Shorter sleep: a new potential target to address cardiovascular and metabolic risk?

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Category of manuscript: Invited Editorial

Total word count: 1809

Manuscript word count: 831

Cardiovascular disease (CVD) is a major cause of morbidity and mortality worldwide, with coronary heart disease (CHD) accounting for more than 50% of cases. While recent advances in treatment have led to CVD dipping below cancer as the leading cause of death in some high income countries, it is important to note that 80% of CVD deaths now occur in low and middle-income countries.[1,2] It has long been understood that factors contributing to this large global burden of disease include hypertension, smoking, physical inactivity, obesity and hypercholesterolaemia.[2,3] However, these variables alone do not fully explain the association. More recently, a wealth of evidence has linked low socioeconomic status (SES) to adverse CV outcomes.[4] This evidence has led to SES being incorporated into some risk scores for CV disease, including the ASSIGN score ("ASSessing cardiovascular risk using SIGN")[5] and QRISK3 score,[6] although interestingly, SES has not yet been fully incorporated into SCORE: the European risk score calculator.[7] This strong independent link between socioeconomic status and cardiovascular outcomes has fuelled research to try and determine the underlying mechanisms. Potential factors have included SES-driven differences in smoking, alcohol, obesity, healthcare accessibility,[4] diet and inflammation,[4,8] and recent data from UK Biobank suggest that socioeconomic deprivation potentiates the adverse association between unhealthy lifestyle factors and (CVD and all-cause) mortality.[9] However, other unmeasured factors are also likely to be relevant.

In recent years, sleep has evolved as a potential lifestyle factor which may be relevant to both metabolic and cardiovascular risk. In a meta-analysis of self-reported sleep duration and cardiovascular outcomes in prospective studies, Cappuccio et al, found a ‘U-shaped’ association between sleep duration and risk of developing CHD with both shorter and longer durations of sleep being associated with a greater risk of developing or dying from CHD and stroke disease.[10] The accumulating evidence was thought sufficiently robust for a recent USA-based CVD prevention guideline recommending targeting short sleep duration and poor sleep quality as another method to help lessen risk.[11]

In this issue of Cardiovascular Research, Petrovic and colleagues report the results of a large observational study on eight European Cohorts with a total of more than 111,000 participants. They investigate the role of sleep duration in explaining socioeconomic status links to cardiovascular disease. Their data suggest that both father's and adult occupational position are associated with abnormal sleep duration patterns, with a stronger association for short sleep than long sleep. In addition, they found an inverse association between both life-course SES indicators and CHD, and that the association between adult occupational position and CHD was partly explained by short sleep duration, at least in men. This study has multiple strengths including its large size and being the first to investigate sleep duration and CV disorders across life socioeconomic status. However, there are some limitations which include recall bias of self-reported sleep duration and lack of adjustment for some potential confounders including hypertension, hyperlipidaemia and environmental factors. Even so, this paper adds key insights into our understanding of the associations between SES, sleep and CVD.

Nevertheless, how can we determine whether shorter or longer sleep durations are causal risk factors for adverse CVD outcomes? Here we have to turn to genetic studies. Dashti et al identified 78 (76 novel) gene loci for sleep duration that implicate multiple biological pathways. They then compared observational and genetic data linking sleep to adverse outcomes.[12] Whilst observational data showed short sleep was associated with a 20% higher multivariate adjusted risk of incident myocardial infarction and long sleep with a 34% higher risk, Mendelian randomisation analyses using the discovered sleep genes was consistent only with a casual effect of shorter sleep duration on myocardial infarction in both CARDIoGRAMplusC4D and UK Biobank[13] (Figure 1). Thus while the mechanisms underpinning the association between long sleep duration and CVD risk are still unclear – this may reflect reverse causality (i.e. those with pre-existing illness sleeping longer) or poor sleep quality, which in itself may increase CHD risk,[14] thereby necessitating longer sleep duration to feel rested – there is accumulating evidence that short sleep is likely to play a causal role in mediating CVD risk.

If all of the above is true, can we help short sleepers sleep longer? Recently in a randomised clinical trial of 1711 people, Espie and colleagues reported that the use of digital cognitive behavioural therapy is effective in improving functional health, psychological wellbeing and sleep-related quality of life in people reporting insomnia symptoms.[15] This trial suggested that sleep interventions can improve insomnia symptoms as well as functional health, psychological well-being and sleep-related quality of life. Extending such research, it should be possible to conduct a randomised trial of sleep interventions for the prevention of CV disease or diabetes (Figure 1). Such trials would take time, effort, and careful design, but they are needed if sleep interventions are to have wider impact in preventative medicine. Only by showing sleep interventions improve either proven casual risk factors, or better hard outcomes, will sleep interventions hit prime time in the CV and metabolic arenas.

Conflict of Interest

None declared

Acknowledgements

Thanks to Liz Coyle (University of Glasgow) for her assistance with formatting and drafting the figure.

