

Sleep Quality in Diabetic Patients

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ABSTRACT:

Background: Diabetes mellitus (DM) is a metabolic condition characterized by a persistent rise in blood glucose and a disturbance in the body metabolic state. Sleep is essential for survival and the proper functioning of the body. In diabetes, appropriate sleep is important for handling insulin levels, preventing the build-up of inflammatory cytokines and maintaining body caloric intake.

Objective: This review was conducted to focus on currently available information on sleep changes in diabetic patients.

Methods: An extensive search was conducted on websites, including PubMed, MEDLINE, and Google Scholar, to identify studies that examine the link between sleep quality in patients with type 2 diabetes from 2012 to 2022. Electronic database searches revealed a total number of 24 out of 87 articles that fulfilled the aforementioned criteria for review.

Conclusion: Patients with impaired glucose tolerance have poorer sleep performance which is linked to cognitive impairment. It's well worth looking into if sleep optimization can help those sufferers improve their overall cognitive performance. Support and taking care of patients with diabetes and cognitive impairment is going properly past clinical remedy.

Keywords: sleep, diabetes mellitus, neurological deficits, behavioral defects.

جودة النوم لدى مرضى السكري

الخلاصة: داء السكري (DM) هو حالة أيضية تتميز بارتفاع مستمر في نسبة الجلوكوز في الدم واضطراب في حالة التمثيل الغذائي في الجسم. النوم ضروري للبقاء وللعمل السليم للجسم. في مرض السكري، يعتبر النوم المناسب أمراً مهماً للتعامل مع مستويات الانسولين، ومنع تراكم السايبتوكينات الالتهابية، والحفاظ على السرعات الحرارية في الجسم.

الهدف: أجريت هذه الدراسة للتركيز على المعلومات المتوفرة حالياً حول تغيرات النوم لدى مرضى السكري.

الطرق: تم إجراء بحث مكثف على مواقع الويب، بما في ذلك PubMed و MEDLINE و Google Scholar، لتحديد الدراسات التي تفحص الرابط بين جودة النوم لدى مرضى السكري من النوع 2 من عام 2012 إلى عام 2022. كشفت عمليات البحث في قاعدة البيانات الإلكترونية عن إجمالي عدد 24 من أصل 87 مقالاً استوفت المعايير المذكورة للمراجعة.

الاستنتاج: المرضى الذين يعانون من ضعف في تحمل الجلوكوز يعانون من ضعف أداء النوم المرتبط بضعف الإدراك. يجدر النظر فيما إذا كان تحسين النوم يمكن أن يساعد أولئك الذين يعانون من تحسين أدائهم الإدراكي العام. إن دعم ورعاية مرضى السكري وضعف الإدراك يتخطى العلاج السريري بشكل صحيح.

الكلمات المفتاحية: النوم، السكري، الخلل العصبي، العيوب السلوكية.

INTRODUCTION

Diabetes mellitus (DM) is a metabolic condition characterized by a persistent rise in blood glucose levels and a malfunction of carbohydrate, lipid, and protein metabolism due to problems with

insulin synthesis, and characteristics, or each. Due to variables including growing age, urbanization, obesity, and bodily inaction, the worldwide liability of diabetes is growing. Diabetes is anticipated to affect 9.3% (463

million human beings) of the worldwide population in 2019, rising to 10.2 percent (578 million human beings) through 2030 and 9% (700 million human beings) by way of 2045. Millions of humans in advanced and growing nations go through diabetes (1).

Sleep is essential for survival and the proper functioning of the body. Many important hormones are secreted with the aid of the frame for sleep duration to regulate metabolic and endocrine sports. Sleep's primary feature is to repair the entire body's balance, consisting of the crucial worried implement, and it's for an everyday requirement (2).

In diabetes mellitus patients, appropriate sleep is important for handling insulin levels, preventing the build-up of inflammatory cytokines and maintaining body caloric intake (3). In the diabetic population, negative sleep properly is prime health trouble. It manifests as difficulty beginning and maintaining sleep, excessive sleepiness, a disrupted sleep-wake rhythm, and sleep-associated dysfunctions. Poor sleep quality is a clinical condition characterized by using negative sleep patterns, accelerated sunlight hours' sleepiness, and using sleep drug treatments at more payments (4).

Epidemiological data suggest that sleep duration either short sleep duration (<5–6 h/night) or long sleep duration (≥ 9 h/day) as well as poor sleep quality are linked with a higher risk of T2DM.

