**UNIVERSIDADE FEDERAL DE UBERLÂNDIA**
**PROGRAMA DE PÓS-GRADUAÇÃO EM CIÊNCIAS DA SAÚDE**
**FACULDADE DE MEDICINA**

# ASSOCIAÇÃO ENTRE CURTA DURAÇÃO DO SONO E OBESIDADE: UMA REVISÃO SISTEMÁTICA E META-ANÁLISE DE ESTUDOS DE COORTE

**KISIAN COSTA GUIMARÃES**

**UBERLÂNDIA**
**2020**

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Dissertação apresentada ao programa de Pós-Graduação em Ciências da Saúde da Faculdade de Medicina da Universidade Federal de Uberlândia, como requisito parcial para a obtenção do título de Mestre em Ciências da Saúde.

**Área de Concentração:** Ciências da Saúde.

**Orientador (a):** Profa. Dra. Cibele Aparecida Crispim.

**Coorientador (a):** Prof. Dr. Ricardo de Ávila

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# ATA

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| Defesa de: | Dissertação de Mestrado Acadêmico Nº 025/PPCSA | | | | |
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Reuniu-se em web conferência pela plataforma Mconf-RNP, em conformidade com a PORTARIA Nº 36, DE 19 DE MARÇO DE 2020 da COORDENAÇÃO DE APERFEIÇOAMENTO DE PESSOAL DE NÍVEL SUPERIOR - CAPES, pela Universidade Federal de Uberlândia, a Banca Examinadora, designada pelo Colegiado do Programa de Pós-graduação em Ciências da Saúde, assim composta: Professores Doutores: Tássia do Vale Cardoso Lopes (FoRC USP), Erick Prado de Oliveira (UFU) e Cibele Aparecida Crispim (UFU) orientadora da candidata.

Iniciando os trabalhos o presidente da mesa, Dra. Cibele Aparecida Crispim , apresentou a Comissão Examinadora e a candidata, agradeceu a presença do público, e concedeu a Discente a palavra para a exposição do seu trabalho. A duração da apresentação do Discente e o tempo de arguição e resposta foram conforme as normas do Programa.

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# FOLHA DE APROVAÇÃO

Kisian Costa Guimarães

## ASSOCIAÇÃO ENTRE CURTA DURAÇÃO DO SONO E OBESIDADE: UMA REVISÃO SISTEMÁTICA E META-ANÁLISE DE ESTUDOS DE COORTE

**Presidente da banca:** Profa. Dra. Cibele Aparecida Crispim

Dissertação apresentada ao Programa de Pós-Graduação em Ciências da Saúde da Faculdade de Medicina da Universidade Federal de Uberlândia, como requisito parcial para a obtenção do título de Mestre em Ciências da Saúde.

**Área de Concentração:** Ciências da Saúde

**Banca Examinadora**

**Titular:** Erick Prado de Oliveira

**Instituição:** Universidade Federal de Uberlândia (UFU)

**Titular:** Tássia do Vale Cardoso Lopes

**Instituição:** Food and Research Center – FoRC USP

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# RESUMO

**Introdução:** A curta duração do sono está associada a um risco aumentado de desenvolver obesidade. Revisões sistemáticas vêm sendo realizadas para tentar confirmar este achado, porém são necessárias análises com maior rigor metodológico e sistemático que inclua somente estudos de coortes, o que contribuirá para o aumento da confiança dessas evidências. **Objetivo:** Este estudo teve como objetivo realizar uma revisão sistemática da literatura incluindo estudos de coorte que avaliaram a associação entre duração de sono e desenvolvimento da obesidade e, posteriormente, realizar uma meta-análise. Também foi avaliada a associação entre duração curta do sono e desfechos secundários, como diabetes mellitus tipo 2, síndrome metabólica, risco de doenças cardiovasculares, hipertensão arterial sistêmica, obesidade abdominal, qualidade de vida e mortalidade. **Fontes de dados:** Com a utilização do software Rayyan, foram utilizadas estratégias de buscas com termos similares a *"sleep deprivation"* e *"obesity"* nas bases LILACs, Medline, Central e Embase e a literatura cinza pelo Opengrey foram consultadas sem restrições de idiomas até o mês de julho de 2020. **Seleção do estudo:** A estratégia PECO (P: adultos, E: curta duração do sono, C: duração normal do sono, O: obesidade) foi utilizada, excluindo estudos com gestantes, lactantes ou participantes com deficiências físicas. **Extração de dados:** Após leitura na íntegra dos artigos selecionados no Rayyan segundo os critérios de inclusão e exclusão, vinte e nove artigos foram incluídos na revisão. Dados como desenho do estudo, tamanho da amostra, localização, período de acompanhamento, idade no início do estudo, exposição, desfecho, método estatístico e resultados foram extraídos. **Estatística:** A meta-análise foi realizada utilizando o Cochrane Review Manager 5.3 Software. Foi calculado o *Risk Ratio* para dados dicotômicos e *Odds Ratio* para dados de análises agrupadas. A análise de sensibilidade foi realizada retirando da

análise principal os estudos classificados como qualidade baixa pelo NewCastle-Ottawa (dois estudos). A qualidade da evidência foi realizada usando *Grading of Recommendations Assessment, Development, and Evaluation*. **Resultados:** A meta-análise foi realizada com 22 estudos e mostrou associação significativa entre curta duração do sono e desenvolvimento de obesidade (RR = 1.18, 95% CI, 1.15, 1.26), síndrome metabólica (RR: 1.54; 95%CI: 1.13, 2.11) e diabetes tipo 2 (RR: 1.13; 95%CI: 1.02, 1.25). Na análise com dados de medidas de associações agrupadas, a associação permaneceu significativa entre curta duração do sono e o desenvolvimento de obesidade (OR = 1.26, 95%CI: 1.17, 1.36) e diabetes tipo 2 (OR: 1.25; 95%CI: 1.08, 1.45). **Conclusão:** A curta duração do sono está associada à obesidade, síndrome metabólica e diabetes tipo 2. Registro de revisão: número PROSPERO CRD42019130143. Disponível em: https://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID=130143.

# ABSTRACT

Introduction: Short sleep duration is associated with an increased risk of developing obesity. Systematic reviews have been carried out trying to confirm these findings, however, a review with greater methodological and systematic rigor is needed that includes only cohort studies with the aim of increasing the confidence of this evidence. **Objective:** This review aimed to conduct a systematic review of the literature, including cohort studies that assessed the association between sleep duration and development of obesity and, subsequently, to perform a meta-analysis. There was also an association between short sleep duration and secondary outcomes, such as type 2 diabetes mellitus, metabolic syndrome, risk of cardiovascular disease, systemic arterial hypertension, abdominal obesity, quality of life and mortality. **Data sources:** LILACs, Medline, Central and Embase, in addition to the gray literature by Opengrey were used to find articles without languages limits until July 2020 using Rayyan with "sleep deprivation" and "obesity" as mesh terms. **Study selection:** The PECO strategy (P: adults, E: short sleep duration, C: normal sleep duration, O: obesity) was used, excluding studies with pregnant, lactating or physically disabled participants. **Data extraction:** After reading in full-text the studies selected in Rayyan, according to inclusion and exclusion criteria, twenty-nine studies were included in the review, and data such as study design, sample size, location, follow-up period, age at baseline, exposure, outcome, statistical method and results were extracted. **Statistics:** The meta-analysis was performed using the Cochrane Review Manager 5.3 Software. Risk Ratio was calculated for dichotomous data and Odds Ratio for data from pooled analyses. The sensitivity analysis was performed by removing studies classified as low quality by NewCastle-Ottawa from the main analysis (two studies). The quality of the evidence was performed using the Grading of

