

## SCIENTIFIC INVESTIGATIONS

## The prevalence and impact of pre-existing sleep disorder diagnoses and objective sleep parameters in patients hospitalized for COVID-19

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**Study Objectives:** Obstructive sleep apnea and other sleep disorders overlap with comorbidities associated with poor outcomes related to severe acute respiratory syndrome coronavirus 2 infection. However, the prevalence of obstructive sleep apnea among patients hospitalized for COVID-19 and relationship to outcomes is poorly characterized, and the relevance of other sleep disorders remains unknown. The objective of this study was to identify the prevalence of pre-existing sleep disorders and association with outcomes related to severe COVID-19 illness.

**Methods:** Patients with severe acute respiratory syndrome coronavirus 2 infection admitted to the University of Michigan Hospital System were included. Electronic medical records were queried for sleep disorders diagnostic codes. Data were extracted from polysomnography and home sleep testing in a subgroup with previous diagnostic testing at our center. Logistic regression was used to examine the association of sleep disorders with mechanical ventilation requirement, treatment with vasopressors, and death and Cox proportional hazards regression for time to discharge.

**Results:** Among n = 572 adult patients hospitalized for COVID-19, 113 (19.8%) patients had obstructive sleep apnea, 4 patients had central sleep apnea (0.7%), 5 had hypoventilation (0.9%), 63 had insomnia (11.0%), and 22 had restless legs syndrome or periodic limb movements disorder (3.9%). After adjusting for age, sex, body mass index, and race, no significant relationship was apparent between sleep disorders diagnoses or indices of sleep-disordered breathing severity and outcomes.

**Conclusions:** This is the first study to determine the prevalence of obstructive sleep apnea and other sleep disorders in a well-characterized cohort of patients hospitalized for COVID-19. Once hospitalized, a significant contribution of sleep disorders to outcomes was not identified. Therefore, future evaluations should focus on earlier outcomes, such as infection or clinical manifestations after exposure to severe acute respiratory syndrome coronavirus 2.

**Keywords:** COVID-19, sleep disorders in hospitalized patients, mechanical ventilation, mortality

**Citation:** Goldstein CA, Rizvydeen M, Conroy DA, et al. The prevalence and impact of pre-existing sleep disorder diagnoses and objective sleep parameters in patients hospitalized for COVID-19. *J Clin Sleep Med*. 2021;17(5):1039–1050.

### BRIEF SUMMARY

**Current Knowledge/Study Rationale:** Many have hypothesized that sleep disorders, particularly obstructive sleep apnea, are relevant in patients infected with severe acute respiratory syndrome coronavirus 2 given the overlap of with comorbidities associated with worse outcomes related to COVID-19. However, objective data regarding the prevalence of sleep disorders and association with outcomes in patients hospitalized with COVID-19 are minimal.

**Study Impact:** Sleep disorders were common in individuals hospitalized for COVID-19 but did not contribute to mortality or other critical outcomes. Therefore, earlier outcomes such as the development of illness after exposure to severe acute respiratory syndrome coronavirus 2 or requirement of hospitalization warrant further investigation. The role of sleep disorders in COVID-19 is particularly important given the disproportionate impact of both sleep disorders and COVID-19 on individuals with unfavorable social determinants of health.

### Σχόλιο:

Σε 577 ασθενείς με COVID 19 που εισέρχονται στο νοσοκομείο για νοσηλεία η ύπαρξη αποφρακτικής υπνικής άπνοιας διαπιστώθηκε σε 113 (19,8%), η ύπαρξη κεντρικής υπνικής άπνοιας σε 4 (0,7%), η ύπαρξη αυπνίας σε 63 (11%) και η ύπαρξη συνδρόμου ανήσυχων άκρων -RLS- σε 22 (3,9%).

Η ύπαρξη αποφρακτικής υπνικής άπνοιας δεν φάνηκε να χειροτέρευε την πρόγνωση της COVID 19.

Δεν διερευνήθηκε στη μελέτη αυτή η τυχόν επίδραση της αποφρακτικής υπνικής άπνοιας στην ανάπτυξη και συμπτωματολογία της COVID 19 σε προνοσοκομειακό επίπεδο.

Επιλογή άρθρου – Σχολιασμός: Μάνος Βαγιάκης

## SCIENTIFIC INVESTIGATIONS

## Sleeping patterns and childhood obesity: an epidemiological study in 1,728 children in Greece

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**Study Objectives:** Sleep is an essential normal function for children's growth and development, but over the years, lifestyle changes have resulted in insufficient sleep, a factor that may be associated with increased childhood obesity. The aim of this study was to evaluate the association between sleep duration and sleep patterns separately on weekdays and weekends regarding children's weight status.

**Methods:** This study was conducted among Greek students (55.1% girls) in 2014–2016. Children's weight status was classified according to the International Obesity Task Force tables and guidelines. Sleep duration was determined based on the sleep and wake time that children reported, separately for weekdays and weekends. Classification and regression tree analysis was used to derive sleep patterns and evaluate their relation to children's weight status.

**Results:** Multiadjusted analysis revealed an inverse association between average duration of sleep on weekdays and weekends with the likelihood of being overweight/obese (odds ratio per 1 hour 0.82; 95% confidence interval, 0.73–0.92). This was more prominent on weekends than on weekdays. Children who had lower duration on weekdays, but catch-up sleep duration on weekends, were 2% (95% confidence interval, 0.97–0.99) less likely to be overweight/obese compared to those children having both less or increased sleep duration on weekdays and weekends.

**Conclusions:** Sleep duration and sleep patterns seem to be associated with childhood weight status. Interventions should be developed to educate parents on the importance of an adequate sleep duration and healthy sleep patterns for their children's healthy development.

**Keywords:** sleep patterns, sleep duration, overweight and obesity, children, CART analysis

**Citation:** Kanellopoulou A, Notara V, Magriplis E, et al. Sleeping patterns and childhood obesity: an epidemiological study in 1,728 children in Greece. *J Clin Sleep Med*. 2021;17(5):1093–1101.

### BRIEF SUMMARY

**Current Knowledge/Study Rationale:** In recent years, sleep duration has begun to be studied. However, the aim of this study was to investigate the effect of sleep duration and sleep patterns during weekdays and weekends, separately, on the likelihood of overweight/obesity in pre-adolescents in Greece.

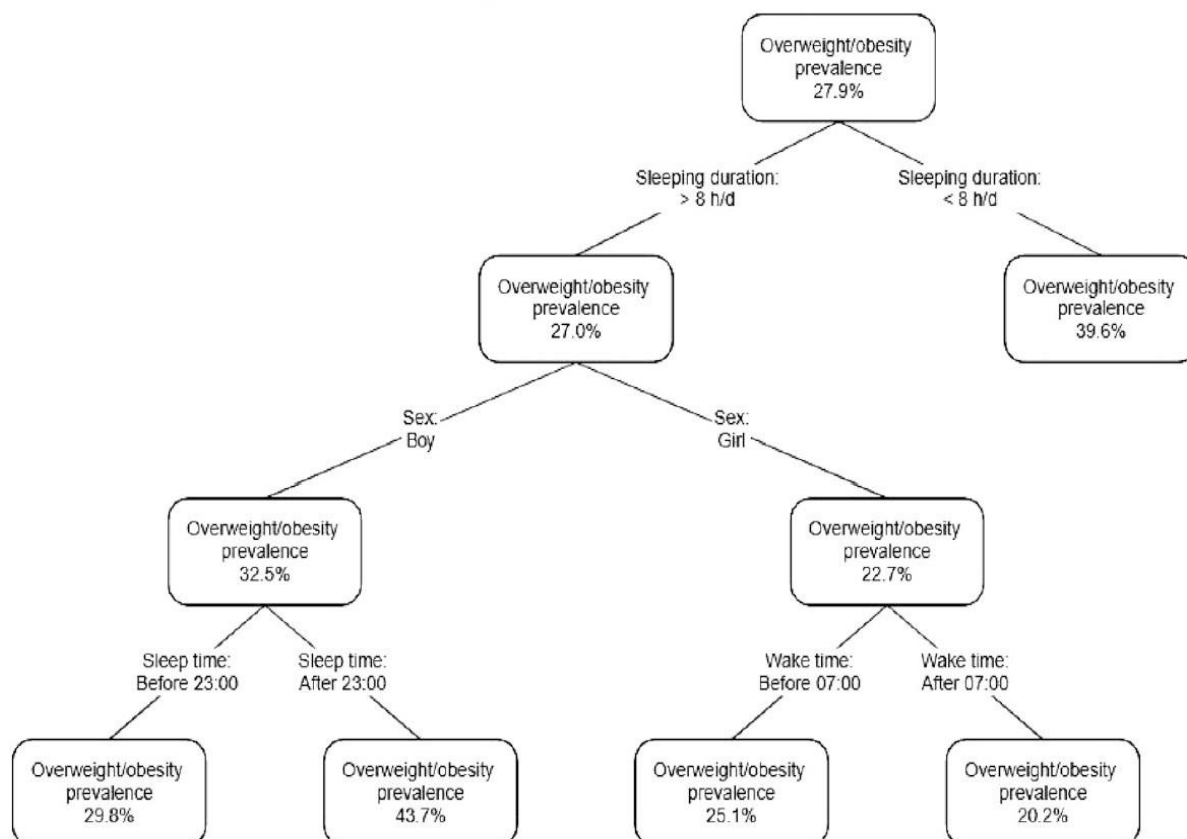
**Study Impact:** Nowadays, there are still uncertainties about sufficient sleep patterns. Parents need to understand their role in ensuring a healthy sleep pattern in their children.

