

## EDITORIAL

## Who Needs Sleep Apnea Treatment for Safety Critical Tasks—Are We There Yet?

Commentary on Karimi et al. Sleep apnea related risk of motor vehicle accidents is reduced by continuous positive airway pressure: Swedish traffic accident registry data. *SLEEP* 2015;38:341–349.

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Normalizing cognitive function is key to optimizing road and workplace safety and is one of the main reasons why clinicians identify and treat obstructive sleep apnea (OSA). Whilst numerous studies have found that OSA increases the risk of motor vehicle crashes, few have applied ideal research designs to conclusively validate the relationship,<sup>1</sup> and importantly, to demonstrate that treatment of OSA reduces the risk of motor vehicle crashes.<sup>2</sup> In this issue of *SLEEP*, Karimi and colleagues<sup>3</sup> attempt to redress the limitations of past research with respect to OSA and motor vehicle crash risk, for the first time assessing the impact of CPAP treatment adherence. Karimi et al. highlight an elevated risk of crash associated with OSA, reflecting previous findings.<sup>1</sup> The authors extend the current literature by using an objective measure of crash (police reports) and assess crash risk using two perspectives, both retrospective and prospective, among a cohort of patients referred for suspected OSA compared to an external cohort.

There are several challenges in optimally designing crash risk studies for OSA. While objective crash statistics are preferable, the low rate of police reported crashes necessitates a large sample. Clinical equipoise to leave a range of OSA patients untreated to assess crash risk is challenging because of safety concerns for severely sleepy patients.<sup>4</sup> Bias may occur when a clinical population is used in that some patients may present because they have had a crash. Using a prospective community cohort, the Wisconsin cohort study found an increased road crash risk in men with OSA, but not women.<sup>5</sup> Case (road crash drivers) control (drivers who have not had a crash) studies are an alternative, with assessment of OSA after the crash, and support increased crash risk in those with OSA.<sup>6</sup> The findings of Karimi et al.<sup>3</sup> are consistent with these previous studies. Some limitations must be acknowledged, though, including the potential for presentation bias that might increase the risk estimate in a clinical sample. OSA, sleepiness, and other confounders were not measured in the control cohort; hence it could have included some drivers with OSA and excessive sleepiness.<sup>3</sup> Nevertheless, the study by Karimi is one of only a few controlled investigations to assess and identify a reduction in crash risk with CPAP treatment.<sup>2,7,8,3</sup>

and it appears to be the first to demonstrate the importance of CPAP adherence (use  $\geq 4$  h/night). As for OSA crash risk, the designs of these studies have not been ideal (observational cohorts rather than randomized trials) due to the same challenges. The adherent CPAP users could have behaved differently to the non-adherent group (e.g., less speeding), which could be at least partly responsible for their reduced crash risk.

Disease severity was not related to crash risk within the OSA group of Karimi et al.,<sup>3</sup> suggesting that respiratory indices (e.g., apnea hypopnea index [AHI]) may not be the best way of determining OSA-related cognitive impairment.<sup>9,10</sup> Previous work has been divided on whether AHI predicts crash risk.<sup>1,5</sup> Patient sleepiness may also be highly variable despite comparable OSA severity. Moreover, individuals vary in their susceptibility to sleep loss.<sup>11</sup> Some consistently and rapidly develop sleepiness and cognitive impairment during restricted sleep; others are more resistant. Recently, this concept has been explored in OSA patients; some maintain normal driving performance following restricted sleep, while others develop substantial impairment.<sup>12</sup> Supporting this concept both subjective and objective measures of sleepiness hold only modest relationships with respiratory indices of OSA severity.<sup>13</sup> This is not surprising given that sleepiness can be influenced by many factors, including age, medications, and genetic factors.<sup>14</sup> Given the poor relationship between OSA severity and crash risk, and the apparent variable impact of OSA on cognitive function and sleepiness, there is a need for alternative methods to assess crash risk in OSA patients. Severe subjective sleepiness is related to crash risk<sup>15,16</sup>; however, this can be unreliable when licensing is at risk,<sup>17</sup> particularly in occupational settings. Sleep latency testing is recommended when driving safety is in question and relates to driving performance,<sup>18</sup> although its relationship to crash risk appears weak.<sup>19</sup> Robust studies of current and alternative objective markers of sleepiness or cognitive function are required to better determine those OSA patients who require treatment in order to undertake safety critical tasks and adequacy of treatment.

The concept that individuals may have different cognitive responses to OSA and sleep loss raises the possibility that those in high-risk occupations might self-select to be more resistant to conditions that cause sleepiness.<sup>20</sup> Commercial vehicle drivers have a high prevalence of OSA.<sup>15,21</sup> Their response to sleep loss appears to be similar to the general population<sup>22</sup>; however, some large studies have not identified a relationship between OSA and crash risk.<sup>23</sup> Many other influences are evident here. Shift work, circadian misalignment, and sleep

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restriction may be more important in this population as found by Karimi et al.<sup>3</sup> and others.<sup>24</sup> Hence, it is important clinically to assess a range of individual factors associated with sleepiness and motor vehicle crash risk.<sup>25</sup> It is also important to consider that individuals operate in complex transport and workplace systems with many opportunities to intervene on key risk factors that impact on sleepiness at the system level. For example, improving heavy vehicle driver schedules may also improve sleep and crash risk.<sup>23,26,27</sup>

Despite the challenges in designing ideal studies, OSA appears to increase crash risk with some indication that treatment of OSA may reduce crash risk. For the first time Karimi<sup>3</sup> provides evidence that good CPAP adherence in particular is associated with reduced risk. This is not the first time, however, that OSA severity appears to be a poor discriminator of crash risk. Hence, there is an opportunity to improve stratification of risk and assessment of response to treatment through improved objective assessment of the cognitive impact of OSA, including sleepiness, a field of research that has not been sufficiently advanced in sleep medicine. It is important for sleep clinicians to address other factors that impact crash risk in their patient, in particular sleep duration and circadian effects in shift workers, and identify those activities and conditions that could help to mitigate this risk.

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