In hypertensive individuals, sleep time and sleep efficiency did not affect the number of angina episodes: a cross-sectional study

Ahmad H. Alghadir1, Masood Khan1,*, Mohammed Mansour Alshehri2, Abdul fattah S. Alqahtani2 & Mishal Aldaihan1

Previous studies have reported adverse effects of short and long sleep duration on cardiovascular health. However, how sleep time and sleep efficiency affect angina have not been studied in hypertensive individuals. This study aimed to assess the relationship of sleep with angina. Using a cross-sectional design, data from 1563 hypertensive individuals were collected from the parent Sleep Heart Health Study (SHHS). Age, alcohol use, average diastolic blood pressure (ADBP), average systolic blood pressure (ASBP), cigarette use, sleep time, sleep efficiency, percent time in stage N3 of sleep, and body mass index (BMI) were used as covariates. Multiple linear regression, the Chi-Square test, and Pearson’s correlation coefficient were used for data analysis. Unadjusted sleep efficiency, sleep time, ADBP, and age were significant (p < 0.05) predictors of the number of angina episodes (Angina_n). When the covariates were adjusted, only ADBP and ASBP were significant (p < 0.05) predictors of Angina_n. Sleep efficiency, BMI, ADBP, sleep time, and age had a significant (p < 0.05) correlation with Angina_n. In hypertensive individuals, sleep time and sleep efficiency did not affect Angina_n when adjusted for covariates. ADBP and ASBP were found to be significant predictors of Angina_n when the covariates were adjusted.

Abbreviations

Angina_n: Number of angina episodes
BMI: Body mass index
REM: Rapid eye movement
NREM: Non-rapid eye movement
BP: Blood pressure
ADBP: Average diastolic blood pressure
ASBP: Average systolic blood pressure
SHHS: Sleep heart health study

To maintain good emotional, mental, and physical health, individuals are required to have good sleep1. Several advantages of good sleep are reported. Normal sleep reduces the workload on the cardiovascular system, therefore, it may enhance cardiovascular longevity, and insufficient sleep may cause adverse consequences2.

Reduction in blood pressure (BP) is reported during normal sleep, where systemic BP decreases by an average of 5–10% in stages N1 and N2 of non-rapid eye movement (NREM) sleep and by 10–15% in stage N33,4. The reduction in heart rate is also observed by 5–10% during NREM sleep. During rapid eye movement (REM) sleep, greater variability is observed in both BP and heart rate. Cardiac output also decreases during NREM sleep3,4.

Therefore, there are several benefits of nocturnal sleep on the cardiovascular system, especially through the reduction in systemic BP. Thus, if total sleep time is reduced due to any disorder then the cardiovascular system will be deprived of several benefits it accrues from good nocturnal sleep. The prevalence of sleep problems has been reported from 1.6 to 56% in several studies conducted in different countries throughout the world7–9.

It’s reported that the ability to perform daily activities of living is directly affected in individuals having sleep disturbances10, which in turn induces a sedentary lifestyle11 that ultimately affects the health and quality of life.

1Department of Rehabilitation Sciences, College of Applied Medical Sciences, King Saud University, Riyadh, Saudi Arabia. 2Physical Therapy Department, Jazan University, Jazan, Saudi Arabia. *email: raomasood22@gmail.com
Systolic and diastolic BPs were measured to the nearest 2 mmHg. Measurements were taken with a 5-min interval in between each reading, with the use of a mercury gauge sphygmomanometer.

The participants were asked to rest for 5 min, then in a sitting position, 3 BP readings were taken with a 5-min interval in between each reading, with the use of a mercury gauge sphygmomanometer. Systolic and diastolic BPs were measured to the nearest 2 mmHg.