The categories of sleep disturbances that are associated with a higher risk of T2DM include the following: (1) alterations of sleep duration, chronic sleep restriction, and excessive sleep; (2) alterations in sleep architecture; (3) sleep fragmentation; (4) circadian rhythm disorders and disruption (i.e., shift work); and (5) OSA. Sleep initiation difficulty and sleep maintaining difficulty increase the risk of T2DM by 55% and 74% respectively.

People with sleep disturbance experience insulin resistance and consequently, increase blood glucose. Also, sleep disorders affect the hypothalamic-pituitary-adrenocortical system leading to a higher release of glucocorticoids. As a result, glucose metabolism is altered which affects glycemic control. Sleep disorder

plays an important role in the occurrence and development of diabetes (5).

OBJECTIVE:

We do this review to focus on currently available information on sleep changes in diabetic patients.

METHODS:

To accomplish this study, an extensive search was conducted on many websites, including PubMed, MEDLINE, and Google Scholar, to identify studies that examine the link between sleep quality and duration in patients with type 2 diabetes, the search included a period extending from 2012 to 2022. The search was conducted using the English language. The initial search included multiple keywords including, "sleep", "diabetes", "insomnia", "neurological deficits", and "behavioral defects". In addition to adding multiple terms, including, "OSA (obstructive sleep apnea)", "metabolic disorder", "neurological deficits" and "behavioral defects". Electronic database searches revealed a total number of 24 out of 87 articles that fulfilled the aforementioned criteria for review. For the articles identified from the database search (87 articles), the titles were screened manually and the abstract was read according to those which were relevant to the research questions. Any articles that appeared to provide an answer to the research questions were included. Then, articles that were duplicated in the pool of screened articles were discarded and the total number of articles left after duplication were assessed for eligibility. The eligible articles were retrieved and evaluated based on the inclusion and exclusion criteria. **Inclusion criteria** were: (a) studies conducted on adult patients with type 2 diabetes that examine the relationship between sleep disturbance and diabetes, (b) community-based study, (c) trials for assessment of proposed etiology and outcome, and (d) availability of baseline information. The studies were excluded based on: (a) letters or articles of unreliable sources, and (b) if the English version of the full text was not available. The research includes major topics, the most important of which are:

Sleep Length and Quality in Diabetes

In the modern world, poor sleep and chronic sleep loss are very common. Poor sleep high-quality or sleep loss has a long-time deleterious effect on morbidity and mortality and an improved risk of growing diabetes mellitus. Lower glucose tolerance and lower insulin sensitivity have been connected to sleep length and are good in numerous experimental trials. These findings returned epidemiological studies that advise prolonged sleep loss. However, most of these investigations were conducted in Western international locations, with few statistics available in Eastern nations (4).

Poor sleep is a usual problem among people with diabetes, in accordance to research. Poor sleep satisfaction afflicted 47% of diabetes worldwide. Reduced saturation degrees, discomfort, restless leg syndrome, nocturnal polyuria, and nocturnal hypoglycemia can all contribute to bad sleep quality in people with diabetes. In addition, individuals with DM may enjoy mental impairment because of negative sleep, which might reduce their functioning potential. According to the investigation, poor sleep quality in diabetic patients has been connected to age, gender, BMI, noisy settings, smoking, and drinking behavior (6).

Insomnia and Diabetes

Temporary insomnia is part of normal life. If a person wakes up refreshed in the morning and experiences a good quality of life, it is not a type of insomnia that requires treatment. However, prolonged insomnia increases the risk of many illnesses and accidents, impairs functioning, and impairs quality of life (7). By recognizing newly started insomnia and good treatment, it is possible to prevent the development of long-term insomnia. The diagnosis of insomnia is based primarily on a careful medical history, clinical examination, and keeping a sleep diary. The primary treatment for temporary insomnia is drug-free treatment (8). Key issues include patient support, finding and addressing the underlying causes and triggers, and guidance for self-care

in sleep. In the treatment of long-term insomnia, the best results are achieved by cognitive-behavioral methods. Therefore, in long-term insomnia, the need for medication should be assessed individually.

