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Effects of sleep and insomnia on cardiovascular disease - literature review

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Abstract

Introduction:

Sleep disorders, including insomnia, obstructive sleep apnea (OSA) and other sleep disorders, are increasingly recognized as important risk factors for cardiovascular diseases such as hypertension and coronary artery disease. This review aims to analyze the current literature on the impact of sleep disorders on cardiovascular health, focusing on the underlying pathophysiological mechanisms and the effectiveness of diagnostic and therapeutic

approaches. The results highlight the importance of early diagnosis and treatment of sleep disorders to reduce cardiovascular risk.

Aim of the Study:

The main objective of this study is to review and summarize recent findings on the relationship between sleep disorders and cardiovascular diseases, with a particular focus on hypertension and coronary artery disease. This study aims to elucidate the pathophysiological mechanisms linking these conditions and to evaluate the effectiveness of current diagnostic and therapeutic strategies.

Materials and Methods:

This review was conducted by searching PubMed for articles published in the last ten years (2014-2024) using keywords such as "insomnia", "obstructive sleep apnea", "hypertension", "coronary heart disease", "polysomnography".

Conclusions:

The evidence reviewed in this article suggests that sleep disorders are important and independent risk factors for cardiovascular disease. Insomnia, obstructive sleep apnea and other sleep disorders contribute to cardiovascular morbidity through mechanisms such as increased sympathetic activity, systemic inflammation and metabolic dysregulation. Effective diagnosis and treatment of sleep disorders, including the use of CPAP therapy for obstructive sleep apnea and cognitive-behavioral therapy for insomnia, can mitigate these risks and improve cardiovascular outcomes.

Keywords: "insomnia", "obstructive sleep apnea", "hypertension", "coronary heart disease", "polysomnography".

Introduction

Sleep is an essential physiological process that plays a critical role in maintaining overall health and well-being. Adequate sleep is necessary for cognitive function, emotional stability, and the regulation of various physiological processes, including metabolic and cardiovascular functions. Despite its importance, sleep disorders are highly prevalent in modern society, affecting millions of individuals globally. These disorders, which include insomnia, obstructive sleep apnea (OSA), restless legs syndrome (RLS), and circadian rhythm disorders, can have profound effects on health, particularly on cardiovascular health.

Insomnia, characterized by difficulty initiating or maintaining sleep, is one of the most common sleep disorders. It affects approximately 10% to 30% of the general population, with higher prevalence rates observed in older adults and individuals with chronic medical conditions [1]. Chronic insomnia is associated with a range of adverse health outcomes, including an increased risk of developing hypertension, coronary artery disease, and other cardiovascular conditions [2].

Obstructive sleep apnea (OSA) is another prevalent sleep disorder, affecting an estimated 9% to 38% of adults [3]. OSA is characterized by recurrent episodes of partial or complete upper airway obstruction during sleep, leading to intermittent hypoxia, sleep fragmentation, and a range of physiological disturbances. The condition is more common in men, older adults, and individuals with obesity. OSA has been strongly linked to cardiovascular diseases, including hypertension, atrial fibrillation, myocardial infarction, and stroke [4].

Restless legs syndrome (RLS) and circadian rhythm disorders, such as shift work sleep disorder, also contribute to cardiovascular risk. RLS is characterized by an uncontrollable urge to move the legs, usually accompanied by uncomfortable sensations, which can significantly disrupt sleep [5]. Circadian rhythm disorders, which involve misalignment between the endogenous circadian clock and the external environment, are increasingly common in modern society due to factors such as shift work and exposure to artificial light at night [6]. These disorders have been associated with an increased risk of metabolic syndrome, hypertension, and coronary artery disease [7].

The pathophysiological mechanisms linking sleep disorders to cardiovascular diseases are complex and multifaceted. Chronic sleep deprivation and poor sleep quality can lead to increased sympathetic nervous system activity, hormonal imbalances, systemic inflammation, and metabolic dysregulation. These factors contribute to the development and progression of cardiovascular diseases [8]. For instance, sleep deprivation increases levels of cortisol and catecholamines, which can lead to hypertension and other cardiovascular issues [9]. Furthermore, intermittent hypoxia associated with OSA promotes oxidative stress and endothelial dysfunction, which are key contributors to atherosclerosis and cardiovascular morbidity [10].

The impact of sleep disorders on cardiovascular health extends beyond the traditional risk factors of hypertension and coronary artery disease. Studies have shown that sleep disorders are associated with an increased risk of heart failure, arrhythmias, and sudden cardiac death [11]. These associations highlight the importance of early recognition and effective management of sleep disorders to mitigate their adverse cardiovascular effects.

