EGAS MONIZ SCHOOL of HEALTH & SCIENCE | INSTITUTO UNIVERSITÁRIO EGAS MONIZ

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MESTRADO INTEGRADO EM CIÊNCIAS FARMACÊUTICAS

OBESITY AND SLEEP DISTURBANCE : A VICIOUS CIRCLE. ANALYSIS OF CAUSES, CONSEQUENCES AND TREATMENTS

Trabalho submetido por
Angélique Socheata Sisowath
para a obtenção do grau de Mestre em Ciências Farmacêuticas

novembro de 2025

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Prof. Doutor José Camolas

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Resumo

A obesidade, definida como uma acumulação anormal ou excessiva de gordura corporal, é um importante problema de saúde pública na Europa e está associada a um risco acrescido de muitas doenças crónicas, incluindo doenças cardiovasculares, diabetes de tipo 2 e certos tipos de cancro.

As perturbações do sono são definidas como distúrbios na quantidade/qualidade/regularidade do sono, com ênfase na sua prevalência crescente na Europa. Estes distúrbios incluem doenças como a insónia, a síndrome da apneia obstrutiva do sono e a síndrome da alimentação nocturna, todas elas susceptíveis de alterar os ritmos circadianos e perturbar o metabolismo.

A relação entre a obesidade e as perturbações do sono será o foco da análise, destacando síndromes específicas.

O papel da regulação circadiana do sono e da vigília será estudado, nomeadamente em relação ao metabolismo e ao comportamento alimentar. As perturbações dos ritmos circadianos podem induzir desequilíbrios metabólicos, alterando a regulação do apetite e contribuindo para a obesidade.

Por fim, será analisado o impacto dos tratamentos, distinguindo entre abordagens farmacológicas e não farmacológicas. A tese examinará como a regulação do sono pode potencialmente melhorar ou eliminar a obesidade e, inversamente, como a perda de peso pode levar a uma melhoria da qualidade do sono.

O objetivo desta tese é explorar a complexa relação entre a obesidade e os distúrbios do sono, através de uma revisão narrativa da literatura científica. A investigação está estruturada em torno de vários temas-chave para estabelecer uma compreensão abrangente e actualizada das interações entre estas duas condições.

Palavras-chave: Obesidade, Perturbações do sono, Europa, Desregulação Metabólica

Abstract

Obesity, defined as an abnormal or excessive accumulation of body fat, is a major public health problem in Europe and is associated with an increased risk of many chronic diseases, including cardiovascular disease, type 2 diabetes, and certain types of cancer.

Sleep disorders are defined as disturbances in the quantity/quality/regularity of sleep, with a focus on their increasing prevalence in Europe. These disorders include conditions such as insomnia, obstructive sleep apnea syndrome, and night eating syndrome, all of which are likely to alter circadian rhythms and disrupt metabolism.

The relationship between obesity and sleep disorders will be the focus of the analysis, with an emphasis on specific syndromes.

The role of circadian regulation of sleep and wakefulness will also be studied, particularly in relation to metabolism and eating behavior. Circadian rhythm disorders can induce metabolic imbalances, alter appetite regulation, and contribute to obesity.

Finally, the impact of treatments will be analyzed, distinguishing between pharmacological and non-pharmacological approaches. The thesis will examine how sleep regulation can potentially improve or eliminate obesity and, conversely, how weight loss can lead to improved sleep quality.

The objective of this thesis is to explore the complex relationship between obesity and sleep disorders through a systematic review of scientific literature. The research focuses on several key themes in order to establish a comprehensive and up-to-date understanding of the interactions between these two conditions.

Keywords: Obesity, Sleep disorders, Europe, Metabolic Dysregulation

Résumé

L'obésité, définie comme une accumulation anormale ou excessive de graisse corporelle, est un problème de santé publique important en Europe et est associée à un risque accru de nombreuses maladies chroniques, notamment les maladies cardiovasculaires, le diabète de type 2 et certains types de cancer.

Les troubles du sommeil sont définis comme des perturbations de la quantité/qualité/régularité du sommeil, l'accent étant mis sur leur prévalence croissante en Europe. Ces troubles comprennent des maladies telles que l'insomnie, le syndrome d'apnée obstructive du sommeil et le syndrome de l'alimentation nocturne, qui sont toutes susceptibles de modifier les rythmes circadiens et de perturber le métabolisme.

La relation entre l'obésité et les troubles du sommeil sera au centre de l'analyse, en mettant l'accent sur des syndromes spécifiques.

Le rôle de la régulation circadienne du sommeil et de l'éveil sera étudié, notamment en relation avec le métabolisme et le comportement alimentaire. Les troubles des rythmes circadiens peuvent induire des déséquilibres métaboliques, modifier la régulation de l'appétit et contribuer à l'obésité.

Enfin, l'impact des traitements sera analysé, en distinguant les approches pharmacologiques et non pharmacologiques. La thèse examinera comment la régulation du sommeil peut potentiellement améliorer ou éliminer l'obésité et, inversement, comment la perte de poids peut conduire à une amélioration de la qualité du sommeil.

L'objectif de cette thèse est d'explorer la relation complexe entre l'obésité et les troubles du sommeil, à travers une revue narrative de la littérature scientifique. La recherche s'articule autour de plusieurs thèmes clés afin d'établir une compréhension globale et actualisée des interactions entre ces deux conditions.

Mots-clés : Obésité, Troubles du sommeil, Europe, Dysrégulation métabolique

Table of contents

Abstract 3
Introduction 15
1. Obesity 17
1.1. Definition and classification 17
1.1.1. Definitions of obesity 17
1.1.2. Prevalence in Europe and epidemiological context 20
1.2. Risk factors and determinants 21
1.3. Health consequences of obesity 23
1.3.1. Cardiovascular diseases 23
1.3.2. Type 2 diabetes 23
1.3.3. Cancers 23
1.3.4. Respiratory diseases 24
2. Sleep disorders 25
2.1. Normal sleep 25
2.1.1. Sleep architecture: cycles, stages, circadian rhythms 25
2.1.2. Physiological role of sleep (cognition, metabolism, immunity) 26
2.2. Types of sleep disorders 27
2.2.1. Insomnia 27
2.2.2. Obstructive sleep apnea 27
2.2.3. Nocturnal feeding syndrome 28
2.2.4. Specific obesity-related syndrome (Pickwick or OHS) 28
2.3. Prevalence 30
2.3.1. Sleep duration by age 30
2.3.2. Epidemiological data in Europe 30
2.4. Risk factors and determinants influencing sleep 30
2.4.1. Behavioral factors: diet, sedentary, lifestyle 30
2.4.2. Genetic factors 31
2.4.3. Environmental and social factors 32
3. Interactions between obesity and sleep disorders 33
3.1. A bidirectional relationship 33
3.1.1. Sleep disorders promote weight gain 33
3.1.2. Obesity aggravates sleep disorders 34
3.2. Pathophysiological mechanisms 35
3.2.1. Hormonal imbalances (leptin, ghrelin, cortisol, melatonin) 35
3.2.2 Subclinical inflammation and insulin resistance 37
3.2.3. Circadian desynchronization and metabolism 37

3.2.4. Disruption of appetite regulation and eating behavior 39
3.3. Clinical and public health consequences 39
3.3.1. Vicious circle 39
3.3.2 Impact on quality of life 40
4. Therapeutic perspectives 42
4.1. Non-pharmacological approaches 42
4.1.1. Nutrition and healthy living 42
4.1.2. Sleep hygiene and circadian regularity 44
4.1.3. Physical activity 44
4.1.4. Cognitive behavioral therapy for insomnia (CBT-I) 45
4.1.5. Continuous Positive Airway Pressure 46
4.1.6. Non-Invasive Ventilation 47
4.2. Pharmacological approaches 47
4.2.1. GLP-1 receptor agonists 47
4.2.2. Dual agonists 52
4.2.3. Triple agonists 54
4.2.4. Other obesity treatments 56
4.2.5. Medication/hormones for sleep disorders 58
5. The role of the pharmacist 63
6. Conclusion 65
References 67

Index of Figures

Figure 1 - BMI-for-age Growth Charts for boys 0-5years. Source: de WHO Standards 18
Figure 2 - BMI-for-age Growth Charts for girls 0-5years. Source: WHO Standards.... 19
Figure 3 - Analysis of body fat composition at the same weight and height. Source: NFX NaturalFlex 20
Figure 4 - Hypnogram of Sleep Stages and Cycles. A hypnogram illustrating the stages of sleep, including rapid-eye movement (REM) and the 3 stages of non–rapid eye movement (NREM). (Source: RazerM, Public Domain, via Wikimedia Commons) 25
Figure 5 - Causes Complications of Sleep Apnea (Source: Fort Worth ENT, 2024).... 28
Figure 6 - Pulmonary alveoli. gas exchange in a lungs. Respiratory bronchioles with Alveolar sacs. Cross section of the alveolus and capillary. Respiratory system. Vector illustration (Source: Dreamstime, Designua) 29
Figure 7 - Secretion and release of hormones related to sleep in the human body. (Source: Diabetol Metab Syndr, 2025) 36
Figure 8 - Circadian Rhythms and SCN. (Source: National Institute of General Medical Sciences)..... 38
Figure 9 - Melatonin synthesis from tryptophan: dietary cofactors can influence daytime levels. (Source: Cambridge University Press, Miller, 2023) 43
Figure 10 - A CPAP (continuous positive airway pressure) machine helps treat sleep apnea. (Source: (Cleveland Clinic Medical, 2024)..... 46

List of Tables

Table 1 - Class of medications associated with weight gain (Source : Biomedpharmajournal, 2025)..... 22
Table 2 - Nutrients and their potential dietary sources. (Source : Cambridge University Press, Miller, 2023)..... 43
Table 3 - Main GLP-1 agonists in use or under development (Source : original)..... 51
Table 4 - Hormonal components of the hormone replacement therapy (HRT) treatment regimen and their respective roles. (Source : original) 61
Table 5 - STOP-BANG screening questionnaire for SA (Source : Pharmacy Magazine, 2024) 63

List of Abbreviations and Acronyms

BMI – Body Mass Index

CBT-I – Cognitive Behavioral Therapy for Insomnia

CPAP – Continuous Positive Airway Pressure

CRP – C-Reactive Protein

DORA – Dual Orexin Receptor Antagonists

EMA – European Medicines Agency

GCG – Glucagon

GIP – Gastric Inhibitory Polypeptide (or Glucose-dependent Insulinotropic Polypeptide)

GLP-1 – Glucagon-Like Peptide-1

HDL – High-Density Lipoprotein

HPA – Hypothalamic-Pituitary-Adrenal Axis

HRT – Hormone Replacement Therapy

IL-6 – Interleukin-6

IR – Immediate-Release

LDL – Low-Density Lipoprotein

NAION – Non-Arteritic Anterior Ischemic Optic Neuropathy

NCDs – Noncommunicable Diseases

NREM - Non-rapid eye movement

OHS – Obesity Hypoventilation Syndrome

OSA – Obstructive Sleep Apnea

REM - Rapid Eye Movement

SDB – Sleep-Disordered Breathing

SCN – Suprachiasmatic Nucleus

SWD – Shift Work Disorder

TRE – Time-Restricted Eating

WHO – World Health Organization

WMSs – Weight Management Services

Introduction

Obesity is a complex, multifactorial disease characterized by excessive accumulation of adipose tissue. Obesity is considered a priority public health issue worldwide. In the European region, it is identified as a major cause of disability and death (WHO, 2022), and is linked to an increased risk of noncommunicable diseases (NCDs), including cardiovascular disease, several types of cancer, type 2 diabetes and chronic respiratory diseases such as obstructive sleep apnea (OSA). (WHO, 2025).

Beyond obstructive sleep apnea, many other sleep disorders also represent a public health issue. These include insomnia, sleep deprivation, disruption of sleep cycles and circadian rhythms, nocturnal feeding syndrome, and obesity-specific forms such as Pickwick's syndrome and obese hypoventilation.
These disorders can disrupt metabolic regulation, leading to hormonal imbalances - notably a decrease in leptin, an increase in ghrelin and cortisol - and stimulate the immune system. (Sharma & Kavuru, 2010).
This interaction promotes subclinical inflammation, insulin resistance and risk factors for diseases such as type 2 diabetes and obesity. (Rohm et al., 2022).

The amount of sleep required varies according to age and individual (INSV, 2022), and is partly influenced by genetic factors.
In Europe, sleep disorders affect all age groups. (Galan-Lopez et al., 2021).
This finding underlines the scale of this public health problem, since good sleep quality, as much as its duration, is essential for maintaining cognitive functions, hormonal balance and metabolic regulation.
Numerous epidemiological data suggest an association between insufficient sleep (both in duration and quality) and poorer health outcomes (both physical and psychological), while also pointing out that these behaviors are biologically influenced by genetic determinants contributing to variations between individuals.

There is a bidirectional relationship between obesity and sleep disorders, creating a vicious circle in which lack of sleep promotes weight gain, while obesity aggravates sleep disorders. This dynamic is particularly worrying in Europe, where the prevalence of obesity and sleep disorders is constantly on the rise. Understanding this interaction is therefore of major scientific and medical interest, as it opens new perspectives for the

prevention and integrated management of these two conditions, notably through approaches linked to nutrition and pharmaceutical support.

This thesis aims to analyze the mechanisms linking obesity and sleep disorders, review the available treatment options (pharmacological and non-pharmacological), and clarify the role of pharmacists in the overall management of these patients.

1. Obesity

1.1. Definition and classification

1.1.1. Definitions of obesity

Obesity correspond to an abnormal or excessive accumulation of adipose tissue, likely to impair health and quality of life, particularly sleep and physical activity. It is a chronic, non-communicable disease (NCD). (WHO, 2024).
Recent knowledge distinguishes between different stages or types of obesity: (Rubino et al., 2025)

Preclinical obesity: Excessive accumulation of adipose tissue, without leading to major organ or tissue dysfunction. However, this condition increases the danger of progression to clinical obesity and other NCDs, such as type 2 diabetes, cardiovascular disease or certain types of cancer.
Clinical obesity: Stage where excessive adiposity causes systemic changes and organ dysfunction, which may manifest as specific signs, functional limitations or reduced quality of life.
Clinical obesity remission: Lasting reduction (≥ 6 months) in the clinical and biological symptoms associated with obesity, achieved through treatment (weight loss, surgery, etc.), although a complete cure is not guaranteed.

Clinically, obesity can be generalized, central/visceral, which are strongly associated with metabolic complications, or subcutaneous. Specific forms include sarcopenic obesity, where fat mass is associated with age-related loss of muscle mass, metabolically healthy obesity, defined by excess weight without major metabolic disturbance, and hormonal obesity, linked to endocrine imbalances. (S. K. Ahmed & Mohammed, 2025).
In practice, obesity is diagnosed using what is known as the body mass index (BMI). BMI is calculated by dividing weight (kg) by height squared (m^2).
In adults, a BMI ≥ 25 kg/ m^2 defines overweight, and a BMI ≥ 30kg/ m^2 defines obesity.

In children aged between 5 and 19, obesity is defined as a weight-to-height ratio greater than 2 standard deviations above the median of WHO growth standards.
In children under 5, obesity is defined as weight for height greater than 3 standards deviations above the median of WHO growth norms, with separate reference curves for gender (female or male), as illustrated in Figure 1 and Figure 2. (WHO, 2025).