### INTRODUCTION

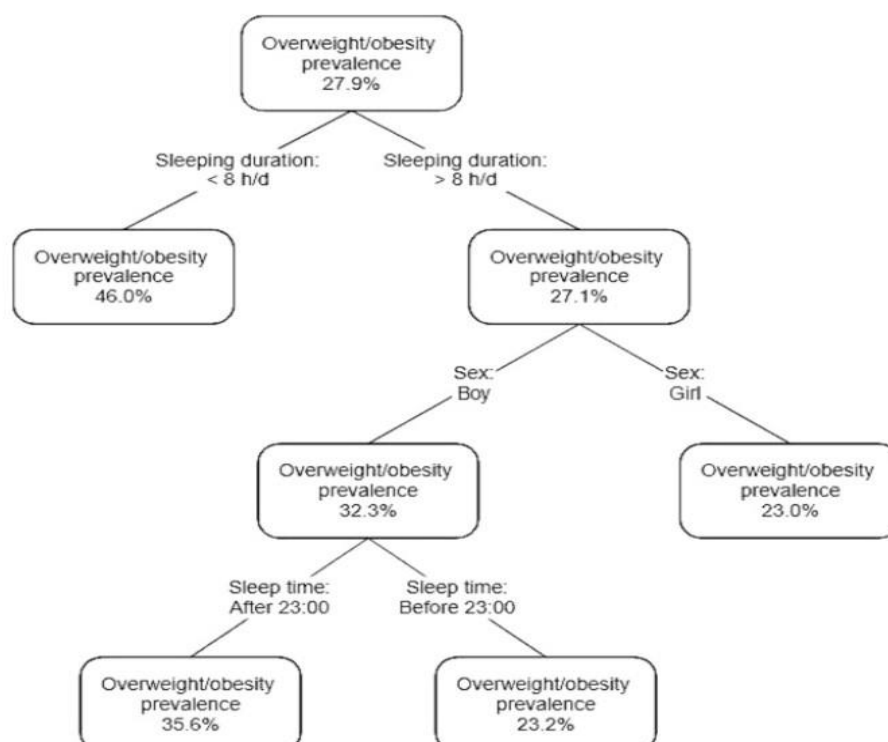
Sleep is a normal, necessary biological process, which affects the human body in multiple ways.<sup>1</sup> Proper and adequate sleep enhances the immune function<sup>2</sup> and may reduce the likelihood of developing a number of diseases, such as cardiovascular disease,<sup>3</sup> diabetes,<sup>4</sup> and stroke.<sup>5</sup> It has also been found to improve memory and to help learning<sup>6</sup> and to regulate the secretion of growth hormone,<sup>7</sup> which is responsible for the physical development of children and adolescents. It has been proposed that the body's ability to regulate its endocrine function is affected by sleep duration and patterns.<sup>8</sup> Sleep deprivation leads to the deregulation of 2 appetite-related hormones, ghrelin<sup>9</sup> and leptin.<sup>10</sup> Ghrelin is a hormone that increases the feeling of hunger, and leptin regulates the feeling of satiety. Disturbed sleep may result in an increased feeling of hunger and food

consumption through this deregulation.<sup>11</sup> Moreover, insulin, which is associated with sleep duration<sup>12</sup> and responsible for blood sugar levels, may also be deregulated, resulting in increased blood levels, which leads to increased fat deposition—ie, it increases the risk of being overweight and of obesity.<sup>13</sup> Children, however, often have habits that affect sleep, such as the time they spend in front of screens.<sup>14</sup> It has been found that many hours of use of electronic devices during a day are connected with symptoms of insomnia in children.<sup>15</sup> Sleep-specific guidelines have been developed by the American Academy of Sleep Medicine to enhance the healthy growth of children. Specifically, it is recommended that children should sleep 9–12 hours on a daily basis.<sup>16</sup> In recent years, it has been observed that children adopt patterns of restricted sleep<sup>17</sup> as they transition toward adolescence. Also, children have different schedules on weekdays compared to weekends, since they spend most of

**Figure 1**—Classification tree for overweight/obesity based on weekday sleep duration.



**Figure 2**—Classification tree for overweight/obesity based on weekend sleep duration.



Σχόλιο:

Ένα ενδιαφέρον άρθρο από την Ελλάδα (Χαροκόπειο Πανεπιστήμιο, Επιστήμες Διατροφής) που περιλαμβάνει 1482 παιδιά 10-12 ετών από 47 σχολεία.

Η μελέτη έδειξε ότι οι μειωμένες ώρες ύπνου (<8) καθώς και η έναρξη του ύπνου μετά τις 23:00 συνδυάζεται με αυξημένα ποσοστά παχυσαρκίας ιδίως στα αγόρια.

Συμπέρασμα: Βάλτε τα παιδιά να κοιμούνται νωρίς και πάνω από 8 ώρες.

Επιλογή άρθρου – Σχολιασμός: Μάνος Βαγιάκης

## SPECIAL ARTICLES

### The use of telemedicine for the diagnosis and treatment of sleep disorders: an American Academy of Sleep Medicine update

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The COVID-19 pandemic led to widespread use of telemedicine and highlighted its importance in improving access to sleep care and advocating for sleep health. This update incorporates the lessons learned from such widespread utilization of telehealth to build on the American Academy of Sleep Medicine's 2015 position paper on the use of telemedicine for diagnosing and treating sleep disorders. Important key factors in this update include an emphasis on quality and value, privacy and safety, health advocacy through sleep telemedicine, and future directions.

**Keywords:** telemedicine, sleep disorders, sleep medicine, guidance, quality, safety, advocacy

**Citation:** Shamim-Uzzaman QA, Bae CJ, Ehsan Z, et al. The use of telemedicine for the diagnosis and treatment of sleep disorders: an American Academy of Sleep Medicine update. *J Clin Sleep Med*. 2021;17(5):1103–1107.

## BACKGROUND

Telemedicine has grown exponentially since the publication of the American Academy of Sleep Medicine's position paper on the use of telemedicine for the diagnosis and treatment of sleep disorders in 2015.<sup>1</sup> Increasing need for access to specialty care and advancing technologies initially led the change, but it was the novel severe acute respiratory syndrome coronavirus (SARS-CoV-2) that spurred widespread use of telemedicine. The COVID-19 pandemic challenged traditional methods of health care delivery as health systems curtailed nonemergent care at hospitals and sought to provide the safest possible environments for patient care.<sup>2,3</sup> Telemedicine became the cornerstone of providing health care in an environment that was safe for patients, providers, and staff,<sup>2,3</sup> and health care systems reported dramatically increased rates of telemedicine utilization to manage pandemic related stay-at-home orders.

In 2020, the US Department of Health and Human Services made it easier to provide telehealth services by waiving Centers for Medicare & Medicaid Services' restrictions on reimbursement. Novel platforms made care available to patients at any location, from the safety and comfort of their own

homes to public locales. Traditional center-to-home models were expanded to include not only the patient, but also the provider, being out of the center.

In response, the AASM Board of Directors initiated a review and update of the 2015 document. A Telemedicine Presidential Committee was convened, and a review of existing policies, materials and literature was initiated in May 2020. An early finding of the group was that the guidance outlined in the original 2015 document was still relevant and should continue to serve as guiding principles. This current updated document is a supplement to, rather than a replacement of, the original paper, with a summary of the combined guidance listed in **Table 1** and details of the new guidance below.

## UPDATE

A growing body of literature supports effective utilization of telemedicine in the management of patients with sleep disorders. Studies have shown effective use of telemedicine for the diagnosis and management of obstructive sleep apnea,<sup>4–7</sup> most extensively to improve adherence to positive airway pressure therapy.<sup>8–10</sup> Telemedicine has been widely applied in

