The last decade has witnessed a growing body of epidemiological and basic research on sleep and cognitive health. However, the association between sleep duration and cognitive function remains one of the most studied yet controversial topics, with conflicting findings reported by both cross-sectional and prospective studies. To clarify this important question in a large population-based setting, Ma et al. pooled data from 20,065 individuals from the English Longitudinal Study of Ageing (ELSA) and the China Health and Retirement Longitudinal Study (CHARLS), two nationally representative longitudinal cohorts of aging, and found an inverted U-shaped association: those with 4 hours or less and 10 hours or more of sleep per night had worse cognition and faster decline in global cognitive function and memory. Although this investigation is not the first study to report on such an association, the implications of this work go beyond a U-shaped association.

Numerous prior studies, often on a much smaller scale, have produced inconsistent findings regarding the association between sleep duration and cognitive function, whereas larger studies, including meta-analysis, have mostly identified an inverted U-shaped association. This observation makes one wonder if previous null findings could be partly owing to a lack of statistical power to detect a modest association between sleep duration and cognitive function. As one of the largest studies of its kind, the pooled cohort study by Ma et al. presented a unique opportunity to investigate the extreme categories of sleep duration (i.e., ≤4 hours and ≥10 hours of sleep per night), which typically comprise few individuals. The associations were small, especially for longitudinal analyses. For global cognition, there was a pooled β of −0.022 (95% CI, −0.035 to −0.009) SD per year for 4 hours or less and a pooled β of −0.033 (95% CI, −0.054 to −0.011) SD per year for 10 hours or more of sleep per night compared with 7 hours of sleep per night. Worse cognitive function was also observed for 8 or 9 vs 7 hours of sleep in cross-sectional analyses but not longitudinal analyses. Therefore, although Ma et al. should be commended for the large sample size of their study and the ability to examine extreme sleep duration, the interpretation of its public health relevance has been limited by the small effect sizes and the low prevalence of extreme sleep duration among the general population.

Ma et al. suggest there are similar associations in the English and Chinese populations, despite the clearly different baseline characteristics of the 2 populations. Compared with the English participants, the Chinese participants were much more likely to sleep for less than 6 or 10 or more hours per night, had lower body mass index and a lower level of education, had more depressive symptoms, and were less likely to be living alone and to consume alcohol at least once per week. The Chinese participants were also less likely to have hypertension, stroke, cancer, and asthma but were more likely to have coronary heart disease and chronic lung disease. In addition, the Chinese participants had higher memory scores, much lower executive function, and similar orientation. The observed differences might be owing to genetics, culture, environment, lifestyle, or a combination of these. In any case, they are all important factors that might alter both sleep duration and cognition, yet almost nothing is known about how these factors might contribute to the association between sleep duration and cognition in different populations. Although some of these factors were controlled for in the multivariate model, residual confounding is still a possibility. Future cross-cultural comparative studies would be of particular interest.

Another question that deserves further attention is which cognitive domain is most susceptible to changes in sleep patterns. Prior studies have suggested that memory, verbal fluency, and executive function are associated with sleep changes, although no consensus has been reached. It
was previously reported that long sleep duration was associated with more rapid subsequent cortical thinning in frontal and temporal brain regions, which have relevance for language and executive function.\textsuperscript{5} Ma et al\textsuperscript{2} concluded that memory is most altered by variations in sleep duration given that an inverted U-shaped association was observed in longitudinal analyses for memory but not for executive function or orientation. Notably, the tasks that were used to assess each cognitive domain were simple and might be limited in their capacity to reflect each individual's performance. Although the methods for evaluating memory and orientation were largely the same in the ELSA and the CHARLS populations, the associations for sleep duration and each cognitive domain were different in these 2 populations (as summarized in eTables 4, 5, and 6 in the study by Ma et al\textsuperscript{2}). Specifically, the CHARLS participants who had more extreme sleep duration had much faster memory decline compared with the ELSA participants, whereas changes in orientation and executive function did not follow a clear pattern. Therefore, these pooled results should be considered with caution.

Despite the growing epidemiological evidence suggesting a U-shaped association in which both short sleep duration and long sleep duration are associated with worse cognitive outcomes, the cause of this U-shape remains to be elucidated. One key question is whether short and long sleep duration might be risk factors, early markers, or a result of cognitive decline in older adults. Patients with cognitive impairment are known to have shorter and more disrupted sleep; therefore, it is intuitive to think of changes in sleep duration as a behavioral symptom of cognitive impairment. Indeed, the study by Ma et al\textsuperscript{2} also observed a cross-sectional association between 4 hours or less or 8 hours or more of sleep and worse cognitive performance, which was attenuated in longitudinal analyses, especially for a sleep duration of 8 or 9 hours. Consistent with most previous studies,\textsuperscript{4} the longitudinal association for long (\(\geq 10\) hours) sleep duration was stronger than that for short (\(\leq 4\) hours) sleep duration. Although ample evidence supports the negative impact of sleep deprivation on cognitive aging through the promotion of amyloid and tau deposition, endothelial dysfunction, and inflammation,\textsuperscript{9,10} there are no known biological mechanisms that explain why long sleep duration might cause cognitive impairment. It is also important to bear in mind the limitations of subjective reports of sleep duration,\textsuperscript{7} as well as the implications of long sleep duration, which might reflect other sleep disorders or comorbidities, medication use, and frailty. Therefore, clarification of the reasons and implications behind individuals’ sleep duration is an essential step toward understanding the nature of the U-shaped association between sleep duration and cognitive function.

It has been almost 2 decades since sleep duration was first suggested to be associated with cognitive health in older adults. The study by Ma et al\textsuperscript{2} adds to existing evidence by pooled analysis of 2 large nationally representative longitudinal cohorts confirming an inverted U-shaped association between sleep duration and cognitive performance. Prospective studies using objective measures of sleep duration and comprehensive neuropsychological batteries are needed to test the association in different populations and to compare different ethnicities. Use of neuroimaging techniques and biomarkers will help clarify the pathophysiological pathways between sleep duration and cognitive aging. Furthermore, novel statistical approaches (eg, mendelian randomization or causal mediation analysis) should be considered to overcome limitations of traditional observational studies and to elucidate pathways underlying sleep duration and cognitive decline. Ultimately, the study of sleep and cognition needs to go beyond sleep duration. Both sleep quality and sleep quantity should be considered in developing prevention and management strategies for dementia.
REFERENCES