Table 1. Descriptive statistics for participant’s characteristics and dependent and independent variables (total n = 1563, missing data n = 21). BMI: body mass index; SD: standard deviation; ADBP: average diastolic blood pressure; ASBP: average systolic blood pressure; Sleep N3: percent time in stage N3 of sleep.

|                          | Normal (n = 1331) Mean ± SD | Angina present (n = 211) Mean ± SD | Total (1542) Mean ± SD/ frequency (percentage) |
|--------------------------|-----------------------------|-----------------------------------|-----------------------------------------------|
| Sleep efficiency (%)     | 49.2 ± 38.10                | 41.82 ± 38.84                     | 48.19 ± 38.28                                 |
| BMI (kg/m²)              | 25.57 ± 10.75               | 24.66 ± 10.71                     | 25.44 ± 10.75                                 |
| ADBP (mmHg)              | 63.41 ± 24.50               | 58.44 ± 24.19                     | 62.73 ± 24.51                                 |
| ASBP (mmHg)              | 119.04 ± 45.48              | 116 ± 47.05                       | 118.63 ± 45.70                                |
| Sleep N3 (%)             | 9.79 ± 11.56                | 7.37 ± 11.05                      | 9.46 ± 11.51                                  |
| Alcohol use (n)          | 2.47 ± 6.23                 | 2.7 ± 6.40                        | 2.5 ± 6.25                                    |
| Cigarette packs per year (n) | 12.36 ± 19.45           | 20.49 ± 26.43                     | 13.47 ± 20.73                                 |
| Sleep time (minutes)     | 233.5 ± 184.39              | 197.09 ± 186.46                   | 228.52 ± 185.04                               |
| Age (years)              | 71.71 ± 9.60                | 73.8 ± 9.22                       | 71.99 ± 9.58                                  |
| Male (n)                 | 722 (46.2)                  |                                   |                                               |
| Female (n)               | 841 (53.8)                  |                                   |                                               |

Materials and methods

A cross-sectional design was used. The demographic characteristics (gender, age, body mass index (BMI), cigarette smoking, alcohol use), cardiovascular variables (average diastolic blood pressure (ADBP), average systolic blood pressure (ASBP), presence of angina, Angina, and sleep variables (sleep time, percent time in stage N3 of sleep, percentage of time in bed that was spent sleeping) were obtained from the data collected by the parent study Sleep Heart Health Study (SHHS). Only participants of age 40 years or older at the time of the sleep study participated. The specific aims, designs, and protocols of the SHHS have been previously described. The SHHS Manual of Operations contains a comprehensive description of the methods used in study. The primary aim of SHHS was to study the cardiovascular consequences of sleep-disordered breathing. The baseline data for SHHS were obtained from nine ongoing epidemiologic studies of cardiovascular and respiratory disease from December 1995 to January 1998 in diverse populations in the United States.

Only the data of hypertensive individuals were used from the SHHS. In SHHS, hypertension was defined as a resting BP of at least 140/90 mmHg or the use of antihypertensive medication. The parent study (SHHS) included a baseline examination of 5804 participants, of which 3326 were not qualified as hypertensive and a total of 2478 participants qualified as hypertensive. However, out of 2478 participants, 915 participants’ data were missing for one or more variables. These participants were excluded from data analysis. Therefore, ultimately 1563 participants were used for data analysis (Tables 1 and 2). All methods were performed in accordance with the relevant guidelines and regulations.

In SHHS, information related to covariates such as medical history and health-related characteristics was obtained using a standardized questionnaire through an interview by the study technician while visiting participants’ homes. The information regarding cardiovascular health was obtained by asking questions such as if the doctor ever told the participant that he had angina, etc. The responses of the participants were obtained in the form of ‘yes’, ‘no’, or ‘unsure’. Other related information like alcohol use or cigarette packs per year, was also obtained through interviews. Bodyweight, height, and BP were measured during the home visits of the participants using standard protocols. Bodyweight was measured by a portable scale. A manual of operation of SHHS contains detailed information regarding the protocols for these measurements.

BP measurement. The participants were asked to rest for 5 min, then in a sitting position, 3 BP readings were taken with a 5-min interval in between each reading, with the use of a mercury gauge sphygmomanometer.
Measurement of sleep variables. Sleep variables were measured using a single overnight EEG-based polysomnography at the participant’s home and in some cases where the home environment was not conducive to polysomnography, a non-home environment (e.g. a motel) was used. The Compumedics P Series System (Abbotsford, Victoria, Australia) was used for polysomnography. During the evening home visit, this equipment was calibrated and sensors were placed on the participants.

The institutional review board of each participating center approved the study. The signed informed consent was obtained from each participant. Data on smoking were also obtained through a questionnaire. Data regarding cardiovascular disease was also obtained through a questionnaire.