Despite the growing body of evidence linking sleep disorders to cardiovascular diseases, these conditions often remain underdiagnosed and undertreated. This is partly due to the lack of awareness among healthcare providers and the general population about the significance of sleep health. Additionally, the overlap of symptoms between sleep disorders and other medical conditions can complicate diagnosis [12].

The primary aim of this study is to review and synthesize the most recent research findings on the relationship between sleep disorders and cardiovascular diseases, with a specific focus on hypertension and coronary artery disease. This study aims to elucidate the pathophysiological mechanisms linking these conditions and to evaluate the effectiveness of current diagnostic and therapeutic strategies. By increasing awareness and understanding of these associations, this review seeks to highlight the importance of incorporating sleep health into routine cardiovascular care.

Epidemiology of sleep disorders

Epidemiological studies have shown that sleep disorders are highly prevalent in the general population. For instance, the prevalence of insomnia ranges from 10% to 30% in various populations [1]. Similarly, obstructive sleep apnea affects approximately 9% to 38% of adults, with higher rates in men and older adults [3]. These sleep disorders are associated with several risk factors, including obesity, smoking, and a sedentary lifestyle [12].

A meta-analysis conducted by Heinzer et al. (2015) reported that nearly 1 billion people worldwide suffer from moderate to severe obstructive sleep apnea, highlighting the global burden of this conditio [13]. The study also noted significant geographic variations in the prevalence of OSA, with higher rates observed in North America and Asia compared to Europe.

Restless legs syndrome (RLS) is another common sleep disorder, affecting approximately 5% to 10% of the adult population [14]. This condition is characterized by an uncontrollable urge to move the legs, particularly during rest, and can significantly disrupt sleep quality, leading to increased cardiovascular risk.

Pathophysiological mechanisms

Chronic sleep deprivation not only affects the cardiovascular system through increased sympathetic nervous system activity but also leads to hormonal imbalances, including elevated levels of cortisol, a stress hormone that can contribute to hypertension and other cardiovascular issues [9]. Additionally, reduced sleep duration has been linked to increased levels of inflammatory markers such as C-reactive protein and interleukin-6, which are known to play a role in atherogenesis [15].

Further, the intermittent hypoxia caused by obstructive sleep apnea leads to oxidative stress, which damages the endothelium, the inner lining of blood vessels, and contributes to the

development of atherosclerosis [11]. This endothelial dysfunction, coupled with increased sympathetic activity, results in elevated blood pressure and heightened risk for cardiovascular events [10].

The role of the autonomic nervous system in the development of cardiovascular diseases due to sleep disorders is also critical. Sleep deprivation and disturbances lead to increased sympathetic tone and decreased parasympathetic activity, which contribute to hypertension, increased heart rate, and arrhythmias [16]. This autonomic imbalance is particularly evident in patients with OSA, where repeated episodes of apnea and hypopnea result in significant fluctuations in heart rate and blood pressure [17].

In addition to these mechanisms, sleep disorders can impact cardiovascular health through alterations in glucose metabolism and insulin sensitivity. Sleep deprivation and poor sleep quality have been associated with insulin resistance, a condition in which cells in the body become less responsive to insulin, leading to higher blood glucose levels and an increased risk of developing type 2 diabetes [18]. This metabolic disturbance is a well-established risk factor for cardiovascular disease.

Chronic sleep loss also affects lipid metabolism. Studies have shown that individuals with insufficient sleep have higher levels of low-density lipoprotein (LDL) cholesterol and triglycerides, both of which are significant contributors to atherosclerosis [19]. These lipid abnormalities can exacerbate the risk of coronary artery disease and other cardiovascular conditions.

Furthermore, sleep disorders can lead to hypercoagulability, a state in which the blood is more prone to clotting. This condition is particularly dangerous as it can increase the likelihood of thrombotic events, such as myocardial infarction and stroke. Intermittent hypoxia, a characteristic of obstructive sleep apnea, promotes platelet aggregation and increases the levels of coagulation factors, contributing to a prothrombotic state [20].

Insomnia and cardiovascular disease

Numerous studies have demonstrated a significant association between insomnia and cardiovascular diseases. For example, a meta-analysis found that individuals with insomnia have a higher risk of developing hypertension compared to those with normal sleep patterns [2]. Another study reported that chronic insomnia increases the risk of coronary artery disease

[21]. These findings highlight the importance of recognizing and managing insomnia to prevent cardiovascular complications.