Recommendations Assessment, Development, and Evaluation. **Results:** The meta-analysis was carried out in 22 studies and showed a significant association between short sleep duration and the development of obesity (RR = 1.18, 95% CI, 1.15, 1.26), metabolic syndrome (RR: 1.54; 95%CI: 1.13, 2.11) and type 2 diabetes (RR: 1.13; 95%CI: 1.02, 1.25). In the analysis with pooled data, the association remained significant between short sleep duration and the development of obesity (OR = 1.26, 95%CI: 1.17, 1.36) and type 2 diabetes (OR: 1.25; 95%CI: 1.08, 1.45). **Conclusion:** Short sleep duration is associated with obesity, metabolic syndrome and type 2 diabetes. Review record: number PROSPERO CRD42019130143. Available at: https://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID=130143.

# LISTA DE ILUSTRAÇÕES

## FUNDAMENTAÇÃO TEÓRICA



## ARTIGO

# LISTA DE TABELAS

## FUNDAMENTAÇÃO TEÓRICA



## ARTIGO

# LISTA DE ABREVIATURAS E SIGLAS

| | |
|---|---|
| EEG | Eletroencefalograma |
| EMG | Eletromiograma |
| EOG | Eletrooculograma |
| Hz | Hertz |
| IC | Intervalo de Confiança |
| IMC | Índice de Massa Corporal |
| NCD-Risk | National Coverage Determination - Risk Factor Collaboration |
| NREM | *Non-rapid eyes movement* |
| OMS | Organização Mundial de Saúde |
| OR | *Odds Ratio* |
| PSG | Polisonografia |
| REM | *Rapid eyes movement* |
| RR | Risco Relativo |
| VIGITEL | Vigilância de fatores de risco e proteção para doenças crônicas por inquérito telefônico |

# SUMÁRIO

# 1. INTRODUÇÃO

Uma noite adequada de sono é essencial para a saúde humana, principalmente para a restauração celular e consolidação de memórias (BORBÉLY; ACHERMANN, 1992; RASCH; BORN, 2013). Estudos de várias partes do mundo constatam elevada prevalência de adultos com tempo insuficiente de sono (<7 horas por noite) (BAYON et al., 2014; BIN; MARSHALL; GLOZIER, 2013; FORD; CUNNINGHAM; CROFT, 2015; KHUBCHANDANI; PRICE, 2020; KRONHOLM et al., 2008; "QuickStats", 2005). Evidências atuais têm ainda demonstrado que a privação de sono está associada a uma série de doenças crônicas, tais como a síndrome metabólica (FAN et al., 2020; KIM et al., 2018; SMILEY; KING; BIDULESCU, 2019), o diabetes mellitus tipo 2 (KOREN; TAVERAS, 2018; LIN; TSAI; YEH, 2016; NUYUJUKIAN et al., 2016; WORLEY, 2018), as doenças cardiovasculares (CHANDOLA et al., 2010; KHAN; AOUAD, 2017), a hipertensão arterial sistêmica (BUXTON; MARCELLI, 2010; KIM; JO, 2010; KOREN; TAVERAS, 2018; WORLEY, 2018) e a obesidade (AZIZ et al., 2017; BENHAM; GHADDAR; TALAVERA-GARZA, 2017; LIN et al., 2018; SZABO; MÁTÉ; FRIGY, 2019; WU et al., 2019).

A obesidade é considerada um problema de saúde pública que já alcançou níveis pandêmicos no mundo atual, com uma prevalência que triplicou nas últimas décadas (WHO, 2016; YANOVSKI, 2018). Dentre as várias doenças associadas à obesidade estão comorbidades também muito prevalentes, como a hipertensão arterial sistêmica (SERAVALLE; GRASSI, 2017; SUSIC; VARAGIC, 2017), diabetes mellitus tipo 2 (DAOUSI et al., 2006; THOMAS; ZIMMET; SHAW, 2006), doenças cardiovasculares (CSIGE et al., 2018), câncer (ACKERMAN et al., 2017; FONT-BURGADA; SUN; KARIN, 2016) e os distúrbios de sono (KOREN;

TAVERAS, 2018; MUSCOGIURI et al., 2019). Dentre os problemas no padrão de sono frequentes em nível populacional destaca-se a curta duração de sono (AZIZ et al., 2017; BENHAM; GHADDAR; TALAVERA-GARZA, 2017; LIN et al., 2018; SZABO; MÁTÉ; FRIGY, 2019; WU et al., 2019). Nesse sentido, a ligação entre curta duração do sono e obesidade é bem evidenciada na literatura (CAPPUCCIO et al., 2008; ITANI et al., 2017; WU; ZHAI; ZHANG, 2014), porém é evidente a necessidade de se consolidar tal relação com metodologias robustas.

Diante deste cenário, o objetivo do presente estudo é realizar uma revisão sistemática da literatura incluindo estudos de coorte que tenham avaliado a associação entre curta duração de sono e obesidade e, posteriormente, realizar uma meta-análise dos dados encontrados. Nosso objetivo secundário é analisar estudos da busca que tenham avaliado a associação entre curta duração do sono e doenças crônicas não-transmissíveis como a hipertensão arterial sistêmica, a diabetes mellitus tipo 2, as doenças cardiovasculares, a síndrome metabólica, assim como qualidade de vida e mortalidade das populações estudadas.

# 2. FUNDAMENTAÇÃO TEÓRICA

## 2.1. Definição e função do sono

O sono é uma condição fisiológica cíclica presente em seres vivos do reino animal, caracterizado pelo estado completamente ou parcialmente imóvel de um indivíduo, de natureza involuntária e automática, com estímulos externos reduzidos em relação ao estado de vigília (FERNANDES, 2006). Quando os sistemas reguladores do sono estão em perfeito equilíbrio, espera-se durante a noite um episódio de sono estável, seguido de um episódio de vigília consolidado (KIM; LEE; DUFFY, 2013).

O sono possui várias funções no organismo, como a consolidação de memórias (RASCH; BORN, 2013; STICKGOLD, 2005), que se origina da reativação das representações de memória neuronal codificadas que acontecem durante o sono de ondas lentas e, por fim, são transformadas em memória de longo prazo e o sono REM (*Rapid Eyes Movement)* pode subsequente estabilizar memórias transformadas (RASCH; BORN, 2013). Há também a função restauradora do sono, que acontece a partir da mudança da atividade de ondas lentas do eletroencefalograma (BORBÉLY; ACHERMANN, 1992).

O mecanismo fisiológico homeostático e o ciclo circadiano são os dois moduladores básicos do sono. A cota de duração e intensidade do sono são determinados pelo mecanismo homeostático. A conexão de entrada (via aferente) para o controle do ciclo circadiano tem seus receptores na retina e respondem ao nível geral de iluminação ou outros fatores do meio ambiente (GOOLEY et al., 2001).