Data analysis. SPSS statistical software version 26 (SPSS Inc., Chicago, IL, USA) was used for data analysis. A total of 1563 participants’ data was analyzed. The descriptive statistics of the outcome variable (Anginaₐ) and predictors (age, alcohol use, ADBP, ASBP, cigarette smoking, sleep time, sleep N3, BMI, sleep efficiency) are shown in Table 1. Multiple linear regression analysis was performed to predict the relationship of the dependent variable, i.e. Anginaₐ, with predictors. Pearson’s correlation coefficient was used for correlational analysis between Anginaₐ and other covariates. A Chi-square test was performed to test the relationship between categorical variables (presence of angina and gender). The confidence interval was established at 95%, p < 0.05 considered significant.

Table 2. Median and percentile values of ADBP and ASBP. ADBP: average diastolic blood pressure; ASBP: average systolic blood pressure.

|                  | ADBP (mmHg) |                  | ASBP (mmHg) |
|------------------|-------------|------------------|-------------|
|                  | Normal (n = 1331) | Angina present (n = 211) | Total (1542) | Normal (n = 1331) | Angina present (n = 211) | Total (1542) |
| Median           | 70.00       | 65.00            | 69.00       | 129.00          | 127.00         | 129.00         |
| Percentile       |             |                  |             |                |                |                |
| 25               | 60.00       | 59.00            | 60.00       | 115.00          | 111.00         | 114.00         |
| 50               | 70.00       | 65.00            | 69.00       | 129.00          | 127.00         | 129.00         |
| 75               | 78.00       | 72.00            | 77.00       | 142.00          | 140.00         | 142.00         |

Table 3. Multiple linear regression analysis. Association of the number of angina episodes with sleep efficiency, BMI, average diastolic blood pressure, average systolic blood pressure, percent time in stage N3 of sleep, alcohol use, cigarette use, sleep time, age, and gender. BMI: body mass index; ADBP: average diastolic blood pressure; ASBP: average systolic blood pressure; Sleep N3: percent time in stage N3 of sleep. *Significant.

| Covariate                  | Unadjusted for predictors | Adjusted for predictors |
|----------------------------|---------------------------|-------------------------|
|                            | R-value | Adjusted R-square value | Un-standardized beta coefficient | F | t-value | p-value | Standardized coefficients beta | t-value | p-value |
| Sleep efficiency           | 0.061   | 0.003 | −0.001 | 5.895 | −2.428 | 0.015* | −0.123 | −1.125 | 0.261 |
| BMI                        | 0.043   | 0.001 | −0.003 | 2.857 | −1.690 | 0.091 | 0.041 | 1.044 | 0.297 |
| ADBP                       | 0.095   | 0.008 | −0.003 | 14.230 | −3.772 | 0.000* | −0.307 | −4.916 | 0.000* |
| ASBP                       | 0.029   | 0.000 | 0.000  | 1.323 | −1.150 | 0.250 | 0.224 | 3.543 | 0.000* |
| Sleep N3                   | 0.039   | 0.001 | −0.002 | 2.364 | −1.537 | 0.124 | 0.007 | 0.209 | 0.834 |
| Alcohol use                | 0.004   | 0.001 | −0.001 | 0.282 | −0.169 | 0.866 | −0.005 | −0.194 | 0.846 |
| Cigarette packs per year   | 0.031   | 0.000 | 0.001  | 1.500 | 1.225 | 0.221 | 0.025 | 0.965 | 0.335 |
| Sleep time                 | 0.055   | 0.002 | 0.000  | 4.822 | −2.196 | 0.028* | 0.091 | 0.870 | 0.384 |
| Age                        | 0.097   | 0.009 | 0.008  | 14.915 | 3.862 | 0.000* | 0.043 | 1.527 | 0.127 |
| Gender                     | 0.016   | 0.000 | −0.023 | 0.380 | −0.616 | 0.538 |
smoking, sleep efficiency, sleep time, sleep N3, and BMI) were adjusted then only ADBP and ASBP were found to be significant predictors of Angina, (p < 0.05). The adjusted covariates had a significant impact (p < 0.01) on Angina, and were responsible for 2.3% of the variance (Table 4). Pearson’s correlation coefficients between Angina, and other predictors are presented in Table 5. Sleep efficiency, BMI, ADBP, sleep time, and age were found to have a significant (p < 0.05) correlation with Angina. Among these significant correlations, only age had a positive correlation, otherwise, the rest of the covariates had a negative correlation. Pearson correlation coefficient values are presented in Table 5. The Chi-square test revealed a significant difference (p = 0.01, Cramer’s V = 0.066) in the presence of angina with gender differences (male and female) (Table 6). The presence of angina was found to be significantly (p < 0.05) greater in the male hypertensive population than in the female hypertensive population.