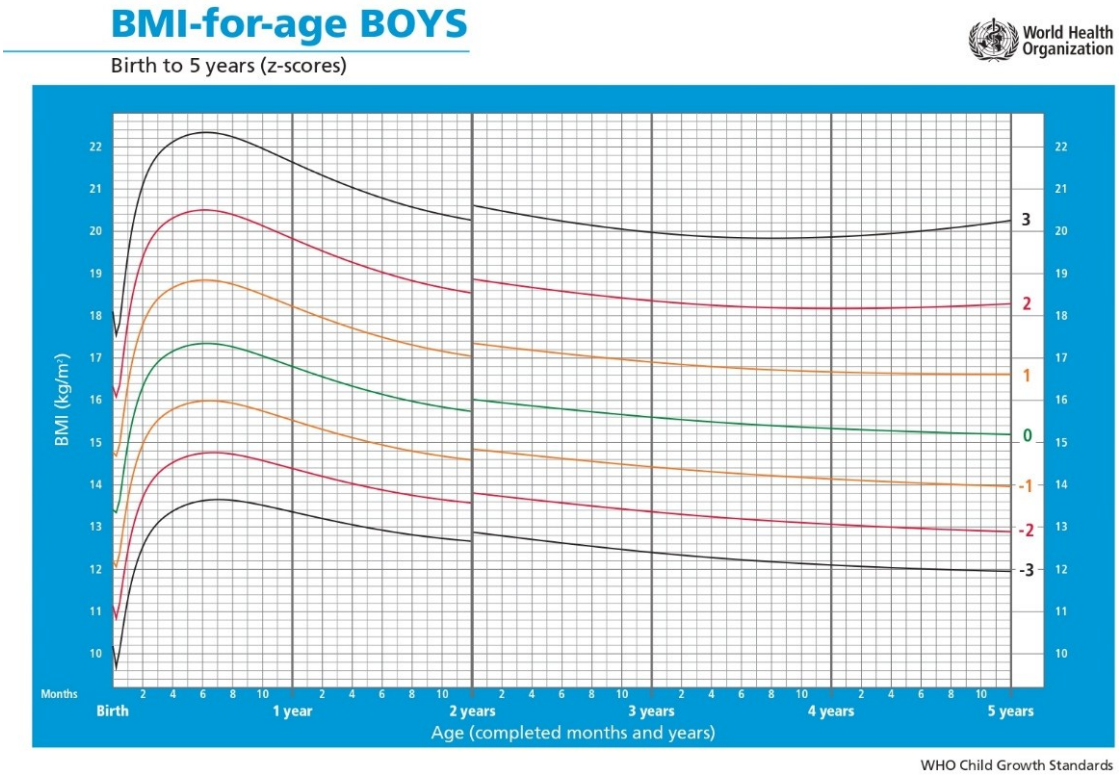

Figure 1 - BMI-for-age Growth Charts for boys 0-5years. Source: de WHO Standards

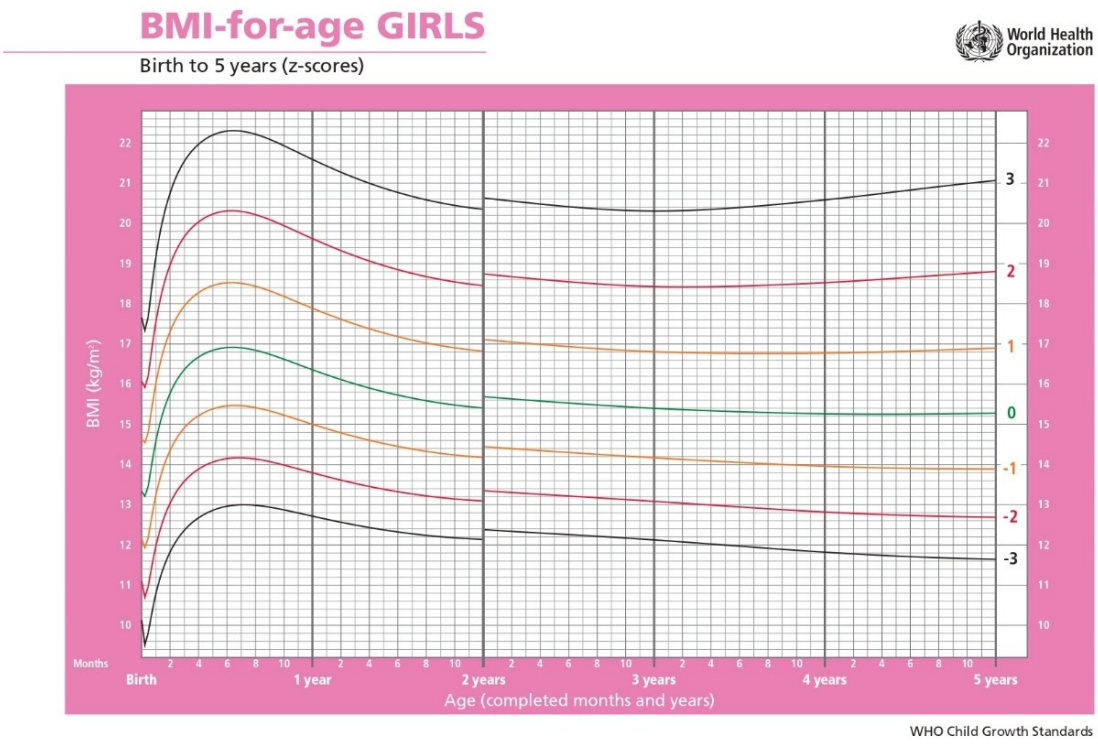

Figure 2 - BMI-for-age Growth Charts for girls 0-5years. Source: WHO Standards

However, BMI does not differentiate between fat and lean body mass (Figure 3), nor does it assess the distribution of fat, all of which play a decisive role in metabolic risk. Nevertheless, BMI remains the most widely used tool for defining obesity, as it is simple and accessible. Current recommendations, however, suggest complementing it with other measurements, such as waist circumference, waist-to-hip ratio, waist-to-height ratio, body fat percentage, relative fat mass or bioelectrical impedance analysis. Except in cases of very high BMI (≥ 40 kg/m^2) where excess adiposity can be considered certain.

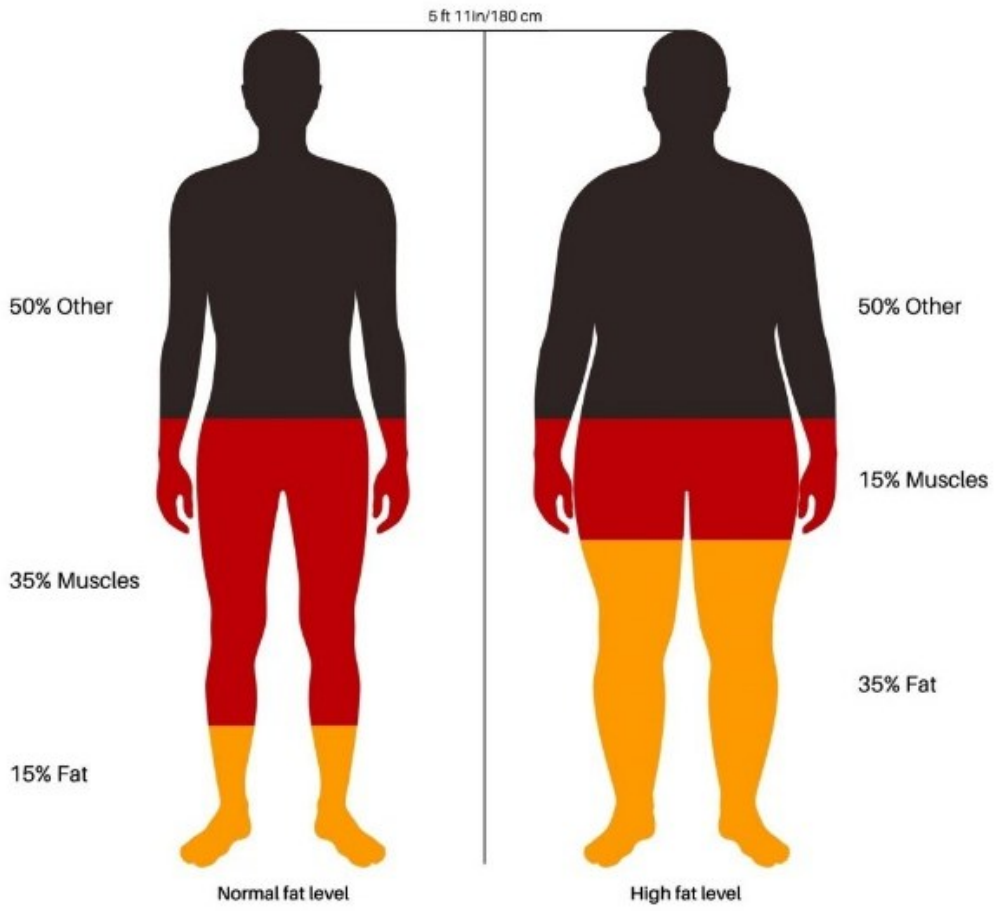

Figure 3 - Analysis of body fat composition at the same weight and height. Source: NFX NaturalFlex

1.1.2. Prevalence in Europe and epidemiological context

This definition of BMI is widely used in epidemiology, public health and clinical practice, and has the advantage of being simple, reproducible and accessible.
Rates of obesity (BMI ≥ 30) in Europe vary widely among women aged 16 or over. They range from 6.1% in Italy to over 23% in Latvia, Estonia and Malta, while among men, they range from 7.9% in Italy to 28.7% in Malta. (Eurostat, 2024).
According to estimates by the NCD Risk Factor Collaboration, the combined prevalence of underweight and obesity was around 11% in Portugal and 26% in France in 1990. In the majority of European countries, obesity accounted for more than 80% of this combined nutritional burden, reflecting a clear dominance of overweight. Between 1990 and 2022, the prevalence of male obesity increased in all countries except France, where no significant change was observed. (The Lancet, 2024).

Generally speaking, prevalence is higher in men than in women. It increases with age (especially between 65 and 74) and remains strongly influenced by socio-educational level. (Eurostat, 2024).
Among children and adolescents (aged 5-19), the combination of thinness and obesity has also increased in almost 70% of European countries. Obesity is more common than thinness in 67% of countries for girls and 63% for boys. (The Lancet, 2024).

1.2. Risk factors and determinants

Obesity is a multifactorial pathology whose mechanisms remain partially elucidated. It results from the interaction of biological and metabolic factors (genetics, insulin resistance, hormonal imbalances, microbiota), environmental factors (urbanization, industrial diet, socio-economic inequalities) and psychosocial factors (stress, emotional eating, stigmatization), which disrupt adipose tissue regulation and lead to excessive fat accumulation. (Rennie et al., 2005).

On a behavioral level, a diet rich in sugars, saturated fats and ultra-processed products, combined with a sedentary lifestyle and low energy expenditure, favors an imbalance between intake and expenditure. Habits such as irregular meals and lack of sleep reinforce this phenomenon. (Rennie et al., 2005).
The speed at which food is consumed is also a significant determinant of energy balance and weight gain. Slowing down the pace of meals helps to limit total calorie consumption, regardless of immediate or delayed feelings of hunger, because eating quickly disrupts physiological satiety signals, particularly those regulated by leptin, ghrelin, cholecystokinin, and peptide YY. Eating too quickly does not allow these hormones time to signal satiety to the brain, leading to overeating before homeostatic regulation kicks in. Conversely, prolonged chewing and longer oral exposure to taste stimuli promote more effective activation of the sensory and hormonal mechanisms of satiety, thereby reducing overall energy intake. (Robinson et al., 2014)

In addition, slowing down the speed of consumption could influence gastric emptying and stomach distension, reinforcing the feeling of gastric fullness. These effects appear to occur without a secondary increase in hunger, suggesting that eating slowly could be a sustainable weight management strategy. (Robinson et al., 2014)

Finally, certain medical factors (endocrine disorders, drug treatments) and molecular mechanisms such as chronic inflammation and adipose tissue dysfunction aggravate this metabolic imbalance. (S. K. Ahmed & Mohammed, 2025).
Several therapeutic classes are particularly implicated in weight gain, notably anticholinergics (antipsychotics, antiretrovirals, antihistamines, hormonal contraceptives, oral hypoglycemic agents) and anticonvulsants, but also glucocorticoids, beta-blockers, insulin, and antidepressants (Table 1).

Table 1 - Class of medications associated with weight gain (Source : Biomedpharmajournal, 2025)

Anti-cholinergics	Anticonvulsants
Antipsychotics	Glucocorticoids
Anti-retroviral agents	Beta-blockers
Antihistamines	Insulin
Hormonal contraceptives	Antipsychotics
Oral hypoglycaemic agents	Antidepressants

1.3. Health consequences of obesity

Obesity has serious health implications. Excess adipose tissue increases the risk of diseases, disorders and cancers. These complications are responsible for significant morbidity and many premature deaths. (WHO, 2024)

1.3.1. Cardiovascular diseases

Obesity increases the risk of cardiovascular disease, notably through weight-related hypertension, which also promotes left ventricular hypertrophy and heart failure. Abdominal obesity contributes to the development of coronary heart disease via inflammation and atherosclerosis. It also increases clot formation, raising the risk of ischemic and hemorrhagic strokes. (S. K. Ahmed & Mohammed, 2025).

1.3.2. Type 2 diabetes

Obesity promotes type 2 diabetes mainly through insulin resistance, linked to excess body fat and inflammation of adipose tissue. This resistance leads to hyperglycemia, hyperinsulinemia and progressive failure of pancreatic β-cells. (Rubino et al., 2025) Obesity is also part of the metabolic syndrome (central obesity, dyslipidemia, hypertension), often associated with NAFLD, which further accentuates this risk. Weight loss improves insulin sensitivity and significantly reduces the likelihood of developing type 2 diabetes. (S. K. Ahmed & Mohammed, 2025).

1.3.3. Cancers

Excess body fat increases the risk of developing several cancers, in particular post-menopausal breast, endometrial, colon and rectal cancers. These links are explained by chronic inflammation, hormonal imbalances (increased estrogen, insulin resistance) and oxidative stress, all of which favor tumor growth. Other cancers are also affected: pancreas, liver, kidney, gall bladder, esophagus (Barrett's esophagus) and ovary. In these cases, obesity contributes to carcinogenesis through metabolic alterations,

disruption of microbiota, hepatic steatosis and resistance to treatment. Overall, obesity is associated with an increased risk of more than 13 types of cancer, accounting for almost 40% of diagnoses worldwide. It also increases cancer mortality due to altered drug metabolism, resistance to chemotherapy and accelerated carcinogenesis. (S. K. Ahmed & Mohammed, 2025) (Rubino et al., 2025).

1.3.4. Respiratory diseases

Excess body fat, particularly in the abdominal and thoracic regions, exerts pressure on the diaphragm and reduces lung compliance, resulting in reduced respiratory capacity and shortness of breath, particularly during exertion or respiratory infections. (Rubino et al., 2025).
Obese people have an increased risk of OSA (obstructive sleep apnea), OHS (Obesity hypoventilation syndrome) and asthma. (S. K. Ahmed & Mohammed, 2025).
OSA is very common in obese people. Fat accumulation around the neck and upper airways obstructs airflow during sleep, leading to respiratory arrest, daytime fatigue and increased cardiovascular risk. Weight loss significantly improves respiratory symptoms and sleep quality. (Health Risks of Overweight & Obesity, 2023).

OHS is characterized by chronic respiratory failure due to hypoventilation during sleep. This condition can progress to daytime hypercapnia and chronic fatigue, but weight loss and assisted ventilation (PAP) reduce its effects. (S. K. Ahmed & Mohammed, 2025).

Finally, asthma is more frequent and more severe in obese people. Inflammation reduced lung function and increased airway reactivity aggravate symptoms. Weight control and bariatric surgery can often improve respiratory outcomes. (Health Risks of Overweight & Obesity, 2023)

2. Sleep disorders

2.1. Normal sleep

2.1.1. Sleep architecture: cycles, stages, circadian rhythms

Sleep is a succession of phases. There are 2 phases: slow wave sleep (SWS or NREM (non-rapid eye movement)) and REM (Rapid Eye Movement) sleep. These 2 phases follow one another to form a cycle, of which there are 4 to 5 cycles per night, each lasting around 90 minutes. Each phase comprises several stages which follow one another in an orderly fashion to enable physical and mental recovery.
The architecture of sleep can be represented by a hypnogram (Figure 4), showing the succession of sleep phases (slow wave sleep and REM sleep) throughout the night, influenced by physiological parameters such as heart rate, respiration and muscular activity. (Sound Sleep Health, 2020).

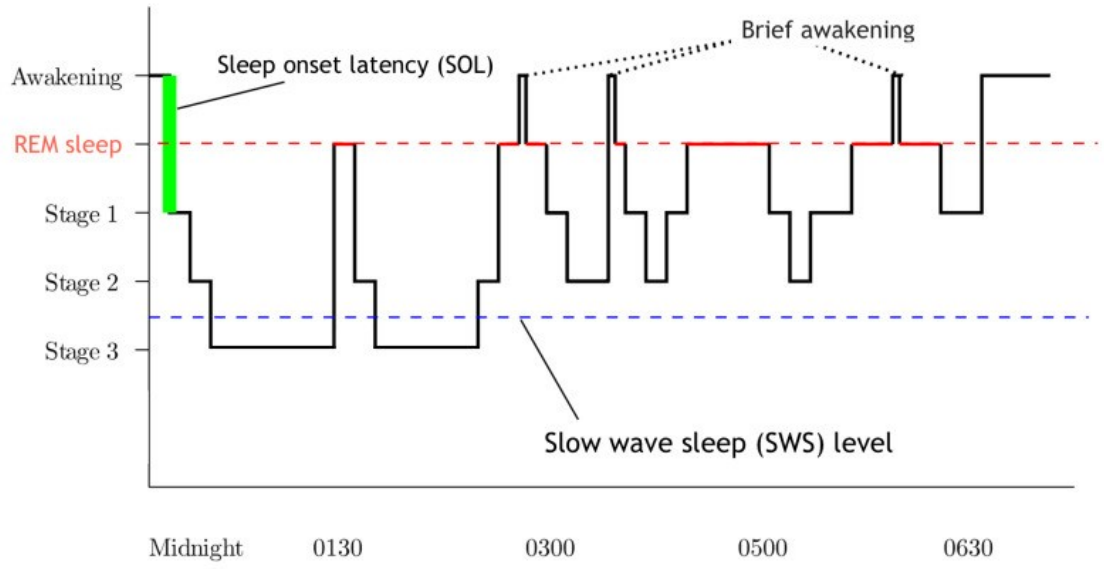

Figure 4 - Hypnogram of Sleep Stages and Cycles. A hypnogram illustrating the stages of sleep, including rapid-eye movement (REM) and the 3 stages of non–rapid eye movement (NREM). (Source: RazerM, Public Domain, via Wikimedia Commons)

In a cycle, there are two phases: slow wave sleep (stage1: light sleep, stage2: deeper sleep and stage3: deepest non-REM sleep) and REM sleep (sometimes called stage 4). Environmental factors, health problems such as diabetes, and certain medications can disrupt these cycles, leading to frequent awakenings or poor-quality sleep. Balanced sleep requires a good cycle, alternating between slow-wave sleep (essential for physical recovery) and REM sleep (for brain regeneration). (Sound Sleep Health, 2020).

Circadian rhythms are the expression of the internal 24-hour biological clock, which regulates many essential functions such as sleep, hormone secretion, body temperature and energy metabolism. The rhythms are synchronized by natural light, which acts on the suprachiasmatic nucleus (SCN). This is a clock that controls melatonin production and coordinates the rhythms of the various organs.
When these rhythms are out of sync, this can lead to sleep disorders and metabolic imbalances. This can increase the risk of obesity, diabetes, cardiovascular disease, blood pressure, mood disorders and cancer. (Circadian Rhythms | National Institute of General Medical Sciences, n.d.).