## 2.2. Fisiologia do sono

A arquitetura do sono é baseada em parâmetros fisiológicos e investigada por meio de eletroencefalograma (EEG), eletromiograma (EMG) e eletro-oculograma (EOG). A polissonografia (PSG) é atualmente considerada como padrão ouro para avaliação do sono, permitindo classificar os estágios *Rapid eyes movement* (REM) e *Non-rapid eyes movement* (NREM) (BASSETTI; DOGAS; PEIGNEUX, 2014).

O período da vigília é caracterizado no EEG por ondas beta de baixa amplitude e ritmo alfa de alta frequência (40-300 Hz), enquanto que no EMG e no EOG a atividade segue contínua (Figura 1) (BASSETTI; DOGAS; PEIGNEUX, 2014). O sono é então iniciado pela ativação de neurônios serotoninérgicos da rafe no tronco encefálico, que inibe a transmissão de impulsos sensoriais para o córtex cerebral e inibe a atividade motora diretamente ou por meio do tálamo (FERNANDES, 2006). A constituição do sono é dada por meio da alternância dos estágios REM e NREM (FERNANDES, 2006). O sono NREM é composto por quatro fases (as fases 3 e 4 correspondem a ondas lentas ou delta), enquanto que sono REM é caracterizado por ondas dessincronizadas no EEG e de baixa amplitude (ALÓE; AZEVEDO; HASAN, 2005).

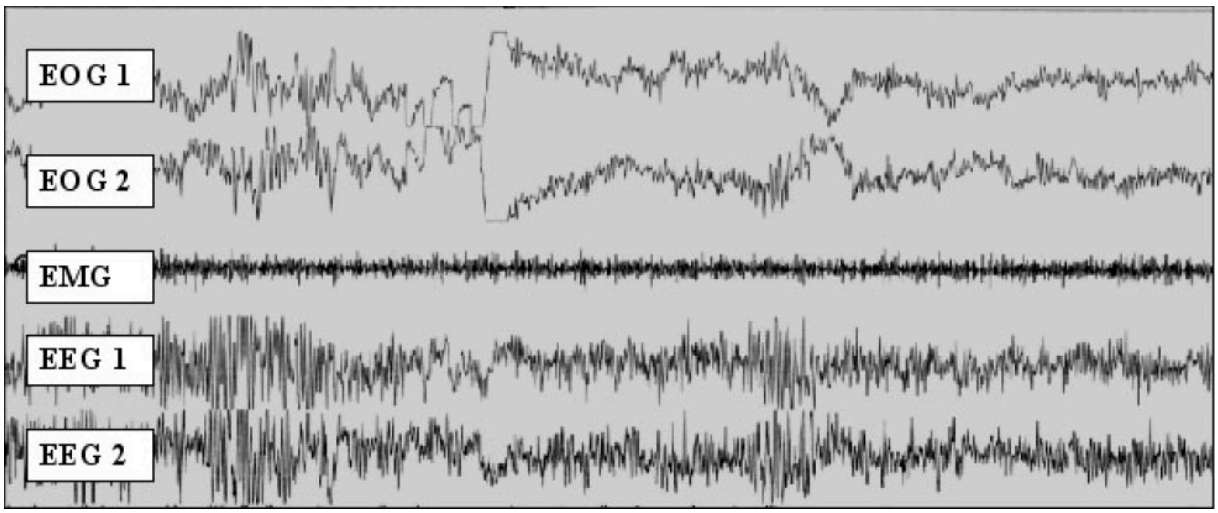

**Figura 1.** Trecho de 30 segundos de vigília em traçado polissonográfico; EOG-1- eletro-oculograma do olho esquerdo; EOG-2- eletro-oculograma do olho direito; EMG – eletromiograma submentoniano; EEG – canais de encefalograma (FERNANDES, 2006).

O sono NREM, também chamado de sono de ondas lentas, pode ser fracionado em três fases pelo EEG (fase 1 a fase 3) (BASSETTI; DOGAS; PEIGNEUX, 2014). Tais fases representam uma progressiva continuidade do aprofundamento do sono, sendo a fase 1 mais baixa e a 3 a mais elevada (RENTE; PIMENTEL, 2004). Na fase 1 as ondas alfa vão progressivamente sendo substituídas pelo ritmo teta (6-9 Hz) (Figura 2); na fase 2 há surtos curtos de ondas de frequência rápida (Figura 3); na transição da fase 2 para a 3 surgem surtos de ondas deltas amplas e de baixa frequência ( 0,5-4 Hz); e ainda na fase 3 do sono há uma predominância do sono de ondas lentas (Figura 4) (RENTE; PIMENTEL, 2004). O sono REM é descrito por uma predominância de ritmos teta (6-9 Hz) e gamma (30-300 Hz), de baixa e alta amplitude (Figura 5), também chamado de sono paradoxal (BASSETTI; DOGAS; PEIGNEUX, 2014). É importante ressaltar que em adultos durante a fase delta do sono (estágios 3 e 4), a maior parte do hormônio o crescimento (GH) é secretada, com pulsos de grandes amplitudes, responsáveis por exercer fatores estimuladores e inibidores respectivamente.