### Discussion

The results of the present study revealed that unadjusted sleep efficiency, sleep time, ADBP, and age were significant predictors of Angina, in hypertensive individuals. When all covariates (age, BMI, alcohol use, ADBP, ASBP, cigarette smoking, sleep time, sleep N3, and sleep efficiency) were adjusted, then only ADBP and ASBP were found to be significant predictors of Angina. Adjusted covariates were found to be responsible for only 2.3% of the variance in Angina. This indicates that there will be several factors other than the above-mentioned covariates that can predict more variation in the Angina. The present study aimed to know the association of sleep time and sleep efficiency with Angina, which has not been found when sleep time and efficiency were adjusted to other covariates. Therefore, in the present study, hypertension played a major role in predicting the Angina, rather than sleep time and efficiency.

Previous epidemiological studies have shown that impaired sleep patterns like long and short sleep duration are related to several cardiometabolic impairments such as hypertension, diabetes, obesity, hypercholesterolemia, stroke, and myocardial infarction.

In the present study, it should be noted that the mean sleep efficiency was 48.33%, which is quite low. Several factors could be responsible for low sleep efficiencies, such as participants belonging to the older age group (mean age 64.1 ± 11.7 years). The mean ADBP was 123.73 ± 16.84 mmHg, and ASBP was 180.69 ± 15.57 mmHg. The mean BMI was 26.81 ± 4.68 kg/m², and the mean alcohol consumption was 24.26 ± 15.94 g/day. The mean sleep time was 7 hours and 25 minutes, and the mean sleep efficiency was 48.33%.

The findings of this study highlight the importance of sleep efficiency and time as significant predictors of Angina. Further research is needed to investigate the underlying mechanisms of these associations and to develop interventions to improve sleep quality and reduce the risk of cardiovascular disease.
The present study revealed that, when unadjusted, age is a significant predictor of $\text{Angina}_n$, and was responsible for 0.9% variance. Age was also found to have a significant positive correlation, although small ($r = 0.097$), with $\text{Angina}_n$. But when adjusted for other covariates, no significant impact of age was found on $\text{Angina}_n$. However contrary findings were reported by the study of Fisher et al., which reported that older people were more likely to have angina and more severe symptoms when compared with people with a similar extent of disease. They reported that age is an independent and significant predictor of the presence and severity of angina, even after adjusting for covariates. Several factors may explain the association of aging with the presence of angina, such as deconditioning due to a sedentary lifestyle, physiological factors related to aging, and the disease process.

An interesting finding from the present study is that no association was found between the number of cigarette packs used in a year and $\text{Angina}_n$. Similar findings were reported by Pujades-Rodriguez who reported no differences in lifetime risks for stable angina according to the smoking status. However, a study by Merry et al. reported that smoking increased the risk of unstable angina. Also, the study by Wilmink et al. reported a relative risk of 1.3 for angina for current smokers compared to non-smokers.

This study used gold standard measurements for sleep parameters and cardiovascular health. However, some limitations are needed to be mentioned for future studies. Cardiovascular medication adherence was not controlled, which has an impact on BP and cardiovascular health. Depression and anxiety symptoms increase during aging which has an impact on overall sleep quality. Future studies are needed to assess the impact of sleep on cardiovascular health with controlled psychological symptoms. Future studies should control extraneous variables like physical activity and sedentary lifestyle because they affect cardiovascular health.

**Conclusion**

In hypertensive individuals, sleep time and sleep efficiency did not affect $\text{Angina}_n$ when adjusted for covariates. Average diastolic and systolic BP were found to be significant predictors of $\text{Angina}_n$ when covariates were adjusted.

**Data availability**

The datasets generated and/or analyzed during the current study are not publicly available due but are available from the corresponding author on reasonable request.