Insomnia is not only associated with an increased risk of hypertension and coronary artery disease but also with stroke and heart failure. A large cohort study found that individuals with chronic insomnia had a significantly higher risk of stroke, independent of other cardiovascular risk factors. Additionally, a longitudinal study demonstrated that persistent insomnia symptoms were associated with a 27% increased risk of developing heart failure [22].

The impact of insomnia on cardiovascular health is mediated through several pathways, including increased sympathetic activity, hormonal imbalances, and inflammation. Insomnia leads to a chronic stress response, which elevates cortisol levels and promotes a pro-inflammatory state. These physiological changes contribute to endothelial dysfunction and atherogenesis, increasing the risk of cardiovascular events [23].

Obstructive sleep apnea and cardiovascular disease

The relationship between obstructive sleep apnea (OSA) and cardiovascular disease is welldocumented. OSA causes intermittent hypoxia, which leads to increased sympathetic activity and systemic inflammation, both of which are detrimental to cardiovascular health. Studies have shown that OSA is an independent risk factor for hypertension, with untreated OSA patients having a significantly higher incidence of resistant hypertension [24]. Furthermore, OSA has been linked to an increased risk of atrial fibrillation, stroke, and myocardial infarction, underscoring the importance of diagnosing and treating this sleep disorder [25].

The nocturnal hypoxia experienced by OSA patients activates several harmful pathways, including oxidative stress and inflammation, which contribute to the pathogenesis of atherosclerosis and other cardiovascular diseases. Effective treatment of OSA with CPAP therapy has been shown to reduce these risks significantly [25]. Long-term studies indicate that CPAP therapy not only improves sleep quality but also has a favorable impact on cardiovascular outcomes by reducing blood pressure and preventing myocardial infarction and stroke [26].

Sleep disorders and cardiovascular disease

Other sleep disorders, such as restless legs syndrome (RLS) and circadian rhythm disorders, have also been implicated in cardiovascular disease. Restless legs syndrome, characterized by an uncontrollable urge to move the legs, particularly during rest, has been associated with an increased risk of cardiovascular diseases, possibly due to the frequent sleep disturbances and sympathetic overactivity it causes [27]. Circadian rhythm disorders, such as shift work sleep disorder, disrupt the normal sleep-wake cycle and have been linked to an increased risk of hypertension and coronary artery disease [28].

A comprehensive review by Vyas et al. (2012) demonstrated that shift workers have a 40% increased risk of cardiovascular events compared to non-shift workers [29]. The disruption of circadian rhythms leads to metabolic and hormonal imbalances that adversely affect cardiovascular health [30].

Diagnostic and therapeutic methods

Accurate diagnosis and effective treatment of sleep disorders are crucial in mitigating their impact on cardiovascular health. Polysomnography remains the gold standard for diagnosing sleep apnea, while actigraphy and sleep diaries are commonly used for diagnosing insomnia and other sleep disturbances [12]. Treatments for insomnia typically involve cognitive-behavioral therapy (CBT-I) and pharmacotherapy, which have been shown to improve sleep quality and reduce associated cardiovascular risks [31]. Continuous positive airway pressure (CPAP) therapy is the standard treatment for OSA and has been proven to lower blood pressure and improve cardiovascular outcomes in patients with OSA [32].

In addition to CPAP, other treatment options for OSA include oral appliances and lifestyle modifications, such as weight loss, which have shown efficacy in reducing the severity of apnea and improving cardiovascular health [33]. For patients with severe OSA who do not respond to these treatments, surgical options such as uvulopalatopharyngoplasty (UPPP) may be considered [34].

Emerging treatments, such as hypoglossal nerve stimulation, offer promising alternatives for patients with moderate to severe OSA who are intolerant to CPAP therapy. This approach has shown significant improvements in both sleep apnea symptoms and cardiovascular outcomes [35].

Pharmacological treatments for insomnia, including benzodiazepines and non-benzodiazepine sleep aids, can be effective but must be used with caution due to potential side effects and dependency risks. Recent studies suggest that melatonin and other chronobiotic agents may help manage circadian rhythm disorders and improve cardiovascular outcomes by aligning the sleep-wake cycle with the natural circadian rhythm [36].

Behavioral interventions, such as sleep hygiene education and relaxation techniques, are also beneficial in managing sleep disorders and reducing cardiovascular risks. These non-pharmacological approaches aim to improve sleep quality and duration by addressing lifestyle factors that contribute to sleep disturbances [37].