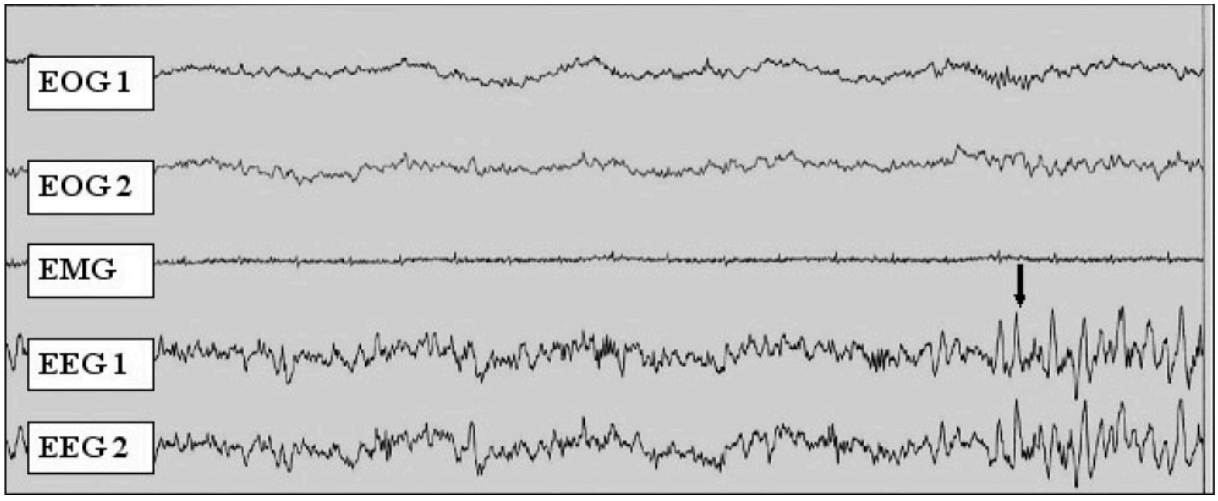

**Figura 2.** Trecho de 30 segundos em estágio 1 do sono NREM (FERNANDES, 2006).

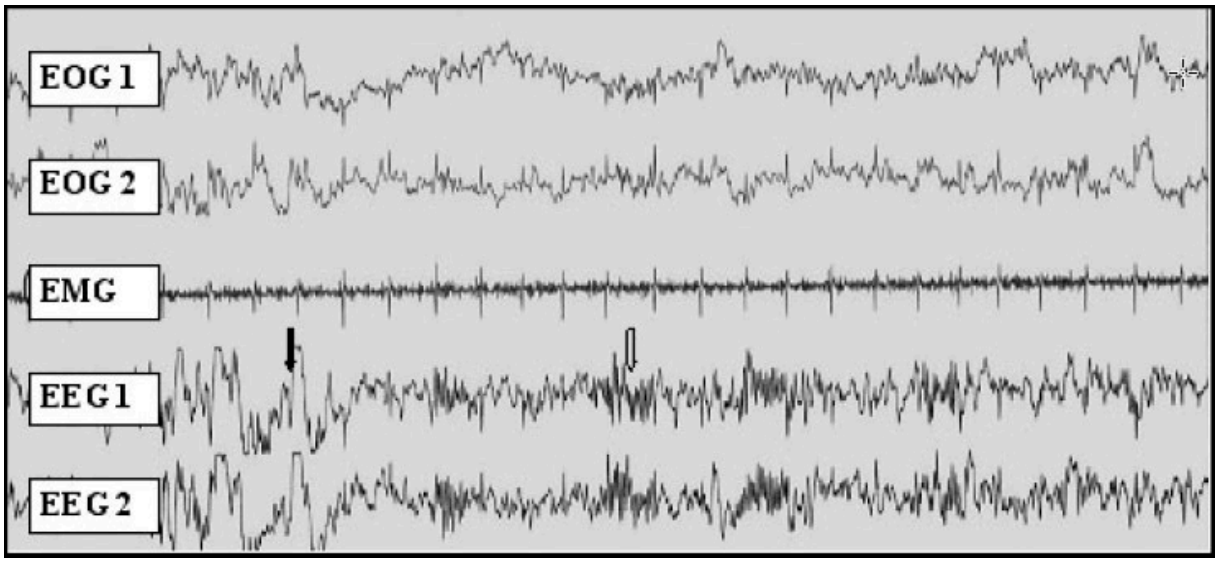


**Figura 3.** Trecho de 30 segundos em estágio 2 do sono (FERNANDES, 2006).

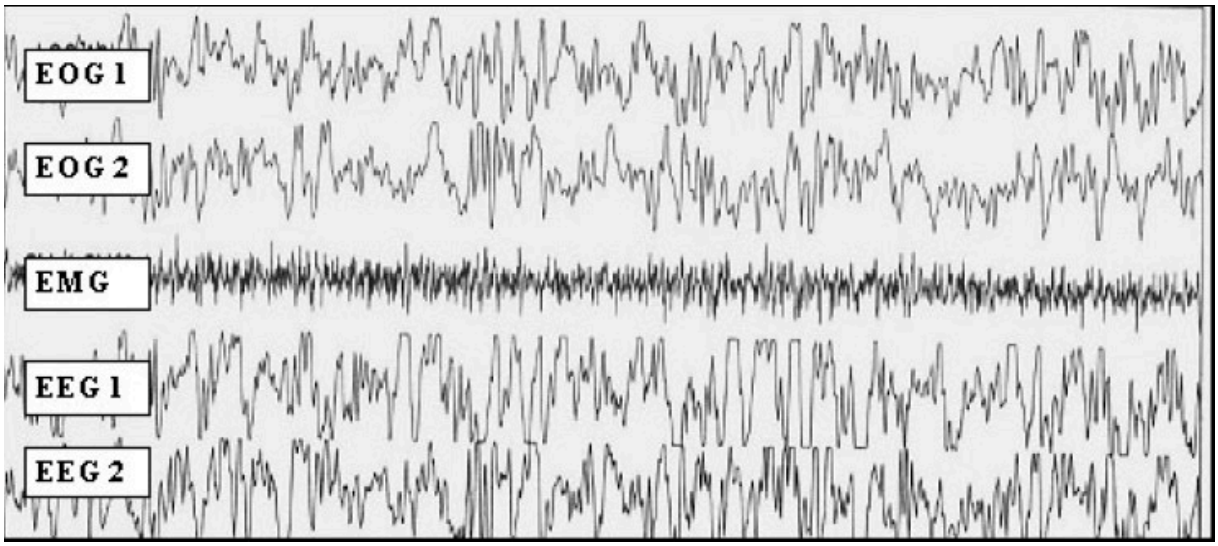


**Figura 4.** Trecho de 30 segundos em estágio 3 do sono (FERNANDES, 2006).

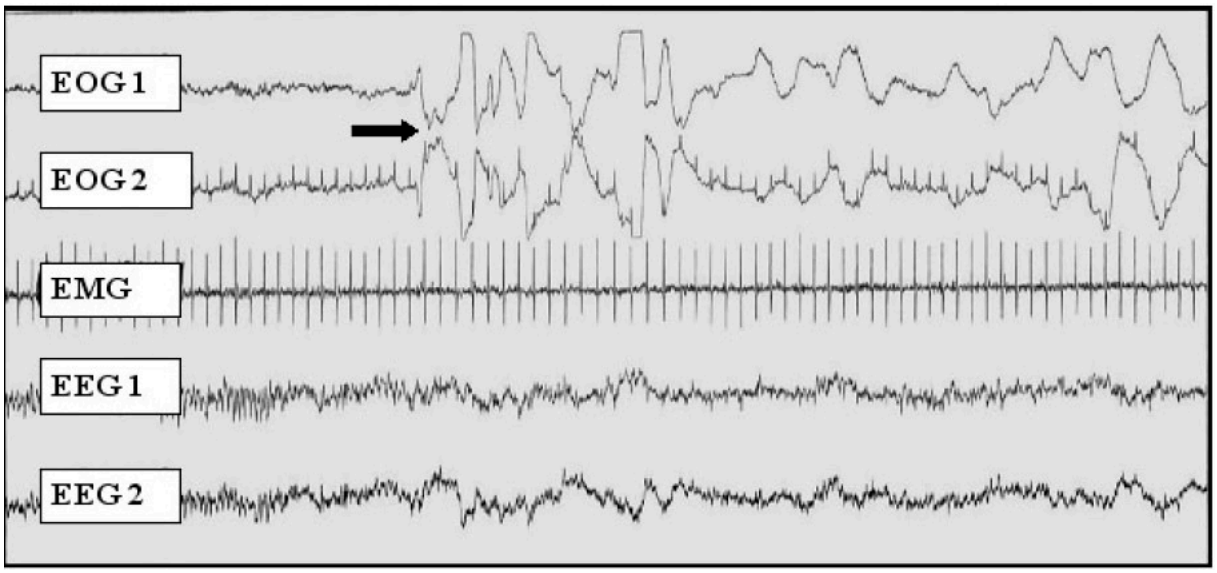


**Figura 5.** Trecho de 30 segundos em sono REM (FERNANDES, 2006).

**Tabela 1.** Caraterísticas do sono (NREM e REM)

| Tipo de sono | Estágio do sono |
|---|---|
| NREM | Estágio 1: período de transição entre a vigília e o sono, durando geralmente de 5 a 10 minutos. A frequência cardíaca diminui e os olhos se movimentam lentamente. |
| | Estágio 2: Estágio mais profundo que o estágio 1 do sono em que os movimentos oculares começam a desaparecer. Há um relaxamento nos músculos esqueléticos e poucos movimentos corporais. Esse estágio representa metade do período do sono total em adultos. |
| | Os estágios 3 e 4 são agrupados em um único estágio, também chamado de estágio do sono delta. É o estágio mais profundo do sono, onde há uma redução da frequência respiratória e não há movimentos oculares ou atividade muscular. |
| REM | Este estágio é caracterizado por uma redução no tônus muscular e por paralisia muscular. Também é possível |

| | |
|---|---|
| | observar respiração irregular, aumento da frequência cardíaca, movimentos oculares rápidos, os músculos das vias áreas relaxam e o consumo de oxigênio cerebral aumenta. Ele compreende cerca de 20% do sono do adulto. |

