowska, M., Kumari, M. & Septoe, A. Sleep and biomarkers in the English Longitudinal Study of Ageing: associations with C-reactive protein, fibrinogen, dehydroepiandrosterone sulfate and hemoglobin. *Psychoneuroendocrinology* **38**, 1484–1493, https://doi.org/10.1016/j.psyneuen.2012.12.015 (2013).

26. Cappuccio, F. P. et al. Gender-specific associations of short sleep duration with prevalent and incident hypertension: the Whitehall II Study. *Hypertension* **50**, 693–700, https://doi.org/10.1161/HYPERTENSIONAHA.107.099547 (2007).

27. Kim, S. I. et al. Genetic association of short sleep duration with hypertension incidence—a 6-year follow-up in the Korean genome and epidemiology study. *Circulation journal: official journal of the Japanese Circulation Society* **76**, 907–913, JST.JSTAGE/circj/CJ-11-0713 (2012).

28. Wu, S. et al. Prevalence of ideal cardiovascular health and its relationship with the 4-year cardiovascular events in a northern Chinese industrial city. *Circulation. Cardiovascular quality and outcomes* **5**, 487–493, https://doi.org/10.1161/CIRCOUTCOMES.111.963694 (2012).

29. Song, Q. et al. Long Sleep Duration Is an Independent Risk Factor for Incident Atrial Fibrillation in a Chinese Population: A Prospective Cohort Study. *Scientific reports* **7**, 3679, https://doi.org/10.1038/s41598-017-00348-4 (2017).

30. Foley, D. J. An epidemiological perspective on one tale of a two-tailed hypothesis. *Sleep medicine reviews* **8**, 155–157; discussion 175–156, https://doi.org/10.1016/j.smrv.2004.02.002 (2004).

31. Rosen, C. L. et al. Obstructive sleep apnea and sickle cell anemia. *Pediatrics* **134**, 273–281, https://doi.org/10.1542/peds.2013-4223 (2014).

32. Khan, A. M., Ashizawa, S., Hlebowicz, V. & Appel, D. W. Anemia of aging and obstructive sleep apnea. *Stroke & thrombosis: research* **15**, 29–34, https://doi.org/10.1177/113525-010-0326-7 (2011).

33. Grandner, M. A. et al. Extreme sleep durations and increased C-reactive protein: effects of sex and ethnoracial group. *Sleep* **36**, 769–779E, https://doi.org/10.5665/sleep.2646 (2013).

34. Patel, S. R. et al. Sleep duration and biomarkers of inflammation. *Sleep* **32**, 200–204 (2009).

35. Meier-Ewert, H. K. et al. Effect of sleep loss on C-reactive protein, an inflammatory marker of cardiovascular risk. *Journal of the American College of Cardiology* **43**, 678–683, https://doi.org/10.1016/j.jacc.2003.07.050 (2004).

36. Punjabi, N. M. The epidemiology of adult obstructive sleep apnea. *Proceedings of the American Thoracic Society* **5**, 136–143, https://doi.org/10.1513/pats.200709-155MG (2008).

37. Song, Q., Liu, X., Wang, X. & Wu, S. Age- and gender-specific associations between sleep duration and incident hypertension in a Chinese population: the Kailuan study. *Journal of human hypertension* **30**, 503–507, https://doi.org/10.1016/j.jhh.2015.118 (2016).

38. Zhang, Q. et al. Ideal cardiovascular health metrics and the risks of ischemic and intracerebral hemorrhagic stroke. *Stroke* **44**, 2451–2456, https://doi.org/10.1161/STROKEAHA.113.768839 (2013).

39. Zhu, J. et al. 2016 update of the Chinese Guideline on the Prevention and Treatment of Dyslipidemia in Adults. *Chinese circulation journal* **31**, 937–953 (2016).

40. Cai, J. et al. Evaluation of the Efficiency of the Reticulocyte Hemoglobin Content on Diagnosis for Iron Deficiency Anemia in Chinese Adults. *Nutrients* **9**, https://doi.org/10.3390/nu9050430 (2017).

**Acknowledgements**

We thank the project development and management teams at the Kailuan Group.

**Author Contributions**

X.W. and S.W. conceived and designed this study, X.L. directed data analysis, Q.S. and X.L. writing the paper, W.H., X.H., J.G. and X.Z. prepared the database and reviewed the paper, X.W. and S.W. conducted the quality assurance, reviewed and edited the paper. All authors reviewed the manuscript.