Received: 20 October 2021; Accepted: 12 September 2022
Published online: 29 September 2022

**References**

1. Altenvogt, B. M. & Colten, H. R. Sleep disorders and sleep deprivation: an unmet public health problem. (2006).
2. Parish, J. M. & Shepard, J. W. Jr. Cardiovascular effects of sleep disorders. Chest 97, 1220–1226 (1990).
3. Cappuccio, F. P. et al. Sleep duration and cardiovascular disease: a systematic review of prospective studies. Sleep Med. Rev. 16, 131–141 (2012).
4. Khatri, I. M. & Freis, E. D. Hemodynamic changes during sleep. J. Appl. Physiol. 22, 867–873 (1967).
5. Bristow, J., Honour, A., Pickering, T. & Sleight, P. Cardiovascular and respiratory changes during sleep in normal and hypertensive subjects. *Cardiovasc. Res.* 3, 476–485 (1969).

6. Miller, J. & Horvath, S. Cardiac output during human sleep. *Nature* 73, 2455 (1976).

7. Koyanagi, A. & Stickley, A. The association between sleep problems and psychotic symptoms in the general population: A global perspective. *Sleep* 38, 1875–1885 (2015).

8. Léger, D., Poursain, B., Neubauer, D. & Uchiyama, M. An international survey of sleeping problems in the general population. *Curr. Med. Res. Opin.* 24, 307–317 (2008).

9. Stranges, S., Tigbe, W., Gómez-Olivé, F., Thorogood, M. & Kandala, N.-B. Sleep problems: An emerging global epidemic? Findings from the INDEPTH WHO-SAGE study among more than 40,000 older adults from 8 countries across Africa and Asia. *Sleep* 35, 1173–1181 (2012).

10. Lepp, S. et al. The epidemiology of sleep quality, sleep patterns, consumption of caffeinated beverages, and khat use among ethiopian college students. *Sleep Disord.* 2012, 11 https://doi.org/10.1155/2012/583510 (2012).

11. Lie, I., Arnesen, H., Sandvik, L., Hamilton, G. & Bunch, E. H. Predictors for physical and mental health 6 months after coronary artery bypass grafting a cohort study. *Eur. J. Cardiovasc. Nurs.* 9, 238–243 (2010).

12. Redeker, N. S., Ruggiero, J. & Hedges, C. Patterns and predictors of sleep pattern disturbance after cardiac surgery. *Res. Nurs. Health* 27, 217–224 (2004).

13. Redeker, N. S., Ruggiero, J. S. & Hedges, C. Sleep is related to physical function and emotional well-being after cardiac surgery. *Nurs. Res.* 53, 154–162 (2004).

14. Chaput, J. P., Després, J. P., Bouchard, C. & Tremblay, A. Short sleep duration is associated with reduced leptin levels and increased adiposity: Results from the Quebec family study. *Obesity* 15, 253–261 (2007).

15. Forquer, L. M., Camden, A. E., Gabriau, K. M. & Johnson, C. M. Sleep patterns of college students at a public university. *J. Am. Coll. Health* 56, 563–565 (2008).

16. Knutsson, K. L. et al. Association between sleep and blood pressure in midlife: The CARDIA sleep study. *Arch. Intern. Med.* 169, 1055–1061 (2009).

17. Koren, D., Arnon, I., Lavie, P. & Klein, E. Sleep complaints as early predictors of posttraumatic stress disorder: A 1-year prospective study of injured survivors of motor vehicle accidents. *Am. J. Psychiatry* 159, 855–857 (2002).

18. Kripke, D. F., Garfinkel, L., Wingard, D. L., Klauber, M. R. & Marler, M. R. Mortality associated with sleep duration and insomnia. *Arch. Gen. Psychiatry* 59, 131–136 (2002).

19. Meero, P., Sgoifo, A. & Suchecki, D. Restricted and disrupted sleep: effects on autonomic function, neuroendocrine stress systems and stress responsivity. *Sleep Med. Rev.* 12, 197–210 (2008).