Conclusions

Sleep disorders, including insomnia, obstructive sleep apnea, and other sleep disturbances, significantly impact cardiovascular health through mechanisms involving sympathetic overactivity, systemic inflammation, and hormonal imbalances. Recognizing and managing these disorders is essential for preventing cardiovascular complications and improving overall health outcomes. Future research should continue to explore the pathophysiological links between sleep disorders and cardiovascular disease, as well as develop and refine effective treatment strategies.

Author's contribution

Conceptualization, Julita Gmitrzuk; methodology, Julita Gmitrzuk and Martyna Opatowska; software, Tomasz Kucharski and Joanna Jakubiec; check, Katarzyna Wiśniewska and Maciej Karasiński; formal analysis, Julita Gmitrzuk and Zuzanna Malinka; investigation, Julita Gmitrzuk and Anna Jachymek; resources, Martyna Opatowska and Maciej Karasiński; data curation, Joanna Jakubiec, Katarzyna Wiśniewska; writing – rough preparation, Julita Gmitrzuk; writing - review and editing, Julita Gmitrzuk and Tomasz Kucharski; visualization, Julita Gmitrzuk, Zuzanna Malinka and Anna Jachymek; supervision, Joanna Jakubiec and Martyna Opatowska; project administration, Julita Gmitrzuk, Katarzyna Wiśniewska. All authors have read and agreed with the published version of the manuscript.

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References:

- M. M. Ohayon, "Epidemiology of insomnia: what we know and what we still need to learn.," *Sleep Med. Rev.*, vol. 6, no. 2, pp. 97–111, Apr. 2002, https://doi.org/10.1053/smrv.2002.0186
- F. Sofi, F. Cesari, A. Casini, C. Macchi, R. Abbate, and G. F. Gensini, "Insomnia and risk of cardiovascular disease: a meta-analysis.," *Eur. J. Prev. Cardiol.*, vol. 21, no. 1, pp. 57–64, Jan. 2014, https://doi.org/10.1177/2047487312460020
- P. E. Peppard, T. Young, J. H. Barnet, M. Palta, E. W. Hagen, and K. M. Hla,
 "Increased prevalence of sleep-disordered breathing in adults.," *Am. J. Epidemiol.*, vol. 177, no. 9, pp. 1006–1014, May 2013,
 <u>https://doi.org/10.1093/aje/kws342</u>
- [4] J. M. Marin *et al.*, "Association between treated and untreated obstructive sleep apnea and risk of hypertension.," *JAMA*, vol. 307, no. 20, pp. 2169–2176, May 2012,

https://doi.org/10.1001/jama.2012.3418

- [5] R. P. Allen *et al.*, "Restless legs syndrome/Willis-Ekbom disease diagnostic criteria: updated International Restless Legs Syndrome Study Group (IRLSSG) consensus criteria--history, rationale, description, and significance.," *Sleep Med.*, vol. 15, no. 8, pp. 860–873, Aug. 2014, https://doi.org/10.1016/j.sleep.2014.03.025
- [6] W. D. P. Gusmão, I. R. O. M. Pureza, and C. R. C. Moreno, "Shift Work and Early Arterial Stiffness: A Systematic Review.," *Int. J. Environ. Res. Public Health*, vol. 19, no. 21, Nov. 2022, https://doi.org/10.3390/ijerph192114569
- [7] C. Vetter, E. E. Devore, C. A. Ramin, F. E. Speizer, W. C. Willett, and E. S. Schernhammer, "Mismatch of Sleep and Work Timing and Risk of Type 2 Diabetes.," *Diabetes Care*, vol. 38, no. 9, pp. 1707–1713, Sep. 2015, https://doi.org/10.2337/dc15-0302
- [8] K. Spiegelhalder, C. Scholtes, and D. Riemann, "The association between insomnia and cardiovascular diseases.," *Nat. Sci. Sleep*, vol. 2, pp. 71–78, 2010, <u>https://doi.org/10.2147/nss.s7471</u>
- P. Meerlo, A. Sgoifo, and D. Suchecki, "Restricted and disrupted sleep: effects on autonomic function, neuroendocrine stress systems and stress responsivity.," *Sleep Med. Rev.*, vol. 12, no. 3, pp. 197–210, Jun. 2008, https://doi.org/10.1016/j.smrv.2007.07.007
- [10] L. Lavie, "Oxidative stress in obstructive sleep apnea and intermittent hypoxia--revisited--the bad ugly and good: implications to the heart and brain.," *Sleep Med. Rev.*, vol. 20, pp. 27–45, Apr. 2015, https://doi.org/10.1016/j.smrv.2014.07.003
- [11] P. Lévy *et al.*, "Obstructive sleep apnoea syndrome.," *Nat. Rev. Dis. Prim.*, vol. 1, p. 15015, Jun. 2015, https://doi.org/10.1038/nrdp.2015.15
- [12] V. K. Kapur *et al.*, "Clinical Practice Guideline for Diagnostic Testing for Adult Obstructive Sleep Apnea: An American Academy of Sleep Medicine Clinical Practice Guideline.," *J. Clin. sleep Med. JCSM Off. Publ. Am. Acad. Sleep Med.*, vol. 13, no. 3, pp. 479–504, Mar. 2017,

