The relevance of insomnia in relation to other high-impact pathologies. A systematic literature review

Egea C[1], Romero O[2], Bellido C[3], Mur C[4], Espallardo O[5], Comellas M[6], Aceituno, S[6]

EPH184

1. Servicio de Neumología y Sueño, Hospital Universitario Araba, Vitoria-Gasteiz, Spain. Presidente de FESMES. 2. Unidad del Sueño, Hospital Universitario Vall d'Hebron, Barcelona, Spain. 3. Servicio de Prevención de Riesgos Laborales, Hospital General Universitario de Castellón, Castellón de la Plana, Spain. 4. Servei de Salut Mental, Servei Andorrà d'Atenció Sanitària, Andorra. 5. Market Access & Public Affairs, Idorsia, Madrid, Spain. 6. Outcomes'10, Castellón de la Plana, Spain.

RATIONALE

Insomnia, recognized as the foremost sleep disorder for clinical consultations[1,2], affects 14% of population in Spain[3]. However, on a global scale, epidemiological studies estimate that 6-10% of the general population suffers from chronic insomnia[4,5].

This condition associates with both physical and psychiatric morbidity[1,6], and affects Health-Related Quality of Life (HRQoL)[7]. Furthermore insomnia represents a predisposing risk factor for the onset or exacerbation of conditions including cardiometabolic disorders and psychiatric disorders.

However, despite its impact, insomnia is often an underrecognized disorder[8]. Raising awareness and understanding of its relationship with other high-impact diseases, as defined as by the Ministry of Health based on the significant volumen of consultations they generat in heatlhcare[9,10], is crucial for enhanced management[11].

OBJECTIVE

We aim to describe the current burden of insomnia, exploring its relevance in relation to other high-impact pathologies.

METHODS

A systematic literature review was conducted in Pubmed/Medline to identify studies examining insomnia's association or burden with other high-impact pathologies (COVID-19, cancer survivors, cardiometabolic diseases, neurodegenerative diseases, and mental illness). Observational studies, reviews, and meta-analyses evaluating insomnia using established diagnostic criteria, conducted in Europe, United States and Canada, and published in Spanish/English between 2017-2023 were included. Clinical trials, opinion articles, letters to the editor, conference proceedings, and studies focused on specific populations and/or lacking established insomnia diagnostic criteria were excluded. The Oxford Center for Evidence-Based Medicine levels of evidence were employed to assess the evidence level and quality of the studies reviewed.

RESULTS

Of the total 604 studies identified, sixteen publications were finally included (Figure 1). These publications comprised observational studies (81.0%), narrative reviews (13.0%) and systematic reviews (6.0%) (Figure 2). The evidence levels for these included studies were as follows: 1b (38.0%), 2a (13.0%), 2b (3.0%), 3a (6.0%), and 3b (6.0%). The definition of insomnia and/or chronic insomnia used in the articles reviewed shows heterogeneity. Therefore, hereafter, the term 'insomnia' will be used in any case. Among the selected studies examining insomnia's association or burden with other high-impact pathologies, 56.2% focused on cardiometabolic diseases (heart failure [HF] and cardiovascular disease [CVD], arterial hypertension [AHT], coronary heart disease [CHD], type 2 diabetes [DM2], and metabolic syndrome [MS]) 12.5% addressed COVID-19, 12.5% mental illness (anxiety and depression), 12.5% cancer survivors and, 6.2% neurodegenerative diseases, particularly Alzheimer's disease. The majority of the studies were conducted in Europe (43.8%) and the United States (43.8%).