**Table 1—American Academy of Sleep Medicine guidance for the use of telemedicine in sleep medicine.**

|                                                                                                                                                                                                                                                                                                                                     |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Position Paper for the Use of Telemedicine in Sleep Medicine (2015)<sup>1</sup></b>                                                                                                                                                                                                                                              |
| Clinical care standards for telemedicine services should mirror those of live office visits, including all aspects of diagnosis and treatment decisions as would be reasonably expected in traditional office-based encounters.                                                                                                     |
| Clinical judgment should be exercised when determining the scope and extent of telemedicine applications in the diagnosis and treatment of specific patients and sleep disorders.                                                                                                                                                   |
| Live interactive telemedicine for sleep disorders, if utilized in a manner consistent with the principles outlined in this document, should be recognized, and reimbursed in a manner competitive or comparable with traditional in-person visits.                                                                                  |
| Roles, expectations, and responsibilities of providers involved in the delivery of sleep telemedicine should be defined, including those at originating sites and distant sites.                                                                                                                                                    |
| The practice of telemedicine should aim to promote a care model in which sleep specialists, patients, primary care providers, and other members of the health care team aim to improve the value of health care delivery in a coordinated fashion.                                                                                  |
| Appropriate technical standards should be upheld throughout the telemedicine care delivery process, at both the originating and distant sites, and specifically meet the standards set forth by the Health Insurance Portability and Accountability Act (HIPAA).                                                                    |
| Methods that aim to improve the utility of telemedicine exist and should be explored, including the utilization of patient presenters, local resources and providers, adjunct testing, and add-on technologies.                                                                                                                     |
| Quality assurance processes should be in place for telemedicine care delivery models that aim to capture process measures, patient outcomes, and patient/provider experiences with the model(s) employed.                                                                                                                           |
| Time for data management, quality processes, and other aspects of care delivery related to telemedicine encounters should be recognized in value-based care delivery models.                                                                                                                                                        |
| The use of telemedicine services and its equipment should adhere to strict professional and ethical standards so as not to violate the intent of the telemedicine interaction while aiming to improve overall patient access, quality, and/or value of care.                                                                        |
| When billing for telemedicine services, it is recommended that patients, providers, and others rendering services understand payor reimbursements, and that there be financial transparency throughout the process.                                                                                                                 |
| Telemedicine utilization for sleep medicine is likely to rapidly expand, as are broader telehealth applications in general; further research into the impact and outcomes of these are needed.                                                                                                                                      |
| <b>Additional Guidance for the Use of Telemedicine in Sleep Medicine (2021)</b>                                                                                                                                                                                                                                                     |
| High quality, comprehensive sleep care can be provided via telehealth modalities, which are not limited by geographic boundaries.                                                                                                                                                                                                   |
| Synchronous telehealth visits may be performed in lieu of live in-person office visits if they mirror the live visits in quality and process and comply with all licensing, state, federal and HIPAA regulations for both originating and distant sites, even when <i>both</i> sites are located outside of the traditional office. |
| Asynchronous telehealth modalities may be used to augment clinical care and access to sleep medicine services.                                                                                                                                                                                                                      |
| A telemedicine program must maintain a culture of good patient safety encompassing professional accountability, risk assessment, risk management, and infection control, with special consideration for both the physical and psychological safety of the patient at the time of the telemedicine visit.                            |
| Telehealth may play a vital role in preserving the continuity of sleep health, but advocacy for greater access to telehealth systems to reduce health disparities is needed.                                                                                                                                                        |
| Moving forward, clinical pathways to diagnose and manage sleep disorders are needed to determine the best way to integrate in-person care with telemedicine, including the incorporation of data from sleep-specific and consumer-based technologies.                                                                               |

behavioral health to improve access with success in a number of disorders.<sup>11</sup> Several small studies have shown that the benefits from cognitive behavioral therapy for insomnia (CBT-I) and brief behavioral therapy for insomnia delivered via telemedicine are similar to those delivered via traditional in-person office visits.<sup>12,13</sup> Because of the shortage of trained behavioral sleep therapists, online application-based CBT-I programs have been developed and a recent systematic review and meta-analysis found that internet-delivered CBT-I is effective in improving sleep.<sup>14</sup>

Telemedicine has also been used to manage sleep disorders in pediatric populations. Telehealth follow-up visits, primarily via telephone, have been used for chronic management of obstructive sleep apnea and internet delivered CBT-I has been shown to be effective in adolescents with insomnia.<sup>15</sup>

Telemedicine management has not been studied explicitly in other sleep disorders such as restless legs syndrome or

parasomnias. However, studies showing the success of management of other medication- treated disorders, such as asthma, hypertension and diabetes,<sup>16,17</sup> suggest that management of these other sleep disorders via telemedicine would be successful as well.

TECHNOLOGY-BASED CARE

As detailed in the 2015 position paper,<sup>1</sup> sleep care delivered through telemedicine modalities may occur synchronously or asynchronously. Synchronous telemedicine services occur in real-time with audio and video communications between a patient at the originating site and a provider at the distant site and must mirror live office visits. Other providers, caregivers, and staff may also be included in the telemedicine encounter, as routinely needed during the traditional office visit.

A tele-presenter may be added to assist with the technology and examination at the originating site during a telemedicine visit. Asynchronous telemedicine services in which the patient and provider are separated not only by distance, but also time, include remote interpretation of store-and-forward systems, electronic communications between patients and providers, electronic consultations between providers, and self-directed care mechanisms such as data from health apps. Additional details can be found in the 2015 position paper.<sup>1</sup>

### Updates for synchronous telemedicine services

In addition to the center-to-center and center-to-home models in which the provider is at the health care facility and the patient is at another center or at home, fully out-of-center models may also provide comprehensive care, as long as they mirror live office visits. Out-of-center models incorporate both the originating and distant sites outside of the traditional office, and may occur at any private, safe location of the patient's and provider's choosing. These interactions may be performed utilizing multimedia communications equipment which permit, at a minimum, audio and video two-way, real time, interactive communication. Examples include smart phones and tablets in addition to traditional laptop and desktop computers. In any form of mobile communication technology, both privacy should be ensured, in compliance with the Health Insurance Portability and Accountability Act (HIPAA) and state and federal regulations, as well as the quality of the interaction. Patients should be informed that the telehealth visit is in lieu of the live in-person office visit. Patient safety should be ensured, and procedures for activating emergency services (eg, e-911) should be in place in case an emergency is witnessed during the telemedicine encounter. A backup plan should be developed in advance to address connection troubles or poor signal quality. Consent for synchronous care through a telehealth modality should also be obtained at each visit.

### Updates for asynchronous telemedicine services

Store-and-forward systems are now used routinely in sleep medicine. Communications through patient portals, remote patient monitoring incorporating review of data obtained remotely from a positive airway pressure device, and remote interpretation of home sleep apnea tests are examples of store-and-forward technologies commonly used in the care of sleep medicine patients. Electronic consultations incorporating review of medical data with clinical decision-making communicated to referring providers, electronic communications with patients, and virtual patient check-ins through the electronic health record platforms are also examples of asynchronous telemedicine services. As with synchronous telemedicine, asynchronous services require patient consent, and consent for asynchronous care should be obtained at least annually. As a result of the COVID-19 pandemic, more asynchronous telemedicine services have become reimbursable; however, providers should consult payers regularly to ensure ongoing reimbursement for these services.

### Updates to technology-based requirements

Technical requirements for performing telemedicine visits will continue to change as technology evolves. However, any

telehealth technology used should ensure privacy and security of protected health information in compliance with HIPAA. Some present-day examples include password or biometric-ID protection of the device and/or platform used to deliver care, encryption of data transmitted or stored, and access to telehealth platforms restricted to authorized users. Popular, audio-video chat applications used to provide synchronous telehealth services during the current pandemic emergency must be "non-public" facing to limit participation to only the intended parties (patient, provider, caregiver, etc.) and require HIPAA business associate agreements with the technology vendor to ensure compliance with HIPAA.<sup>18</sup> Whether their use will continue postpandemic will depend on regulatory changes.

## REGULATORY GUIDELINES

Regardless of the mode of telemedicine used, adherence to federal and state regulations and compliance with HIPAA are vital. Providers practicing across state lines are subject to requirements in all states in which the provider and patient are located at the time of the encounter. This includes clinical encounters, sleep testing, as well as the prescription of controlled substances. Providers are encouraged to consult state and federal regulatory bodies routinely for updates. Interstate compacts have been developed to ease the process of applying for licenses in multiple states.<sup>19</sup> Telemedicine offers the unique opportunity to also practice across international borders. In such cases, providers will also need to ensure licensure and compliance with regulations of the country in which the patient is located at the time the care is provided.

## PATIENT SAFETY

The COVID-19 pandemic accelerated the use of telemedicine to minimize risk to patients and their health care teams from the SARS CoV-2 virus, avoid exposures during transit or at in-person appointments, and prevent spread of disease. Although center-to-home and out-of-center models offer great advantages and convenience over center-to-center models, more diligence is needed by providers and provider organizations to ensure patient privacy, safety, and compliance with HIPAA.

Competence in the use of telemedicine is fundamental in providing ethical and safe health care. Providers need to understand the limitations of telemedicine care delivery, including impact on diagnostic capabilities, that may affect care. Education, training, preparedness, and awareness are key factors in mitigating patient safety risk. Moreover, quality assurance plans for telemedicine should be in place to maintain a culture of good patient safety encompassing professional accountability, risk assessment and risk management related to its use. The ideal model needs to incorporate strategies to ensure provisions are in place for patients who are technologically challenged, those who do not have access to broadband/internet, or those with lower levels of digital health literacy. Providers also need to ensure accommodations are in place for patients with language barriers or those with visual or hearing impairments.

The safety of the patient and provider at the time of the visit should always be considered. For example, care should not be delivered in a moving vehicle while the patient or provider is driving. Ideally, telemedicine should mirror and meet the quality and standards of in-person visits. Providers must also be cognizant of the limitations of telemedicine as they relate to patient safety.<sup>20</sup> They need to ensure all data security and encryption protocols are up-to-date and all possible risks are disclosed to the patient prior to enrollment (eg, informed consent). There is concern that virtual visits can increase the risk of medical error by missing something that could have been caught in an in-person visit, particularly in relation to physical examination findings. In addition, the psychological safety and well-being of patients pose unique challenges when care is delivered through telehealth modalities, as factors out of sight of the camera (eg, abusive partner/household member) influencing the patient encounter may not be visible. As such, telemedicine in the home setting puts the onus on the patient (or personal caregiver) to participate in and manage their own health care needs which can impact patient safety. Lastly, escalation protocols should be developed (personalized to the sleep medicine practice) to dictate when a patient receiving telehealth services should be transitioned to urgent in-person follow-up care or receive emergency services.

## ADVOCACY

The COVID-19 pandemic has shown us that telemedicine can be used to provide comprehensive care to patients with sleep disorders, and sleep medicine has shown itself to be a specialty that can offer complete and quality care remotely. Telemedicine increases access to sleep care to geographically remote and underserved areas, to vulnerable populations, and to all in times of national emergencies or natural disasters. Vulnerable populations who may benefit from telehealth services include the elderly, children, lower socio-economic groups, high risk immunocompromised or sleepy patients, those with physical or mental limitations, and those lacking a safe means of traveling to or from medical appointments. In fact, telehealth may help reduce some of the health disparities and inequities associated with the traditional health care model. However, a clear digital divide exists today based on geographic and socio-economic factors,<sup>21</sup> and telehealth care delivery is highly dependent on access to high-speed internet/broadband. It is important to identify and address the potential to worsen health disparities, especially in highly rural areas with limited internet connectivity and high poverty/low-income areas with limited financial resources to afford internet or smart electronic devices.