**Adaptado de:** MAGALHÃES; MATARUNA, 2007

## 2.3. Reguladores do sono

A cronobiologia é uma ciência que estuda fenômenos biológicos que se repetem com determinadas periodicidades e influenciam variáveis fisiológicas mais longas, como o ciclo menstrual, ou mais curtas, como o sono. Essa ritmicidade de variáveis fisiológicas, morfológicas e comportamentais é chamada de ritmos ou ciclos biológicos (JANSEN et al., 2007).

Os ritmos biológicos são classificados em circadianos, que obedecem um período de aproximadamente 24 horas; ultradianos, com período inferior a 20 horas; infradianos, que compreende períodos superiores a 28 horas; circanuais, com período de aproximadamente um ano; circalunares, com período de aproximadamente uma lunação; circasseptanos, com período de aproximadamente uma semana; e circamarés, período de aproximadamente 12 horas (JANSEN et al., 2007).

O termo circadiano vem da palavra em latim *circa diem,* que significa cerca de um dia (TOH, 2008). O ritmo circadiano é controlado por meio do relógio endógeno localizado no núcleo supraquiasmático do hipotálamo e é responsável por definir o período de sono durante cada ciclo (MURILLO-RODRIGUEZ et al., 2012). Este por sua vez, é responsável por sincronizar o sono entre as necessidades do indivíduo e o ambiente (OUYANG et al., 1998), portanto esse sistema de manutenção de tempo produzirá o ciclo circadiano ainda que as indicações de tempo (*zeitgebers*) estejam ausentes (TOH, 2008).

O ciclo claro-escuro é um dos sincronizadores dos ritmos biológicos relacionados ao sono. A luz pode mudar a fase do relógio circadiano por uma série de eventos no interior do núcleo supraquiasmático. Assim, esse sinal ambiental ou sua ausência são transmitidos por meio do trato retino-hipotalâmico localizado na retina para o núcleo suprasquiasmático e, em seguida, para a glândula pineal, que regula a secreção de melatonina (WEINERT, 2000). A melatonina desempenha o papel de sincronização como marcador do ritmo circadiano, sendo produzida durante o período da noite e atingindo o pico entre as 2:00h e 4:00 da madrugada (JANSEN et al., 2007). Em contrapartida, a secreção de melatonina é suprimida na presença de luz, que faz com que ocorra diminuição no momento do despertar (WEINERT, 2000). Portanto, a melatonina desempenha um papel de sinalizador temporal para o sistema nervoso central, arrastando o ritmo sono-vigília para o ciclo 24 horas (claro/escuro) (ZISAPEL, 2001).

### 2.4. Duração do sono

A duração de sono ideal e recomendada é variável para cada fase da vida (HIRSHKOWITZ et al., 2015**)**. A Tabela 2 descreve as recomendações da duração de sono em diferentes faixas etárias.

**Tabela 2.** Recomendação de duração de sono em diferentes faixas etárias.

| **Idade** | **Recomendação (h)** | **Não recomendado (h)** |
|---|---|---|
| **Recém-nascido** | 14 a 17 | <11 |
| **0 a 3 meses** | | >19 |
| **Bebês** | 12 a 15 | <10 |
| **4 a 11 meses** | | >18 |

| | | |
|---|---|---|
| **Crianças** | 11 a 14 | <09 |
| **1 a 2 anos** | | >16 |
| **Pré-escolares** | 10 a 13 | <08 |
| **3 a 5 anos** | | >14 |
| **Criança em idade escolar** | 09 a 11 | <07 |
| **6 a 13 anos** | | >12 |
| **Adolescentes** | 08 a 10 | <07 |
| **14 a 17 anos** | | >11 |
| **Jovens adultos** | 07 a 09 | <06 |
| **18 a 25 anos** | | >11 |
| **Adultos** | 07 a 09 | <06 |
| **26 a 64 anos** | | >10 |
| **Adultos mais velhos** | 07 a 08 | <05 |
| **>65 anos** | | >09 |

**Fonte:** Adaptado de HIRSHKOWITZ et al., 2015**.**

Segundo a *American Heart Association* e *The United States National Sleep Foundation* (HIRSHKOWITZ et al., 2015; ST-ONGE et al., 2016), é recomendado que um adulto tenha a duração do sono entre sete e oito horas por dia. Essa demanda de sono varia de indivíduo para indivíduo, ou seja, cada indivíduo possui uma recomendação de duração de sono por noite para manter o bom desempenho durante a vigília (ORZEŁ-GRYGLEWSKA, 2010). Ainda que a recomendação do tempo de sono considere o estágio da vida, o sexo e o cronotipo são também determinantes individuais para a duração do sono (FERRARA; DE GENNARO, 2001), uma vez que é reportado na literatura que mulheres e indivíduos com cronotipo vespertino geralmente apresentam maior necessidade de sono (BROMAN; LUNDH; HETTA, 1996; FERRARA; DE GENNARO, 2001; TAILLARD; PHILIP; BIOULAC, 1999).

### 2.4.1. Curta duração do sono

Nas últimas décadas a duração do sono tem sido encurtada devido às demandas da vida moderna (FORD; CUNNINGHAM; CROFT, 2015; KRONHOLM et al., 2008; LÉGER et al., 2011; "QuickStats", 2005). Uma pesquisa multinacional mostrou a prevalência da curta duração do sono em diversos países, com elevada frequência no Canadá (11,2%-11,5%) e menos comum na Holanda (<1%). Tal prevalência tem também aumentado na Austrália e Noruega (BIN; MARSHALL; GLOZIER, 2013). Já nos Estados Unidos, numa população de 158.468 indivíduos, a prevalência de curta duração de sono em adultos aumentou significativamente no período de 2010 a 2018 (30,9% e 35,6%, respectivamente), sendo 24% maior em 2018 (OR: 1.24, 95%CI: 1,17, 1,31) e mais comum entre as categorias de emprego relacionadas a serviços de proteção e forças armadas (50%), serviços de assistência à saúde (45%), transporte de materiais e cargas (41%) e serviços de produção (41%) (KHUBCHANDANI; PRICE, 2020).

A curta duração do sono pode levar a consequências no organismo, como tempo de reação prolongado, distúrbios na atenção e concentração, dificuldade de memorização e, em seu nível mais alto, pode causar estresse, cansaço e diminuição da eficácia no trabalho (ORZEŁ-GRYGLEWSKA, 2010). Dentre os fatores de risco que podem influenciar a duração do tempo de sono estão o sexo feminino, o consumo de álcool e de substâncias ilícitas, o diagnóstico de angina, a depressão e a obesidade (SIMÕES et al., 2019).