Figure 1. Selected studies in accordance with the PRISMA recommendations

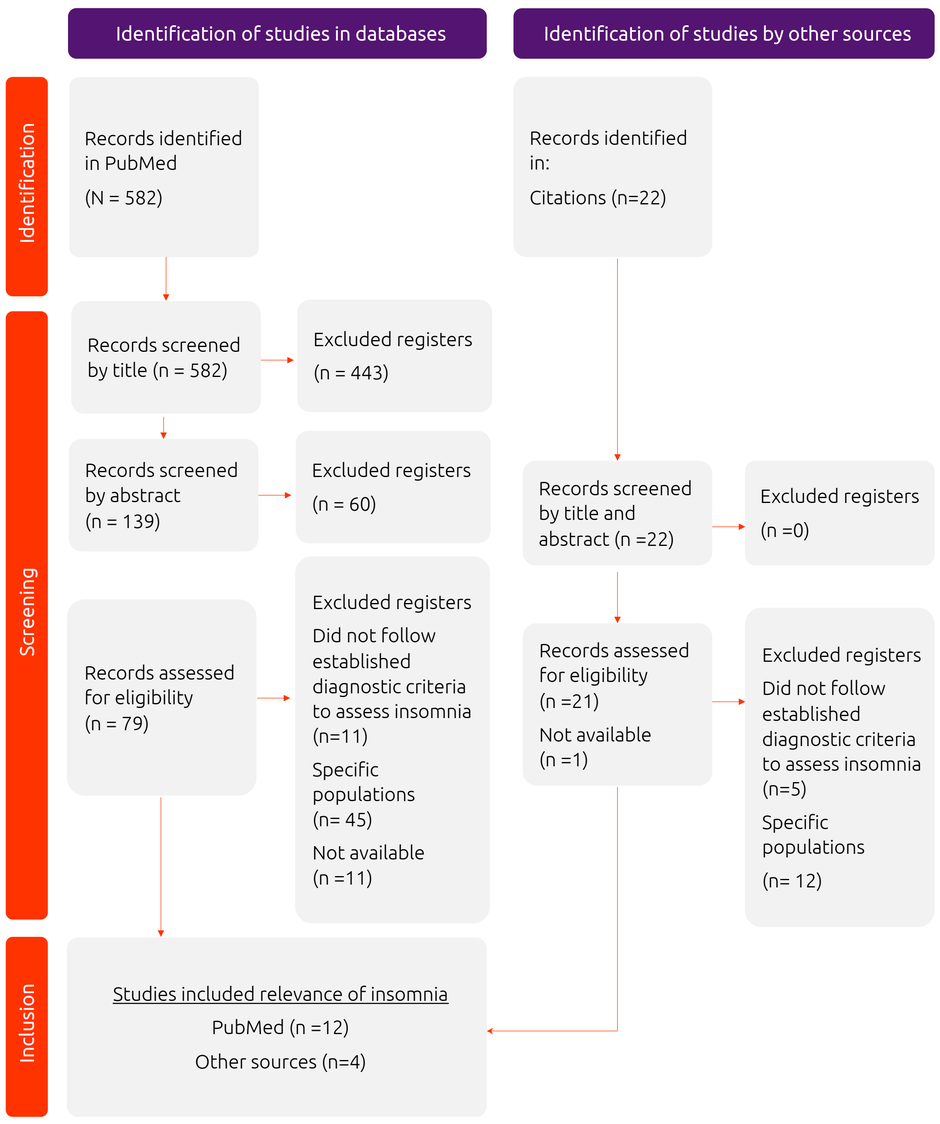
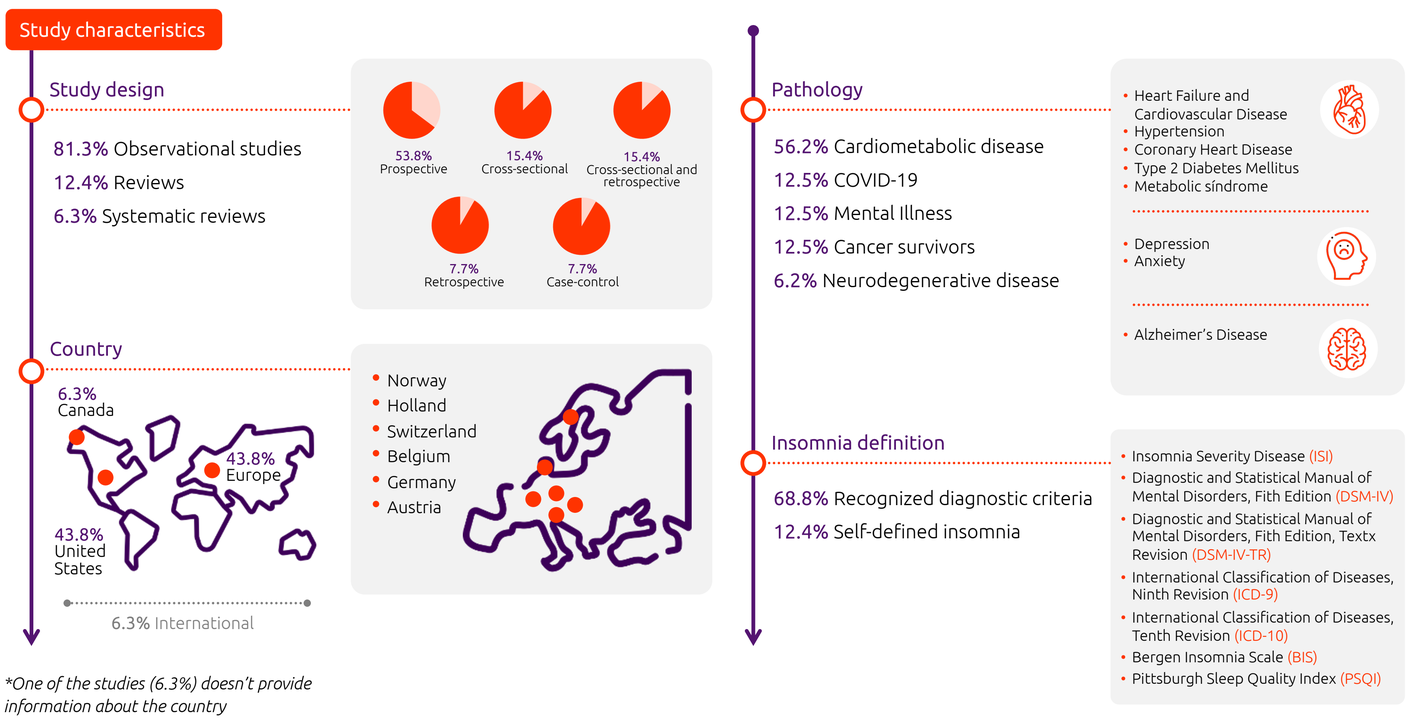