Figure Legend

This figure depicts the observational associations between sleep duration and cardiovascular outcomes. Generally, both short and long sleep are associated with greater CV risks compared to those who sleep between 6 to 9 hours per night. That noted, recent genetic work suggest shorter sleep may be causally linked to such CV outcomes whereas this appears not to be the case for longer sleep durations. As many conditions can lead people to sleep for longer, this association may represent reverse causality or residual confounding. In particular, long sleep may be a consequence of poor sleep quality, which in itself may be associated with CHD risk. The totality of work sets the scene for sleep intervention trials in the cardiovascular arena.

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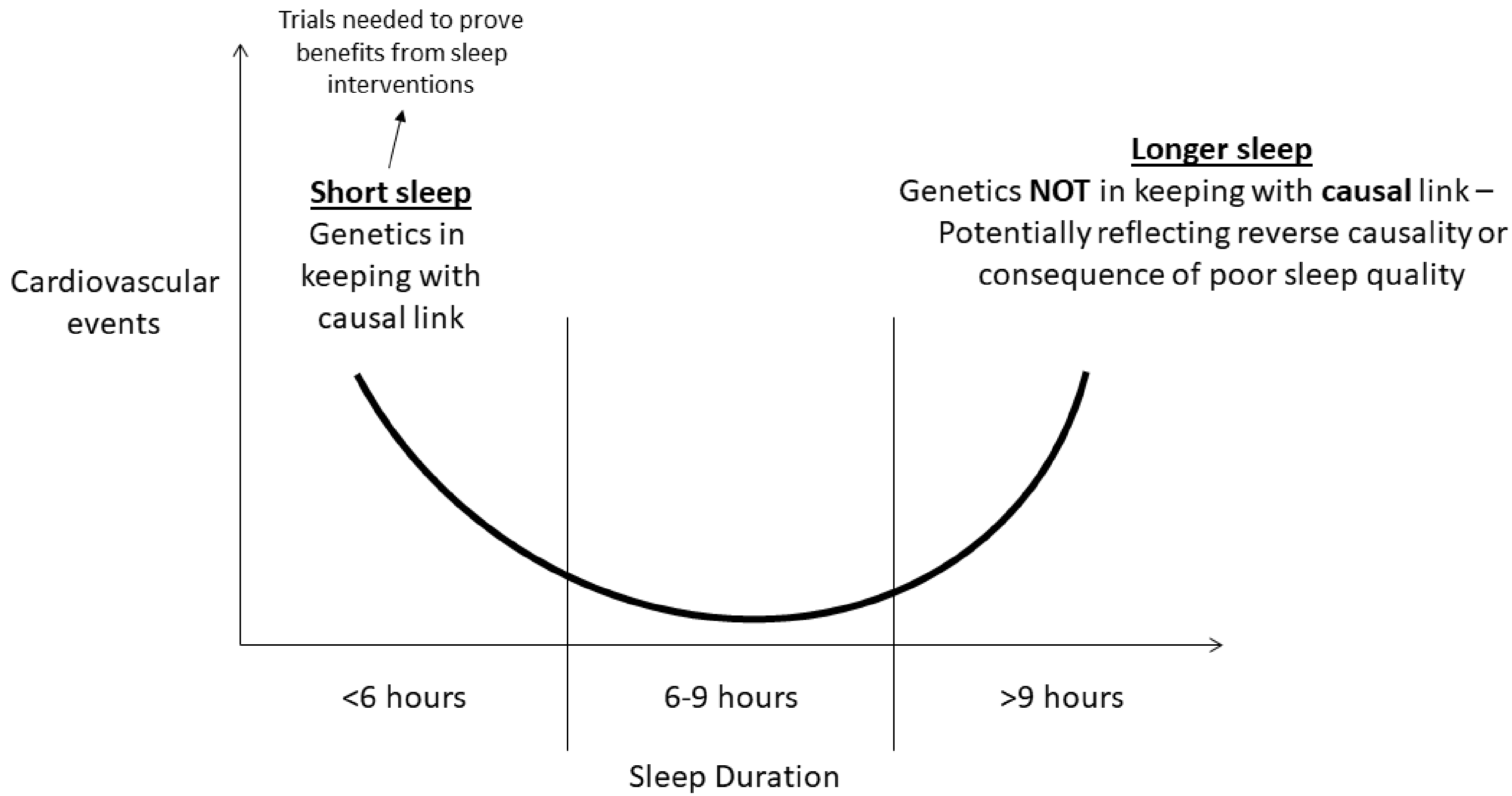
Figure 1


Trials needed to prove benefits from sleep interventions
Short sleep
Genetics in keeping with causal link
Longer sleep
Genetics NOT in keeping with causal link – Potentially reflecting reverse causality or consequence of poor sleep quality
Cardiovascular events
<6 hours
6-9 hours
>9 hours
Sleep Duration