In addition, state licensing regulations have posed significant barriers to the widespread utilization of telemedicine, creating inequities in access to specialized expertise. Medical licensing falls under the purview of individual states, and while some states allow for cross-border care, others forbid it. Providers are required to be licensed in the states where they practice (distant site) as well as the states in which their patients reside at the time of the telehealth encounter (originating site). Although Interstate Medical Licensure Compacts<sup>19</sup> may help facilitate and

expedite medical licensure across states, multistate licensing can still be onerous and expensive. In the age of telemedicine, in which geographical distance no longer limits access to care, these regulations impose unnecessary restrictions that curtail access. While many state licensure requirements were waived during the COVID-19 pandemic, allowing for providers to care for patients irrespective of the location of the provider or patient, such waivers need to become permanent, or new regulations implemented that permanently allow for cross-border care, as is the case for the Department of Veterans' Affairs.

We need to continue to move forward to provide safe, compassionate, and potentially cost-effective quality care through telehealth modalities without introducing new health inequities or exacerbating existing health inequities. Improved connectivity and increased access to high-speed internet need to grow together with telehealth expansion. Telehealth may play a vital role in preserving the continuity of sleep health, but we will need to advocate for greater access to telehealth systems to reduce health disparities.

## FUTURE DIRECTIONS

An important area of research is to look at the efficacy of telemedicine when compared to traditional in-person models of care. Clearly telemedicine is a viable way to deliver care, but we must examine how clinical outcomes compare to in-person interactions. Equivalence or noninferiority needs to be demonstrated. Additionally, novel models of care, such as shared medical appointments, may be conducted more easily via telemedicine since barriers, such as physical space and multiple simultaneous patient check-ins, are obviated.

Most of the discussion about using telemedicine for sleep disorders has focused on how to diagnose and manage patients with sleep apnea remotely. The next step is to look at other common sleep disorders such as insomnia, narcolepsy, restless legs syndrome, parasomnias and circadian rhythm sleep-wake disorders to create recommended workflows and templates to diagnose and manage those conditions. It will be important to determine which elements of a sleep disorder can be assessed virtually and which require in-person care. Once these elements are identified, telemedicine can provide more options to interact with patients, either synchronously or asynchronously. Using the quality measures that were published in 2015 by the AASM for sleep disorders would be one method to compare telemedicine versus in-person visits.<sup>22</sup>

Consumer sleep technologies such as mobile apps and wearables have already found widespread use among patients, and the large volumes of data generated by medical devices and consumer wearables may aid in developing algorithms for remote patient monitoring. More research is needed to evaluate not only their validity, as new technologies emerge, but also their impact on sleep behaviors and their potential role in the sleep care of patients.

More research is needed regarding the impact of telehealth on access to care, health care navigation, resource mobilization, and health inequities to influence health policy and create systemic change. The role of industry and consumer technology

in diagnosing and managing sleep patients should also be examined. We must identify and share successes in telemedicine during the COVID-19 pandemic to secure broader and more flexible policies to support the expanded use of telemedicine in medical care.

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## SUBMISSION & CORRESPONDENCE INFORMATION

Submitted for publication February 16, 2021

Submitted in final revised form February 16, 2021

Accepted for publication February 16, 2021

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## DISCLOSURE STATEMENT

The development of this paper was funded by the American Academy of Sleep Medicine. Dr. Won serves on the Society of Sleep and Anesthesia Board of Directors. Dr. Jain serves on the Board of Registered Polysomnographic Technologists Board of Directors. The participation of Drs. Won and Jain does not imply endorsement by the respective organizations on which they serve as Board of Directors members. Dr. Epstein serves as a consultant for AIM Specialty Health, eviCore Healthcare, Somnoware, and the American Academy of Sleep Medicine. Dr. Trotti serves on the AASM Board of Directors. The other authors report no conflicts of interest.

## Σχόλιο:

Το κείμενο αυτό περιλαμβάνει τις επίσημες θέσεις της AASM για το θέμα της χρήσης της τηλεϊατρικής στην Ιατρική του ύπνου. Η επιδημία COVID 19 επιτάχυνε τις διαδικασίες της εξ' αποστάσεως εξέτασης και παρακολούθησης των ασθενών με τη χρήση των σύγχρονων τεχνολογιών.

Στην ανάπτυξη της δραστηριότητας αυτής συντέλεσε και η απόφαση του 2020 του Department of Health and Human Services που κατήργησε τους περιορισμούς στην οικονομική αποζημίωση των γιατρών που χρησιμοποιούν τηλεϊατρική. Η τηλεϊατρική έχει φανεί ότι είναι αποτελεσματική στη διάγνωση και διαχείριση της υπνικής άπνοιας (λήψη ιστορικού, διάγνωση, παρακολούθηση) όσο και της άπνοιας (γνωσιακή – συμπεριφορική θεραπεία).

Οι υπηρεσίες τηλεϊατρικής μπορεί να είναι συγχρονισμένες όπως η συζήτηση και λήψη ιστορικού χρησιμοποιώντας ήχο και εικόνα σε πραγματικό χρόνο και ασύγχρονες όπως η παρακολούθηση της μνήμης της συσκευής CPAP και η αποστολή οδηγιών στον ασθενή.

Άλλα θέματα που αναφέρονται στις οδηγίες είναι η εμπιστευτικότητα της διαδικασίας και η συναίνεση σε αυτήν του ασθενούς.

Επιλογή άρθρου – Σχολιασμός: Μάνος Βαγιάκης

# Pitolisant for Residual Excessive Daytime Sleepiness in OSA Patients Adhering to CPAP

## A Randomized Trial



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**BACKGROUND:** Excessive daytime sleepiness (EDS) in individuals with OSA syndrome persisting despite good adherence to CPAP is a disabling condition. Pitolisant is a selective histamine H<sub>3</sub>-receptor antagonist with wake-promoting effects.

**RESEARCH QUESTION:** Is pitolisant effective and safe for reducing daytime sleepiness in individuals with moderate to severe OSA adhering to CPAP treatment but experiencing residual EDS?

**STUDY DESIGN AND METHODS:** In a multicenter, double-blind, randomized (3:1), placebo-controlled, parallel-design trial, pitolisant was titrated individually at up to 20 mg/day and taken over 12 weeks. The primary end point was change in the Epworth Sleepiness Scale (ESS) score in the intention-to-treat population. Key secondary end points were maintenance of wakefulness assessed by the Oxford Sleep Resistance Test, Clinical Global Impressions scale of severity, the patient's global opinion, EuroQoL quality-of-life questionnaire score, Pichot fatigue questionnaire score, and safety.

**RESULTS:** Two hundred forty-four OSA participants (82.8% men; mean age, 53.1 years; mean Apnea Hypopnea Index with CPAP, 4.2/h; baseline ESS score, 14.7) were randomized to pitolisant (n = 183) or placebo (n = 61). ESS significantly decreased with pitolisant compared with placebo (−2.6; 95% CI, −3.9 to −1.4;  $P < .001$ ), and the rate of responders to therapy (ESS  $\leq 10$  or change in ESS  $\geq 3$ ) was significantly higher with pitolisant (71.0% vs 54.1%;  $P = .013$ ). Adverse event occurrence (mainly headache and insomnia) was higher in the pitolisant group compared with the placebo group (47.0% and 32.8%, respectively;  $P = .03$ ). No cardiovascular or other significant safety concerns were reported.

**INTERPRETATION:** Pitolisant used as adjunct to CPAP therapy for OSA with residual sleepiness despite good CPAP adherence significantly reduced subjective and objective sleepiness and improved participant-reported outcomes and physician-reported disease severity.

**TRIAL REGISTRY:** ClinicalTrials.gov; No.: NCT01071876; URL: [www.clinicaltrials.gov](http://www.clinicaltrials.gov); EudraCT N°: 2009-017248-14; URL: [eudract.ema.europa.eu](http://eudract.ema.europa.eu)

CHEST 2021; 159(4):1598-1609

**KEY WORDS:** CPAP; OSA; pitolisant; residual excessive daytime sleepiness

**ABBREVIATIONS:** EDS = excessive daytime sleepiness; ESS = Epworth Sleepiness Scale; ITT = intention-to-treat; LOCF = last observation carried forward; OSleR = Oxford Sleep Resistance Test; PP = per-protocol; QTcF = QT interval (using Fredericia's correction); TEAE = treatment-emergent adverse event

**AFFILIATIONS:** From the HP2 Laboratory (J.-L. Pépin, R. Tamisier, P. Lévy), INSERM U1042, University Grenoble Alpes, and EFCR Laboratory, Grenoble Alpes University Hospital, Grenoble, France; the Department of Internal Medicine, Pulmonology (O. Georgiev), Alexandrovska Hospital Medical University, Sofia, Bulgaria;

Σχόλιο:

Σε αυτή τη διπλή-τυφλή τυχαιοποιημένη μελέτη, διάρκειας 12 εβδομάδων, εξετάστηκε η αποτελεσματικότητα και η ασφάλεια του pitolisant, ενός εκλεκτικού ανταγωνιστή των H3 υποδοχέων της ισταμίνης, σε ασθενείς με μέτριας βαρύτητας και σοβαρό ΣΑΑΥ οι οποίοι εμφάνιζαν ημερήσια υπνηλία παρά την ικανοποιητική συμμόρφωση στη CPAP. Βρέθηκε ότι το pitolisant οδήγησε σε στατιστικά σημαντική μείωση της ημερήσιας υπνηλίας στους ασθενείς αυτούς, χωρίς σοβαρές ανεπιθύμητες ενέργειες. Είναι σημαντικό το γεγονός ότι περίπου οι μισοί ασθενείς που περιελήφθησαν στη μελέτη έπασχαν από καρδιαγγειακά ή μεταβολικά νοσήματα. Φάνηκε, λοιπόν, ότι το φάρμακο αυτό μπορεί να χορηγηθεί με ασφάλεια σε ασθενείς με καρδιαγγειακές συννοσηρότητες.