Sleeping pills prolong but also alleviate night sleep. All benzodiazepines and similar drugs reduce the amount of deep sleep and REM sleep that are important to the body, and other significant side effects have been reported. (Risk for falls, produce rebound insomnia with prolonged use, disrupt normal sleep architecture, and promote misuse and abuse in patients with a history of substance-related disorders). The use of conventional sleeping pills (benzodiazepines and similar medicines) in the elderly may be more harmful than beneficial and should be used with caution. Monitoring patient care is essential. The possible underlying conditions of insomnia should be treated appropriately.

One patient with diabetes has sleep problems due to their blood glucose levels fluctuating and other diabetes-related signs and symptoms. Insomnia and weariness the following day can result from excessive blood sugar (hyperglycemia) or low blood sugar (hypoglycemia) during the night. Like many continual issues, feelings of despair, or challenges, approximately the sickness itself can keep you unsleeping at night. In addition, the kidneys overcompensate for high blood sugar levels by making you urinate extra frequently—these frequent excursions to the bathroom throughout the night purpose sleep disruption. High blood sugar can also produce headaches, thirst, and exhaustion, making it difficult to fall asleep. Low blood sugar tiers at night can also be because of going too long without ingesting or taking the flawed mixture of diabetic medications (6). As a result, patients could experience nightmares, wake up in a sweat, or experience agitated or disoriented when they wake up.

Sleep disorders appear to play a role in diabetes, simply as diabetes can result in sleep problems. High blood sugar has been associated with negative sleep or less restorative sluggish-wave sleep in patients with

diabetes and prediabetes. However, it's doubtful whether one influences the other or if there are other elements at play. Researchers agree that sleep deprivation may also affect blood sugar levels because of its consequences on insulin, cortisol, and oxidative strain (9,10). Sleeping less than six hours or more than 8 hours a night time is reported with the aid of one region of people with diabetes, setting them at a better risk of high blood sugar (11). Sleep deprivation is now not the handiest boosts blood sugar degrees in those with diabetes, but it also primarily increases the chance of obtaining insulin resistance(12). This connection can be seen as early as a youth.

In diagnosing insomnia, laboratory tests are performed only as needed, mainly to rule out other diseases. Consider Current treatment recommendations for Sleep apnea (obstructive sleep apnea in adults), Urinary incontinence (women), COPD, diabetes. and thyroid dysfunction. Sleep recordings, including night polygraphs, are not required to diagnose normal insomnia. However, a night polygraph may be considered if, for example, an overweight or low-jaw patient is suspected of having sleep apnea. In certain groups of patients, such as diabetic, hypertensive, and psychiatric patients, a large waist circumference and a small chin space itself give rise to suspicion of sleep apnea (13). The current treatment recommends sleep apnea (obstructive sleep apnea in adults); in unclear and severe cases, a physician experienced in sleep medicine should be consulted, or the patient should be referred directly to specialist care.

In these situations, referral of a patient to specialist care should be agreed upon locally, as well-established practices or treatment pathways for referral to Finland have not yet been established.

Further research in public sector specialist care and private sleep clinics may be needed to investigate a prolonged or unclear background sleep disorder. Long-term home-based, approximately one-week recording of an actigraphy (wrist motion sensor) helps determine the cause and type of insomnia, especially when a circadian arrhythmia is

suspected. It also helps assess the amount and quality of sleep. Extensive full-night sleep polygraphy in a sleep laboratory may be appropriate to determine the cause of problematic insomnia (14). Melatonin secretion may be examined when a chronobiological sleep disorder is suspected. This could be, for example, the determination of the onset of dim light melatonin onset at night (DLMO). As an alternative to the determination of melatonin, the circadian rhythm can be examined with a sleep monitor diary, actigraphy, and repeated body temperature measurements.

Breathing Pattern During Sleep in Diabetes

Obstructive sleep apnea is a sleep problem wherein a person pauses respiration for seconds at some stages in the night (15). The character is commonly unaware that is going on, even though a bedmate may additionally be aware of loud night breathing and gasping. Micro-arousals (very quick awakenings) is due to these pauses in breathing, which disrupt the usual sequence of sleep stages and decrease sleep quality. Obese people are much more likely to broaden OSA because their neck circumference is thicker, obstructing the airway (8). A continuous positive airway pressure therapy (CPAP) tool can treat the disorder, which keeps the airway open to restore ordinary breathing and save sleep disturbances (16).