Figure 2. Characteristics of the selected studies



*One of the studies (6.3%) doesn't provide information about the country

Nine studies assessed insomnia's relationship to cardiometabolic diseases[12-20], showing that insomnia is a risk factor for the development of HF and CVD. Patients with insomnia have a higher risk of experiencing incident CVD compared to those without insomnia (HR:1.29, 95% CI:1.00-1.66)[14]. Further, exists a bidirectional relationship between insomnia and AHT. On one hand, patients with AHT have a higher prevalence of insomnia compared to those without AHT (14.9% vs. 12.8%; OR:1.07, 95% CI:1.01-1.13)[15]. On the other hand, insomnia patients have a 21.0% increased risk of developing hypertension compared to those without insomnia (HR=1.21, 95% CI:1.01-1.76, p=0.040)[15]. Additionally, insomnia is a risk factor of CHD, with insomnia patients showing a 68.0% increased risk of experiencing a myocardial infarction (HR= 1.68, 95% CI:1.31-2.16, p<0.001) and an 85.0% increased risk of stroke (HR=1.85, 95% CI:1.62-2.12, p<0.001)[13]. Insomnia also increases the risk of MS, with patients with insomnia experiencing approximately twice the risk compared to those without insomnia (OR:1.97, 95% CI:1.00-3.86, p=0.041)[20]. Furthermore, there's a bidirectional association between DM2 and insomnia. The prevalence of DM2 among individuals with insomnia stands at 21.1%[19], and it is a contributing factor to the development of insomnia (OR: 1.83, 95% CI:1.17-2.87, p= 0.009)[18].