Το pitolisant φαίνεται να αποτελεί ένα σημαντικό εργαλείο στη διαχείριση ασθενών με αποφρακτική άπνοια και υπολειπόμενη υπνηλία. Η κλινική πράξη θα επιβεβαιώσει, περαιτέρω, την αποτελεσματικότητά του.

Επιλογή άρθρου – Σχολιασμός: Αθηνά Βλάχου

## Regulation of tissue regeneration by the circadian clock

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First published: 23 April 2021 | <https://doi.org/10.1111/ejn.15244>

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi:10.1111/ejn.15244

### Abstract

Circadian rhythms are regulated by a highly conserved transcriptional/translational feedback loop that maintains approximately 24-hour periodicity from cellular to organismal levels. Much research effort is being devoted to understanding how the outputs of the master clock affect peripheral oscillators, and in turn, numerous biological processes. Recent studies have revealed roles for circadian timing in the regulation of numerous cellular behaviors in support of complex tissue regeneration. One such role involves the interaction between the circadian clockwork and the cell cycle. The molecular mechanisms that control the cell cycle create a system of regulation that allows for high fidelity DNA synthesis, mitosis, and apoptosis. In recent years, it has become clear that clock gene products are required for proper DNA synthesis and cell cycle progression, and conversely, elements of the cell cycle cascade feed back to influence molecular circadian timing mechanisms. It is through this crosstalk that the circadian system orchestrates stem cell proliferation, niche exit, and control of the signaling pathways that govern differentiation and self-renewal. In this review, we discuss the evidence for circadian control of tissue homeostasis and repair and suggest new avenues for research.

### Σχόλιο

Σε αυτό το άρθρο ανασκόπησης του EJN, αποκαλύπτεται ο ρόλος του κηράδιου συγχρονισμού στη ρύθμιση πληθώρας κυτταρικών λειτουργιών που αφορούν την ιστική αναγέννηση. Η αλληλεπίδραση μεταξύ κυτταρικού κύκλου και κηράδιου ρολογιού έχει κεντρικό ρόλο σε πολλαπλές βιολογικές διαδικασίες, όπως η υψηλής πιστότητας σύνθεση DNA, η μίτωση και η απόπτωση. Φαίνεται καθαρά από σειρά πρόσφατων μελετών πως τα προϊόντα των λεγόμενων clock genes είναι απαραίτητα για την κυτταρική αναγέννηση και πως, αντίστροφα, στοιχεία του καταρράκτη του κυτταρικού κύκλου ανατροφοδοτούν το κηράδινο ρολόι σε μοριακό επίπεδο!

Οι αποδείξεις της κηράδιας ενόρχησης σπουδαίων μονοπατιών που αφορούν την ομοιότητα και την επιδιόρθωση ιστών ανοίγει, σύμφωνα με τους συγγραφείς, νέους ερευνητικούς δρόμους. Σε μια εποχή που το τεχνητό φως και η ανατροπή των βιολογικών ρυθμών από τον κυρίαρχο δυτικό τρόπο ζωής, η κατανόηση των μηχανισμών ελέγχου της αναγέννησης των ιστών μοιάζει ιδιαίτερα προκλητική και πολλά υποσχόμενη.

# Current and Future Roles of Consumer Sleep Technologies in Sleep Medicine



Cathy Goldstein, MD, MS

## KEYWORDS

• Consumer sleep technology • Actigraphy • Remote patient monitoring

## KEY POINTS

- Consumer sleep technologies are products marketed directly to consumers for the purpose of tracking sleep and can be coarsely grouped into wearables, nearables, and stand-alone mobile apps.
- Consumer sleep technology is the system of sensors within the device and the associated mobile application and cloud-based platform for data management and visualization.
- These technologies include sensors that measure motion, heart rate, oximetry, respiration, temperature, neuronal activity, and other parameters to differentiate sleep from wake, determine sleep stages, and identify other relevant sleep metrics.
- Some consumer sleep technologies provide feedback to the user through mobile application delivered behavioral recommendations or acoustic or physical intervention.
- Clinical adoption of consumer sleep technologies is limited by lack of validation studies in the peer-reviewed literature and absent clearance by the US Food and Drug Administration.

## INTRODUCTION

The world market for wearable devices is expected to exceed \$60 billion by 2025 and the health care industry is forecasted as the greatest end-user of wearable mobile technologies.<sup>1</sup> Approximately one-third of the US population reports regularly tracking their sleep with use of smartphones or other digital technologies<sup>2</sup> and, not surprisingly, sleep medicine providers have witnessed the permeation of consumer products into everyday clinical practice.

Our field is well-positioned to benefit from products marketed directly to patients and used in the home owing to the following paradox present in sleep medicine. Sleep disorders are chronic, and symptoms typically result from persistent, daily exposure to disturbances in sleep quality and/or duration. However, the cornerstone for diagnostic testing and gold-standard for sleep measurement

is the polysomnogram (PSG) which, owing to the requirement of a sleep laboratory, technicians, and monitoring of multiple physiologic parameters, is typically restricted to the assessment of sleep over 1 or 2 nights.<sup>3</sup>

Objective, longitudinal sleep measurement in the clinical setting is currently available through the use of US Food and Drug Administration (FDA) cleared actigraphy, which uses wrist-worn accelerometry devices that measure movement to estimate sleep. Actigraphy is well-accepted by the medical and research communities, given the large body of peer-reviewed evidence has assessed sleep estimation accuracy against PSG<sup>4–6</sup>; however, significant inadequacies limit usefulness, such as expense, the requirement of a trained member of the sleep team to set up the device and recover the data, and lack of easy integration between actigraphy software and the

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Sleep Med Clin 15 (2020) 391–408

<https://doi.org/10.1016/j.jsmc.2020.05.001>

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#### Σχόλιο:

- Το άρθρο αναλύει τις πιθανές εφαρμογές στην τηλεϊατρική, και την ιατρική του ύπνου γενικότερα, των νεότερων προϊόντων που διατίθενται στην αγορά, διαθέτουν τεχνολογία ανίχνευσης κίνησης και καταγραφής ύπνου και άλλων δεδομένων υγείας και απευθύνονται στο ευρύ κοινό, χωρίς να έχουν λάβει άδεια χρήσης ως ιατρικές διαγνωστικές συσκευές (Consumer Sleep Technologies ή CST, θα μπορούσαμε να τα περιγράψουμε με τον όρο καταγραφικά ύπνου ευρείας κατανάλωσης, ΚΥΕΚ). Τα προϊόντα αυτά διακρίνονται σε συσκευές που φοριούνται πάνω στο σώμα, πχ. ρολόγια και δαχτυλίδια (wearables), σε άλλα προϊόντα που τίθενται σε λειτουργία στον χώρο όπου κοιμάται ο χρήστης (nearables) και σε εφαρμογές έξυπνων κινητών με αυτόνομο λογισμικό (apps).
- Το κάθε ΚΥΕΚ είναι ένα σύστημα που αποτελείται από τους αισθητήρες που υπάρχουν ενσωματωμένοι μέσα στη συσκευή, τη σχετιζόμενη εφαρμογή κινητού και την πλατφόρμα υπηρεσιών υπολογιστικού νέφους για τη διαχείριση και απεικόνιση των δεδομένων.
- Διαθέτουν τεχνολογία που περιλαμβάνει αισθητήρες που ανιχνεύουν κίνηση, καρδιακό παλμό, οξυμετρία, αναπνοή, θερμοκρασία, νευρονική δραστηριότητα και άλλες παραμέτρους με τις οποίες γίνεται δυνατός ο διαχωρισμός του ύπνου από την εγρήγορση, ο καθορισμός των σταδίων ύπνου και η αλίευση άλλων σημαντικών παραμέτρων ύπνου.
- Ορισμένα ΚΥΕΚ παρέχουν τη δυνατότητα στον χρήστη, μέσω εφαρμογών κινητών ή μέσα από ακουστικές και σωματικές παρεμβάσεις, να τροποποιεί τη συμπεριφορά του, ανάλογα με τα δεδομένα χρήσης και ακολουθώντας αλγόριθμους του ενσωματωμένου λογισμικού.
- Η κλινική τους εφαρμογή περιορίζεται λόγω έλλειψης βιβλιογραφικών δεδομένων και απουσίας σαφούς πλαισίου κατευθυντήριων οδηγιών από τον FDA.

Περίπου 1 στους 3 Αμερικανούς αναφέρει τακτική χρήση έξυπνων κινητών ή άλλων τεχνολογικών προϊόντων με στόχο την παρακολούθηση του ύπνου του και, δεδομένων των δυσκολιών στην εξέταση και παρακολούθηση ασθενών εν μέσω της πανδημίας, τα ΚΥΕΚ θα μπορούσαν ίσως να συμβάλουν στην επίλυση πολλών προβλημάτων που προκύπτουν από το φόρτο των ιατρείων και εργαστηρίων ύπνου.