2.1.2. Physiological role of sleep (cognition, metabolism, immunity)

Sleep is essential for the proper functioning of cognitive functions, i.e. memory, attention, vigilance and concentration. Insufficient sleep duration or quality is detrimental to cognitive performance. To strengthen them, it is important to have a good balance of slow-wave and REM sleep. A number of sleep-enhancing interventions, including melatonin, glycine and plant extracts (Menta spicata, Coriandrum sativum), have been shown to have a positive impact on wakefulness and cognitive functions. (De Longis et al., 2024).

Sleep also fulfils essential metabolic functions, including the regulation of insulin sensitivity, energy balance, carbohydrate and lipid metabolism. Sleep deprivation, frequent awakenings or circadian desynchronization promote insulin resistance, hyperglycemia, dyslipidemia and weight gain. (Baranwal et al., 2023).
Restorative sleep can strengthen immune defense by supporting pathogen elimination, immune memory and inflammation regulation. Conversely, poor sleep promotes chronic low-grade inflammation, with elevated pro-inflammatory cytokines (IL-6, TNF-α),

impaired T lymphocytes and NK cells, and dysregulation of prostaglandins. This imbalance impairs immune balance and increases the risk of metabolic and cardiovascular diseases. (Singh et al., 2024).

2.2. Types of sleep disorders

2.2.1. Insomnia

Insomnia is defined as difficulty in falling asleep, maintaining sleep or waking up early. This results in unrefreshing sleep and altered daytime functioning, such as fatigue, reduced concentration or irritability.
Insomnia has a variety of causes, including stress, anxiety, depression, chronic pain, metabolic diseases, stimulant use and poor sleep hygiene.
It can be acute (often linked to stress or a temporary change) or chronic (>3 nights a week for 3 months) and, if left untreated, can promote weight gain and increase the risk of type 2 diabetes, hypertension and cardiovascular disease. (Suni & Rehman, 2025).

2.2.2. Obstructive sleep apnea

Obstructive sleep apnea (OSA) is a respiratory disorder characterized by repeated episodes of partial or complete obstruction of the upper airway (Figure 5) during sleep, leading to respiratory arrest. It is defined by the occurrence of at least 5 episodes of hypopnea or apnea per hour of sleep, leading to oxygen desaturation (>3%) and micro-arousals. It is strongly associated with obesity, overweight, hypertension, type 2 diabetes and cardiovascular disease. Key risk factors include accumulation of cervical fat, male gender, advanced age, alcohol or sedative use, and certain anatomical abnormalities of the airways. The most common symptoms are intense snoring, daytime sleepiness, chronic fatigue, morning headaches, concentration problems, and a higher risk of road accidents. OSA affects around 10% of the world's population, with an estimated prevalence of 14% in men and 5% in women. This rate increases significantly after the menopause (47-67%). (Hynes & Mansfield, 2024). (Nag et al., 2024).

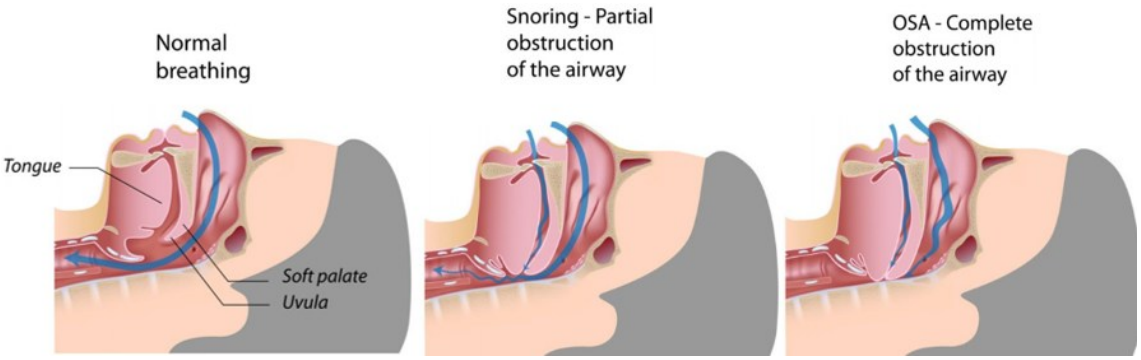

Figure 5 - Causes Complications of Sleep Apnea (Source: Fort Worth ENT, 2024)

2.2.3. Nocturnal feeding syndrome

Nocturnal eating syndrome (NES) is an eating disorder characterized by excessive food consumption in the evening or at night. This disorder is often accompanied by insomnia and a lack of appetite in the morning. Sufferers typically consume 25% or more of their daily caloric intake after dinner, thus disrupting energy metabolism and circadian rhythms. Episodes occur in full awareness, unlike food sleepwalking, and are often accompanied by feelings of loss of control or guilt. The disrupted circadian rhythm affects hunger- and sleep-regulating hormones such as melatonin, leptin and ghrelin. It is closely linked to sleep disorders and psychiatric disorders, notably depression and anxiety. NES promotes weight gain, insulin resistance and, in the long term, increases the risk of type 2 diabetes and cardiovascular disease.
(Pacheco, D., & Singh, A. 2025). (Salman & Kabir, 2022).

2.2.4. Specific obesity-related syndrome (Pickwick or OHS)

OHS (Obesity hypoventilation syndrome) is defined as awake alveolar hypoventilation in an obese patient (BMI ≥ 30), excluding any other identifiable causes of daytime hypercapnia ($PaCO_2$ > 45 mmHg).
From a pathophysiological perspective, this alveolar hypoventilation results in reduced gas exchange in the pulmonary alveoli, with decreased CO2 elimination and reduced O2 supply, as illustrated in Figure 6.

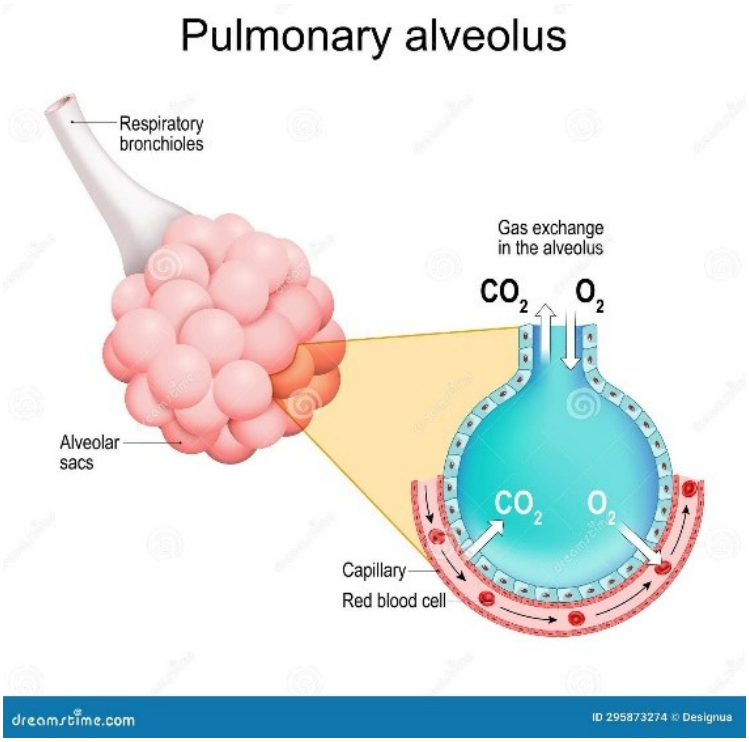

Figure 6 - Pulmonary alveoli. gas exchange in a lungs. Respiratory bronchioles with Alveolar sacs. Cross section of the alveolus and capillary. Respiratory system. Vector illustration (Source: Dreamstime, Designua)

This syndrome is based on several factors: firstly, excess adipose mass in the thoracoabdominal and cervical regions, which exerts a mechanical constraint on the ribcage and diaphragm, limiting respiratory amplitude and reducing the amount of air inspired with each breath. Secondly, impaired central control of ventilation manifests itself in a reduced response to carbon dioxide (CO_2) and hypoxia, as the brain no longer reacts correctly to these chemical signals. This leads to chronic hypoventilation and a progressive accumulation of CO_2 in the blood. Finally, the frequent simultaneous presence of OSA accentuates episodes of oxygen desaturation and worsens CO_2 retention, contributing to the severity of the respiratory disorder. Typical signs include loud snoring, nocturnal breathing pauses, excessive daytime sleepiness, morning headaches, dyspnea, edema and sometimes signs of right heart failure.
It is therefore diagnosed by the presence of symptoms, a BMI ≥ 30, $PaCO_2 > 45$ mmHg in the awake state and the exclusion of other causes of hypoventilation (ex. neuromuscular diseases, pulmonary conditions). (Vultur et al., 2025). (Ghimire et al., 2025).

2.3. Prevalence

2.3.1. Sleep duration by age

The amount of sleep required varies with age: newborns sleep an average of 15 to 17 hours a day, teenagers need 9 to 10 hours, and most adults need at least 7 to 8 hours. (INSV, 2022). However, the optimum duration varies from one individual to another, as it is partly determined by genetic factors.

In newborns, the very long duration of sleep reflects its fundamental biological role in brain maturation. Rapid eye movement (REM) sleep, which is particularly abundant during this period, supports the maturation and differentiation of sensory and motor areas, promotes neural plasticity, and prepares the brain to adapt to the postnatal environment. (De Groot et al., 2024).

With age, several studies show that sleep duration and subjective sleep restorativeness may decrease, and that sleep problems increase with aging. (Åkerstedt et al., 2018). This could be related to changes in sleep architecture and efficiency due to neural aging.

2.3.2. Epidemiological data in Europe

In Europe, sleep disorders affect all age groups. Among teenagers, for example, 68% to 69% do not sleep the recommended 9 to 10 hours and suffer from poor sleep quality. (Galan-Lopez et al., 2021).

2.4. Risk factors and determinants influencing sleep

2.4.1. Behavioral factors: diet, sedentary, lifestyle

A study carried out on children and adolescents in five Mediterranean countries (the "DELICIOUS" project) examined eating habits, diet quality (via a "Youth Healthy Eating Index") and other lifestyle behaviors in relation to so-called adequate sleep

duration (defined as 8-10h). This study shows that better diet quality, meal structure, among others, are associated with a greater probability of having a normal sleep duration. (Godos et al., 2025). Similarly, the level of physical activity and time spent in a seated position play a decisive role in sleep regulation. Sedentary behavior is often defined as prolonged sitting, particularly in front of a screen or in the workplace. There is a relationship between this sedentary behavior and the frequency of sleep disorders.

A recent study analyzed this relationship: participants were divided into quartiles, i.e. into four groups according to their level of sedentariness, ranging from the least sedentary (1st quartile) to the most sedentary (4th quartile). The results showed that individuals in the 3rd and 4th quartiles had a significantly higher risk of sleep disorders than the least sedentary group. Statistical analysis showed that beyond around 300 minutes of daily sitting, the probability of developing a sleep disorder increased significantly. (Ju et al., 2025). Data from the Nurses' Health Study confirmed the link between sedentary lifestyle, sleep duration and overall health. In adults over the age of 50, two extra hours of television a day reduced the probability of "healthy aging" by 12%, while replacing one hour of television with one hour of light physical activity or extra sleep significantly improved the chances of healthy aging. (Shi et al., 2024). These results show that diet and physical inactivity interact within the same lifestyle. A balanced diet combined with regular physical activity and a less sedentary lifestyle help to preserve sleep quality and duration.

2.4.2. Genetic factors

Sleep mechanisms are strongly influenced by genetic components that regulate the duration, quality and synchronization of sleep-wake cycles. According to studies carried out on twins and families, this is partly based on heritability. Our internal circadian clock is controlled by specific genes: CLOCK, BMAL1, PER (1-3) and CRY (1-2). These genes function as a loop of activation and inhibition that repeats itself approximately every 24 hours. When the CLOCK and BMAL1 genes are activated, they trigger the production of PER and CRY proteins, which once accumulated, return to block CLOCK and BMAL1. Genetic variations modify the speed of the circadian cycle, explaining the different chronotypes: morning sleepers have an advanced sleep phase, while evening sleepers have a delayed phase. In the study of twins, the heritability of

the chronotype varies between 12 and 50%, confirming the genetic influence on the circadian rhythm of sleep. Sleep homeostasis, i.e., what determines the length and depth of sleep required for recovery, can be mutated. In adults, the majority sleep between 7 and 9 hours a night, but some people naturally sleep much less without showing any functional deficit, a phenomenon known as "familial natural short sleep" (FNSS). This particular profile has been associated with a mutation in the DEC2 gene. This gene, identified in families, shows that they sleep 1h30 less than the average, yet remain fit, because this mutation leads to an increase in wakefulness and a reduction in deep and REM sleep (due to modulation of the hormone involved in maintaining wakefulness, orexin).

There are other genetic mutations that can naturally reduce sleep duration, such as the ADRB1, NPSR1 and GRM1 genes, which are involved in communication between neurons. Variations in these genes result in about 1 hour less sleep and greater resistance to sleep deprivation (Zou et al., 2024).

If certain genetic variations reduce sleep duration, then this may influence hormonal regulation and metabolism, thus increasing risks such as obesity.

2.4.3. Environmental and social factors

Indoor environmental conditions have a significant impact on sleep quality. A moderate room temperature (generally between 18ºC and 22ºC) favors continuity of sleep, whereas temperatures that are too low or too high can weaken rest. Evening exposure to short-wave light (around 460-480 nm) disrupts the circadian rhythm. Also nocturnal noise levels (above approx. 35bB(A) have been associated with REM disturbances. There is also the accumulation of CO_2 or fine particles (PM2.5) in poorly ventilated bedrooms, which can contribute to more frequent awakenings and fragmented sleep. (Yasmeen et al., 2025).

A systematic review by Batool-Anwar and Quan (2024) showed that in many countries, racial/ethnic minorities and people of low socio-economic status have shorter sleep durations and poorer sleep quality than better-off populations individuals with low socio-economic status were 1.62 times more likely to sleep less than recommended. In a context of high-income inequality, social and environmental conditions (housing, commuting and exposure to urban nuisances) influence sleep duration and latency. (Lok et al., 2025).

3. Interactions between obesity and sleep disorders

3.1. A bidirectional relationship

3.1.1. Sleep disorders promote weight gain

Sleep disorders are now recognized as independent factors contributing to the development of overweight and obesity. Among these disorders, the restriction of sleep time, specifically less than 6 hours per night, is associated with an increased risk of obesity and metabolic syndrome. This lack of sleep disrupts the regulation of energy and glucose metabolism, reducing enerrgy expenditure and promoting fat storage. Sleeping less than 6 hours a night increases the likelihood of developing insulin resistance and weight gain. In fact, short or fragmented sleep disrupts several physiological processes. It alters the regulation of blood sugar and blood pressure, while modifying appetite hormones. Leptin, the satiety hormone, decreases, while ghrelin, the hunger-stimulating hormone, increases, which increases appetite and encourages excessive calorie consumption.

At the same time, sleep deprivation or poor sleep quality activates inflammatory pathways and promotes chronic low-grade inflammation, considered a central mechanism linking sleep disorders to metabolic syndrome and obesity. This chronic sleep deprivation stimulates the hypothalamic-pituitary-adrenal (HPA) axis, increasing the production of cortisol, a stress hormone that promotes the storage of visceral fat. (Direksunthorn, 2025).

In addition to sleep deprivation, we have sleep fragmentation and repeated micro-awakenings, in particular caused by OSA, leading to marked daytime fatigue and sleepiness. This can lead to a lack of motivation for physical activity, and therefore a reduction in daily energy expenditure. This decrease in activity contributes to a positive energy imbalance, in which caloric intake exceeds expenditure, leading to a progressive accumulation of body fat. (Figorilli et al., 2025).

Thus, sleep disorders, whether they involve restriction, fragmentation or poor quality of rest, exert a direct influence on hormonal, metabolic and behavioral regulation, contributing to weight gain.

3.1.2. Obesity aggravates sleep disorders

Obesity exerts profound effects on the body through metabolic, neuroendocrine and autonomic mechanisms. These physiological alterations contribute to an increase in the frequency and severity of sleep disorders, particularly OSA. (Figorilli et al., 2025).
Indeed, excess weight is one of the major risk factors for OSA: 60% to 90% of OSA patients are obese. (Noyed & DeBanto, 2025).
Anatomically speaking, the accumulation of adipose tissue in the neck and upper airways reduces their caliber and promotes respiratory obstruction during sleep. This obstruction is often aggravated by the nocturnal redistribution of fat to the cervical and thoracic regions, resulting in mechanical resistance to breathing. (Chopra, 2025).
The mechanisms observed above, notably activation of the HPA axis and increased cortisol in response to sleep deprivation, are also found in the opposite direction. Indeed, obesity is also accompanied by chronic stimulation of this axis and increased cortisol secretion, disrupting the regulation of sleep-wake cycles. (Figorilli et al., 2025).
In OHS, excess adipose tissue in the thorax, abdomen and upper airways increases the mechanical load on the respiratory system, reduces thoracic compliance and increases airway resistance. OHS is often associated with OSA and illustrates how overweight directly interferes with respiratory mechanics. (Ghimire et al., 2025).
Thus, obesity is not just a risk factor, but a genuine physiological amplifier of sleep disorders. Several studies indicate that even moderate weight loss improves sleep quality and reduces the severity of OSA, confirming the interaction between obesity and sleep disorders. (Chopra, 2025). (Noyed & DeBanto, 2025).

