

## EDITORIAL

## Mend the Mind and Mind the “MCC”

Commentary on Kim et al. Correlates and escitalopram treatment effects on sleep disturbance in patients with acute coronary syndrome: K-DEPACS and EsDEPACS. *SLEEP* 2015;38:1105–1111.

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The World Health Organization (WHO) has stated that mental illnesses are the leading causes of disability worldwide and account for 37% of healthy years lost from non-communicable diseases.<sup>1</sup> Non-communicable diseases—such as cardiovascular disease, chronic respiratory disease, cancer, diabetes, and mental health conditions—are estimated to result in \$47 trillion loss, which, in turn, accounts for 75% of the global Gross Domestic Product [GDP].<sup>2</sup> Depression alone is expected to be responsible for one-third of health years lost to disability from mental illness.<sup>1,2</sup> Mental illnesses such as depression and physical ailments such as ischemic heart disease are examples of 17 chronic conditions that coexist in at least one in four Americans and such co-location is termed multiple (two or more) concurrent chronic conditions (MCC).<sup>3</sup> MCC accounts for approximately 66% of total health care expenditures in the U.S. that is spent on 27% of Americans.<sup>3</sup> Importantly, combinations of MCC, such as co-occurrence of coronary artery disease and depression may have synergistic interactions and lead to worse health outcomes of individuals with such serious mental illnesses due to poor attention to treatment adherence and disease understanding.<sup>4</sup> It naturally follows that the participants of the Grand Challenges in Global Mental health identified the need for integrating the treatment of mental disorders with chronic disease care and suggested redesign of healthcare systems.<sup>5</sup>

In this issue of *SLEEP*, Jae-Min Kim and colleagues<sup>6</sup> report having successfully integrated treatment of a mental health condition (i.e., depression) in patients with a common medical condition (i.e., acute coronary syndrome), and demonstrated both the high prevalence of depression in patients with acute coronary syndrome and that sleep outcomes can be improved through treatment of depression. They should not only be commended for an arduous and well done study in such a challenging population, but also for setting the stage for coordinated care across mental and physical health domains.

In this study of Kim et al., both sleep and depression were evaluated within two weeks of the acute coronary syndrome episode, which is much earlier than that in other similar studies of sleep and depression in patients with ischemic

heart disease.<sup>7–9</sup> However, a recent study by Lafitte and colleagues examined the prevalence of depression within a few days of acute coronary syndrome and noted a prevalence of major depression in 29% of such patients.<sup>10</sup> They found that a prior personal history of depression was a good marker to select patients who should be screened for depression after an ACS with an adjusted hazard ratio of 11.<sup>10</sup> In another recent study, Notara and colleagues found that among “not married” patients, a 1-point increase in the Center for Epidemiological Studies Depression score was associated with a 2% greater risk of having non-fatal and 4% increased risk for fatal cardiac events.<sup>11</sup> There may be multiple mechanisms through which depression increases cardiac risk, and poor sleep may represent one such mechanism.

The domains of the Leeds Sleep Evaluation Questionnaire—getting to sleep, quality of sleep, awakening from sleep, and behavior following wakefulness—correspond individually to insomnia with good consistency, reliability, and validity.<sup>12</sup> Poor sleep labelled as “insomnia” has in turn been associated with increased cardiovascular and all-cause mortality.<sup>13–25</sup> One of the criticisms of such subjective sleep complaints is that poor sleep or insomnia do not lend themselves well to objective measurements. However, it has been argued that a composite of both sleep duration and sleep quality may be measuring the various facets of poor sleep much better and may have a more direct (and simple) relationship with mortality rather than the curvilinear relationship between sleep duration and mortality.<sup>26–28</sup>

Poor sleep or insomnia may lead to systemic inflammation in experimental conditions.<sup>29</sup> Recently, in a 20-year cohort, persistent insomnia was associated with steeper increments in systemic inflammation measured with serum levels of C-reactive protein (CRP).<sup>25</sup> Elevated CRP levels have, in turn, been independently associated with increased risk for cardiovascular disease and death.<sup>30</sup> However, the duration of such exposure to both poor sleep and increased levels of inflammation mediated by poor sleep may be important. In a short-term study of biomarkers in patients with depression following acute coronary syndrome there was no association between CRP, fibrinogen, or atherosclerosis burden at any time-point over a 9-month follow-up period.<sup>10</sup> In contrast, cognitive behavioral therapy for insomnia reduced systemic inflammation, and Tai Chi Chih therapy reduced cellular inflammatory responses, and both treatments reduced expression of genes encoding pro-inflammatory mediators in older adults with insomnia.<sup>31</sup> Such improvements in systemic inflammation through a sleep-intervention may benefit patients with acute coronary syndrome by

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reducing atherosclerotic plaque rupture facilitated by systemic inflammation.

In the study by Jae-Min Kim and colleagues,<sup>6</sup> the randomized placebo controlled trial of escitalopram revealed temporal improvements in sleep in both the placebo and treatment arms. Conceivably, the temporal pattern of resolution of insomnia versus persistence of insomnia, and the duration of “exposure” to the insult of lost sleep, may determine the adverse effects of poor sleep on cardiovascular health. While the implications of their intervention are significant in how patients with depression following acute coronary syndrome should be treated, future research needs to also identify individuals at-risk for persistence of poor sleep. In the era of precision medicine, such personalized approaches using a composite of clinical characteristics and biomarker predictors are needed.

Jae-Min Kim and colleagues have taken a bold step of demonstrating the improvements in sleep in patients with depression and acute coronary syndrome following treatment with escitalopram. Future research needs to investigate whether such improvement in sleep can improve long-term outcomes in patients with MCC that includes mental health conditions such as depression. As healthcare systems strive to integrate the delivery of healthcare to MCCs in the mental and physical domains, sleep bridges this gap nicely and serves as a potential target for well-planned interventions. Future research on better sleep and mental health screening, care delivery and coordination is urgently needed. The results of this research may lead to prevention of new chronic conditions and improved self-management of existing chronic conditions. We need to mind the “implementation” gap!

#### CITATION

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