Ως προτεινόμενες εφαρμογές χρήσης τους περιγράφονται η ακτιγραφία, η συλλογή νέων δεδομένων, όπως το περιβάλλον όπου κοιμάται ο χρήστης (φωτισμός, θερμοκρασία χώρου, ποιότητα αέρα και ήχος), ακόμα και – όταν πρόκειται για παρακολούθηση ασθενών με υπνοαπνοϊκό σύνδρομο που κάνουν χρήση συσκευών θετικής πίεσης αεραγωγών – τη δυνατότητα υπολογισμού του χρόνου κατά τον οποίο ο ασθενής κοιμάται χωρίς CPAP.

Επιπλέον, θα μπορούσαν να χρησιμοποιηθούν στα πλαίσια μιας ψηφιακά καθοδηγούμενης συμπεριφοριστικής θεραπείας της αϋπνίας, σε συνδυασμό με εφαρμογές για κινητά. Ως άλλη εφαρμογή τους στην κλινική πράξη προτείνεται η δυνατότητα πρόβλεψης, μέσω των δεδομένων καταγραφής, μιας ενδεχόμενης παρόξυνσης ΧΑΠ ή ΣΚΑ.

Και βέβαια, ως τελευταίο αλλά όχι μικρότερης σημασίας, αναφέρεται το γεγονός πως η χρήση των τεχνολογικών αυτών συσκευών μπορεί να συνδυαστεί μαζί με άλλες ψηφιακές διαγνωστικές συσκευές, κάτι που προσφέρει τη δυνατότητα ταυτόχρονης καταγραφής πολλών δεδομένων υγείας, όπως για παράδειγμα την πρόσληψη θερμίδων, την κατανάλωση αλκοόλ, την άσκηση, την ημέρα του κύκλου έμμηνης ρύσης και τη διάθεση, καθώς επίσης και την σύνδεση με άλλες έξυπνες συσκευές, πχ. ζυγαριές, πιεσόμετρα, οξύμετρα κ.ά. Τρανό παράδειγμα της χρησιμότητας της ενσωμάτωσης διαφόρων πηγών δεδομένων υγείας στην τεχνολογία των κινητών αποτελεί ένα ψηφιακό προϊόν υγείας, που αρχικά προοριζόταν αποκλειστικά για προσωπική χρήση και πλέον θεωρείται ότι παρέχει αξιόπιστες μετρήσεις ανά πάσα στιγμή, το μόνιτορ συνεχούς καταγραφής γλυκόζης, για το οποίο σήμερα υπάρχει εφαρμογή εγκεκριμένη από τον FDA που παρέχει εργαλεία για δοσολογικά σχήματα χορήγησης ινσουλίνης και άλλες παρεμβάσεις.

Στην τηλεϊατρική, τα ΚΥΕΚ μπορούν τέλος να παρέχουν πληροφορίες για τις συνήθειες ύπνου, την ανάγκη για τροποποίηση της θεραπείας (πχ. προσαρμογή πιέσεων CPAP), καθώς και να κινητοποιήσουν επιπλέον τον χρήστη για συνεχιζόμενη αλλαγή συμπεριφοράς του και προσκόλληση στη θεραπεία με CPAP ή άλλες θεραπείες.

Στον αντίποδα, οι περιορισμοί στη χρήση των συσκευών αυτών στην καθημερινή κλινική πράξη δεν είναι λίγοι. Ο σημαντικότερος είναι η έλλειψη σταθμισμένων ερευνητικών δεδομένων, για τα οποία είναι απαραίτητη η συντονισμένη προσπάθεια από κατασκευαστικές εταιρείες, ερευνητές και κλινικούς.

Ακόμα και αν οι κλινικοί ιατροί είχαν μεγαλύτερη εμπιστοσύνη στα δεδομένα που συλλέγονται με τις συσκευές αυτές, η εφαρμογή στην ιατρική του ύπνου πάλι δεν θα ερχόταν χωρίς τη διακύβευση της ευαισθησίας και της ειδικότητας. Ο χρήστης μπορεί να επαφίεται περισσότερο στην ανάλυση των δεδομένων που καταγράφει η συσκευή παρά στη δική του αίσθηση και είτε να υποεκτιμά είτε να υπερεκτιμά δεδομένα ασαφούς κλινικής σημασίας.

Τέλος, ηθικά διλήμματα και νομικά θέματα μπορεί να προκύψουν, όπως η διασφάλιση των προσωπικών δεδομένων και δεδομένων ασφάλειας, ενώ ελλοχεύει και ο κίνδυνος τα δεδομένα που συλλέγονται από τα ΚΥΕΚ, πέρα από το να υποκλαπούν, να χρησιμοποιηθούν από εταιρείες για να ελέγξουν τους εργαζόμενους ή από τη δικαιοσύνη για απόδοση ευθυνών σε περιπτώσεις ατυχημάτων.

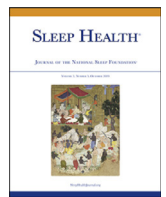
Επιλογή άρθρου – Σχολιασμός: Αγησίλαος Δέρβας



Contents lists available at ScienceDirect

## Sleep Health

Journal of the National Sleep Foundation

journal homepage: [sleephealthjournal.org](https://www.sleephealthjournal.org)

## Associations between dietary inflammatory index and sleep problems among adults in the United States, NHANES 2005–2016

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## ARTICLE INFO

## Keywords:

Sleep  
Dietary Inflammatory Index  
Nutrition  
NHANES  
Sleep duration

## ABSTRACT

**Objectives:** To examine the associations between Dietary Inflammatory Index (DII) scores and sleep measures of sleep duration and self-reported sleep disturbance.

**Design:** Cross-sectional study.

**Setting:** The United States.

**Participants:** Participants from the 2005–2016 National Health and Nutrition Examination Survey (NHANES) who were 20 years old or older (n = 30,121).

**Measurements:** Sleep duration, classified as short ( $\leq 6$  hours), long ( $\geq 9$  hours) and recommended (6–9 hours) duration, and the presence of self-reported sleep disturbance were the outcome variables. The energy-adjusted DII (E-DII) was computed based on the dietary intake data using a single-day 24-hour dietary recall. Multinomial logistic regression was used to examine the associations.

**Results:** After adjusting for confounders, participants in the highest quintile (most proinflammatory E-DII) had a 40% increase in the odds of short sleep duration compared to the lowest quintile (most anti-inflammatory E-DII) ( $OR_{\text{quintile5vs1}} = 1.40$  [95% confidence interval {CI}, 1.21, 1.61]). The odds of short sleep duration was increased by 26% in quintile 4 compared to quintile 1 ( $OR_{\text{quintile4vs1}} = 1.26$  [95% CI, 1.10, 1.43]). Similarly, the odds of long sleep duration was increased in higher E-DII quintiles ( $OR_{\text{quintile5vs1}} = 1.23$  [95% CI, 1.03, 1.46] and  $OR_{\text{quintile4vs1}} = 1.24$  [95% CI, 1.03, 1.49]). Participants in the highest E-DII quintile also were more likely to report sleep disturbances ( $OR_{\text{quintile5vs1}} = 1.14$  [95% CI, 1.02, 1.27]).

**Conclusions:** Adults consuming proinflammatory diets were more likely to have short sleep duration, long sleep duration, and/or self-reported sleep disturbances. Future, especially longitudinal, studies need to examine the impact of anti-inflammatory diets in mitigating extreme sleep durations and sleep disturbances.

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## Σχόλιο:

Το άρθρο που αναλύεται αφορά μεγάλη έρευνα στις Ηνωμένες Πολιτείες Αμερικής στην οποία συμμετείχαν 30.121 άτομα, ηλικίας 20 ετών και άνω. Το άρθρο στηρίζεται στο γεγονός ότι η κατανάλωση ορισμένων τροφών, που περιέχουν επεξεργασμένους υδατάνθρακες, κορεσμένα λίπη, ροφήματα υψηλής περιεκτικότητας σακχάρων, τηγανητά, και ωμέγα 6 λιπαρά οξέα σχετίζεται με αύξηση των δεικτών συστηματικής φλεγμονής, όπως η CRP, IL-6 και η IL-10. Η έρευνα έδειξε ότι τα άτομα που καταναλώνουν τέτοιες τροφές, παρουσιάζουν αύξηση των δεικτών φλεγμονής και είναι πιο πιθανό να αναφέρουν διαταραχές στην ποιότητα ή τη διάρκεια του ύπνου τους.

Επιλογή άρθρου - Σχολιασμός: Αικατερίνη Μπάου

## Early View

Original article

# Sleep apnoea and incident malignancy in type 2 diabetes

Sarah Driendl, Michael Arzt, Claudia S. Zimmermann, Bettina Jung, Tobias Pukrop, Carsten A. Böger, Sebastian Haferkamp, Florian Zeman, Iris M. Heid, Stefan Stadler

Please cite this article as: Driendl S, Arzt M, Zimmermann CS, *et al.* Sleep apnoea and incident malignancy in type 2 diabetes. *ERJ Open Res* 2021; in press (<https://doi.org/10.1183/23120541.00036-2021>).

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## **Abstract**

**Background:** Sleep apnoea (SA) and type 2 diabetes (T2D) have been linked to malignancy. The aim of the present study was to evaluate the association between SA and incidence of malignancy in patients with T2D.

