

LETTERS TO THE EDITOR

## Thoughts on the 2019 American Academy of Sleep Medicine position statement on chronic opioid therapy and sleep

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We would like to express a few thoughts about the recent position statement by the American Academy of Sleep Medicine (AASM) on chronic opioid therapy and sleep.<sup>1</sup> The opioid crisis has lasted over a decade now, which makes this position statement much needed and welcomed. It provides a comprehensive coverage of the issues and highlights the risks that opioids pose for sleep-disordered breathing, including obstructive sleep apnea and central sleep apnea (CSA).

**Opioid use and comedications:** There is an evident opioid crisis, which is primarily fueled by the illicit use of opioids.<sup>2</sup> However, the misuse of opioids by patients with pain who are prescribed long-term opioid therapy may also potentially lead to fatal consequences. In 2016, the US Centers for Disease Control and Prevention published the *CDC Guideline for Prescribing Opioids for Chronic Pain* (updated in 2018). Among others, this guideline mentions the use of coprescribed medications such as benzodiazepines as risk factors for opioid-related harms: <https://www.cdc.gov/drugoverdose/prescribing/guideline.html>

Concurrent use of benzodiazepine, alcohol, and other central nervous system depression medications, including gabapentin, pregabalin, or cocaine, and other illicit drugs, should also be factored in as potential risks. Clinicians who prescribe opioids and sleep doctors who assess opioid-related breathing risks<sup>3-9</sup> must take all these factors into consideration. Sleep doctors need to review the patient's full list of medications and determine whether there is substance co-use and/or abuse to assess the risk for disturbed sleep.

**Restless legs syndrome and opioids:** The position statement addresses a critical and paradoxical issue: chronic opioid therapy for individuals with severe or refractory restless legs syndrome (RLS) for whom other therapies have failed to control the symptoms.<sup>10</sup> It is widely believed that these individuals are less prone to develop misuse or addiction. However, solid evidence for this belief is lacking. Therefore, the National RLS Opioid Registry is of major importance to assess the long-term safety and effectiveness of opioid medications for RLS: <https://www.massgeneral.org/rls-registry>.

**Phenotyping the risks of opioid use for sleep disorders:** In the era of personalized medicine and phenotyping, the position statement makes a timely conclusion: "Collaboration among medical providers is encouraged to provide high quality, patient-centered care for people who are treated with chronic opioid therapy." Opioid analgesics are not a panacea. They do not work for everyone. Moreover, they tend to act differently between acute and chronic pain situations, and long-term opioid use may lead to opioid-induced hyperalgesia.<sup>11-13</sup> There is moderate to strong evidence that opioids, in either acute or chronic cases, can affect both sleep breathing and sleep quality.<sup>3,14-19</sup> However, although the risk of opioids for sleep-disordered breathing is recognized, so far we have failed to identify exactly who is at risk. A 2015 review concludes that CSA is present in 24% of opioid users.<sup>5</sup> A recent sleep laboratory study confirmed that 16% of chronic opioid users present CSA (central apnea index  $\geq 5$ ) and 32% obstructive sleep apnea (apnea-hypopnea index  $\geq 15$  events/h) with a clear dose effect for CSA and higher prevalence ( $> 1.6$  times) of Mallampati score ( $> 3$ ).<sup>20</sup> Dose over 200 equivalent in milligram is considered as the threshold.<sup>18</sup> We need to identify different at-risk phenotypes, similar to the work on sleep apnea and opioid-induced ventilatory impairment in the postoperative period.<sup>21-24</sup> Phenotyping for genetic, enzymatic, psychosocial, and physiological risk factors will help prevent the long-term consequences of opioid use for sleep and reduce the fatality risks.

**Polysomnography to assess sleep in chronic opioid users:** In addition to the 2019 position statement, clinicians should keep in mind the 2017 AASM *Clinical Practice Guideline for Diagnostic Testing of Adult Obstructive Sleep Apnea*. Polysomnography testing, and not home sleep apnea testing, is recommended for vulnerable patients such as those with chronic opioid use.<sup>24</sup> Furthermore, titration and follow-up control sleep recordings are probably critical to optimize positive airway pressure treatment in that vulnerable population.

**Responsibility of medical providers toward patients with pain on long-term opioid therapy:** In the United States and

Canada, the responsibility for prescribing opioids to treat pain falls on the shoulders of physicians, dentists, and nurses. In addition, pharmacists are ideally positioned to keep track of multiple or rapid renewals of opioid prescriptions. Clinicians are obliged to inform their patients of the possible and probable risks of opioid use (eg, addiction) as well as potential side effects, including those that affect sleep. The possibility of disrupted sleep homeostasis and sleep-disordered breathing need to be part of the equation. Other health care providers, such as psychologists and physical and respiratory therapists, can collaborate on sleep-related issues. Importantly, they can also identify opioid misuse and other problematic opioid use behaviors.

#### Opioids for cancer pain at end of life versus noncancer pain:

Opioids may sometimes be the only acceptable choice to manage cancer pain at the end of life. However, it is still important to inform patients, family, and close friends about the risks of opioids. Although rates of opioid misuse and addiction have long been assumed to be relatively low among patients with cancer, evidence suggests that rates of problematic opioid use are higher than previously assumed.<sup>25,26</sup> As cancer survivorship increases, patients undergoing curative cancer treatment may be exposed to opioids for increasingly longer periods of time. It is important to reiterate the 2018 statement by the International Association for the Study of Pain: although it confirms that “Opioids are indispensable for the treatment of severe short-lived pain during acute painful events and at the end of life, such as pain associated with cancer,” it also cautions against “open-ended and indiscriminate long-term prescribing” for treating chronic pain (<https://www.iasp-pain.org/PublicationsNews/NewsDetail.aspx?ItemNumber=7221>).

**No harm or stigmatization:** The opioid crisis has led to a stigmatization of chronic pain patients who need opioids for pain. Although opioid misuse is a critical problem, the majority of patients take their opioids responsibly. According to a systematic review, opioid addiction rates among patients with chronic pain prescribed long-term opioid therapy range from 8 to 12%, and opioid misuse rates range from 21 to 29%.<sup>27</sup> However, the incidence of iatrogenic opioid use disorder (ie, addiction) among those prescribed opioids on a short-term basis (eg, after surgery or an emergency medicine visit) is less than 1%.<sup>28</sup> As sleep doctors, we should be careful not to stigmatize patients with chronic pain or RLS who regularly take opioids, as this could decrease the quality of care and lead to an undertreatment of those who suffer from pain.

As rightfully highlighted through the position statement by the AASM on *Chronic Opioid Therapy and Sleep*,<sup>1</sup> opioids may pose a risk for some patients with sleep-disorder breathing. However, opioid reduction (ie, tapering) approaches should be accompanied by alternative evidence-based therapies to manage pain (eg, psychotherapy, physical therapy, nonopioid analgesic medications, or devices). Patients without a clear alternative treatment plan and those who are forced to abruptly discontinue opioids might turn to illicit sources of opioids to self-manage their pain, which in turn could lead to harmful consequences and ultimately to fatal opioid overdose.<sup>29</sup>

## CITATION

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All the authors have read and approved the manuscript. Gilles J. Lavigne holds a Canada Research Chair in Pain, Sleep and Trauma and it is Member of the Order of Canada. Marc O. Martel holds a Canada Research Chair (Tier 2) in Chronic Pain, Mental Health, and Opioid Use. The authors report no conflict of interests.