3.2. Pathophysiological mechanisms

3.2.1. Hormonal imbalances (leptin, ghrelin, cortisol, melatonin)

Sleep disorders profoundly disrupt hormonal regulation, affecting several essential endocrine axes. Sleep deprivation, sleep fragmentation or the disorganization of circadian rhythms caused by sleep disorders lead to increased activation of the HPA axis, resulting in higher levels of cortisol. This activation is a central process and explains how sleep deprivation or poor sleep quality disrupts sugar (glucose) metabolism, reduces the body's ability to respond to insulin, and promotes visceral fat storage. (Jiao et al., 2025).

Another major hormonal mechanism concerns appetite hormones. Sleep deprivation reduces levels of the satiety hormone leptin and increases levels of the hunger-stimulating hormone ghrelin. These hormonal changes promote increased food intake, often of the hyperphagia type, and contribute to weight gain. These hormonal effects depend not only on the number of hours of sleep, but also on the quality of sleep, i.e. whether it is deep, continuous and well-structured. They operate via hypothalamic circuits integrating leptin, ghrelin, orexin and insulin. (Liu et al., 2022).
Sleep disorders also affect melatonin secretion. This hormone, secreted by the pineal gland according to a circadian rhythm, regulates the sleep-wake cycle and plays a major role in energy metabolism, adipogenesis, thermogenesis of brown adipose tissue and lipolysis. Its decrease, often linked to circadian desynchronization or light exposure, therefore translates into increased fat accumulation, altered adipose activity and increased adipose tissue inflammation - many factors favoring obesity. (Ratwani et al., 2025). Circadian rhythms are generally coordinated when melatonin levels rise and cortisol levels fall, and reciprocally. (Miller, 2023).

On a mechanistic level, melatonin also participates in the temporal organization of metabolic processes by modulating insulin secretion and action, stimulating GLUT-4 translocation, and promoting the browning of white adipose tissue. A reduction in melatonin secretion is accompanied by insulin resistance, glucose intolerance, and

metabolic desynchronization, which can be partially corrected by exogenous supplementation. (Cipolla-Neto et al., 2014).

These disturbances are part of the overall impairment of the hypothalamic-pituitary axis, where the hypothalamus, pituitary gland, pineal gland, and peripheral glands (adrenal, thyroid, and gonads) interact to regulate the secretion of cortisol, thyroid hormones, melatonin, and sex hormones, as illustrated in the diagram below. gonads) interact to regulate the secretion of cortisol, thyroid hormones, melatonin, and sex hormones, as illustrated in Figure 7.

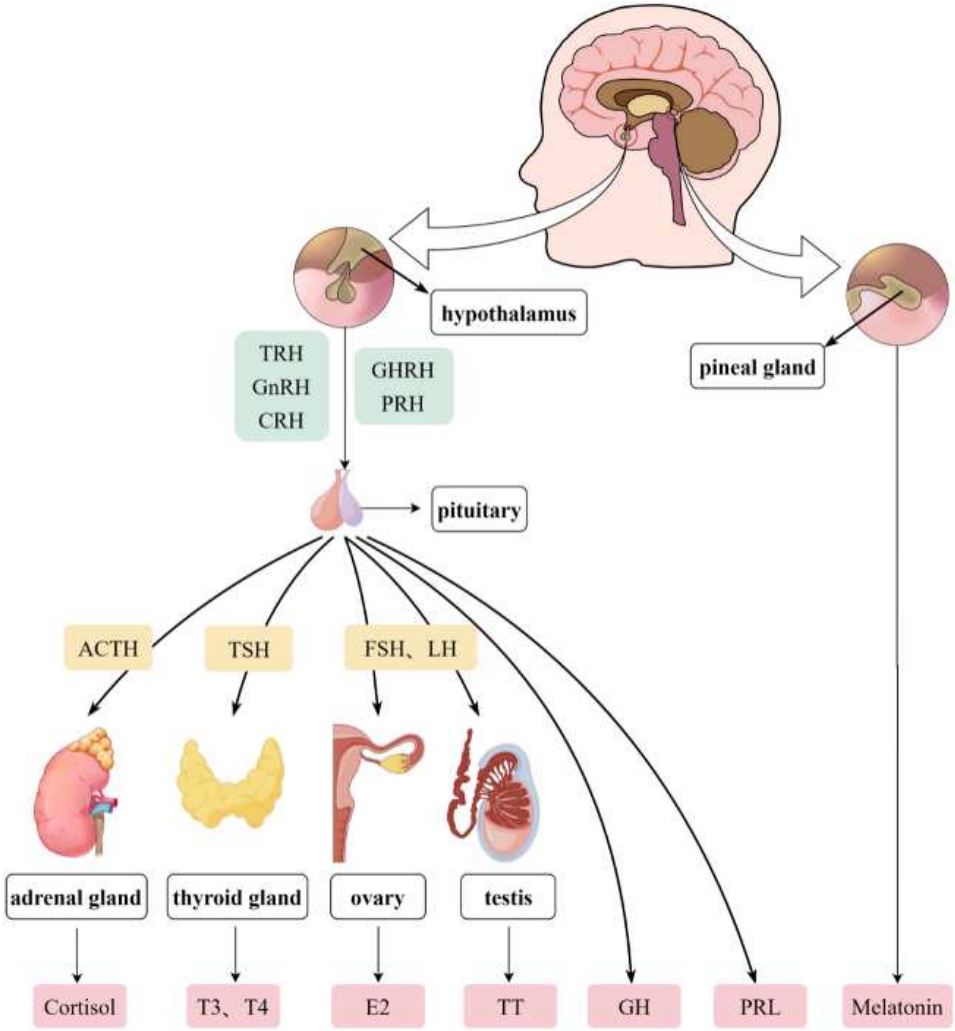

Figure 7 - Secretion and release of hormones related to sleep in the human body. (Source: Diabetol Metab Syndr, 2025)

Overall, hormonal imbalances due to sleep disturbances take several forms: metabolic stress via the HPA axis and cortisol, appetite regulation via leptin and ghrelin, and circadian regulation via melatonin.

3.2.2 Subclinical inflammation and insulin resistance

Sleep disorders or obesity induce chronic low-grade inflammation (subclinical inflammation), which plays a central role in the onset of insulin resistance. (Jiao et al., 2025). This inflammation is characterized by elevated systemic markers such as C-reactive protein (CRP), interkeulin-6 (IL-6) and TNF-α (Direksunthorn, 2025).
A study of obese children showed that those with sleep disorders had significantly higher levels of CRP and HOMA-IR (Homeostasis Model Assessment of Insulin Resistance). This results in increased inflammation and insulin resistance. This inflammation could form a pathophysiological bridge linking impaired sleep, obesity and early metabolic derangements. (Konuksever & Karakaya, 2023).

Moreover, sleep deprivation promotes activation of the sympathetic nervous system and the HPA axis, inducing increased cortisol secretion and stimulating the production of pro-inflammatory cytokines. (Direksunthorn, 2025).
These cytokines disrupt insulin signaling in peripheral tissues and promote visceral fat storage, aggravating insulin resistance. (Jiao et al., 2025). Obesity itself sustains this inflammation: the adipose tissue of obese people secretes more CRP and cytokines (IL-6, TNF-α), creating a vicious circle in which inflammation, sleep disorders and insulin resistance are self-reinforcing. (Figorilli et al., 2025).

Thus, the combination of impaired sleep and excess body fat results in persistent immune activation that disrupts glucose regulation and contributes to the progression of metabolic syndrome. (Direksunthorn, 2025). (Jiao et al., 2025). (Figorilli et al., 2025).

3.2.3. Circadian desynchronization and metabolism

Circadian desynchronization corresponds to a disruption between the central biological clock, located in the SCN of the hypothalamus, and the peripheral clocks present in

metabolic tissues such as the liver, pancreas or adipose tissue. This disruption is frequently caused by sleep disorders, nocturnal exposure to light, night work or eating at irregular hours. (Begemann et al., 2025).

As illustrated in Figure 8, the central clock located in the suprachiasmatic nucleus (SCN) of the hypothalamus receives light information from the environment and synchronizes all peripheral clocks, a process that is profoundly disrupted in cases of circadian desynchronization.

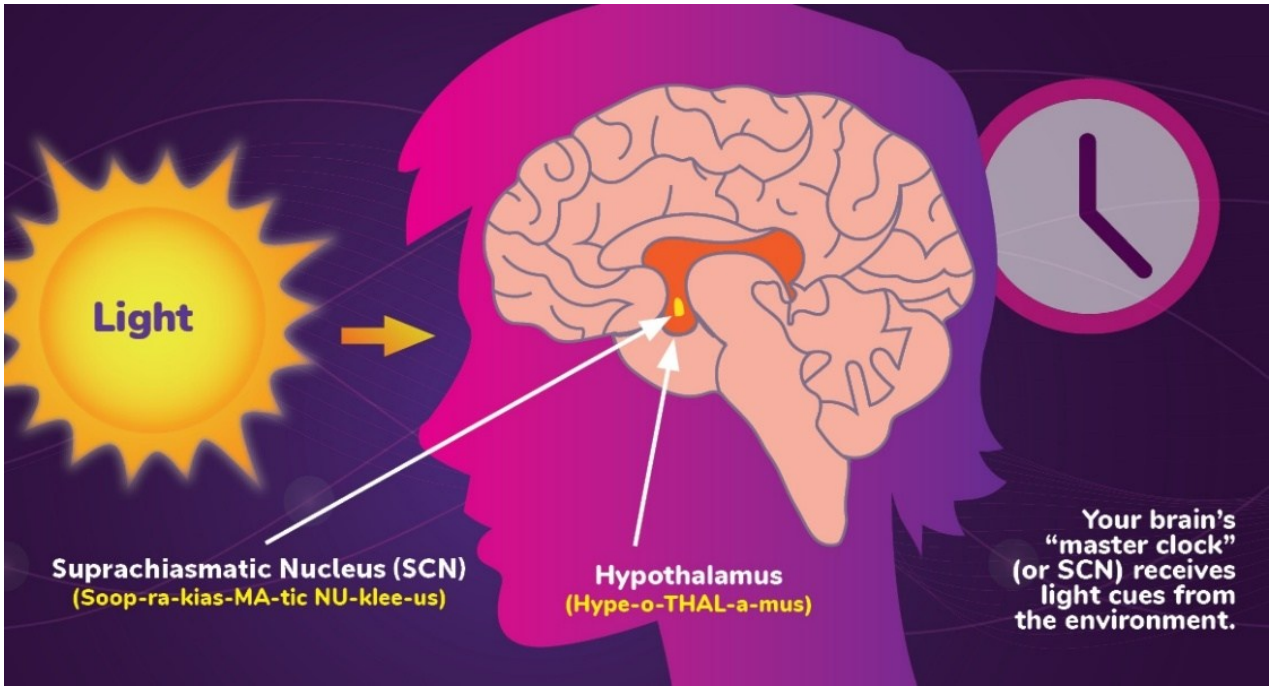

Figure 8 - Circadian Rhythms and SCN. (Source: National Institute of General Medical Sciences)

This temporal disorganization alters the hormonal signals that punctuate energy metabolism. The cyclical secretions of melatonin, cortisol, insulin and leptin, which normally adjust to the sleep-wake cycle, become desynchronized. This disrupts the mechanisms regulating glycemia, lipolysis and thermogenesis. (Begemann et al., 2025) (Chaput et al., 2022).

Circadian desynchronization is the key point where several pathological mechanisms come together and feed-off each other. It links sleep, hormones and metabolism. This disorganizes hormone signaling, promotes inefficient glucose utilization and triggers excessive energy storage. Restoring circadian rhythms is therefore essential to prevent insulin resistance and obesity-related metabolic disorders.

(Begemann et al., 2025) (Direksunthorn, 2025) (Chaput et al., 2022).

3.2.4. Disruption of appetite regulation and eating behavior

Sleep disorders profoundly disrupt the mechanisms regulating appetite and eating behavior. They can increase ghrelin and decrease leptin, thus encouraging excessive food intake. (Muszyński & Ulewicz, 2025).

They can also increase cortisol and thus promote the accumulation of visceral fat. These altered neuroendocrine signals will disrupt neural circuits via the dopaminergic reward pathway, amplifying the attraction for high-calorie, sugary foods, and impulsive eating behaviors. (Jiao et al., 2025). (Muszyński & Ulewicz, 2025). These behaviors include the nocturnal snacking described in the « Night Eating Syndrome ». (Pacheco, D., & Singh, A. 2025). This behavior is reinforced by the nocturnal decrease in melatonin observed in cases of disturbed sleep. This hormone interferes with metabolic signals and promotes nocturnal hunger. (Muszyński & Ulewicz, 2025).

Finally, there is evidence that disturbed breathing during sleep in obese individuals exacerbates metabolic dysregulation. Increased inflammatory mediators and leptin resistance observed in sleep apnea contribute to increased appetite and difficulty in controlling food intake. (Griffin et al., 2025).

3.3. Clinical and public health consequences

3.3.1. Vicious circle

Obesity and sleep disorders form a two-way vicious circle, in which each condition reinforces the other. On the one hand, excess weight promotes the onset of sleep disorders, notably OSA, through mechanical and inflammatory mechanisms. On the other, insufficient or fragmented sleep disrupts hormonal regulation of appetite, energy metabolism and glycemic control, facilitating weight gain and progression to obesity. (Figorilli et al., 2025). Induced fatigue also reduces motivation for physical activity, contributing to energy imbalance and the risk of weight gain. (Huang et al., 2024). This interaction contributes to a worsening of cardiometabolic complications, including type 2 diabetes, hypertension and cardiovascular disease. (Figorilli et al., 2025).

Beyond the individual consequences, this dynamic contributes to a significant public health burden, linked to increased healthcare costs, reduced quality of life, and a loss of professional productivity. (Boers et al., 2025).

3.3.2 Impact on quality of life

The association between obesity and sleep disorders exerts a cumulative negative impact on quality of life, encompassing both physical and psychological dimensions. (Figorilli et al. 2025). In addition, a survey was carried out among overweight/obese healthcare professionals, as they constitute a population at high risk of sleep disorders due to their irregular schedules, professional stress and fatigue associated with clinical work, despite their theoretical knowledge of health-promoting behaviors. The study revealed a significantly higher prevalence of poor sleep quality: 36.1% in overweight/obese people versus 22.5% in normal weights. (Huang et al., 2024).

This association has a cumulative effect on well-being and quality of life. Although OSA and OHS present distinct respiratory profiles, their subjective consequences (fatigue, altered sleep and mood disorders) remain comparable and unfavorable.
It reinforces the need for multidisciplinary care combining weight control, sleep treatment such as Continuous Positive Airway Pressure (CPAP) and Non-Invasive Ventilation (NIV). (Georgakopoulou et al., 2025).

Furthermore, in obese patients with OSA, the combination of excess weight and sleep-disordered breathing (SDB) affects overall quality of life, with an impact on physical and psychosocial well-being. Lifestyle improvements and weight loss can reduce the severity of OSA and improve health-related quality of life. However, interventions such as lifestyle modification, exercise or behavioral sleep therapy improve not only OSA symptoms, but also patients' overall health and well-being. (Wilson & Akbarshahi, 2024).

Finally, in obese people, the combination of unfavorable eating habits and impaired sleep contributes to a deterioration in psychological well-being, reflected in increased

fatigue, mood disorders and reduced body satisfaction, impacting overall quality of life. (Wang et al., 2024).

4. Therapeutic perspectives

4.1. Non-pharmacological approaches

4.1.1. Nutrition and healthy living

Sleep is part of a global strategy to promote health and cannot be dissociated from dietary and lifestyle habits. The review by R. Liu et al, 2024, shows that in overweight or obese children and adolescents, interventions including a sleep component did not lead to a significant reduction in BMI, except in a single low-bias study. This indicates that sleep improvement alone is not sufficient to induce a lasting weight effect without concomitant dietary and lifestyle modifications. (R. Liu et al., 2024).

Thus, nutritional hygiene needs to be adjusted in parallel with sleep hygiene to potentiate metabolic benefits. Diet quality modulates the impact of sleep deprivation on weight gain, particularly in young people, indicating that diet can mitigate the adverse metabolic effects associated with insufficient sleep. (Lin et al., 2025). A diet rich in nutrients co-factors of melatonin synthesis helps to optimize sleep-wake regulation and associated metabolic signals. Dietary sources of B vitamins, magnesium, iron, zinc, calcium and vitamin C support the conversion of tryptophan to serotonin and then to melatonin. As illustrated in Figure 9, these micronutrients are involved in various stages of the metabolic pathway from tryptophan to serotonin and then to melatonin, highlighting the importance of adequate dietary intake to support the synthesis of this sleep hormone. For example, tuna, lentils and avocados are rich in B vitamins, while salmon, wholegrain cereals and green leafy vegetables provide magnesium. Broccoli and dairy products are sources of calcium, while peppers or oranges provide vitamin C. (Table 2). In addition, sour cherries, rich in melatonin, have been shown to have beneficial effects on sleep quality. On the other hand, certain foods and substances can disrupt sleep, such as caffeine and tea, which block adenosine receptors and promote wakefulness, justifying limiting sleep at the end of the day. (Miller, 2023).