**Methods:** The DIACORE (DIABetes COHoRtE) study is a prospective, population-based cohort study in T2D patients. In the SDB (sleep-disordered breathing) sub-study, the apnoea-hypopnoea index (AHI), oxygen desaturation index (ODI) and percentage of night-time spent below a peripheral oxygen saturation of 90% (TSat90%) were assessed using a two-channel ambulatory monitoring device. Malignancy diagnoses were gathered using self-reported medical history data validated by medical records. Hazard ratios (HR) for incident malignancy were derived by Cox regression adjusting for sex, age, body-mass index, smoking status, alcohol intake, socioeconomic status and HbA1c.

**Results:** Of 1239 patients with T2D (mean age 67 years, 41% female, mean body-mass index 30.9 kg/m<sup>2</sup>), 79 (6.4%) were first-time diagnosed with a malignancy within a median follow-up period of 2.7 (interquartile range 2.2; 4.5) years. AHI, ODI and TSat90% were not associated with incident malignancy. In subgroup analysis, women showed increased cancer risk per AHI unit (adjusted HR 1.03 per AHI unit, 95% CI [1.00-1.06], p=0.028) and severe SA (defined as AHI≥30/h; adjusted HR 4.19, 95% CI [1.39-12.77], p=0.012). This was not seen in men, and a significant interaction was observed (interaction terms, p=0.048, p=0.033, respectively).

**Conclusion:** SA was not associated with incident malignancy in T2D patients. However, stratified analysis revealed a significant association between SA and incident malignancy in women, but not in men.

**Keywords:** Sleep-disordered breathing, apnoea/hypopnoea, hypoxia, malignancy, type 2 diabetes

Σχόλιο:

Ο επιπολασμός μέτριου-σοβαρού ΣΑΑΥ (επεισόδια >15/ώρα), είναι 49% στους άνδρες και 23% στις γυναίκες με βαθμιαία αύξηση τις τελευταίες δύο δεκαετίες. Η διαλείπουσα υποξυγοναιμία σχετίζεται με αυξημένη επίπτωση ανάπτυξης χημειοανθεκτικών-ακτινοανθεκτικών καρκίνων. Επίσης η σχέση T2D και ΣΑΑΥ είναι αμφίδρομη (αλληλεπιδρούν το ένα στην εμφάνιση του άλλου). Στη μελέτη DIACORE 1239 διαβητικοί τύπου 2, μελετήθηκαν με το φορητό σύστημα (Apnea link, Res Med, two channel monitoring device) και καταγράφηκαν τρεις παράμετροι: AHI, ODI 4% και T90% (a measure of cyclic and continuous nocturnal hypoxemia, cut off 10,4%). Βρέθηκε ότι οι γυναίκες με ΣΑΑΥ και διαβήτη είχαν αυξημένο κίνδυνο νεοπλασίας (HR=1.03 (i.e. 3% per unit increase in AHI) και για το σοβαρό ΣΑΑΥ περαιτέρω αύξηση (HR 4.19 (CI 1.39-12.77, p=0.012, adjusted for covariates). Το ΣΑΑΥ εμπλέκεται στην εμφάνιση νεοπλασιών μέσω της διαλείπουσας υποξυγοναιμίας και κατακερματισμού του ύπνου με αποτέλεσμα τη συστηματική φλεγμονή, ανοσοκαταστολή και παρουσία οξειδωτικού stress.

Επιλογή άρθρου – Σχολιασμός: Παναγιώτης Πανάγου

## SCIENTIFIC INVESTIGATIONS

# Short-term insomnia disorder in health care workers in an academic medical center before and during COVID-19: rates and predictive factors

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**Study Objectives:** This study investigated risk factors and estimated rates of acute insomnia disorder in health care workers at the onset of the coronavirus disease 2019 (COVID-19) pandemic.

**Methods:** A Qualtrics survey of more than 2,300 health care providers was conducted in a single academic health system on May 15, 2020, including practicing attending physicians, residents and fellows in training, advanced practice providers, and nurses. Six hundred and sixty-eight responded (29% response rate). The survey employed the Research Diagnostic Criteria for insomnia disorder to diagnose acute insomnia disorder.

**Results:** Five hundred seventy-three respondents had no missing data pertaining to sleep, with a mean age of  $43.4 \pm 12.5$  years and 72% women. The rate of insomnia disorder before COVID-19 was 44.5%, while after COVID-19 it was 64.0%. Of persons with insomnia disorder before COVID-19 10.2% stated it had resolved during COVID-19, while 43.4% of persons who did not have insomnia disorder before COVID-19 developed acute insomnia disorder during COVID-19 ( $\chi^2 = 145.2$ ;  $df = 1$ ;  $P < .0001$ ). New cases of acute insomnia disorder were related positively to female sex, advancing age, and less time spent in direct patient care.

**Conclusions:** Acute insomnia disorder was exceptionally common in this sample of tertiary care health care workers. The effects of sex and age were similar to what has been generally described as risk factors for insomnia. The surprising finding that less time spent in direct patient care was associated with more cases of acute insomnia disorder might be explained by the poorly understood stresses of working from home during COVID-19.

**Keywords:** COVID-19, health care workers, insomnia, acute insomnia disorder

**Citation:** McCall WV, Mensah-Bonsu D, Withers AE, Gibson RW. Short-term insomnia disorder in health care workers in an academic medical center before and during COVID-19: rates and predictive factors. *J Clin Sleep Med*. 2021;17(4):749–755.

## BRIEF SUMMARY

**Current Knowledge/Study Rationale:** The rate of new cases of acute insomnia disorder in health care workers during COVID-19 is unknown. Insomnia disorder may impact the mental health and performance of health care workers.

**Study Impact:** Our survey of health care workers revealed a surprising high rate of acute insomnia disorder. This implies a need for awareness on the part of health care system leaders of the pandemic's impact on their health care workers, both in the health care setting and in the home when working from home.

## INTRODUCTION

Insomnia disorder is a common sleep disorder that includes both acute and chronic forms, with respective annual prevalence of at least 8–9% and 6%.<sup>1,2</sup> Insomnia is associated with the risk of developing other psychiatric disorders,<sup>3</sup> poor quality of life,<sup>4,5</sup> and an increased risk of suicidal ideation and suicidal behavior.<sup>6,7</sup> It would be valuable to public health to understand both the modifiable and the unmodifiable risk factors for insomnia that might inform prevention strategies for insomnia and its psychiatric complications. While there is some lack of consensus as to what constitutes acute vs chronic insomnia,<sup>8,9</sup> acute insomnia disorder is typically defined as covering a timeframe of a few weeks, while chronic insomnia disorder may last months to years. Not surprisingly, acute insomnia may progress into chronic insomnia, only to eventually remit and then recur.<sup>10</sup>

Precipitating life events often precede acute insomnia disorder,<sup>11,12</sup> and the precipitating factors can either be pleasant

(like a wedding or a new job) or unpleasant (such as divorce or job loss). Most of life's pleasant and unpleasant events/stressors are private in nature, and it is unusual to witness the sudden emergence of a near universal stressor across an entire population. Pandemics such as SARS are examples of population-wide stressors that may serve as a natural laboratory for acute insomnia research, including insomnia in health care workers (HCWs).

In 2007, Su et al examined the prevalence of psychological symptoms and adaptation among nurses in a SARS unit in Taiwan. In this cohort, insomnia was more prevalent among SARS unit nurses than non-SARS unit nurses (37% vs 9.7%). Insomnia was less marked in nurses who took care of the more severely affected or intubated SARS patients.<sup>13</sup>

A recent review article on the psychological impact of pandemics in HCWs found a prevalence of insomnia symptoms in 34–36.1%.<sup>14</sup> Jing Qi et al compared sleep disturbances among frontline HCWs and non-frontline HCWs in Hubei

**William V. McCall, MD, MS, Demetra Mensah-Bonsu, BA, Allison E. Withers, BS, Robert W. Gibson, PhD**

**Short-term insomnia disorder in health care workers in an academic medical center before and during COVID-19: rates and predictive factors**

<https://jcsn.aasm.org/doi/10.5664/jcsn.9034> (Πλήρες κείμενο)

**ΠΕΡΙΛΗΨΗ**

**ΣΤΟΧΟΙ ΜΕΛΕΤΗΣ:** Η παρούσα μελέτη διερεύνησε παράγοντες κινδύνου και εκτιμώμενα ποσοστά οξείας διαταραχής αϋπνίας στους εργαζομένους στον τομέα της υγείας κατά την έναρξη της πανδημίας της νόσου του κορωνοϊού 2019 (COVID-19).

**ΜΕΘΟΔΟΙ:** Μια έρευνα της Qualtrics για περισσότερους από 2.300 παρόχους υγειονομικής περίθαλψης διεξήχθη σε ένα ενιαίο ακαδημαϊκό σύστημα υγείας στις 15 Μαΐου 2020, το οποίο συμπεριλάμβανε ειδικευμένους ιατρούς, ειδικευόμενους, ιατρούς σε πρόγραμμα εξειδίκευσης, παρόχους προηγμένης περίθαλψης και νοσηλευτές. Εξακόσιοι εξήντα οκτώ απάντησαν (ποσοστό απόκρισης 29%). Η έρευνα χρησιμοποίησε τα Research Diagnostic Criteria (RDC) σχετικά με τη διαταραχή της αϋπνίας για τη διάγνωση της οξείας διαταραχής της αϋπνίας.