Though sleep apnea does not cause diabetes at once, it's miles a dangerous issue for diabetes. It has been discovered to raise insulin resistance in adults who're neither diabetic nor overweight(17). The National Center for Biotechnology Information enhances technological know-how and fitness via supplying access to biomedical and genetic information. According to American Diabetes Association, National Library of Medicine and Biotech Information, OSA influences one in four patients with diabetes, and a quarter of people with diabetes have every other sleep-related respiratory issue (11).

Overweight and obese adults are more likely to expand OSA and sort two diabetes. Even after correcting for fats, OSA appears to impair

insulin resistance and glucose control (18). OSA disrupts sluggish-wave sleep by inflicting sleep fragmentation, but it also shuts off the body's oxygen delivery on a normal foundation. Insulin resistance and glucose metabolism are the effects of these interactions (19). Short-time sleep apnea remedy seems to improve blood sugar levels in many trials; however, long-term CPAP therapy improves blood sugar and insulin resistance. However, other studies have found no difference in blood glucose levels after treating obstructive sleep apnea, prompting a few professionals to link it with other factors, including weight (19).

Diabetes as a Causative Agent for Sleep disturbances

Diabetes and sleep are inextricably linked, and many people with diabetes have insomnia or negative sleep (20). The critical news is that paying close interest to patients' nutrients, exercise, and blood sugar levels can improve their sleep and, as a result, your standard health. Sleep deprivation reasons ghrelin, the hunger hormone, to boom and leptin, which makes us experience complete, to drop (21). People who sleep badly may be more vulnerable to seeking comfort in foods that elevate blood sugar and put them vulnerable to weight problems, which is a chance component for diabetes to compensate for lower electricity levels (22). Adults with diabetes who have hassle sleeping or waking up regularly at night may be less likely to comply with different diabetes self-care recommendations, acquire enough exercise, and monitor blood glucose levels (23).

Poor sleep will have a protracted-time period impact on humans with diabetes, further to its acute consequences on blood sugar levels (24). Those who use sleep remedies or have difficulty dozing are more susceptible to revel in extreme mental discomfort. Additionally, people with diabetes who do not get sufficient sleep are more likely to have cognitive impairment later in life (23).

Dementia in Diabetic Patients

Diabetes can cause a variety of troubles, including blood vessel damage. In addition,

diabetes is connected to a multiplied hazard of vascular dementia. This kind of dementia is a brain injury frequently due to diminished or obstructed blood flow to the brain. Many people with diabetes developed brain abnormalities similar to those seen in Alzheimer's ailment and vascular dementia. According to a few researchers, every contamination exacerbates the harm produced with the aid of the other.

Diabetes might also enhance the threat of moderate cognitive impairment (MCI), an ailment wherein human beings have extra pondering (cognitive) and memory impairments than they could commonly have as they age (25). According to numerous studies, hyperglycemia may additionally boost the danger of MCI progressing to dementia. Alzheimer's disorder and different styles of dementia may be preceded or observed via slight cognitive impairment. Researchers are searching into the hyperlinks between diabetes and Alzheimer's disorder (26), in addition to possible methods to prevent or deal with both issues. However, a recent look at intranasal insulin found no benefit in phrases of cognition (27).

Management of Diabetes-Induced Cognitive Impairments

Diabetes causes cognitive impairment, which is common trouble (28). This may be due to diabetes-related brain alterations, but the co-prevalence of diabetes and cognitive dysfunction surely suggests similar chance factors, the most outstanding of which is age. The worldwide occurrence of diabetes in adults over sixty-five years is currently 18.8%. The range of people aged 65–99 years living with diabetes turned into estimated to be Eight million in 2017. This is predicted to double within the subsequent three years, due to a rise within the range of humans over sixty-five. The populace traits for dementia are comparable. Dementia impacts 6–7% of adults over the age of 60 in the sector, with little difference between regions (25). According to estimates from 2015, forty-six million people were living with dementia global at the time, with the range expected to double in the subsequent two

decades. According to information from a massive veteran's registry within the United States, dementia and cognitive impairment prevalence were thirteen (27). 1% among those with diabetes elderly 65–74 years and 24.2% among those aged seventy-five years and older. Although people with diabetes are getting privy to cognitive disorders due to the disorder, the knowledge of other diabetes outcomes is still missing. For example, patients say their dogs have a tough time handling cognitive problems because of diabetes. Professional diabetic associations regularly include information on cognitive dysfunction in instructional programmers, recognizing this critical information hole.