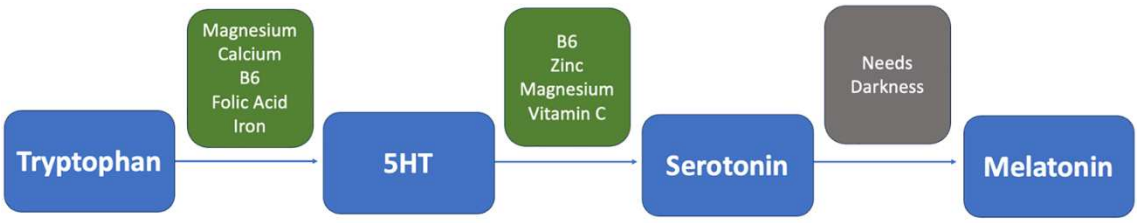

Figure 9 - Melatonin synthesis from tryptophan: dietary cofactors can influence daytime levels. (Source: Cambridge University Press, Miller, 2023)

Table 2 - Nutrients and their potential dietary sources. (Source : Cambridge University Press, Miller, 2023)

Nutrient	Examples of potential dietary sources
Magnesium	Whole Grains, Salmon, Green Leafy Vegetables
Calcium	Broccoli, Beans, Dairy
B Vitamins	Tuna, Lentils, Broccoli, Avocados
Folic Acid	Dark Green Leafy Vegetables, Avocado, Lentils, Nuts
Iron	Dark Chocolate, Lentils, Beef, Chickpeas
Zinc	Spinach, Shellfish, Nuts, Seeds
Vitamin C	Bell Peppers, Kiwifruit, Oranges, Broccoli, Tomatoes

It's also advisable to avoid heavy, spicy or high-fat meals, full-fat dairy products, acidic food and alcohol in the evening. (Fountain & Singh, 2025).
Limiting food intake to a defined time window during the day, known as Time-Restricted Eating (TRE), and concluding meals several hours before bedtime, appears to be beneficial for metabolic regulation and sleep quality. (Benedict & Heilbronn, 2025). However, while TRE may promote weight loss and improved circadian synchronization, these positive effects could be partially offset by increased nighttime hunger, which may disrupt sleep continuity. (Benedict & Heilbronn, 2025).

A study on young women showed that a longer interval between the last meal and the middle of the sleep period is associated with lower adiposity, underlining the importance of dinner timing in metabolic regulation and maintaining a healthy weight. (Zerón-Rugerio et al., 2020). However, neither the optimal duration of the feeding window nor the precise time before bedtime has yet been standardized. (Benedict & Heilbronn, 2025). (Zerón-Rugerio et al., 2020).

4.1.2. Sleep hygiene and circadian regularity

A stable circadian rhythm is based on the synchronization of daily behaviors, i.e. bedtime, wake-up time, mealtimes, physical activity and exposure to light, with natural light-dark cycles. This circadian coherence contributes directly to the regulation of metabolism, blood sugar and appetite hormones. (Knutson et al., 2025). The biological clock interacts closely with endocrine systems, reinforcing the idea that circadian desynchronization is a central factor in metabolic dysregulation. (Begemann et al., 2025).

Getting enough sleep on a regular basis is the foundation of good sleep hygiene. (Suni & Rehman, 2025).

Thus, several measures can support circadian regularity:

- Maintain consistent wake-up and bedtimes (Knutson et al., 2025)
- Encourage exposure to morning light to reinforce circadian training (Begemann et al., 2025)
- Avoid exposure to screens and bright light sources in the evening to prevent melatonin inhibition (Begemann et al., 2025)
- Limit late-night food intake and stimulants such as caffeine. (Benedict & Heilbronn, 2025) (Miller, 2023)

These behavioral changes improve sleep quality and efficiency and contribute to better metabolic regulation. (Knutson et al., 2025). (R. Liu et al., 2024).

4.1.3. Physical activity

Data from the systematic review by R. Liu et al. indicate that several included studies reported improved physical activity after intervention, particularly when objective tools such as accelerometry were used to measure physical activity levels, intensity, duration of movement and time spent sitting or inactive. However, assessment methods varied from study to study, sometimes making it difficult to interpret the results. In some studies, a significant increase in moderate to vigorous physical activity time was

observed following intervention programs, underlining the role of structured programs in improving active behavior among young people. (R. Liu et al., 2024).
Supervised exercise is also associated with reductions in BMI, waist circumference and body fat, as well as increases in lean body mass. Prolonged programs (>24 weeks), comprising 2-3 weekly sessions of moderate to sustained intensity, are effective. The addition of exercises combining endurance and resistance seems to produce greater effects on metabolic and body parameters than programs focusing solely on aerobics. (Li et al., 2024).

4.1.4. Cognitive behavioral therapy for insomnia (CBT-I)

CBT-I is the non-pharmacological reference treatment for chronic insomnia (Suni & Rehman, 2025), including in people suffering from obesity or associated metabolic disorders. CBT-I combines behavioral techniques (restriction of time spent in bed, stimulus control, sleep education) and cognitive work on beliefs and attitudes towards sleep, often coupled with relaxation strategies and healthy lifestyle measures. (Savin et al., 2022).

A recent study in overweight or obese adults suffering from insomnia showed that CBT-I significantly improved perceived sleep quality and increased self-reported sleep duration, while reducing daytime sleepiness. The intervention also promotes better control of food cravings and a reduction in cravings for sweet and salty products, suggesting an indirect role for sleep in regulating eating behavior. (Merchant et al., 2025).

A recent meta-analysis confirms that CBT-I-based interventions contribute to lasting behavioral changes, particularly in weight management and maintenance of health habits. Although the impact on certain metabolic parameters such as glycemia remains less constant, this work underlines the potential of cognitive-behavioral approaches as complementary tools in the comprehensive management of obesity. (Mesarič et al., 2023).

In this way, CBT-I not only improves sleep, it also contributes to a broader behavioral dynamic that promotes weight control and overall well-being.

4.1.5. Continuous Positive Airway Pressure

CPAP (Continuous Positive Airway Pressure) is the non-pharmacological therapeutic reference for the treatment of OSA, often associated with obesity. (Figorilli et al., 2025). This device keeps the upper airway open during sleep by applying continuous positive air pressure, (Pharmacy Magazine, 2024) thus preventing the obstructive episodes that cause respiratory interruptions, hypoxia and sleep fragmentation. (Figorilli et al., 2025).

Regular use of CPAP improves sleep quality, reduces daytime sleepiness, and significantly reduces obstructive respiratory events. It also helps reduce the cardiovascular and metabolic risk associated with OSA. (Figorilli et al., 2025). However, its efficacy is highly dependent on patient compliance, often limited by discomfort or side effects. (Zota et al., 2023).

In obese patients, CPAP is recommended as first-line treatment for moderate to severe OSA (Figorilli et al., 2025), and must be combined with weight reduction interventions to maximize lasting clinical benefits. (Nunez, 2025).

In short, CPAP is a central pillar of non-pharmacological treatment for obesity-related sleep-disordered breathing, acting as an effective means of improving sleep and overall health. (Figorilli et al., 2025) (Pharmacy Magazine, 2024).

CPAP delivers a continuous flow of air through a nasal or full-face mask connected to a machine, preventing the upper airway from closing during sleep and reducing apneas. (Figure 10).

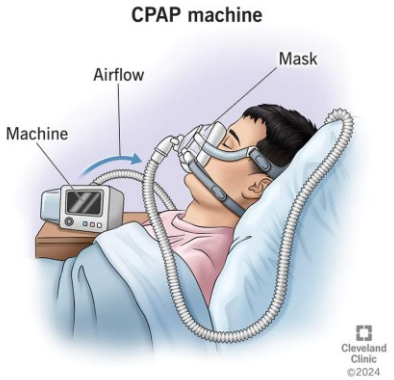

Figure 10 - A CPAP (continuous positive airway pressure) machine helps treat sleep apnea. (Source: (Cleveland Clinic Medical, 2024)

4.1.6. Non-Invasive Ventilation

In OHS, NIV (Non-Invasive Ventilation) is recommended when the ventilatory disorder is mainly the result of central hypoventilation, while CPAP is mainly indicated in cases of associated severe obstructive apnea. (Masa et al., 2016) (Huertas et al., 2025).
NIV delivers differentiated positive pressures during inspiration and expiration, increasing tidal volume and helping to eliminate carbon dioxide, thus correcting hypoventilation. (Masa et al., 2016). It significantly improves daytime PaCO2, sleepiness, polysomnographic parameters and certain aspects of quality of life, compared with hygienic-dietary interventions alone. These effects are explained by an improvement in alveolar ventilation and better elimination of carbon dioxide. (Huertas et al., 2025). NIV reduces the respiratory load on ventilatory muscles, promotes alveolar recruitment, and helps restore nocturnal ventilation and oxygenation, thus improving the overall health of severely affected obese patients. (Masa et al., 2016).

4.2. Pharmacological approaches

4.2.1. GLP-1 receptor agonists

Several therapeutic classes have been shown to be effective in reducing weight and improving metabolic parameters by acting on appetite, energy expenditure, or nutrient absorption, which can significantly improve sleep quality and reduce symptoms of sleep disorders such as OSA.
Recent treatments are mainly based on GLP-1 (glucagon-like peptide 1) agonists, a hormone that promotes satiety, reduces food intake, and improves blood sugar regulation. (Roomy et al., 2024). These treatments are recommended as a supplement to a low-calorie diet and regular physical activity for people who are obese or overweight with comorbidities. (Vidal, 2025).

Liraglutide

This treatment leads to a significant reduction in fat mass and an improvement in lipid and glycemic profiles, confirming its central role in the pharmacological management of obesity. (S. K. Ahmed & Mohammed, 2025).
A marked reduction in visceral adipose tissue and an improvement in cardiometabolic profile, particularly beneficial in individuals at increased risk of diabetes or metabolic syndrome. (Schmidt et al., 2025).

Mechanistically, liraglutide mimics the action of the endogenous hormone GLP-1. It acts on pancreatic β cells by stimulating glucose-dependent insulin secretion while inhibiting glucagon (GCG) secretion. This dual effect promotes better glycemic control without causing hypoglycemia. At the same time, it acts centrally, particularly on the hypothalamic satiety centers, leading to decreased appetite and reduced caloric intake. This combination of peripheral and central effects explains the sustained weight loss observed in patients. (Cerrillo & Parmar, 2024).

Administered subcutaneously once daily, liraglutide has a bioavailability of approximately 55% and a half-life of 13 hours, allowing for a single injection per day. For the management of type 2 diabetes, the recommended starting dose is 0.6 mg/day, increased gradually to 1.2–1.8 mg/day depending on glycemic response. For weight loss, the target dose is 3 mg/day, reached in weekly increments of 0.6 mg. (Cerrillo & Parmar, 2024).

The most common side effects are gastrointestinal (nausea, diarrhea, constipation, dyspepsia), generally transient and related to the titration phase. More rare effects, such as acute pancreatitis, gallbladder disorders, or increased heart rate, have been reported. (Cerrillo & Parmar, 2024).

All of these data confirm that liraglutide, through its ability to reduce visceral fat mass, improve insulin sensitivity, and act on central appetite regulation, is a standard treatment for obesity and type 2 diabetes, with an overall favorable safety profile. (Ahmed et al.,2025b) (Cerrillo & Parmar, 2024) (Schmidt et al., 2025).

Liraglutide is administered by daily injection, while semaglutide is administered by weekly injection, which may promote adherence to treatment. (Cshp_Editeur, 2025).

Sémaglutide

This peptide is a physiological incretin that stimulates glucose-dependent insulin secretion, inhibits glucagon release, slows gastric emptying, and acts on the hypothalamic satiety centers. These combined effects lead to reduced caloric intake and significant weight loss, justifying its use in the treatment of type 2 diabetes and obesity. (Ojeniran et al., 2021) (VIDAL, 2019).

Therapeutically, semaglutide is available in injectable and oral forms. In injectable form, it is administered once a week subcutaneously, with gradual titration: starting at 0.25 mg/week, increased to 0.5 mg, then possibly to 1 mg/week depending on tolerance and clinical response.
In oral form, it is taken once daily, on an empty stomach, in doses of 3 mg, 7 mg, or 14 mg, depending on the phase of treatment. (VIDAL, 2025).
The main adverse effects reported are digestive (nausea, vomiting, diarrhea), often transient. These effects result from slowed gastric emptying and central action on satiety. (Ojeniran et al., 2021).
However, a recent pharmacovigilance signal led the European Medicines Agency (EMA) to initiate a review of medicines containing this active substance in January 2025, following concerns about a potential increased risk of non-arteritic anterior ischemic optic neuropathy (NAION). (PRAC, 2025).

In obese patients, semaglutide remains an effective therapeutic option for weight reduction and metabolic profile improvement, with indirect benefits on sleep quality through reduced fat mass and risk of obstructive apnea. However, clinical monitoring remains essential, particularly in terms of vision and vascular health, pending the EMA's conclusions. (Ojeniran et al., 2021) (VIDAL, 2019).

According to recent studies, semaglutide leads to greater weight loss on average than liraglutide, with reductions in body mass of up to 15% after 68 weeks of treatment, compared with around 6-8% for liraglutide. (Dummy, 2025).

Orforglipron

Orforglipron (LY3502970) is a new generation of GLP-1 receptor agonists, distinguished by its non-peptide structure and daily oral administration route. (Medical Lilly, 2025). Unlike injectable peptide analogues such as semaglutide or liraglutide, orforglipron does not require any dietary or fluid restrictions, which facilitates therapeutic compliance. (Miller & Parveen, 2025). It acts by binding to the same receptor site as endogenous GLP-1, stimulating the G-protein/cAMP pathway while limiting the activation of β-arrestin, which is responsible for receptor desensitization. This agonist bias promotes prolonged physiological signaling and improved metabolic regulation. (Medical Lilly, 2025). Activation of the GLP-1 receptor by orforglipron stimulates glucose-dependent insulin secretion, inhibits glucagon, slows gastric emptying, and reduces appetite by modulating hypothalamic satiety signals. (Medical Lilly, 2025). (Pratt et al., 2023). These mechanisms result in improved glycemic control and reduced body weight. (Pratt et al., 2023).

The clinical and pharmacodynamic results reported by Pratt et al. (2023) and Miller & Parveen (2025) confirm that orforglipron is an oral GLP-1 receptor agonist demonstrating significant metabolic efficacy, both in terms of glycemic control and weight reduction, with a tolerance profile comparable to that of injectable analogues. Its simple oral administration and non-peptide mechanism make it a promising therapeutic option for the management of type 2 diabetes and obesity, likely to improve treatment adherence and reduce associated metabolic complications, particularly those related to sleep disorders in obese patients.
Pharmacokinetics showed a half-life of between 28 and 49 hours, compatible with once-daily dosing, and oral bioavailability of 20 to 40%, which is higher than that of oral semaglutide. (Pratt et al., 2023) (Miller & Parveen, 2025)

Although current trials have not specifically evaluated sleep quality, they have demonstrated significant metabolic effects, particularly a reduction in body weight and improved glycemic control (Pratt et al., 2023; Miller & Parveen, 2025). The observed decrease in waist circumference suggests a reduction in visceral adipose tissue. (Miller & Parveen, 2025).

Orforglipron acts through a mechanism involving the stimulation of glucose-dependent insulin secretion and the inhibition of glucagon. (Medical Lilly, 2025). According to broader scientific literature, these metabolic results could have indirect beneficial effects on certain comorbidities associated with obesity, particularly sleep-disordered breathing.

Table 3 compares the main GLP-1 agonists currently in use or under development, detailing for each molecule the class, route of administration, frequency of use, and main indication.

Table 3 - Main GLP-1 agonists in use or under development (Source : original)

Molecule	Class	Route	Frequency	Primary indication
Liraglutide	Agonist GLP-1	Subcutaneous	1 injection per day	Type 2 diabetes, obesity
Semaglutide	Agonist GLP-1	Subcutaneous/oral	1 per week (injectable) / 1 per day (oral)	Type 2 diabetes, obesity
Orforglipron	Agonist GLP-1 (non-peptide)	Oral	1 per day	Obesity (in development)

Recent data also support the hypothesis that GLP-1 agonists could improve OSA not only through weight loss, but also via potential direct effects on the upper airway and systemic inflammation. However, these results must be interpreted with caution: the majority of current evidence comes from studies with tirzepatide, while data on semaglutide remain more limited and of heterogeneous quality. These treatments should not be considered as an alternative to OSA-specific therapies, particularly in obese patients for whom weight loss is a major therapeutic lever. (Mifsrud et al., 2025).
These results suggest that GLP-1 agonists could be a complementary therapeutic strategy in the management of obesity-related OSA syndrome, enhancing the benefits of weight loss when hygienic-dietary and behavioral approaches are not sufficient.

However, their use must remain individualized and take account of the patient's profile, as long-term data on their direct effect on sleep are still limited. (Roomy et al., 2024).

4.2.2. Dual agonists

Dual agonists represent a new generation of metabolic therapeutics that simultaneously target several intestinal receptors, in particular GLP-1 and glucose-dependent insulinotropic polypeptide (GIP) receptors. This dual action results in significantly greater weight loss and more marked improvement in metabolic disorders than GLP-1 agonists alone. (Roomy et al., 2024).

Tirzépatide

Tirzepatide is the main representative of dual agonists. Tirzepatide is a combined GIP and GLP-1 agonist (Paitraud, 2024). It is indicated as a complement to a hypocaloric diet and increased physical activity for weight control. (EMA, 2021).
Its action is based on the synergistic dual activation of GIP and glucagon-like peptide-1 (GLP-1) receptors, enabling coordinated improvement in energy metabolism. This simultaneous interaction acts on several metabolically active organs, promoting increased glucose-dependent insulin secretion, inhibition of glucagon release, and slowing of gastric emptying, contributing to feelings of satiety and reduced caloric intake.This joint modulation of incretin pathways results in enhanced glycemic control and greater weight loss than that achieved with GLP-1 agonists alone, thanks to the potentiation of the insulinotropic signal and improved peripheral glucose utilization. In addition, the prolonged half-life of tirzepatide, estimated at approximately five days, allows for weekly injection, ensuring the stability of its metabolic effects. (Roomy et al., 2024).