**ΑΠΟΤΕΛΕΣΜΑΤΑ:** Πεντακόσιοι εβδομήντα τρεις ερωτηθέντες δεν είχαν ελλιπή στοιχεία σχετικά με τον ύπνο, με μέση ηλικία  $43,4 \pm 12,5$  ετών και 72% γυναίκες. Το ποσοστό διαταραχής της αϋπνίας πριν από τον COVID-19 ήταν 44,5%, ενώ μετά τον COVID-19 ήταν 64,0%. Από άτομα με διαταραχή αϋπνίας πριν από τον COVID-19, το 10,2% δήλωσε ότι η αϋπνία είχε υποχωρήσει κατά τη διάρκεια του COVID-19, ενώ το 43,4% των ατόμων που δεν είχαν διαταραχή αϋπνίας πριν τον COVID-19 ανέπτυξε οξεία διαταραχή αϋπνίας κατά τη διάρκεια του COVID-19 ( $\chi^2 = 145,2$ ;  $df = 1$ ;  $P < .0001$ ). Νέες περιπτώσεις οξείας διαταραχής αϋπνίας είχαν θετική συσχέτιση με το γυναικείο φύλο και την προχωρημένη ηλικία και αρνητική συσχέτιση με το χρόνο που αφιερώθηκε στην άμεση φροντίδα των ασθενών.

**ΣΥΜΠΕΡΑΣΜΑΤΑ:** Η οξεία διαταραχή της αϋπνίας ήταν εξαιρετικά συχνή στο παρόν δείγμα εργαζομένων υγείας στην τριτοβάθμια περίθαλψη. Οι επιδράσεις του φύλου και της ηλικίας ήταν παρόμοιες με αυτές που έχουν γενικά περιγραφεί ως παράγοντες κινδύνου για την αϋπνία. Το απροσδόκητο εύρημα ότι ο χρόνος που αφιερώθηκε στην άμεση περίθαλψη των ασθενών συσχετίστηκε αρνητικά με περισσότερες περιπτώσεις οξείας διαταραχής αϋπνίας ίσως μπορεί να εξηγηθεί από τα ανεπαρκώς κατανοητά στρες της εργασίας από το σπίτι κατά τη διάρκεια του COVID-19.

## Σχόλιο

Φαίνεται ότι υπήρξε μια σημαντική αύξηση σε περιπτώσεις οξείας διαταραχής αϋπνίας μεταξύ εργαζομένων στον τομέα της υγείας σε ένα διάστημα 90 ημερών από την έναρξη της πανδημίας COVID-19 και η αϋπνία αυτή ήταν κλινικά σημαντική για πολλούς εργαζομένους. Επιπροσθέτως, οι περιπτώσεις οξείας διαταραχής αϋπνίας συσχετίστηκαν με συμπτώματα κατάθλιψης και άγχους, ειδικά για πρωτοεμφανισθέντα περιστατικά. Ο συνδυασμός αϋπνίας και άγχους έναντι του COVID-19 αντιπροσωπεύει έναν ισχυρό κίνδυνο για αυτοκτονικό ιδεασμό.

Παραδόξως, οι εργαζόμενοι που αφιέρωναν λιγότερες από 30 ώρες την εβδομάδα στη φροντίδα των ασθενών συσχετίστηκαν με αυξημένη πιθανότητα εμφάνισης οξείας διαταραχής αϋπνίας. Αυτό ήταν ένα απροσδόκητο εύρημα, καθώς οι συγγραφείς υπέθεσαν ότι ο περισσότερος χρόνος με ασθενείς θα οδηγούσε σε μεγαλύτερη έκθεση στον COVID-19, περισσότερη ανησυχία και αυξημένη αϋπνία. Αυτό έρχεται σε αντίθεση με βιβλιογραφία που αναφέρει ότι η αποχώρηση από το χώρο εργασίας κατά την συνταξιοδότηση οδηγεί σε λιγότερες αφυπνίσεις νωρίς το πρωί και σε μεγαλύτερους χρόνους ύπνου.

Οι συγγραφείς τονίζουν την ανάγκη ευαισθητοποίησης των ηγετών του συστήματος υγείας σχετικά με τον αντίκτυπο της πανδημίας στους εργαζομένους τους, τόσο εντός του περιβάλλοντος της υγειονομικής περίθαλψης όσο και στην εργασία από το σπίτι. Οι παρεμβάσεις μπορεί να περιλαμβάνουν την εκπαίδευση των εργαζομένων στις αρχές της καλής υγιεινής του ύπνου και στην διαχείριση ποικίλων στρεσογόνων παραγόντων που δύνανται να οδηγήσουν σε οξεία διαταραχή αϋπνίας.

Επιλογή άρθρου - Σχολιασμός : Ιωάννης Παπαδόπουλος

## ORIGINAL ARTICLE

# Association of proton pump inhibitor and histamine H<sub>2</sub>-receptor antagonists with restless legs syndrome

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## Abstract

Restless legs syndrome (RLS) is a common sensorimotor disorder, which can disrupt sleep and is thought to be caused in part by low cellular iron stores. Proton pump inhibitors (PPI) and histamine H<sub>2</sub>-receptor antagonists (H<sub>2</sub>A) are among the most commonly used drugs worldwide and show evidence of causing iron deficiency. We conducted a case/non-case observational study of blood donors in the United States (N = 13,403; REDS-III) and Denmark (N = 50,323; Danish Blood Donor Study, DBDS), both of which had complete blood count measures and a completed RLS assessment via the Cambridge-Hopkins RLS questionnaire. After adjusting for age, sex, race, BMI, blood donation frequency, smoking, hormone use, and iron supplement use, PPI/H<sub>2</sub>A use was associated with RLS (odds ratio [OR] = 1.41; 95% confidence interval [CI], 1.13–1.76; p = 0.002) in REDS-III for both PPI (OR = 1.43; CI, 1.03–1.95; p = 0.03) and H<sub>2</sub>A (OR = 1.56; CI, 1.10–2.16; p = 0.01). DBDS exhibited a similar association with PPIs/H<sub>2</sub>As (OR = 1.29; CI, 1.20–1.40; p < 0.001), and for PPIs alone (OR = 1.27; CI, 1.17–1.38; p < 0.001), but not H<sub>2</sub>As alone (OR = 1.18; CI, 0.92–1.53; p = 0.2). We found no evidence of blood iron stores mediating this association. The association of PPI, and possibly H<sub>2</sub>A, consumption with RLS independent of blood iron status and other factors which contribute to RLS risk suggest the need to re-evaluate use of PPI/H<sub>2</sub>A in populations at particular risk for RLS.

## Statement of Significance

Restless legs syndrome (RLS) afflicts up to 15% of adults in the Western Hemisphere and although its causes are not fully understood, low cellular iron stores appears to be a major contributor. Common antacid medications, proton pump inhibitors, and histamine H<sub>2</sub>-receptor antagonists appear to cause iron deficiency and are among the most consumed drugs worldwide. To date, no link between consumption of these drugs and RLS has been found. In this study, we sought to measure the association between antacid use and the risk of having RLS. Evidence of these drugs contributing to RLS risk could suggest a need to re-evaluate the use of antacids in those at higher risk for developing RLS.

**Key words:** restless legs syndrome; RLS; iron deficiency; blood donors; ferritin

Submitted: 23 June, 2020; Revised: 17 September, 2020

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Σχόλιο:

Το σύνδρομο ανήσυχων ποδιών είναι μία συχνή κινητικοαισθητική διαταραχή που αφορά περίπου το 14% του ενήλικου πληθυσμού του δυτικού κόσμου. Η αιτιολογία αυτής της διαταραχής είναι πολυπαραγοντική και κυρίως φαίνεται να σχετίζεται με την ομοιόσταση του σιδήρου και την ρύθμιση της ντοπαμίνης. Ενδιαφέρον παρουσιάζει ότι αρκετά φάρμακα σχετίζονται με αυτό το σύνδρομο.

Νεότερα δεδομένα καταδεικνύουν συσχέτιση μεταξύ χρήση PPIs (αναστολείς αντλίας πρωτονίων) - H2As (ανταγωνιστών υποδοχέων H2) και του συνδρόμου ανήσυχων ποδιών.

Αυτά είναι συχνά χρησιμοποιούμενα φάρμακα και υπολογίζεται ότι το 8% του ενήλικου πληθυσμού στις USA και ειδικότερα το 22% σε ηλικία >65 ετών τα λαμβάνουν. Η ευρεία αυτή χρήση θα μπορούσε να επηρεάσει και τα ποσοστά εμφάνισης του σύνδρομο ανήσυχων ποδιών.

Στην παραπάνω μελέτη συμμετείχαν αιμοδότες, που εκτιμήθηκαν οι εξετάσεις αίματος και συμπληρώσανε το ερωτηματολόγιο CAMBRIDGE-HOPKINS RLS. Στις ΗΠΑ στους 13.403 συμμετέχοντες ανευρέθηκε RLS στο 4,2% του υπό μελέτη πληθυσμού ενώ στους 50.323 συμμετέχοντες από την ΔΑΝΙΑ το αντίστοιχο ποσοστό είναι 7,1%.

Μετά την προσαρμογή των παραμέτρων ηλικίας, φύλου, φυλής, BMI, συχνότητα αιμοδοσίας, καπνίσματος, ορμονοθεραπείας, θεραπείας υποκατάστασης σιδήρου, η χρήση PPIs και H2As βρέθηκε πως σχετίζεται με το σύνδρομο ανήσυχων ποδιών.

Αυτή η ένδειξη υποδηλώνει την ανάγκη επαναξιολόγησης την χρήση αυτών των φαρμάκων σε άτομα έχουν υψηλότερο κίνδυνο εμφάνισης RLS.

Επιλογή άρθρου – Σχολιασμός: Ευαγγελία Φλώρου