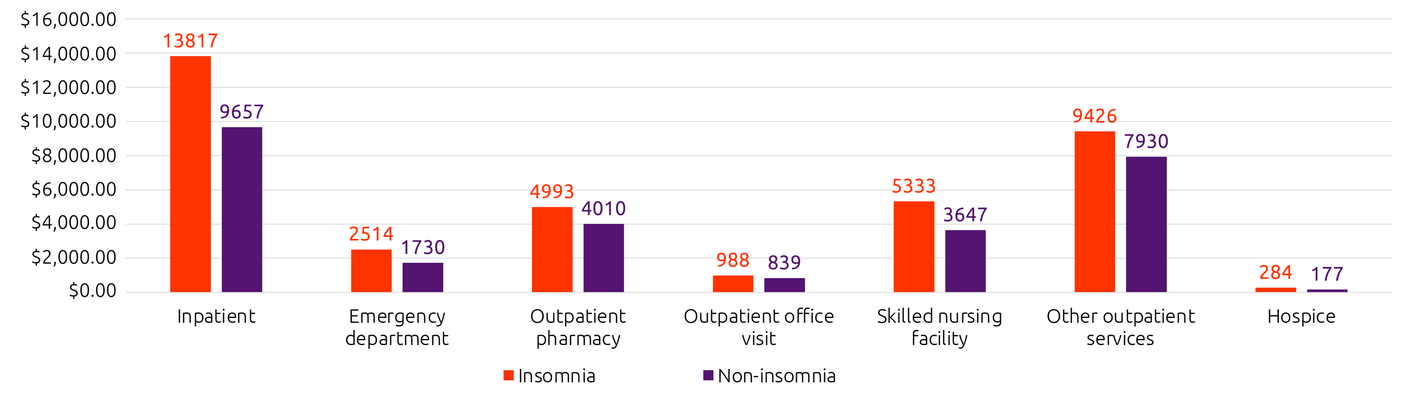
Insomnia's relationship with COVID-19 pandemic was evaluated in two studies[21,22]. The prevalence of insomnia in the general population increased from 16.8% before the onset of the COVID-19 pandemic in 2018 to 19.0% in 2020, during the pandemic[22]. Moreover, sleep quality, as measured by the Pittsburgh Sleep Quality Index (PSQI) worsened significantly (mean [SD – Standard Deviation]: 5.5 [0.1] in 2018 vs. 6.0 [0.1] in 2020; p=0.001). However, insomnia severity, assessed using the Insomnia Severity Index (ISI), decreased (mean [SD]: 6.7 [0.2] in 2018 vs. 6.3 [0.2] in 2020; p=0.029)[22]. This decrease may be attributed to the fact that the new cases of insomnia were generally mild, resulting in a reduction in the mean ISI score[22].

Insomnia has a bidirectional relationship with anxiety. Thus, patients with insomnia had significantly higher anxiety levels compared to those who rarely or never exhibit insomnia symptoms (mean [SD]: 2.5 [2.4] vs. 5.5 [3.7]; p<0.001)[23], and anxiety symptoms were established determinants of insomnia (OR: 5.61; CI 95%: 3.37-9.35; p<0.001)[18].

Insomnia's burden in cancer survivors was evaluated in two studies[24,25], revealing an estimated prevalence of 17.4%[24]. Among patients receiving cancer treatment, 49.4% experience insomnia, with 12.8% having moderate-to-severe insomnia (ISI>14)[25]. These percentages remain similar one year after starting treatment (47.2% and 13.6%, respectively)[25]. Notably, insomnia is related to worse neurocognitive performance in cancer survivors, as evidenced by significant (p<0.050) declines in various cognitive domains, including verbal reasoning (♂: b=-0.34; ♀: b=-0.57), long-term memory (♂: b=-0.60; ♀: b=-0.36, sustained attention (♂: b=-0.85; ♀: b=-0,42) , and cognitive flexibility (♂: b=-0.70; ♀: b=-0.40)[24].