Beyond its metabolic effects, tirzepatide is attracting growing interest in the treatment of obesity-related sleep disorders, notably OSA. Tirzepatide has been identified as the first drug therapy to demonstrate a significant and sustained reduction in the severity of OSA, independent of weight loss. There was a marked reduction in the apnea-hypopnea index, suggesting direct beneficial mechanisms on the upper airways or systemic inflammation. (Aquinde, 2024). These findings were further supported by the

SURMOUNT-OSA clinical trials, which confirmed the efficacy of tirzepatide in significantly reducing OSA severity in obese individuals. (Figorilli et al., 2025).

These results reinforce the idea that dual agonists could play a major role in the management of obese patients with OSA syndrome, complementing hygienic-dietary interventions, and standard treatments such as CPAP. However, further studies are needed to confirm their long-term efficacy, clarify their mechanisms of action on sleep, and identify the most responsive patient profiles. (Roomy et al., 2024). (Aquinde, 2024).

Survodutide

Survodutide is another emerging representative of the dual agonist class. It acts as a combined agonist of GLP-1 (glucagon-like peptide-1) and glucagon receptors, aiming to potentiate beneficial metabolic effects while promoting significant body weight reduction. This approach of hormonal co-activation allows for simultaneous improvement in glycemic control and lipid metabolism. The article highlights that joint stimulation of GLP-1 and glucagon receptors could increase energy expenditure while decreasing appetite, contributing to more pronounced weight loss than that observed with GLP-1 agonists alone. Survodutide is currently undergoing clinical trials to evaluate its efficacy and safety in the management of obesity and associated metabolic disorders. (Roomy et al., 2024).

Survodutide is distinguished by its peptide structure derived from human glucagon, featuring amino acid modifications designed to enhance its stability and prolong its biological half-life. These adjustments enable it to resist enzymatic degradation and ensure sustained activity on both target receptors. The article also states that the molecule has a slightly higher affinity for the GLP-1 receptor than for the glucagon receptor, promoting an optimal balance between hypoglycemic effects and stimulation of hepatic lipolysis. (Roux et al., 2025)
On a mechanistic level, Roux et al. (2025) indicate that survodutide activates the production of intracellular cAMP, a key mediator of the GLP-1R and glucagonR pathways, with effective concentrations (EC_{50}) of approximately 1 nM for GLP-1R and 8 nM for glucagonR, suggesting a functional preference for GLP-1. This dual action

results in stimulation of hepatic energy metabolism, increased thermogenesis, and reduced food intake, while maintaining stable glycemic control.
The adverse effects observed are mainly gastrointestinal, similar to those of GLP-1 agonists, but generally moderate and reversible with gradual titration. (Roux et al., 2025).

The SYNCHRONIZE-1 protocol is a study designed to determine whether survo-dutive therapy can achieve significant, sustainable, and safe weight loss in obese adults without type 2 diabetes, while monitoring the associated metabolic and cardiovascular effects. This protocol is scheduled to last a total of 76 weeks and includes assessment of cardiovascular safety, body composition, and hepatic fat content in order to evaluate the overall impact of treatment on the metabolic profile. (Roux et al., 2025).

Survodutide, like tirzepatide, represents a new generation of dual agonists capable of simultaneously targeting multiple metabolic pathways to optimize weight loss and improve glycemic control. (Roomy et al., 2024) (Roux et al., 2025). Its balanced pharmacological profile, combining appetite modulation with stimulation of energy expenditure, makes it a promising candidate for the management of obesity and its metabolic complications. However, long-term studies are still needed to confirm the durability of its effects, its cardiovascular safety, and its potential impact on other associated disorders, such as obesity-related sleep disorders. (Roux et al., 2025).

4.2.3. Triple agonists

Retatrutide

Retatrutide (LY3437943) is a synthetic peptide molecule with agonist activity on three receptors: GIP, GLP-1, and GCG. This peptide is coupled to a diacidic fatty acid group, which prolongs its action and allows for weekly administration. Compared to endogenous ligands, it shows a higher affinity for the GIP receptor (approximately 8.9 times higher), but a lower affinity for the GLP-1 and GCG receptors (decrease in potency of approximately 0.4 and 0.3 times, respectively). Its pharmacokinetic

characteristics are dose-proportional, with an estimated half-life of 6 days, allowing for weekly administration. (Jastreboff et al., 2023).

Weekly administration of retatrutide results in a decrease in body weight proportional to the dose administered. Published results indicate an average weight loss of between -8.7% and -24.2% after forty-eight weeks of treatment, with the highest values observed with doses of 8 mg and 12 mg. This decrease is accompanied by a high proportion of participants achieving clinically defined weight loss thresholds: between 64% and 100% of treated individuals lost at least 5% of their initial weight, 60% to 93% lost more than 10%, and up to 83% had a reduction of more than 15%. These observations reflect a marked dose-dependent effect of retatrutide on weight reduction. (Jastreboff et al., 2023).

The administration of retatrutide was accompanied by an overall improvement in cardiometabolic parameters. There was a decrease in systolic and diastolic blood pressure, as well as a reduction in glycated hemoglobin, fasting glucose and insulin concentrations, and plasma lipid levels, with the exception of high-density lipoprotein cholesterol (HDL). Among participants with prediabetes at baseline, 72% returned to normal blood glucose levels after forty-eight weeks of treatment. (Jastreboff et al., 2023).

With regard to tolerability, the most frequently observed adverse events were gastrointestinal in nature, including nausea, vomiting, diarrhea, and constipation. These events occurred mainly during the dose escalation phase, with their frequency and intensity related to the dose administered. They were mostly mild to moderate and less pronounced when the initial dose was 2 mg compared to 4 mg. A transient increase in heart rate was observed around week 24, followed by a gradual return to previous values. No severe hypoglycemia or neoplastic events were reported during the treatment period. (Jastreboff et al., 2023).

Weekly treatment with retatrutide for 48 weeks in obese adults is associated with a dose-dependent reduction in body weight, and these data support the continuation of clinical trials to confirm the efficacy and safety profile of this molecule. (Jastreboff et al., 2023).

4.2.4. Other obesity treatments

Orlistat

Orlistat is an FDA-approved anti-obesity drug belonging to the class of gastric and pancreatic lipase inhibitors. It acts locally in the gastrointestinal tract by reversibly blocking the hydrolysis of dietary triglycerides, thereby preventing the formation of free fatty acids and absorbable monoglycerides. (Bansal et al., 2024) (DrugBank, 2025). Through this enzyme inhibition, approximately 30% of ingested fats are not absorbed, contributing to a net calorie reduction and therefore weight loss. (Bansal et al., 2024).

The systemic bioavailability of orlistat is very low, which limits systemic effects and reduces the risk of cardiovascular or neurological side effects. The drug is mainly eliminated in the stool, unchanged, at a rate of 95–97%, and undergoes minimal intestinal metabolism. (DrugBank, 2025).

Clinical trials, notably the XENDOS study, demonstrated an average weight loss of approximately 5.6 kg after six months of combining orlistat with a low-calorie diet and physical activity, compared with 2.4 kg in the placebo group. These results were accompanied by an improvement in cardiometabolic profile, including a reduction in total cholesterol, low-density lipoprotein (LDL), waist circumference, and blood pressure. These positive metabolic effects indirectly contribute to better sleep regulation, as the reduction in visceral adiposity and systemic inflammation can alleviate certain sleep comorbidities such as obstructive apnea and excessive daytime sleepiness. (Bansal et al., 2024).

Orlistat should be administered at the recommended dose of 120 mg three times a day, during or within one hour after a meal containing fat. If the meal is fat-free, the dose may be omitted. (Bansal et al., 2024). Optimal treatment is based on an integrated approach combining a balanced low-calorie diet, physical activity, and nutritional monitoring. Daily supplementation with fat-soluble vitamins (A, D, E, K) is essential, as orlistat can reduce their intestinal absorption. (Bansal et al., 2024) (DrugBank, 2025).

From an interdisciplinary care perspective, Bansal et al. (2024) emphasize the central role of pharmacists and dietitians in monitoring effectiveness, preventing vitamin deficiencies, and providing therapeutic education. This collaborative approach promotes sustainable weight loss, which is essential for reducing obesity-related sleep disturbances (fragmentation, obstructive apnea, decreased sleep efficiency). (Bansal et al., 2024).

Thus, orlistat acts primarily as a complementary metabolic tool, improving lipid profile and body composition (Bansal et al., 2024), which can have indirect beneficial effects on sleep quality by mitigating hormonal dysregulation (insulin, leptin, cortisol) associated with excess weight.

It is recommended for certain individuals when oral administration is preferred or in cases where treatments acting on the central nervous system, such as naltrexone/bupropion, are contraindicated. (Roomy et al., 2024).

Naltrexone/Bupropion

The combination of naltrexone and bupropion is classified as a centrally acting anti-obesity treatment: it targets the hypothalamic satiety pathways and acts on the food reward circuits, making it particularly useful in patients with a marked behavioral component to their eating disorder. This treatment helps to limit overeating and compulsive eating, thereby contributing to weight control in patients with a marked behavioral component. (Roomy et al., 2024).

This combination works through a dual mechanism: naltrexone, an opioid receptor antagonist, modulates reward responses related to food intake, while bupropion, a dopamine and norepinephrine reuptake inhibitor, stimulates satiety centers. Their synergistic action promotes a reduction in appetite and the motivation to consume high-calorie foods, thereby supporting weight loss when combined with an appropriate lifestyle. (Thomas et al., 2023).

Randomized clinical trials have shown that this treatment, combined with lifestyle and dietary measures, results in an average weight loss of 4.5 to 6 kg after one year, which is greater than that achieved with placebo. Approximately 38 to 53% of patients achieve a reduction of at least 5% of their initial body weight, compared with 17 to 21% on placebo. (Thomas et al., 2023). The most common adverse effects are gastrointestinal, mainly nausea and constipation, and may lead to discontinuation of treatment in a minority of patients. The recommended dosage regimen is based on gradual titration up to 32 mg of naltrexone and 360 mg of bupropion per day in two doses. (NICE, 2017).

However, despite proven short-term effectiveness, the sustainability of weight loss and prevention of weight regain remain uncertain after treatment is discontinued. Furthermore, the NICE economic evaluation indicates that the cost-effectiveness ratio is considered too uncertain to justify reimbursement in the UK healthcare system, due to the high overall cost and potentially prolonged nature of treatment. For these reasons, the combination is not recommended for routine clinical use in the UK. (NICE, 2017).

Naltrexone–bupropion may indirectly contribute to improving metabolic parameters and nocturnal eating behavior, which are often involved in sleep disturbance. However, no specific studies have yet demonstrated a direct effect on sleep quality, warranting a cautious and individualized approach based on each patient's metabolic profile and tolerance. (NICE, 2017) (Thomas et al., 2023).

4.2.5. Medication/hormones for sleep disorders

Melatonin

Melatonin is the most extensively studied pharmacological option for sleep disorders associated with metabolic dysfunction. It contributes to the regulation of circadian rhythm and has the potential to improve sleep and support metabolic balance, notably by modulating energy metabolism and adipose tissue.
Moreover, the circadian alteration associated with obesity could make certain patients

less sensitive to endogenous melatonin secretion. However, the available syntheses insist on the need to define optimal doses and durations of use before recommending its systematic use. (Genario et al., 2020).

The physiological effects of melatonin are mediated by two specific membrane receptors, MT_1 et MT_2, belonging to the family of G protein-coupled receptors. These receptors are expressed in several areas of the brain, particularly in the SCN of the hypothalamus, which plays a key role in synchronizing circadian rhythms. Exogenous administration of melatonin reproduces this nocturnal signal and helps synchronize sleep-wake rhythms when they are disrupted. (Zisapel, 2018). Clinically, melatonin is a validated treatment option for circadian rhythm disorders, particularly jet lag and, to a lesser extent, shift work disorders (SWD).

In jet lag, several randomized controlled trials have shown that taking melatonin at bedtime reduces sleep latency, improves sleep quality, and alleviates daytime symptoms of circadian maladjustment.

Studies show that melatonin is effective at doses between 0.5 and 5 mg, administered in immediate-release (IR) form. A dose of 0.5 mg already has a noticeable effect on sleep and circadian adjustment, and 5 mg provides only a slightly greater benefit. However, prolonged-release (PRM) forms have been found to be less effective in alleviating jet lag symptoms. Efficacy depends mainly on the time of administration, at local bedtime, rather than the exact dose.

In the case of Shift Work Disorder, defined as a situation where work schedules overlap with the normal sleep period, causing a desynchronization between the internal biological clock and the sleep-wake cycle imposed by work, melatonin can be used as a supplement to phototherapy to promote phase shift and improve circadian adaptation, although clinical evidence remains limited. (Sack et al., 2007).

Beyond its chronobiotic role, melatonin also facilitates sleep, mainly by attenuating the wakefulness signal emitted by the circadian clock in the SCN. This effect, although moderate, helps promote sleep when endogenous secretion is low or misaligned, as is the case in older people or individuals exposed to artificial light at night or shift work schedules. (Zisapel, 2018).

Immediate-release (IR) formulations act quickly and are used primarily to reduce sleep latency without altering total sleep time, while extended-release forms (PRM 2 mg) enable the nocturnal physiological profile of melatonin to be reproduced. This latest formulation maintains effective plasma concentrations throughout the night, improves perceived sleep quality, and preserves the physiological structure of sleep stages, without inducing dependence or impairing morning alertness. (Zisapel, 2018).
Overall, melatonin should be considered a chronotherapeutic agent aimed at realigning biological rhythms, rather than a conventional hypnotic. It is very well tolerated, with an incidence of adverse effects comparable to placebo in clinical trials. (Sack et al., 2007) (Zisapel, 2018).

Hormone replacement therapy (HRT)

In post-menopausal women, the reduction in estrogen and progestin is associated with an increased risk of sleep disorders, particularly OSA, due to reduced upper airway tone and impaired respiratory control. HRT may improve certain sleep parameters and reduce the severity of breathing disorders in some patients. Although some observational studies have suggested a possible protective effect of HRT, clinical data remain limited, conducted on small samples, and trials have not demonstrated significant improvement in SDB. Thus, HRT cannot be recommended specifically for the treatment of OSA in postmenopausal women. (Lindberg et al., 2019).
It is defined as a treatment intended to compensate for the natural decline in ovarian hormones that occurs during menopause. It is based primarily on the administration of estrogen, either alone or in combination with progestin in women with an intact uterus, in order to prevent endometrial hyperplasia. This treatment aims to alleviate vasomotor and metabolic symptoms associated with hormone deficiency, such as hot flashes, sleep disturbances, mood swings, and bone loss, and to restore an endocrine balance conducive to overall well-being.

Physiologically, estrogen acts on the hypothalamus, modulating the activity of the median preoptic nucleus, which is involved in regulating body temperature and the sleep-wake cycle. This action contributes to an average reduction of nearly 85% in vasomotor symptoms, indirectly improving sleep quality and thermoregulation. HRT

can be administered orally, transdermally, or vaginally, depending on the patient's needs and risk profile. (Harper-Harrison et al., 2024).

Estrogen supplementation, either transdermally or orally, has been shown to have a significant beneficial effect on sleep disorders in peri- and postmenopausal women. The treatment regimen combines oral administration of estradiol valerate (estrogens) at a dose of 1 mg/day for 14 days, followed by hydroxyprogesterone acetate (progestogen) 8 mg/day for 14 days, constituting a 28-day cycle. This protocol has shown satisfactory therapeutic effects on sleep quality, although the optimal dosage and duration of hormone replacement therapy have not yet been clearly established. (X. Wang, 2024).

Table 4 presents the main hormonal components of hormone replacement therapy (HRT) treatment regimens, specifying the type of hormone and therapeutic role for each substance.

Table 4 - Hormonal components of the hormone replacement therapy (HRT) treatment regimen and their respective roles. (Source : original)

Substance	Type of hormone	Role
Estradiol valerate	Estrogen (main female hormone)	Used to replace the decline in estrogen during menopause.
Hydroxyprogesterone acetate	Progestogen (progesterone analog)	Protects the uterus from the stimulating effects of estrogen alone and completes the hormonal cycle.

Although some observational studies have suggested a possible protective effect of HRT, clinical data remains limited, based on small sample sizes, and trials have not demonstrated a significant improvement in HRT. Therefore, HRT cannot be specifically recommended for the treatment of OSA in postmenopausal women. (Lindberg et al., 2019).

Dual orexin receptor antagonists (DORA)

DORA are a new class of hypnotics that directly target the neurobiological pathways of wakefulness by blocking the action of orexin. This neuropeptide is essential for promoting wakefulness. They thus promote more physiological sleep, and appear to have fewer cognitive side-effects and dependence risks than benzodiazepines or Z-hypnotics. Among the DORAs currently available, daridorexant (Quviviq), lemborexant (Dayvigo) and suvorexant (Belsomra) are already on the market, while molecules such as seltorexant are still in clinical development. Daridorexants are characterized by a favorable benefit in terms of daytime sleepiness, linked to faster elimination. However, access remains limited, and cost is a major barrier. European recommendations place DORA as a second-line treatment after CBT-I. Finally, emerging data suggest a potential interest for suvorexant in patients with Alzheimer's disease, with possible effects on the regulation of neurotoxic proteins. (Nuwer, 2025).

5. The role of the pharmacist

In the pharmacy, pharmacists play a key role in the initial screening of sleep disorders, particularly OSA, using short screening questionnaires such as STOP-BANG (Table 5) and the Epworth Sleepiness Scale (ESS) to identify patients at risk before referring them to a sleep physician. (Pharmacy Magazine, 2024).