## 2.5. Obesidade

### 2.5.1. Definição de obesidade

A obesidade é definida pela Organização Mundial de Saúde (OMS) como acúmulo anormal ou excessivo de gordura associado ao elevado risco a saúde do indivíduo. Para realizar a triagem da obesidade é recomendado o Índice de Massa corporal (IMC) - peso dividido por altura elevada ao quadrado (WHO, 2000). Para pessoas com mais de 18 anos, valores iguais ou superiores a 25kg/m² são considerados sobrepeso, e maiores ou igual a 30 kg/m² obesidade (WHO, 2016).

A obesidade é considerada uma doença crônica, pois além dos riscos à saúde determinado pelo excesso de peso, potentes mecanismos biológicos são alterados em pessoas obesas, dificultando a perda e promovendo o ganho de peso (BLÜHER, 2019). Estudos têm mostrado que a obesidade é uma doença causada por condições multifatoriais relacionadas ao ambiente, estilo de vida moderno, genética, estresse, iatrogenia farmacêutica, redução do sono, disruptores endócrinos e tabagismo (ABESO, 2016).

### 2.5.2. Prevalência de obesidade no mundo

Nas últimas décadas a prevalência de obesidade no mundo triplicou alcançando níveis pandêmicos (WHO, 2016; YANOVSKI, 2018). Nos Estados Unidos entre os anos de 2013 e 2014, a obesidade afetava 35% dos homens (37,9% hispânicos, 38% negros, 34,7% brancos, 12,6% asiáticos) e 40,4% das mulheres (57,2% negras, 46,9% hispânicas, 38,2% brancas, 12,4% asiáticas) (FLEGAL et al., 2016). Segundo O NCD-Risk (Risk Factor Collaboration) (NCD, 2017), a prevalência de obesidade aumentou em praticamente todos os países do mundo entre os anos de 1975 e 2016. Foi observado aumento significante no sul da Ásia, sudeste da Ásia e sul da América Latina ao longo de 40 anos entre 1975 e 2016 (NCD, 2017). Em

2016 mais de 1,9 bilhão de pessoas (39%) com mais de 16 anos estavam com sobrepeso e, destas, 650 milhões eram obesos (13%) (WHO, 2016). Já em relação a obesidade mórbida (IMC ≥ 35 kg/m²), a prevalência global foi de 0,64% nos homens e de 1,6% nas mulheres (NCD, 2016). No Brasil, a vigilância de fatores de risco e proteção para doenças crônicas por inquérito telefônico (Vigitel) constatou em 2018 que a prevalência de obesidade no Brasil na população adulta foi de 19,8%, sendo que é maior entre as mulheres (20,7%) do que entre os homens (18,7%) (BRASIL, 2019).

### 2.5.3. Relação entre curta duração do sono e obesidade

Vários estudos epidemiológicos recentes conduzidos em populações do mundo todo encontraram relação entre a curta duração do tempo de sono e a obesidade (AZIZ et al., 2017; BENHAM; GHADDAR; TALAVERA-GARZA, 2017; LIN et al., 2018; SZABO; MÁTÉ; FRIGY, 2019; WU et al., 2019).

A relação entre duração de sono e a obesidade mórbida foi investigada em trabalhadores e a prevalência de obesidade mórbida foi de 24% num total de 9505 participantes que dormiam menos do que 6 horas por dia, enquanto que a prevalência foi de 14% entre para os participantes que dormiam 8 horas ou mais. Participantes com duração do sono inferior a seis horas apresentaram duas vezes maiores chances de desenvolverem obesidade mórbida em relação àqueles com tempo de sono regular (6-7,9 horas por dia) (OR = 1,8; 95%IC: 1,5, 2,2) (AZIZ et al., 2017). Em um estudo conduzido com 228 trabalhadores foi constatado que aqueles com duração de sono igual ou inferior a seis horas por dia apresentaram maiores chances de serem obesos quando comparados aos participantes que dormiam entre sete a nove horas (OR = 1,90; 95%IC: 1,04, 3,47) (BENHAM; GHADDAR; TALAVERA-GARZA, 2017). Resultado semelhante foi encontrado em

estudo transversal realizado por Lin et al. (2018), em que os autores avaliaram 1548 adultos com idade entre 20 e 64 anos e identificaram que a duração do sono igual ou inferior a seis horas por dia foi associada ao risco de desenvolver obesidade (OR = 1,31; 95%IC: 1,01, 1,76).

Estudos de coorte encontrados na literatura também avaliaram a associação entre o tempo de sono e o desenvolvimento da obesidade (GUTIÉRREZ-REPISO et al., 2014; KOBAYASHI et al., 2012; NAGAI et al., 2013; THEORELL-HAGLÖW; LINDBERG, 2016; WATANABE et al., 2010; XIAO et al., 2013). Watanabe et al. (2010) investigaram a associação entre a curta duração do sono e o IMC elevado em uma amostra de 35.247 funcionários que foram acompanhados durante um ano. A razão de chance para o desenvolvimento da obesidade foi de 1,91 para participantes que dormiam menos de 5 horas por noite (95% CI: 1,36, 2,67) e 1,50 (95% CI: 1,24, 1,80) para os participantes que dormiam entre cinco e seis horas, comparado com o grupo de referência com duração do sono entre sete e oito horas. Outro estudo de coorte avaliou 21.469 adultos saudáveis com idade igual e superior a 20 anos, os quais foram acompanhados durante três anos para identificar a associação entre duração de sono e obesidade. Comparados com os participantes que dormiam sete horas por noite, participantes que dormiam cinco horas ou menos apresentaram maior chance de se tornarem obesos (OR = 1,5; 95% CI: 1,1-2,0) (KOBAYASHI et al., 2012). Há, porém, resultados conflitantes acerca dessa temática, tendo como exemplo a coorte prospectiva que avaliou 13.629 participantes com idade entre 40 e 79 anos em que os indivíduos foram acompanhados durante os anos de 1995 a 2006. Os resultados desse estudo não demonstraram associação significativa entre a duração do sono e obesidade (OR = 0,96; 95% CI: 0,59, 1,57) (NAGAI et al., 2013).

Além de estudos originais, algumas revisões sistemáticas com meta-análises vêm sendo estudadas com o objetivo de verificar a associação entre

curta duração do sono e obesidade em adultos e, em geral, mostraram resultados semelhantes (CAPPUCCIO et al., 2008; ITANI et al., 2017; WU; ZHAI; ZHANG, 2014). Uma revisão sistemática realizada por Cappuccio et al. (2008) com 45 estudos de diversos delineamentos teve como objetivo analisar a associação entre duração curta do sono ( ≤5horas de sono) e obesidade. Foram avaliados 634 511 participantes entre crianças e adultos, constando maiores chances dos indivíduos com curta duração de sono se tornarem obesos se comparados com os dormidores com durações regulares (OR = 1.55, 95%CI, 1.43, 1.68; $P < 0.0001$). No entanto, esta revisão, além de não apresentar força de evidência científica, incluiu estudos de diferentes delineamentos, sendo, portanto, uma revisão de pouca confiabilidade.