20. Apicella, R. Sleep and cardiac diseases amongst elderly people. *J. Intern. Med.* 236, 65–71 (1994).

21. Quan, S. F. et al. The sleep heart health study: Design, rationale, and methods. *Sleep* 20, 1077–1085 (1997).

22. H. Rapoport David M. Smith Philip L. Kiley James P., S. H. H. R. G. R. S. s. p. c. S. M. H. L. B. K. Q. S. F . I. C. G. D. J. B. W . Group, S. H. H. S. R. Association of sleep-disordered breathing, sleep apnea, and hypertension in a large community-based study. *JAMA* 283, 1829–1836 (2000).

23. Carkasdon, M. A. & Dement, W. C. Normal human sleep: An overview. *Princ. Pract. Sleep Med.* 4, 13–23 (2005).

24. Grandner, M. A., Jackson, N. J., Pak, V. M. & Gehrman, P. R. Sleep disturbance is associated with cardiovascular and metabolic disorders. *J. Sleep Res.* 21, 427–433 (2012).

25. Gangwisch, J. Epidemiological evidence for the links between sleep, circadian rhythms and metabolism. *Obes. Rev.* 10, 37–45 (2009).

26. Dukidkou, I. et al. Longitudinal sleep efficiency in the elderly and its association with health. *J. Sleep Res.* 29, e12898 (2020).

27. Grandner, M. A., Patel, N. P., Gehrman, P. R., Perlis, M. L. & Pack, A. I. Problems associated with short sleep: Bridging the gap between laboratory and epidemiological studies. *Sleep Med. Rev.* 14, 239–247 (2010).

28. Sabanayagam, C. & Shankar, A. Sleep duration and cardiovascular disease: Results from the National Health Interview Survey. *Sleep* 33, 1037–1042 (2010).

29. Chandola, T., Ferrie, J. E., Perski, A., Akbaraly, T. & Marmot, M. G. The effect of short sleep duration on coronary heart disease risk is greatest among those with sleep disturbance: A prospective study from the Whitehall II cohort. *Sleep* 33, 794–794 (2010).

30. Buxton, O. M. & Marcelli, E. Short and long sleep are positively associated with obesity, diabetes, hypertension, and cardiovascular disease among adults in the United States. *Soc. Sci. Med.* 71, 1027–1036 (2010).

31. Tochikubo, O., Ikeda, A., Miyajima, E. & Ishii, M. Effects of insufficient sleep on blood pressure monitored by a new multibiomedical recorder. *Hypertension* 27, 1318–1324 (1996).

32. Spiegel, K., Leproult, R. & Van Cauter, E. Impact of sleep debt on metabolic and endocrine function. *Lancet* 354, 1435–1439 (1999).

33. Kato, M. et al. Effects of sleep deprivation on neural circulatory control. *Hypertension* 35, 1173–1175 (2000).

34. Meier-Ewert, H. K. et al. Effect of sleep loss on C-reactive protein, an inflammatory marker of cardiovascular risk. *J. Am. Coll. Cardiol.* 43, 678–683 (2004).

35. Shearer, W. T. et al. Soluble TNF-a receptor 1 and IL-6 plasma levels in humans subjected to the sleep deprivation model of space-flight. *J. Allergy Clin. Immunol.* 107, 165–170 (2001).

36. Magee, C. A., Caputi, P. & Iverson, D. C. Short sleep mediates the association between long work hours and increased body mass index. *J. Behav. Med.* 34, 83–91 (2011).

37. Watanabe, M., Kikuchi, H., Tanaka, K. & Takahashi, M. Association of short sleep duration with weight gain and obesity at 1-year follow-up: A large-scale prospective study. *Sleep* 33, 161–167 (2010).

38. Cappuccio, F. P., Cooper, D., D’Elia, L., Strazzullo, P. & Miller, M. A. Sleep duration predicts cardiovascular outcomes: A systematic review and meta-analysis of prospective studies. *Eur. Heart J.* 32, 1484–1492 (2011).

39. Stranges, S. et al. Correlates of short and long sleep duration: A cross-cultural comparison between the United Kingdom and the United States: The Whitehall II Study and the Western New York Health Study. *Am. J. Epidemiol.* 168, 1533–1564 (2008).

40. Krueger, P. M. & Friedman, E. M. Sleep duration in the United States: A cross-sectional population-based study. *Am. J. Epidemiol.* 169, 1052–1063 (2009).

41. Qureshi, A. I., Giles, W. H., Croft, J. B. & Bliwise, D. L. Habitual sleep patterns and risk for stroke and coronary heart disease: A 10-year follow-up of the NHANES I. *Neurology* 48, 904–910 (1997).