Table 5 - STOP-BANG screening questionnaire for SA (Source : Pharmacy Magazine, 2024)

Stop		
Do you **S**NORE loudly (louder than talking or loud enough to be heard through closed doors)?	YES	NO
Do you often feel **T**IRED, fatigued or sleepy during daytime?	YES	NO
Has anyone **O**BSERVED you stop breathing during your sleep?	YES	NO
Do you have or are you being treated for high blood **P**RESSURE?	YES	NO
Bang		
BMI more than 35kg/m^2?	YES	NO
AGE over 50 years old?	YES	NO
NECK circumference >16 inches (40cm)?	YES	NO
GENDER: Male?	YES	NO

Interpretation and use :

- 0-2 : low risk of moderate to severe OSA
- 3-4 : intermediate risk
- 5-8 : high risk

For patients with a score of 3 or 4, additional criteria (BMI > 35 or male gender) may classify the patient as high risk. (Chung et al., 2015)

He can provide structured, non-pharmacological advice, focusing on sleep hygiene measures such as regular scheduling, reducing stimulants and improving the night-time environment, in order to promote restful sleep and avoid inappropriate use of medication. It also carries out an assessment of current treatments to identify drugs that may be disrupting the sleep cycle, and guides patients towards appropriate solutions when these treatments are at the root of the problem. (Pharmacy Times, 2018).

Community pharmacists can offer weight management services (WMSs) including identification of overweight or obese patients, measurement of anthropometric parameters (weight, BMI, waist circumference), personalized advice on diet, physical activity and health behavior modification, as well as regular progress monitoring and referral to other healthcare professionals if necessary. These interventions have shown a positive impact on reducing body weight and improving metabolic markers, confirming the potential of pharmacists in the prevention and management of obesity.
However, pharmacists report major obstacles to implementing these services in pharmacies, including lack of time, absence of confidential consultation areas, insufficient specialist training, and lack of dedicated funding. (AlMukdad et al., 2021).

6. Conclusion

Obesity and sleep disorders are now two major public health issues, closely linked by complex pathophysiological, hormonal, and behavioral mechanisms. Their bidirectional interaction, now well documented, maintains a vicious circle in which sleep deprivation or fragmentation promotes weight gain, while excess weight alters sleep quality through mechanical, metabolic, and inflammatory effects. This imbalance results in hormonal dysregulation involving leptin, ghrelin, cortisol, and melatonin, disrupting signals of satiety, energy expenditure, and circadian rhythms.

The accumulation of visceral adipose tissue and the desynchronization of biological rhythms are central elements of this pathological cycle. Conversely, restoring regular sleep and circadian rhythms helps improve insulin sensitivity, energy metabolism, and hormone regulation, confirming that these two aspects of health must be addressed jointly. European epidemiological data show a parallel increase in these two conditions, particularly among adolescents and middle-aged adults. This trend can be explained by biological determinants as well as environmental and societal factors: sedentary lifestyles, processed foods, chronic stress, exposure to artificial light, and socioeconomic disparities.

From a therapeutic perspective, non-pharmacological interventions remain the cornerstone of management. A structured lifestyle, balanced diet, regular physical activity, and consistent sleep schedule promote circadian stability and reduce cardiometabolic risk. Innovative approaches, such as time-restricted eating (TRE) and cognitive behavioral therapy for insomnia (CBT-I), have shown promising outcomes in improving sleep quality, weight control, and eating behaviors. By synchronizing daily habits with biological rhythms, these strategies offer a coherent and sustainable approach to the prevention of metabolic disorders.

Recent pharmacological advances also offer encouraging prospects. GLP-1 receptor agonists, such as liraglutide and semaglutide, as well as new dual or triple agonists (GLP-1/GIP, GLP-1/GIP/GCG), have been shown to be effective in reducing fat mass,

improving insulin sensitivity, and reducing the severity of obstructive sleep apnea. The emergence of oral treatments, such as orforglipron, the first non-peptide GLP-1 agonist, is a promising step forward in improving treatment adherence and promoting a more personalized approach. These innovations reflect a shift towards integrated metabolic medicine, where weight control and sleep quality are considered complementary goals.

Respiratory treatments, such as CPAP and NIV, remain essential in the management of obesity-related apnea or hypoventilation syndromes. However, their effectiveness depends on patient motivation and adherence, which highlights the need for educational, motivational, and interdisciplinary support.

In this regard, pharmacists play a key role. As local healthcare professionals, they can actively contribute to the screening of sleep disorders, the promotion of healthy lifestyles, and the therapeutic follow-up of obese or at-risk patients, through their interventions, advice on sleep patterns, monitoring of treatment compliance, and identification of medication side effects.
The pharmacist may recommend medicinal plants such as valerian, passionflower, or hops, while ensuring that there are no drug interactions or contraindications, particularly in patients taking multiple medications simultaneously, in order to guarantee their safety. (VIDAL, 2023) . (Schaad, 2003). Its work thus reinforces continuity of care and prevention in community health.

In the future, research will need to deepen our understanding of the links between sleep, metabolism, and chronobiology. The study of gut microbiota, chrononutrition, and circadian hormones could pave the way for new prevention strategies. In addition, the emergence of artificial intelligence in monitoring sleep and eating behaviors offers promising prospects: it could identify at-risk profiles, anticipate metabolic imbalances, and tailor interventions to individual needs.

Ultimately, this thesis underscores the need for a comprehensive, multidisciplinary approach to break the vicious cycle connecting obesity and sleep disorders. Maintaining synchronization between biological rhythms, metabolism, and lifestyle habits is both a clinical and public health priority, fostering the development of targeted and sustainable therapeutic strategies to improve sleep, metabolic balance, and population health.

References

Ahmed, F., Merghani, T., Alkhatry, M., Hisham, H. A., Hamad, F., Qashlan, A., Kedir, L., & Alawad, A. (2025b). Liraglutide in Obesity management: Evidence of weight and lipid improvements in a UAE cohort. The Open Public Health Journal, 18(1). https://doi.org/10.2174/0118749445420434250723055026

Ahmed, S. K., & Mohammed, R. A. (2025). Obesity: Prevalence, causes, consequences, management, preventive strategies and future research directions. Metabolism Open, 27, 100375. https://doi.org/10.1016/j.metop.2025.100375

AlMukdad, S., Zaghloul, N., Awaisu, A., Mahfoud, Z. R., Kheir, N., & Hajj, M. S. E. (2021). Exploring the role of community pharmacists in obesity and weight management in Qatar: A mixed-methods study. Risk Management and Healthcare Policy, 14, 2771–2787. https://doi.org/10.2147/rmhp.s309142

Andy, A., Choudhary, R. P., Andy, D., & Siddalingegowda, S. M. (2025). Optimizing weight management: A collaborative strategy with clinical pharmacists. Biomedical & Pharmacology Journal, 18(1), 517–526. https://doi.org/10.13005/bpj/3104

Aquinde, L. (2024, June 21). Study identifies first drug therapy for sleep apnea. University of California San Diego Health. https://health.ucsd.edu/news/press-releases/2024-06-21-study-identifies-first-drug-therapy-for-sleep-apnea/

Åkerstedt, T., Discacciati, A., Miley-Åkerstedt, A., & Westerlund, H. (2018). Aging and the change in fatigue and sleep – a longitudinal study across 8 years in three age groups. Frontiers in Psychology, 9, 234. https://doi.org/10.3389/fpsyg.2018.00234

Bansal, A. B., Patel, P., & Khalili, Y. A. (2024, February 14). Orlistat. StatPearls - NCBI Bookshelf. https://www.ncbi.nlm.nih.gov/books/NBK542202/

Baranwal, N., Yu, P. K., & Siegel, N. S. (2023). Sleep physiology, pathophysiology, and sleep hygiene. Progress in Cardiovascular Diseases, 77, 59–69. https://doi.org/10.1016/j.pcad.2023.02.005

Batool-Anwar, S., & Quan, S. F. (2024). Sleep health disparity and race/ethnicity, socioeconomic status, and gender: A systematic review. Sleep Medicine Research, 15(3), 139–150. https://doi.org/10.17241/smr.2024.02152

Bcps, M. B. P. (2018, March 8). The role of a pharmacist in managing sleep disorders. Pharmacy Times – Pharmacy Practice News and Expert Insights. https://www.pharmacytimes.com/view/the-role-of-a-pharmacist-in-managing-sleep-disorders

Begemann, K., Rawashdeh, O., Olejniczak, I., Pilorz, V., De Assis, L. V. M., Osorio-Mendoza, J., & Oster, H. (2025). Endocrine regulation of circadian rhythms. Deleted Journal, 2(1). https://doi.org/10.1038/s44323-025-00024-6

Benedict, C., & Heilbronn, L. K. (2025). Time-restricted eating, sleep, and quality of life—Timing your bites to tune your nights. JAMA Network Open, 8(6), e2517280. https://doi.org/10.1001/jamanetworkopen.2025.17280

Boers, E., Barrett, M. A., Benjafield, A. V., Barnet, J. H., Ravelo, L. A., Kaye, L., Cistulli, P. A., Pépin, J., Armitstead, J., Sterling, K. L., Nunez, C. M., Peppard, P. E., Malhotra, A., … Malhotra, A. (2025). Projecting the 30-year burden of obstructive sleep apnoea in the USA: A prospective modelling study. The Lancet Respiratory Medicine. https://doi.org/10.1016/s2213-2600(25)00243-7

Cerillo, J. L., & Parmar, M. (2024, October 6). Liraglutide. StatPearls - NCBI Bookshelf. https://www.ncbi.nlm.nih.gov/books/NBK608007/#:~:text=acts%20on%20the%20pancreatic%20%CE%B2%2Dcells%20to%20release%20endogenous%20insulin

Chaput, J., McHill, A. W., Cox, R. C., Broussard, J. L., Dutil, C., Da Costa, B. G. G., Sampasa-Kanyinga, H., & Wright, K. P. (2022). The role of insufficient sleep and circadian misalignment in obesity. Nature Reviews Endocrinology, 19(2), 82–97. https://doi.org/10.1038/s41574-022-00747-7

Chung, F., Abdullah, H. R., & Liao, P. (2015). STOP-Bang questionnaire. CHEST Journal, 149(3), 631–638. https://doi.org/10.1378/chest.15-0903

Cipolla-Neto, J., Amaral, F. G., Afeche, S. C., Tan, D. X., & Reiter, R. J. (2014). Melatonin, energy metabolism, and obesity: a review. Journal of Pineal Research, 56(4), 371–381. https://doi.org/10.1111/jpi.12137

Circadian Rhythms | National Institute of General Medical Sciences. (n.d.). https://www.nigms.nih.gov/education/fact-sheets/Pages/circadian-rhythms

Circadian rhythms and the SCN | National Institute of General Medical Sciences. (n.d.). https://nigms.nih.gov/image-gallery/6613

Cleveland Clinic Medical. (2024, November 7). CPAP machine. Cleveland Clinic. https://my.clevelandclinic.org/health/treatments/22043-cpap-machine

Cshp_Éditeur. (2025, August 13). Injections obésité : traitements, résultats et Mounjaro – CSHP Paris. https://www.cshp.fr/2025/08/13/injections-contre-lobesite-un-traitement-efficace-pour-perdre-du-poids/

De Groot, E. R., Dudink, J., & Austin, T. (2024). Sleep as a driver of pre- and postnatal brain development. Pediatric Research, 96(6), 1503–1509. https://doi.org/10.1038/s41390-024-03371-5

De Longis, E., Kassis, A., Rémond-Derbez, N., Thota, R., Darimont, C., Donato-Capel, L., & Hudry, J. (2024). Cognitive benefits of sleep: A narrative review to explore the relevance of glucose regulation. SLEEP Advances, 6(1). https://doi.org/10.1093/sleepadvances/zpae095

Direksunthorn, T. (2025). Sleep and cardiometabolic health: A narrative review of epidemiological evidence, mechanisms, and interventions. International Journal of General Medicine, 18, 5831–5843. https://doi.org/10.2147/ijgm.s563616

DrugBank. (2025, 4 novembre). Orlistat : uses, interactions, mechanism of action. DrugBank Online. https://go.drugbank.com/drugs/DB01083

Dummy, C. (2025, October 31). Le sémaglutide dans l'obésité, en dehors du diabète. CBIP. https://www.cbip.be/fr/le-semaglutide-dans-lobesite-en-dehors-du-diabete/

Figorilli, M., Velluzzi, F., & Redolfi, S. (2025). Obesity and sleep disorders: A bidirectional relationship. Nutrition, Metabolism and Cardiovascular Diseases, 104014. https://doi.org/10.1016/j.numecd.2025.104014

Fort Worth ENT. (2024, October 18). Causes and complications of sleep apnea. Fort Worth ENT & Sinus. https://fortworthent.net/ear-nose-throat/snoring-obstructive-sleep-apnea-osa/sleep-medicine-snoring-or-sleep-apnea/

Fountain, L., & Singh, A. (2025, July 16). Is eating before bed bad? Sleep Foundation. https://www.sleepfoundation.org/nutrition/is-it-bad-to-eat-before-bed

Galan-Lopez, P., Domínguez, R., Gísladóttir, T., Sánchez-Oliver, A. J., Pihu, M., Ries, F., & Klonizakis, M. (2021). Sleep quality and duration in European adolescents (The AdolesHealth Study): A cross-sectional, quantitative study. Children, 8(3), 188. https://doi.org/10.3390/children8030188

Genario, R., Cipolla-Neto, J., Bueno, A. A., & Santos, H. O. (2020). Melatonin supplementation in the management of obesity and obesity-associated disorders: A review of physiological mechanisms and clinical applications. Pharmacological Research, 163, 105254. https://doi.org/10.1016/j.phrs.2020.105254

Georgakopoulou, V. E., Lazaridou, A., Voulgaris, A., Archontogeorgis, K., Dalamaga, M., Nena, E., & Steiropoulos, P. (2025). Sleep quality and well-being in obesity-hypoventilation syndrome versus obstructive sleep apnea with obesity: A comparative study. Metabolism Open, 26, 100367. https://doi.org/10.1016/j.metop.2025.100367

Ghimire, P., Sankari, A., Antoine, M. H., Bollu, P. C., & Kaul, P. (2025, June 30). Obesity-hypoventilation syndrome. StatPearls – NCBI Bookshelf. https://www.ncbi.nlm.nih.gov/books/NBK542216/

Godos, J., Rosi, A., Scazzina, F., Bonifaz, M. A. T., Giampieri, F., Abdelkarim, O., Ammar, A., Aly, M., Frias-Toral, E., Pons, J., Vázquez-Araújo, L., Alemany-Iturriaga, J., Monasta, L., Mata, A., Chacón, A., Busó, P., & Grosso, G. (2025). Diet, eating habits, and lifestyle factors associated with adequate sleep duration in children and adolescents living in five Mediterranean countries: The DELICIOUS Project. Nutrients, 17(7), 1242. https://doi.org/10.3390/nu17071242

Griffin, W., Roux, C. W. L., Heneghan, H. M., O'Shea, D., & Garvey, J. F. (2025b). The role of weight management in sleep-disordered breathing. Breathe, 21(3), 250182. https://doi.org/10.1183/20734735.0182-2025

Harper-Harrison, G., Carlson, K., & Shanahan, M. M. (2024, October 6). Hormone replacement therapy. StatPearls - NCBI Bookshelf. https://www.ncbi.nlm.nih.gov/books/NBK493191/

Health Risks of Overweight & Obesity. (2023, May). National Institute of Diabetes and Digestive and Kidney Diseases. https://www.niddk.nih.gov/health-information/weight-management/adult-overweight-obesity/health-risks

Huertas, J. H., Amarilla, C. E., Acevedo, F. T., Jerez, F. R., & Gutiérrez, A. M. F. (2025). Challenges in the treatment of obesity hypoventilation syndrome with persistent nocturnal hypoxemia: CPAP vs. NIV. Open Respiratory Archives, 7(4), 100477. https://doi.org/10.1016/j.opresp.2025.100477

Huang, H., Yu, T., Liu, C., Yang, J., & Yu, J. (2024b). Poor sleep quality and overweight/obesity in healthcare professionals: A cross-sectional study. Frontiers in Public Health, 12, 1390643. https://doi.org/10.3389/fpubh.2024.1390643

Hynes, D., & Mansfield, D. (2024). Diagnosis and management of obstructive sleep apnoea in adults. Australian Prescriber, 47(2), 52–56. https://doi.org/10.18773/austprescr.2024.010

INSV – Institut National du Sommeil et de la Vigilance. (2022, June 20). Comment le sommeil évolue avec l'âge ? https://institut-sommeil-vigilance.org/comment-le-sommeil-evolue-avec-lage/

Jastreboff, A. M., Kaplan, L. M., Frías, J. P., Wu, Q., Du, Y., Gurbuz, S., Coskun, T., Haupt, A., Milicevic, Z., & Hartman, M. L. (2023). Triple–Hormone-Receptor agonist retatrutide for obesity — a phase 2 trial. New England Journal of Medicine, 389(6), 514–526. https://doi.org/10.1056/nejmoa2301972

Jiao, Y., Butoyi, C., Zhang, Q., Adotey, S. A. A. I., Chen, M., Shen, W., Wang, D., Yuan, G., & Jia, J. (2025). Sleep disorders impact hormonal regulation: Unravelling the relationship among sleep disorders, hormones and metabolic diseases. Diabetology & Metabolic Syndrome, 17(1). https://doi.org/10.1186/s13098-025-01871-w

Ju, K., Liu, N., Wu, R., & Shi, X. (2025). The relationship between sedentary behavior, sleep duration, and sleep disorders: Analysis of the 2007–2014 National Health and Nutrition Examination Survey. Frontiers in Neurology, 16. https://doi.org/10.3389/fneur.2025.1488443