No entanto, duas dessas meta-análises - Itani et al. (2017) e Wu et al. (2014) - analisaram exclusivamente estudos de coortes, porém não apresentaram análise de força de evidência, nem utilizaram dados dicotômicos para realizar as análises. Itani et al. (2017) incluíram 21 estudos de coortes e estudos clínicos randomizados, com população acima de 20 anos, e foi encontrado que indivíduos com curta duração de sono apresentaram maior risco de se tornarem obesas se comparadas com as que dormem regularmente (RR = 1.38 95%CI, 1.25, 1.53). Wu et al. (2014) realizaram outra meta-análise incluindo 11 estudos de coortes prospectivas, com um total de 197 906 participantes, e constatou que pessoas com curta duração de sono tinham maiores chances de se tornarem obesas em comparação com os que dormiam regularmente (OR = 1.45 95%CI, 1.25, 1.67) (WU; ZHAI; ZHANG, 2014).

### 2.5.4. Mecanismos que explicam a relação entre sono curto e obesidade

Estudos vêm apontando que a privação do tempo de sono pode estar associada a um padrão alimentar inadequado, tendo em vista que um

consumo elevado de alimentos de alta densidade energética, com grande quantidade de carboidratos, gordura saturada e sódio, e baixo consumo de frutas e vegetais são comuns em indivíduos privados de sono (FANG et al., 2015; KANT; GRAUBARD, 2014).

Kant et al. (2014) realizaram estudo transversal com 15.199 adultos com o objetivo de avaliar a associação entre duração do sono e hábitos alimentares. Foi observado que mulheres com tempo curto de sono (≤ 6 horas) apresentaram consumo de açúcares totais e cafeína maior quando comparado às mulheres com duração média de sono (7-8 horas) (120g *versus* 116g para açúcares totais, p=0,04; 200mg *versus* 184mg para cafeína, p=0,0001).

Um estudo crossover randomizado realizado por Hogenkamp et al. (2013) com 16 participantes teve como objetivo comparar a escolha do tamanho das porções após uma noite de sono regular (8 horas) e após uma noite de vigília. Foi observado que após a privação total do sono noturno, os participantes escolheram maiores porções de alimentos independente da composição (p=0,02). Houve aumento da fome (p<0,001) e escolha de porções maiores de lanches durante o período da manhã (p=0,02) na condição de privação total do sono quando comparado à condição com tempo de sono regular.

Fang et al. (2015) realizaram um estudo experimental com 34 participantes que foram submetidos a privação total do sono e 12 participantes que compuseram o grupo controle, com média de oito horas de sono por noite. Os autores compararam a ingestão alimentar entre os dois grupos e observaram que, quando comparado ao grupo com tempo de sono regular, o grupo privado de sono consumiu maior porcentagem de calorias provenientes de gorduras (p=0,006) e menor porcentagem de consumo de carboidratos (p=0,004).

Assim, o aumento do consumo calórico pode explicar a associação entre curta duração do sono e maior risco de desenvolver obesidade. Destaca-se, nesse sentido, uma cascata de mecanismos que explicam o porquê do indivíduo que dorme pouco terem um aumento do consumo alimentar. Entre eles, destaca-se que indivíduos expostos a privação de sono apresentam alteração hormonal dos níveis de leptina e grelina, hormônios responsáveis pelo controle da fome e saciedade, consequentemente causando um aumento na ingestão de alimentos (BROUSSARD et al., 2016; CRISPIM et al., 2007; SPIEGEL et al., 2004; TAHERI et al., 2004). Ambos hormônios, leptina e grelina, fazem parte do sistema orexina, que além de ser responsável pelo controle da alimentação também regula o sistema de vigília e gasto de energia do corpo que podem explicar o aumento do IMC desses indivíduos (VAN CAUTER et al., 2008). Além disso, pessoas que não dormem o suficiente têm mais oportunidades de consumir alimentos, principalmente pela escolha dos não-saudáveis, com alto teor de carboidratos , açúcares, gordura e sódio (CHAPUT, 2014; COOPER et al., 2018; CRISPIM et al., 2007; CRISPIM; MOTA, 2019). Além do consumo de alimentos não saudáveis, indivíduos com curta duração de sono apresentam geralmente hábitos alimentares inadequados e realizam suas refeições em horários mais tardios do dia, inclusive próximo ao horário de dormir (REUTRAKUL; VAN CAUTER, 2018), considerado um período inadequado para a ingestão alimentar devido à alteração da eficiência do metabolismo dos nutrientes (BIRKETVEDT et al., 2014; RÁCZ et al., 2018). Pessoas com curta duração do sono também estão relacionadas com maior sensação de fadiga, o que diminui a prática de atividades físicas, o que as torna cada vez mais sedentárias (COOPER et al., 2018; OGILVIE; PATEL, 2017).

## 2.6. Relação entre curta duração do sono e outras comorbidades

Recentemente vários estudos vêm estudando a relação entre a curta duração de sono e outras comorbidades, tais como síndrome metabólica (FAN et al., 2020; KIM et al., 2018; SMILEY; KING; BIDULESCU, 2019), diabetes mellitus tipo 2 (KOREN; TAVERAS, 2018; LIN; TSAI; YEH, 2016; NUYUJUKIAN et al., 2016; WORLEY, 2018), doenças cardiovasculares (CHANDOLA et al., 2010; KHAN; AOUAD, 2017) e hipertensão (BUXTON; MARCELLI, 2010; KIM; JO, 2010; KOREN; TAVERAS, 2018; WORLEY, 2018).

Fan et al. (2020) avaliaram a associação entre a duração do sono e síndrome metabólica em 272 adultos. Foi constatado que o tempo de sono inferior à seis horas por dia foi associado ao maior risco de desenvolver síndrome metabólica (OR = 1,10) (FAN et al., 2020). Em outro estudo transversal realizado com 133.608 adultos com idade entre 40 e 69 anos foi identificado que, comparado com participantes com duração de sono regular (6-<8 horas), indivíduos com curta de sono (<6 horas) foram mais propensos a desenvolverem síndrome metabólica (OR = 1,12, CI95%: 1,05-1,19) (KIM et al., 2018).

A relação entre síndrome metabólica e duração do sono também foi avaliada em estudos de coorte encontrados na literatura (CHAPUT et al., 2013; CHOI et al., 2011; DENG et al., 2017; OTSUKA et al., 2011). Em um desses estudos foram incluídos 1107 adultos com idade entre 40 e 70 anos, e a associação entre tempo de sono e síndrome metabólica foi avaliada. Participantes com menos de seis horas de sono apresentaram maior probabilidade de desenvolver síndrome metabólica em relação aos participantes que dormiam entre 6 e 7,9 horas por dia (HR: 1,798; 95%CI: 1,06-3,05) (CHOI et al., 2011). Chaput et al. (2013) avaliaram 293 adultos com idades entre 18 e 65 anos durante o período de seis anos. O risco de desenvolver síndrome metabólica foi significativamente maior entre

participantes que dormiam menos (≤ 6 horas por dia), comparado aos participantes que dormiam entre 7 e 8 horas de sono (RR = 1,74; 95%CI: 1,05-2,72) (CHAPUT et al., 2013).