https://doi.org/10.5664/jcsm.6506

- [13] R. Heinzer *et al.*, "Prevalence of sleep-disordered breathing in the general population: the HypnoLaus study.," *Lancet. Respir. Med.*, vol. 3, no. 4, pp. 310–318, Apr. 2015, <u>https://doi.org/10.1016/S2213-2600(15)00043-0</u>
- [14] R. P. Allen *et al.*, "Evidence-based and consensus clinical practice guidelines for the iron treatment of restless legs syndrome/Willis-Ekbom disease in adults and children: an IRLSSG task force report," *Sleep Med.*, vol. 41, pp. 27–44, Jan. 2018, https://doi.org/10.1016/J.SLEEP.2017.11.1126
- [15] M. R. Irwin, R. Olmstead, and J. E. Carroll, "Sleep Disturbance, Sleep Duration, and Inflammation: A Systematic Review and Meta-Analysis of Cohort Studies and Experimental Sleep Deprivation.," *Biol. Psychiatry*, vol. 80, no. 1, pp. 40–52, Jul. 2016, <u>https://doi.org/10.1016/j.biopsych.2015.05.014</u>
- [16] F. Sauvet *et al.*, "Effect of acute sleep deprivation on vascular function in healthy subjects.," *J. Appl. Physiol.*, vol. 108, no. 1, pp. 68–75, Jan. 2010, <u>https://doi.org/10.1152/japplphysiol.00851.2009</u>
- [17] M. Kohler and J. R. Stradling, "Mechanisms of vascular damage in obstructive sleep apnea.," *Nat. Rev. Cardiol.*, vol. 7, no. 12, pp. 677–685, Dec. 2010, <u>https://doi.org/10.1038/nrcardio.2010.145</u>
- K. Spiegel, R. Leproult, and E. Van Cauter, "Impact of sleep debt on metabolic and endocrine function.," *Lancet (London, England)*, vol. 354, no. 9188, pp. 1435–1439, Oct. 1999,

https://doi.org/10.1016/S0140-6736(99)01376-8

- [19] D. Tsiptsios *et al.*, "Association between sleep insufficiency and dyslipidemia: a cross-sectional study among Greek adults in the primary care setting.," *Sleep Sci. (Sao Paulo, Brazil)*, vol. 15, no. Spec 1, pp. 49–58, 2022, https://doi.org/10.5935/1984-0063.20200124
- [20] F. De Torres-Alba, D. Gemma, E. Armada-Romero, J. R. Rey-Blas, E. López-de-Sá, and J. L. López-Sendon, "Obstructive sleep apnea and coronary artery disease: from pathophysiology to clinical implications.," *Pulm. Med.*, vol. 2013, p. 768064, 2013, <u>https://doi.org/10.1155/2013/768064</u>
- [21] M. A. Miller and N. E. Howarth, "Sleep and cardiovascular disease.," Emerg. Top. life

Sci., vol. 7, no. 5, pp. 457–466, Dec. 2023, https://doi.org/10.1042/ETLS20230111

