Invited Commentary

Invited Commentary: Validity of Case-Control Studies of Sleep Duration and Breast Cancer

Richard G. Stevens*

*Correspondence to Dr. Richard G. Stevens, University of Connecticut Health Center, 263 Farmington Avenue, Farmington, CT 06030-6325 (e-mail: bugs@uchc.edu).

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The light-at-night theory of breast cancer causation states that a portion of the high breast cancer risk in the industrialized world, and of the rising risk in the developing world, is due to the introduction and increasing use of electricity to light the night. It is difficult to test this idea in human populations, partly because almost everyone in the modern world uses electric lighting after the sun sets. Specific hypotheses that have been tested include the notions that shift workers should be at higher risk, blind women should be at lower risk, and reported sleep duration should be inversely associated with risk. Girschik et al. (Am J Epidemiol. 2013;177(4):316–327) have tested the latter in a case-control study. Although the case-control design is useful for many questions, it is probably not useful for studies of sleep duration and health.

breast cancer; case-control studies; circadian rhythm; sleep; sleep duration; sleep quality

In this issue of the Journal, Girschik et al. (1) report finding no association between self-reported sleep duration and breast cancer risk in a case-control study in Australia. They did a good job of considering, and then attempting to quantify by means of sensitivity analyses, the potential impact of various types of bias on their results. They are refreshingly candid about their exposure assessment and the difficulty of assessing sleep duration and quality, citing their own study of the validity of self-reported sleep duration (2). They note that their subjective assessment of sleep duration showed poor validity in comparison with wrist actigraphy in a sample of subjects. In their case-control study, there was a low response fraction, especially among controls; under various assumptions about the sleep duration of the nonresponders, the authors modeled possible effects on the odds ratios. Overall, they concluded that the odds ratios would not have been appreciably altered by these inadequacies, but they also stressed the need for better methods for assessment of sleep quality and duration in epidemiologic studies.

CONTEXT: THE LIGHT-AT-NIGHT THEORY

The light-at-night theory of breast cancer causation is easy to state: A portion of the high risk in industrialized societies, and the rising risk in developing societies, is due to the introduction and increasing use of electricity to light the night (3, 4). Although the theory is easy to state, it is quite difficult to generate reliable evidence in humans upon which to eventually decide whether, and to what extent, light at night does play a role in breast cancer risk. It is an important question, because there are clear intervention and mitigation strategies which could be implemented if it were true.

A variety of predictions associated with the theory have been investigated, the most evidence for which is the hypothesis on non–day shift work (5), which has resulted in the classification of shift work as a “probable human carcinogen, 2A” by the International Agency for Research on Cancer (6). There is a strong experimental model which is a hybrid of human and rodent physiology (7); however, direct epidemiologic evidence is very much needed as well, before any policy action can be contemplated.

Another prediction, first tested by Verkasalo et al. (8), is that self-reported sleep duration should be inversely associated with risk. This was based on the idea that “sleep duration” might be a surrogate for hours of darkness during the night, albeit a crude one. A longer dark period is more permissive of full and robust nocturnal melatonin production...
and the optimal functioning of other aspects of circadian rhythmicity, including circadian control of system-wide DNA damage response (9), cell-cycle regulation (10), and metabolism (11). It has become evident that even ordinary room light in the evening can delay melatonin onset and blunt its nocturnal peak in humans (12).

DARKNESS VS. SLEEP

Adequate daily sleep is required for maintenance of cognitive function and for a vast array of other capabilities that are only partially understood. Sleep is not, however, required for synchronization of the endogenous circadian rhythm, whereas a stable 24-hour light-dark cycle is required (13). The epidemiologic and laboratory research on sleep and health cannot entirely separate effects of sleep duration from duration of exposure to darkness (14). The distinction is quite important, because a requirement for a daily and lengthy period of darkness to maintain optimal circadian health has different implications than a requirement that a person must be asleep during this entire period; it may be normal to experience a wakeful period in the middle of a dark night (15).

Exposure to light during the night will disrupt circadian function as well as sleep, and the health consequences of short sleep and of chronic circadian disruption are both now the subject of intense research (16). A growing number of both observational and clinical studies of “sleep” and metabolism suggest an alarming and important impact of short sleep on health (17, 18); however, it is not clear that sleep and darkness have been entirely disentangled in these studies. An example of the difficulty of interpreting the “sleep” studies is the carefully conducted analysis of Taheri et al. (19), who reported that sleep duration, as verified by polysomnography, was associated with morning blood levels of leptin in a sample of 1,024 adults in Wisconsin. In the same analysis, however, the duration of typical sleep reported by each subject was more strongly associated with leptin levels. By each subject was more strongly associated with leptin levels.

In this case-control study to be, Girschik et al. (1) make a valuable contribution on assessment of various strengths and limitations of epidemiologic studies of sleep and health.

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Author affiliation: University of Connecticut Health Center, Department of Community Medicine and Health Care, School of Medicine, University of Connecticut, Farmington, Connecticut (Richard G. Stevens).

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REFERENCES