CONCLUSION

Patients with impaired glucose tolerance have poorer sleep performance which is linked to decreased cognitive impairment. It's well worth looking into if sleep optimization can help those sufferers improve their overall cognitive performance. Support and taking care of patients with diabetes and cognitive impairment is going properly past clinical remedy. The impact of cognitive impairment and dementia on human beings afflicted is turning into greater well-identified. There have been sturdy calls for movement (for instance, from the WHO) to enhance dementia care and support for folks with dementia and their careers that will stay a life of that means and dignity. This consists of efforts to make societies greater dementia-friendly, as well as, and that is truly relevant to diabetes control, actively attractive patients and their careers in policymaking and the improvement of character-centered, cost-powerful, sustainable, and low-cost treatment and care methods that contain public fitness standards and cultural elements.

REFERENCES:

1-Alam U, Sloan G, Tesfaye S. Treating pain in diabetic neuropathy: current and developmental drugs. *Drugs*. 2020 Mar;80(4):363-84.

2-Batista AF, Forny-Germano L, Clarke JR, Lyra e Silva NM, Brito-Moreira J, Boehnke SE, Winterborn A, Coe BC, Lablans A, Vital JF, Marques SA. The diabetes drug liraglutide reverses cognitive impairment in mice and attenuates insulin receptor and synaptic pathology in a non-human primate model of Alzheimer's disease. *The Journal of pathology*. 2018 May;245(1):85-100.

3-Irwin MR, Wang M, Ribeiro D, Cho HJ, Olmstead R, Breen EC, Martinez-Maza O, Cole S. Sleep loss activates cellular inflammatory signaling. *Biological psychiatry*. 2008 Sep 15;64(6):538-40.

4-Burr O, Berry A, Joule N, Rayman G. Inpatient diabetes care during the COVID-19 pandemic: A Diabetes UK rapid review of healthcare professionals' experiences using semi-structured interviews. *Diabetic Medicine*. 2021 Jan;38(1):e14442.

5-Anothaisintawee T, Reutrakul S, Van Cauter E, Thakkinstian A. Sleep disturbances compared to traditional risk factors for diabetes development: systematic review and meta-analysis. *Sleep medicine reviews*. 2016 Dec 1;30:11-24.

6-Choudhary P, Campbell F, Joule N, Kar P, Diabetes UK. A Type 1 diabetes technology pathway: consensus statement for the use of technology in Type 1 diabetes. *Diabetic Medicine*. 2019 May;36(5):531-8.

7-Filtness AJ, Armstrong KA, Watson A, Smith SS. Sleep-related vehicle crashes on low speed roads. *Accident Analysis & Prevention*. 2017 Feb 1;99:279-86.

8-Abbasi S, Alimohammadi N, Pahlavanzadeh S. Effectiveness of cognitive behavioral therapy on the quality of sleep in women with multiple sclerosis: a randomized controlled trial study. *International journal of community based nursing and midwifery*. 2016 Oct;4(4):320.

9-Beihl DA, Liese AD, Haffner SM. Sleep duration as a risk factor for incident type 2 diabetes in a multiethnic cohort. *Annals of epidemiology*. 2009 May 1;19(5):351-7.