- [22] L. E. Laugsand, L. B. Strand, C. Platou, L. J. Vatten, and I. Janszky, "Insomnia and the risk of incident heart failure: a population study.," *Eur. Heart J.*, vol. 35, no. 21, pp. 1382–1393, Jun. 2014, https://doi.org/10.1093/eurheartj/eht019
- [23] T. Chandola *et al.*, "Work stress and coronary heart disease: what are the mechanisms?," *Eur. Heart J.*, vol. 29, no. 5, pp. 640–648, Mar. 2008, <u>https://doi.org/10.1093/eurheartj/ehm584</u>
- [24] R. P. Pedrosa *et al.*, "Obstructive sleep apnea: the most common secondary cause of hypertension associated with resistant hypertension.," *Hypertens. (Dallas, Tex. 1979)*, vol. 58, no. 5, pp. 811–817, Nov. 2011, https://doi.org/10.1161/HYPERTENSIONAHA.111.179788
- [25] T. Mooe, K. A. Franklin, K. Holmström, T. Rabben, and U. Wiklund, "Sleepdisordered breathing and coronary artery disease: long-term prognosis.," *Am. J. Respir. Crit. Care Med.*, vol. 164, no. 10 Pt 1, pp. 1910–1913, Nov. 2001, <u>https://doi.org/10.1164/ajrccm.164.10.2101072</u>
- [26] J. M. Marin, S. J. Carrizo, E. Vicente, and A. G. N. Agusti, "Long-term cardiovascular outcomes in men with obstructive sleep apnoea-hypopnoea with or without treatment with continuous positive airway pressure: an observational study.," *Lancet (London, England)*, vol. 365, no. 9464, pp. 1046–1053, Mar. 2005, <u>https://doi.org/10.1016/S0140-6736(05)71141-7</u>
- [27] D. J. Gottlieb, V. K. Somers, N. M. Punjabi, and J. W. Winkelman, "Restless legs syndrome and cardiovascular disease: a research roadmap.," *Sleep Med.*, vol. 31, pp. 10–17, Mar. 2017, https://doi.org/10.1016/j.sleep.2016.08.008
- [28] C. Vetter, "Circadian disruption: What do we actually mean?," *Eur. J. Neurosci.*, vol. 51, no. 1, pp. 531–550, Jan. 2020, https://doi.org/10.1111/ejn.14255
- [29] M. V Vyas *et al.*, "Shift work and vascular events: systematic review and metaanalysis.," *BMJ*, vol. 345, p. e4800, Jul. 2012, <u>https://doi.org/10.1136/bmj.e4800</u>

- [30] E. Haus and M. H. Smolensky, "Biologic rhythms in the immune system.," *Chronobiol. Int.*, vol. 16, no. 5, pp. 581–622, Sep. 1999, https://doi.org/10.3109/07420529908998730
- [31] J. M. Trauer, M. Y. Qian, J. S. Doyle, S. M. W. Rajaratnam, and D. Cunnington, "Cognitive Behavioral Therapy for Chronic Insomnia: A Systematic Review and Meta-analysis.," *Ann. Intern. Med.*, vol. 163, no. 3, pp. 191–204, Aug. 2015, <u>https://doi.org/10.7326/M14-2841</u>
- [32] I. H. Iftikhar *et al.*, "Effects of continuous positive airway pressure on blood pressure in patients with resistant hypertension and obstructive sleep apnea: a meta-analysis.," *J. Hypertens.*, vol. 32, no. 12, pp. 2341–50; discussion 2350, Dec. 2014, https://doi.org/10.1097/HJH.00000000000372
- [33] T. E. Weaver and R. R. Grunstein, "Adherence to continuous positive airway pressure therapy: the challenge to effective treatment.," *Proc. Am. Thorac. Soc.*, vol. 5, no. 2, pp. 173–178, Feb. 2008, https://doi.org/10.1513/pats.200708-119MG
- [34] S. M. Caples *et al.*, "Surgical modifications of the upper airway for obstructive sleep apnea in adults: a systematic review and meta-analysis.," *Sleep*, vol. 33, no. 10, pp. 1396–1407, Oct. 2010, https://doi.org/10.1093/sleep/33.10.1396
- [35] P. J. J. Strollo *et al.*, "Upper-airway stimulation for obstructive sleep apnea.," *N. Engl. J. Med.*, vol. 370, no. 2, pp. 139–149, Jan. 2014, https://doi.org/10.1056/NEJMoa1308659
- [36] J. Arendt, "Melatonin and the pineal gland: influence on mammalian seasonal and circadian physiology.," *Rev. Reprod.*, vol. 3, no. 1, pp. 13–22, Jan. 1998, <u>https://doi.org/10.1530/ror.0.0030013</u>
- [37] C. A. Espie *et al.*, "Randomized controlled clinical effectiveness trial of cognitive behavior therapy compared with treatment as usual for persistent insomnia in patients with cancer.," *J. Clin. Oncol. Off. J. Am. Soc. Clin. Oncol.*, vol. 26, no. 28, pp. 4651–4658, Oct. 2008, https://doi.org/10.1200/JCO.2007.13.9006