Knutson, K. L., Dixon, D. D., Grandner, M. A., Jackson, C. L., Kline, C. E., Maher, L., Makarem, N., Martino, T. A., St-Onge, M., & Johnson, D. A. (2025). Role of circadian health in cardiometabolic health and disease risk: A scientific statement

from the American Heart Association. Circulation. https://doi.org/10.1161/cir.0000000000001388

Konuksever, D., & Karakaya, S. P. Y. (2023). The association between insulin resistance, sleep disorders, and inflammation in obese children. Journal of Clinical Medicine of Kazakhstan, 20(3), 82–87. https://doi.org/10.23950/jcmk/13327

Les médicaments de l'obésité – VIDAL. (2025). VIDAL. https://www.vidal.fr/maladies/metabolisme-diabete/obesite/medicaments.html

Li, L., Sun, F., Du, J., Li, Z., Chen, T., & Shi, X. (2024). Behavior-change lifestyle interventions for the treatment of obesity in children and adolescents: A scoping review. Annals of the New York Academy of Sciences. https://doi.org/10.1111/nyas.15278

Lin, L., Hsu, C., Chao, J. C., Chien, Y., & Chiou, H. (2025). Interactive effects of sleep duration and dietary patterns on obesity moderated by age. Scientific Reports, 15(1). https://doi.org/10.1038/s41598-025-17886-2

Lindberg, E., Bonsignore, M. R., & Polo-Kantola, P. (2019). Role of menopause and hormone replacement therapy in sleep-disordered breathing. Sleep Medicine Reviews, 49, 101225. https://doi.org/10.1016/j.smrv.2019.101225

Liu, R., Figueroa, R., Vanden Brink, H., Vorland, C. J., Auckburally, S., Johnson, L., Garay, J., Brown, T., Simon, S., & Ells, L. (2024). The efficacy of sleep lifestyle interventions for the management of overweight or obesity in children: A systematic review and meta-analysis. BMC Public Health, 24(1). https://doi.org/10.1186/s12889-024-17708-6

Liu, S., Wang, X., Zheng, Q., Gao, L., & Sun, Q. (2022). Sleep deprivation and central appetite regulation. Nutrients, 14(24), 5196. https://doi.org/10.3390/nu14245196

Lok, V., Liu, M., Chung, R., & Kim, J. (2025). 0488 Social determinants and gender differences in sleep health disparities: Preliminary findings from a descriptive analysis in Hong Kong 2024. SLEEP, 48(Suppl. 1), A213. https://doi.org/10.1093/sleep/zsaf090.0488

Masa, J. F., Corral, J., Caballero, C., Barrot, E., Terán-Santos, J., Alonso-Álvarez, M. L., Gomez-Garcia, T., González, M., López-Martín, S., De Lucas, P., Marin, J. M.,

Marti, S., Díaz-Cambriles, T., Chiner, E., Egea, C., Miranda, E., Mokhlesi, B., García-Ledesma, E., Sánchez-Quiroga, M., … Bengoa, M. (2016). Non-invasive ventilation in obesity hypoventilation syndrome without severe obstructive sleep apnoea. Thorax, 71(10), 899–906. https://doi.org/10.1136/thoraxjnl-2016-208501

Merchant, A. M., Gray, S. R., Gray, C. M., Finlayson, G., Manyara, A. M., Trisotti, M. F. G., & Gill, J. M. R. (2025). Effect of a cognitive behavioural therapy intervention to improve sleep on food preferences: A randomized controlled trial in adults with overweight and obesity. Appetite, 212, 108022. https://doi.org/10.1016/j.appet.2025.108022

Mesarič, K. K., Pajek, J., Zakrajšek, B. L., Bogataj, Š., & Kodrič, J. (2023). Cognitive behavioral therapy for lifestyle changes in patients with obesity and type 2 diabetes: A systematic review and meta-analysis. Scientific Reports, 13(1), 12793. https://doi.org/10.1038/s41598-023-40141-5

Mifsrud, C. S., Kolla, B. P., Rushlow, D. R., & Mansukhani, M. P. (2025). The impact of GLP-1 agonists on sleep disorders: Spotlight on sleep apnea. Expert Opinion on Pharmacotherapy. https://doi.org/10.1080/14656566.2025.2574848

Miller, M. A. (2023b). Time for bed: Diet, sleep and obesity in children and adults. Proceedings of the Nutrition Society, 1–8. https://doi.org/10.1017/s0029665123004846

Miller, Z., & Parveen, A. (2025, 2 octobre). Orforglipron : the first oral GLP-1 pill for weight loss and diabetes. Quickmeds. https://quickmeds.co.uk/blog/orforglipron-the-first-oral-glp-1-pill/

Muszyński, J., & Ulewicz, M. (2025b). The relationship between sleep and obesity – Literature review. Environmental Medicine. https://doi.org/10.26444/ms/204284

Nag, D. S., Chatterjee, A., Patel, R., Sen, B., Pal, B. D., & Wadhwa, G. (2024). Recent advances in the management of obstructive sleep apnea. World Journal of Clinical Cases, 12(24), 5456–5461. https://doi.org/10.12998/wjcc.v12.i24.5456

NCD Risk Factor Collaboration (NCD-RisC). (2024, February 27). Worldwide trends in underweight and obesity from 1990 to 2022: A pooled analysis of 3663 population-representative studies with 222 million children, adolescents, and adults. The Lancet. https://doi.org/10.1016/S0140-6736(23)02750-2

NICE. (2017, December 12). Overview | Naltrexone–bupropion for managing overweight and obesity | Guidance | NICE. https://www.nice.org.uk/guidance/ta494

Noyed, D., & DeBanto, J. D. (2025, July 15). How weight affects sleep apnea. Sleep Foundation. https://www.sleepfoundation.org/sleep-apnea/weight-loss-and-sleep-apnea

Nuwer, R. (2025). New treatments to put insomnia to bed. Nature. https://doi.org/10.1038/d41586-025-00963-x

Nunez, C. N. (2025, August 7). FAQ: Anti-obesity medications and obstructive sleep apnea. ResMed. https://www.resmed.com/en-us/sleep-health/resources/emerging-therapies/

Obesity: Health consequences of being overweight. (n.d.). World Health Organization. https://www.who.int/news-room/questions-and-answers/item/obesity-health-consequences-of-being-overweight

Ojeniran, M., Dube, B., Paige, A., Ton, J., & Lindblad, A. J. (2021). Le sémaglutide pour la perte pondérale. Canadian Family Physician, 67(11), e296–e297. https://doi.org/10.46747/cfp.6711e296

Overweight and obesity – BMI statistics. (2024, July). Eurostat. https://ec.europa.eu/eurostat/statistics-explained/index.php?title=Overweight_and_obesity_-_BMI_statistics

Pacheco, D., & Singh, A. (2025, July 16). Night eating syndrome. Sleep Foundation. https://www.sleepfoundation.org/nutrition/night-eating-syndrome

Paitraud, D. (2024, November 19). Mounjaro : nouveau médicament injectable indiqué dans le traitement du diabète de type 2 et de l'obésité. VIDAL. https://www.vidal.fr/actualites/31058-mounjaro-nouveau-medicament-injectable-indique-dans-le-traitement-du-diabete-de-type-2-et-de-l-obesite.html

PRAC : l'EMA lance une révision des médicaments contenant du sémaglutide à la suite d'inquiétudes quant à un risque accru de neuropathie optique ischémique antérieure non artéritique | AFMPS. (2025, June 2). https://www.afmps.be/fr/news/prac_janvier_2025_lema_lance_une_revision_des_medicaments_contenant_du_semaglutide_a_la_suite

Pratt, E., Ma, X., Liu, R., Robins, D., Coskun, T., Sloop, K. W., Haupt, A., & Benson, C. (2023). Orforglipron (LY3502970), a novel, oral non-peptide glucagon-like peptide-1 receptor agonist: A Phase 1b, multicentre, blinded, placebo-controlled, randomized, multiple-ascending-dose study in people with type 2 diabetes. Diabetes Obesity and Metabolism, 25(9), 2642–2649. https://doi.org/10.1111/dom.15150

RÉSUMÉ DES CARACTÉRISTIQUES DU PRODUIT. (2021). Agence Européenne des Médicaments (EMA). https://www.ema.europa.eu/fr/documents/product-information/mounjaro-epar-product-information_fr.pdf

Ratwani, M., Bisht, S., & Prakash, S. (2025). Association between sleep disturbance and metabolic dysfunctions in adipose tissue: Insights into melatonin's role. Biochemical and Biophysical Research Communications, 770, 151978. https://doi.org/10.1016/j.bbrc.2025.151978

Rennie, K. L., Johnson, L., & Jebb, S. A. (2005). Behavioural determinants of obesity. Best Practice & Research Clinical Endocrinology & Metabolism, 19(3), 343–358. https://doi.org/10.1016/j.beem.2005.04.003

Robinson, E., Almiron-Roig, E., Rutters, F., De Graaf, C., Forde, C. G., Smith, C. T., Nolan, S. J., & Jebb, S. A. (2014). A systematic review and meta-analysis examining the effect of eating rate on energy intake and hunger. American Journal of Clinical Nutrition, 100(1), 123–151. https://doi.org/10.3945/ajcn.113.081745

Rohm, T. V., Meier, D. T., Olefsky, J. M., & Donath, M. Y. (2022). Inflammation in obesity, diabetes, and related disorders. Immunity, 55(1), 31–55. https://doi.org/10.1016/j.immuni.2021.12.013

Roomy, M. A., Hussain, K., Behbehani, H. M., Abu-Farha, J., Al-Harris, R., Ambi, A. M., Abdalla, M. A., Al-Mulla, F., Abu-Farha, M., & Abubaker, J. (2024). Therapeutic advances in obesity management: An overview of the therapeutic interventions. Frontiers in Endocrinology, 15. https://doi.org/10.3389/fendo.2024.1364503

Rosenberg, R., Breit, M. J., Clark, K. C., Broussard, J. L., Catenacci, V. A., Depner, C. M., Simon, S. L., Wright, K. P., Zuraikat, F. M., & Creasy, S. A. (2025). Examining the role of sleep in body weight regulation and implications for obesity treatment: A narrative review. Obesity Reviews. https://doi.org/10.1111/obr.70017

Roux, C. W. L., Wharton, S., Bozkurt, B., Platz, E., Bleckert, G., Hussain, S. A., Brueckmann, M., Startseva, E., Kloer, I. M., & Kaplan, L. M. (2025). Survodutide for treatment of obesity: Baseline characteristics of participants in a randomized, double-blind, placebo-controlled, phase 3 trial (SYNCHRONIZE ™-1). Diabetes Obesity and Metabolism. https://doi.org/10.1111/dom.70196

Rubino, F., Cummings, D. E., Eckel, R. H., Cohen, R. V., Wilding, J. P. H., Brown, W. A., Stanford, F. C., Batterham, R. L., Farooqi, I. S., Farpour-Lambert, N. J., Roux, C. W. L., Sattar, N., Baur, L. A., Morrison, K. M., Misra, A., Kadowaki, T., Tham, K. W., Sumithran, P., Garvey, W. T., … Mingrone, G. (2025b). Definition and diagnostic criteria of clinical obesity. The Lancet Diabetes & Endocrinology. https://doi.org/10.1016/s2213-8587(24)00316-4

Salman, E. J., & Kabir, R. (2022, September 14). Night eating syndrome. StatPearls – NCBI Bookshelf. PMID: 36251825. https://www.ncbi.nlm.nih.gov/books/NBK585047/

Savin, K. L., Clark, T. L., Perez-Ramirez, P., Allen, T. S., Parra, M. T., & Gallo, L. C. (2022). The effect of cognitive behavioral therapy for insomnia (CBT-I) on cardiometabolic health biomarkers: A systematic review of randomized controlled trials. Behavioral Sleep Medicine, 21(6), 671–694. https://doi.org/10.1080/15402002.2022.2154213

Schaad, N. (2003). Interactions entre les plantes médicinales et les médicaments. In Médecine&Hygiène (pp. 681–682) [Journal-article]. https://www.medhyg.ch

Schmidt, P. H. S., Pasqualotto, E., Santos, H. V. D., De Souza, L. S. N., Santos, B. E. D., Chavez, M. P., Ferreira, R. O. M., Hohl, A., Ronsoni, M. F., & Van de Sande-Lee, S. (2025). Effects of liraglutide on body composition in people living with obesity or overweight : A systematic review. Obesity Research & Clinical Practice, 19(1), 11-18. https://doi.org/10.1016/j.orcp.2025.01.009

Search media – Wikimedia Commons. (n.d.). https://commons.wikimedia.org/w/index.php?search=stages+of+sleep+razer&title=Special%3AMediaSearch&go=Go&type=image

Sharma, S., & Kavuru, M. (2010). Sleep and metabolism: An overview. International Journal of Endocrinology, 2010, 270832. https://doi.org/10.1155/2010/270832

Shi, H., Hu, F. B., Huang, T., Schernhammer, E. S., Willett, W. C., Sun, Q., & Wang, M. (2024). Sedentary behaviors, light-intensity physical activity, and healthy aging. JAMA Network Open, 7(6), e2416300. https://doi.org/10.1001/jamanetworkopen.2024.16300

Singh, K. K., Ghosh, S., Bhola, A., Verma, P., Amist, A. D., Sharma, H., Sachdeva, P., & Sinha, J. K. (2024). Sleep and immune system crosstalk: Implications for inflammatory homeostasis and disease pathogenesis. Annals of Neurosciences. https://doi.org/10.1177/09727531241275347

Sound Sleep Health. (2020, June 13). Sleep architecture: The stages and cycles of sleep. https://www.soundsleephealth.com/sleep-architecture-the-stages-and-cycles-of-sleep/

Suni, E., & Rehman, A. (2025, July 4). Insomnia: Symptoms, causes, and treatments. Sleep Foundation. https://www.sleepfoundation.org/insomnia

Thomas, B., Lindblad, A. J., Luu, T., & Paige, A. (2023). La naltrexone et le bupropion pour la perte pondérale. Canadian Family Physician, 69(9), e179–e180. https://doi.org/10.46747/cfp.6909e179

Tucker, R. T. (2024b, October 25). Sleep apnoea: A brief guide for pharmacists. Pharmacy Magazine. https://www.pharmacymagazine.co.uk/clinical/sleep-apnoea-a-brief-guide-for-pharmacists

VIDAL. (2019, October 3). Sémaglutide : substance active à effet thérapeutique - VIDAL. https://www.vidal.fr/medicaments/substances/semaglutide-25733.html

VIDAL. (2023, January 16). Phytothérapie - Valériane. https://www.vidal.fr/parapharmacie/phytotherapie-plantes/valeriane-valeriana-officinalis.html

Vultur, M. A., Grigorescu, B. L., Huțanu, D., Ianoși, E. S., Budin, C. E., & Jimborean, G. (2025). A multidisciplinary approach to obesity hypoventilation syndrome: From diagnosis to long-term management—A narrative review. Diagnostics, 15(17), 2120. https://doi.org/10.3390/diagnostics15172120

Wang, W., Chen, Z., Zhang, W., Yuan, R., Sun, Y., Yao, Q., Lu, J., & Zheng, J. (2024). Association between obesity and sleep disorder in the elderly: Evidence from

NHANES 2005–2018. Frontiers in Nutrition, 11, 1401477. https://doi.org/10.3389/fnut.2024.1401477

Wang, X. (2024). Research status of hormone replacement therapy on mood and sleep quality in menopausal women. World Journal of Psychiatry, 14(9), 1289–1293. https://doi.org/10.5498/wjp.v14.i9.1289

What is the mechanism of action of Orforglipron? (2025, March 20). Medical Lilly. https://synapse.patsnap.com/article/what-is-the-mechanism-of-action-of-orforglipron

Wilson, H., & Akbarshahi, N. (2024). Obstructive sleep apnea and obesity: How weight loss improves sleep apnea severity and quality of life – An integrative review. DigitalCommons@Kennesaw State University. https://digitalcommons.kennesaw.edu/mastersprojects/19/

World Health Organization (WHO). (2022, May 2). Nutrition, P. A. & O. https://www.who.int/europe/publications/i/item/9789289057738

World Health Organization (WHO). (2025, May 7). Obesity and overweight. https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight

Yasmeen, S., Li, B., Du, C., & Liu, H. (2025). Exploring the interconnection of sleep quality, indoor environmental factors, and energy efficiency: Strategies for sustainable sleep environments. Indoor Air, 2025(1). https://doi.org/10.1155/ina/8245786

Zerón-Rugerio, M. F., Longo-Silva, G., Hernáez, Á., Ortega-Regules, A. E., Cambras, T., & Izquierdo-Pulido, M. (2020). The elapsed time between dinner and the midpoint of sleep is associated with adiposity in young women. Nutrients, 12(2), 410. https://doi.org/10.3390/nu12020410

Zisapel, N. (2018). New perspectives on the role of melatonin in human sleep, circadian rhythms and their regulation. British Journal of Pharmacology, 175(16), 3190–3199. https://doi.org/10.1111/bph.14116

Zota, I., Roca, M., Leon, M., Cozma, C., Anghel, L., Statescu, C., Sascau, R., Hancianu, M., Mircea, C., Ciocoiu, M., Cumpat, C., & Mitu, F. (2023). Long-term adherence in overweight patients with obstructive sleep apnea and hypertension—A pilot

prospective cohort study. Diagnostics, 13(8), 1447. https://doi.org/10.3390/diagnostics13081447

Zou, X., Ptáček, L. J., & Fu, Y. (2024). The genetics of human sleep and sleep disorders. Annual Review of Genomics and Human Genetics, 25(1), 259–285. https://doi.org/10.1146/annurev-genom-121222-120306