- 10-Gangwisch JE, Heymsfield SB, Boden-Albala B, Buijs RM, Kreier F, Pickering TG, Rundle AG, Zammit GK, Malaspina D. Sleep duration as a risk factor for diabetes incidence in a large US sample. *Sleep*. 2007 Dec 1;30(12):1667-73.
- 11-Dyson PA, Twenefour D, Breen C, Duncan A, Elvin E, Goff L, Hill A, Kalsi P, Marsland N, McArdle P, Mellor D. Diabetes UK evidence-based nutrition guidelines for the prevention and management of diabetes. *Diabetic medicine*. 2018 May;35(5):541-7.
- 12-Thorp AA, Schlaich MP. Relevance of sympathetic nervous system activation in obesity and metabolic syndrome. *Journal of diabetes research*. 2015 Oct;2015.
- 13-Sharifi A, De Bock MI, Jayawardene D, Loh MM, Horsburgh JC, Berthold CL, Paramalingam N, Bach LA, Colman PG, Davis EA, Grosman B. Glycemia, treatment satisfaction, cognition, and sleep quality in adults and adolescents with type 1 diabetes when using a closed-loop system overnight versus sensor-augmented pump with low-glucose suspend function: a randomized crossover study. *Diabetes technology & therapeutics*. 2016 Dec 1;18(12):772-83.
- 14-Nam S, Whittemore R, Jung S, Latkin C, Kershaw T, Redeker NS. Physical neighborhood and social environment, beliefs about sleep, sleep hygiene behaviors, and sleep quality among African Americans. *Sleep health*. 2018 Jun 1;4(3):258-64.
- 15-Hudgel DW. Mechanisms of obstructive sleep apnea. *Chest*. 1992 Feb 1;101(2):541-9.
- 16-Zizi F, Jean-Louis G, Brown CD, Ogedegbe G, Boutin-Foster C, McFarlane SI. Sleep duration and the risk of diabetes mellitus: epidemiologic evidence and pathophysiologic insights. *Current diabetes reports*. 2010 Feb;10(1):43-7.
- 17-Punjabi NM, Sorkin JD, Katzell LI, Goldberg AP, Schwartz AR, Smith PL. Sleep-disordered breathing and insulin resistance in middle-aged and overweight men. *American journal of respiratory and critical care medicine*. 2002 Mar 1;165(5):677-82.
- 18-Punjabi NM, Polotsky VY. Disorders of glucose metabolism in sleep apnea. *Journal of Applied Physiology*. 2005 Nov;99(5):1998-2007.
- 19-Finer S, Robb P, Cowan K, Daly A, Shah K, Farmer A. Setting the top 10 research priorities to improve the health of people with Type 2 diabetes: a Diabetes UK–James Lind Alliance Priority Setting Partnership. *Diabetic Medicine*. 2018 Jul;35(7):862-70.
- 20-Lou P, Qin Y, Zhang P, Chen P, Zhang L, Chang G, Li T, Qiao C, Zhang N. Association of sleep quality and quality of life in type 2 diabetes mellitus: a cross-sectional study in China. *Diabetes research and clinical practice*. 2015 Jan 1;107(1):69-76.
- 21-Walkey HC, Kaur A, Bravis V, Godsland IF, Misra S, Williams AJ, Bingley PJ, Dunger DB, Oliver N, Johnston DG. Rationale and protocol for the After Diabetes Diagnosis REsearch Support System (ADDRESS): an incident and high risk type 1 diabetes UK cohort study. *BMJ open*. 2017 Jul 1;7(7):e013956.
- 22-Harsch IA, Schahin SP, Brückner K, Radespiel-Tröger M, Fuchs FS, Hahn EG, Konturek PC, Lohmann T, Ficker JH. The effect of continuous positive airway pressure treatment on insulin sensitivity in patients with obstructive sleep apnoea syndrome and type 2 diabetes. *Respiration*. 2004;71(3):252-9.
- 23-Abdul Jafar NK, Eng DZ, Cai S. Sleep in pregnancy and maternal hyperglycemia: a narrative review. *Current diabetes reports*. 2019 Dec;19(12):1-4.
- 24-Yaggi HK, Araujo AB, McKinlay JB. Sleep duration as a risk factor for the development of type 2 diabetes. *Diabetes care*. 2006 Mar 1;29(3):657-61
- 25-Sinclair A, Dhatariya K, Burr O, Nagi D, Higgins K, Hopkins D, Patel M, Kar P, Gooday C, Howarth D, Abdelhafiz A. Guidelines for the management of diabetes in care homes

during the Covid-19 pandemic. *Diabetic Medicine*. 2020 Jul;37(7):1090-3..

26-Nunley KA, Rosano C, Ryan CM, Jennings JR, Aizenstein HJ, Zgibor JC, Costacou T, Boudreau RM, Miller R, Orchard TJ, Saxton JA. Clinically relevant cognitive impairment in middle-aged adults with childhood-onset type 1 diabetes. *Diabetes Care*. 2015 Sep 1;38(9):1768-76.

27-Muscogiuri G, Barrea L, Annunziata G, Di Somma C, Laudisio D, Colao A, Savastano S. Obesity and sleep disturbance: the chicken or the egg?. *Critical reviews in food science and nutrition*. 2019 Jul 20;59(13):2158-65.

28-Primožič S, Avbelj M, Dernovšek MZ, Oblak MR. Specific cognitive abilities are associated with diabetes self-management behavior among patients with type 2 diabetes. *Diabetes research and clinical practice*. 2012 Jan 1;95(1):48-54.