Finally, only one study assessed the relationship between insomnia and Alzheimer's disease (AD)[26]. Among newly diagnosed AD patients, 14.6% exhibited symptoms of insomnia or required medication for its management. Notably, individuals with both AD and insomnia showed a higher prevalence of comorbidities such as depression, hyperlipidemia, hypertension, resulting in increased healthcare resource utilization. Therefore, the cost associated with the management of patients with AD and insomnia, compared to those without insomnia, was $37,356 [SD $70, 089] vs. $27,990 [SD $57,179] (p<0.001), representing an additional cost of $10,000 (2018 US dollars)[26] (Figure 3).

Figure 3. All-cause healthcare costs per person/year in AD patients[26]



CONCLUSIONS

Insomnia is associated with several high-impact diseases including COVID-19, cardiometabolic diseases (such as heart failure, cardiovascular disease, hypertension, coronary artery disease, type 2 diabetes, and metabolic syndrome), cancer survivors, neurodegenerative diseases (e.g., Alzheimer's disease), and mental health disorders (e.g., anxiety and depression). Early identification and optimal management of insomnia symptoms are crucial for prevention.

REFERENCES: 1. Ferré-Masó, A. et al. Aten Primaria 52, 345-354. 2. Morin, C. M. et al. Insomnia, hypnotic use, and road collisions: a population-based, 5-year cohort study. Sleep 43. 3. de Entrambasaguas M, Romero O, Guevara JAC, de Larrinaga AÁR, Cañellas F, Salud JP, et al. The prevalence of insomnia in Spain: A stepwise addition of ICSD-3 diagnostic criteria and notes. Sleep Epidemiology. 2023;3. 4. Riemann D, Baglioni C, Bassetti C, Bjorvatn B, Dolenc Groselj L, Ellis JG, et al. European guideline for the diagnosis and treatment of insomnia. J Sleep Res. 2017;26(6):675-700 5. Maire M, Linder S, Dvořák C, Merlo C, Essig S, Tal K, et al. Prevalence and management of chronic insomnia in Swiss primary care: Cross-sectional data from the "Sentinella" practice-based research network. J Sleep Res. 2020;29(5):e13121. 6. Haycock, J. et al. BMC Family Practice 22, 158 (2021). 7. Berkley, A. S. et al. Geriatr Nurs 41, 832-838 (2020). 8. Roy, A. N. et al. Manag Care 24, 42-48 (2015). 9. Ministerio de Sanidad. (2023). Plan INVEAT. Retrieved from https://www.sanidad.gob.es/profesionales/prestacionesSanitarias/PlanINVEAT/pdf/Plan_INVEAT.pdf. 10. Ministerio de Sanidad (2022). Informe Anual del Sistema Nacional de Salud 2020-2021. Retrieved from https://www.sanidad.gob.es/estadEstudios/estadisticas/sisInfSanSNS/tablasEstadisticas/InfAnualSNS2020_21/ASPECTOS_RELEVANTES_2020-21.pdf. 11. Bin, Y. S. et al. Aust N Z J Public Health 36, 462-468 (2012). 12. Mahmood, A. et al. Eur Heart J 42, 4169-4176 (2021). 13. Javaheri, S. & Redline, S. Chest 152, 435-444 (2017). 14. Bertisch, S. M. et al. Sleep 41 (2018). 15. Jarrin, D. C. et al. Sleep Med Rev 41, 3-38 (2018). 16. Bathgate, C. J. & Fernandez-Mendoza, J. Curr Hypertens Rep 20, 52 (2018). 17. Dong, Y. & Yang, F. M. Prev Med 123, 41-47 (2019). 18. Frøjd, L. A. et al. J Clin Sleep Med 17, 931-938 (2021). 19. Hein, M. et al. Sleep Med 46, 37-45 (2018). 20. Zou, D. et al. Eur J Prev Cardiol 28, e26-e28 (2021). 21. Morin, C. M. et al. Sleep Med 87, 38-45 (2021). 22. Morin, C. M. et al. Sleep 45 (2022). 23. Bragantini, D. et al. Sleep Health 5, 370-375 (2019). 24. Tonning Olsson, I. et al. JNCI Cancer Spectr 4, pkaa008 (2020). 25. Schieber, K. et al. Sleep Med 58, 107-113 (2019). 26. Qureshi, Z. P. et al. J Alzheimers Dis 83, 1679-1690 (2021).