42. Maas, A. H. & Appelman, Y. E. Gender differences in coronary heart disease. *Neth. Heart. J.* 18, 598–603 (2010).

43. Prezcott, F., Hippe, M., Schnoor, P., Hein, H. O. & Vestbo, J. Smoking and risk of myocardial infarction in women and men: Longitudinal population study. *BMJ* 316, 1043 (1998).

44. Kones, R. Recent advances in the management of chronic stable angina I: Approach to the patient, diagnosis, pathophysiology, risk stratification, and gender disparities. *Vasc. Health Risk Manag.* 6, 835 (2010).

45. Herringsway, H. et al. Incidence and prognostic implications of stable angina pectoris among women and men. *JAMA* 295, 1404–1411 (2006).

46. Murphy, N. F. et al. Prevalence, incidence, primary care burden and medical treatment of angina in Scotland: Age, sex and socio-economic disparities: A population-based study. *Heart* 92, 1047–1054 (2006).
49. Fisher, L. D., Maynard, C., Rademaker, A. W., Alderman, E. L. & Mock, M. Age variation in the association between angiographic coronary disease and angina from the Coronary Artery Surgery Study (CASS). *Int. J. Cardiol.* **24**, 317–326 (1989).
50. Pujades-Rodriguez, M. *et al.* Heterogeneous associations between smoking and a wide range of initial presentations of cardiovascular disease in 1,937,360 people in England: lifetime risks and implications for risk prediction. *Int. J. Epidemiol.* **44**, 129–141 (2015).
51. Merry, A. H. *et al.* Smoking, alcohol consumption, physical activity, and family history and the risks of acute myocardial infarction and unstable angina pectoris: A prospective cohort study. *BMC Cardiovasc. Disord.* **11**, 1–14 (2011).
52. Wilmink, T. B., Quick, C. R. & Day, N. E. The association between cigarette smoking and abdominal aortic aneurysms. *J. Vasc. Surg.* **30**, 1099–1105 (1999).

**Acknowledgements**

The authors are grateful to the Researchers Supporting Project number (RSP-2021/382), King Saud University, Riyadh, Saudi Arabia for funding this research. This work was supported by National Heart, Lung and Blood Institute cooperative agreements U01HL53940 (University of Washington), U01HL53941 (Boston University), U01HL53938 (University of Arizona), U01HL53916 (University of California, Davis), U01HL53934 (University of Minnesota), U01HL53931 (New York University), U01HL53937 and U01HL64360 (Johns Hopkins University), U01HL63463 (Case Western Reserve University), and U01HL63429 (Missouri Breaks Research). The opinions expressed in this paper are those of the authors and do not necessarily reflect the views of the Indian Health Service. SHHS acknowledges the Atherosclerosis Risk in Communities Study, the Cardiovascular Health Study, the Framingham Heart Study, the Cornell/Mt. Sinai Worksite and Hypertension Studies, the SHHS, the Tucson Epidemiologic Study of Airways Obstructive Diseases, and the Tucson Health and Environment Study for allowing their cohort members to be part of the SHHS and for permitting data acquired by them to be used in the study. SHHS is particularly grateful to the members of these cohorts who agreed to participate in SHHS as well. SHHS further recognizes all of the investigators and staff who have contributed to its success. A list of SHHS investigators, staff, and their participating institutions is available on the SHHS website, http://iws1.jhsph.edu/Research/Centers/CCT/shhs/.

**Author contributions**

A.H.A., M.K., M.M.A., A.S.A., and M.A. conceptualized the study and its methodology. A.H.A. and M.M.A. were involved in supervision. M.K., A.S.A., and M.M.A. did data analysis and interpretation. M.K. and M.A. wrote, reviewed, and edited the final manuscript. All authors read and approved the final manuscript.

**Funding**

Researchers Supporting Project number (RSP-2021/382), King Saud University, Riyadh, Saudi Arabia.

**Competing interests**

The authors declare no competing interests.

**Additional information**

**Correspondence** and requests for materials should be addressed to M.K.

**Reprints and permissions information** is available at www.nature.com/reprints.

**Publisher’s note** Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

---

© The Author(s) 2022