Um estudo recente avaliou a associação entre a duração de sono e diabetes tipo 2 em 1.533 participantes (733 homens e 800 mulheres) entre 19 e 64 anos. Participantes com duração de sono inferior a cinco horas apresentaram 2,04 vezes maior risco de desenvolver diabetes comparado com participantes com tempo superior a sete horas de sono (95%CI: 1,05-3,95) (LIN; TSAI; YEH, 2016). Estudos de coorte também avaliaram a relação entre curta duração de sono e diabetes tipo 2 (FERRIE et al., 2015; GANGWISCH et al., 2007; NUYUJUKIAN et al., 2016), como na coorte americana que acompanhou de 8 a 10 anos 8.992 indivíduos com idade entre 32 e 86 anos. Foi concluído que a duração curta de sono (≤ 5 horas) pode ser um fator de risco significativo para a incidência de diabetes (OR = 1,47; 95%IC: 1,03-2,09) se comparado com indivíduos que dormiam 7 horas por noite (GANGWISCH et al., 2007). Em outra coorte do *The Whitehall II study* com 5 anos de acompanhamento, a curta duração do sono (< 6 horas) foi associada com a incidência de diabetes tipo 2 (OR = 1,35; 95%IC: 1,04-1,76), comparando com indivíduos que dormiam 7 horas por dia (FERRIE et al., 2015). Já em uma coorte de 3 anos de acompanhamento com 1.899 índios americanos nativos do Alasca, a incidência bruta de diabetes entre os indivíduos com curta duração de sono (≤6 horas) foi de 4,6/100 pessoas se comparado com aqueles que dormiam 8 horas ou mais. Além disso, houve um aumento do risco de desenvolver diabetes (HR = 1,55; 95% IC: 1,11-2,17) entre os indivíduos que dormiam pouco (NUYUJUKIAN et al., 2016).

A associação entre a curta duração do sono e hipertensão arterial foi investigada em diversos estudos (BUXTON; MARCELLI, 2010; KIM; JO, 2010; KOREN; TAVERAS, 2018; WORLEY, 2018). Kim et al. (2010) realizaram um estudo com 5.393 coreanos com idade entre 19 e 99 anos para

avaliar a associação entre privação do sono e pressão arterial. Participantes com tempo de sono inferior a cinco horas por dia apresentaram 1,5 vezes maior chance de desenvolver hipertensão arterial quando comparados àqueles com média de tempo de sono de sete horas por dia (IC 95%: 1,19-1,94).

Deng et al. (2017) investigaram o impacto da duração curta do sono no desenvolvimento de hipertensão arterial em uma coorte com 162.121 indivíduos com idade entre 20 e 80 anos. Foi observado que os participantes que dormiam menos do que seis horas por dia apresentaram maior risco (8%) de desenvolver hipertensão arterial quando comparados aos participantes com tempo sono entre seis e oito horas por noite (HR: 1,08; IC 95%: 1,04-1,13).

Deng et al. (2017) também avaliaram a relação com a síndrome metabólica com 162.121 participantes (85.255 mulheres e 76.866 homens) com idade entre 20 e 80 anos em um estudo de coorte que teve como objetivo investigar o impacto da duração do sono no desenvolvimento da síndrome metabólica. Participantes com duração do sono inferior a seis horas por dia apresentaram aumento do risco para o desenvolvimento de síndrome metabólica em 9% (IC 95%: 1,05-1,13). Em contrapartida, o sono prolongado superior a oito horas foi considerado fator protetor (HR: 0,93; IC: 0,88-0,99).

Até o momento, poucos os estudos avaliaram a relação entre privação do sono e qualidade de vida e mortalidade. Nesse tema, o risco de mortalidade foi analisado em um estudo de coorte realizado com 6.928 adultos que foram acompanhados durante nove anos. O estudo, que teve como objetivo investigar a relação entre restrição do sono e mortalidade por diversas causas, incluindo doença isquêmica do coração, câncer e acidente vascular encefálico, encontrou que homens que dormiam menos do que seis horas por dia apresentaram 1,7 vezes maior taxa de mortalidade por qualquer

causa quando comparado aos participantes que dormiam entre sete e oito horas por noite (WINGARD; BERKMAN, 1983).

Kripke et al. (2002) durante seis anos acompanharam mais de 1,1 milhão de homens com idade entre 30 e 102 anos com o intuito de investigar se a duração do sono é um indicativo de melhor tempo de sobrevida e apontar os riscos de mortalidade. O aumento do risco foi superior a 15% para aqueles que dormiam menos do que 4,5 horas.

A relação entre sono encurtado e qualidade de vida também foi estudada recentemente (PAIVA; GASPAR; MATOS, 2015; PALHARES et al., 2014). Foi observado, em um estudo que incluiu 3.476 adolescentes brasileiros com idade entre 12 e 19 anos, que participantes privados de sono (diferença ≥3 horas de sono entre dias de semana e dias de final de semana) apresentaram percepção de qualidade de vida reduzida se comparados com indivíduos sem privação de sono (PAIVA; GASPAR; MATOS, 2015). Palhares et al. (2014) analisaram a associação entre qualidade do sono e qualidade de vida de 264 profissionais de enfermagem, e encontraram uma associação negativa entre qualidade de vida e qualidade do sono nos participantes avaliados ($r=-0,56$; $p<0,001$).

## 3. JUSTIFICATIVA

O sono é uma condição fisiológica de grande importância para todos os seres vivos, tendo em vista que é responsável por funções vitais para o organismo, tais como a função restauradora e consolidadora de memórias. Diante de tal relevância dessa função fisiológica, diversos estudos apontam que a duração do sono precisa ser suficiente para que a manutenção de todos os processos envolvidos durante o sono seja satisfatória.

Sabendo-se que há grande número de estudos na literatura avaliando a curta duração de sono e sua associação com a incidência de várias comorbidades - tais como obesidade, diabetes tipo 2, síndrome metabólica,

hipertensão arterial sistêmica e doenças cardiovasculares -, é necessário conhecer a relevância e força desses achados para diferentes áreas da saúde. Em se tratando especificamente da relação entre sono e obesidade, outras revisões sistemáticas com meta-análise têm avaliado esse tópico e, de maneira geral, mostram que tal associação não apresenta força de evidência confiável, tendo em vista que incluíram estudos transversais, estão desatualizadas ou pelo rigor metodológico limitado utilizado.

Diante disto, este estudo se justifica pela necessidade de compreender melhor a literatura que tem estudado o risco de desenvolver obesidade e sua associação com a curta duração de sono.

# 4. OBJETIVOS

## 4.1. Objetivo Geral

Realizar uma revisão sistemática e meta-análise com estudos de coortes que tenham avaliado a associação entre a curta duração do sono e obesidade.

## 4.2. Objetivos específicos

- Realizar busca em base de dados incluindo as palavras chaves que identifiquem estudos de coorte que avaliaram a associação entre a curta duração de sono e o desfecho primário 'obesidade';
- Selecionar estudos de coorte a serem incluídos na revisão sistemática, seguindo os critérios de inclusão e exclusão;
- Avaliar a qualidade (risco de viés) dos estudos de coortes incluídos;
- Realizar meta-análise com os dados extraídos;
- Avaliar a qualidade da evidência e força de recomendação;
- Avaliar a associação entre duração de sono e os desfechos secundários, diabetes mellitus tipo 2, síndrome metabólica, risco de doenças cardiovasculares, hipertensão arterial sistêmica, obesidade abdominal, qualidade de vida e mortalidade, na busca realizada.

**5. ARTIGO 1**. Is short sleep duration associated with obesity? A systematic review and meta-analysis of cohort studies

**Is short sleep duration associated with obesity? A systematic review and meta-analysis of cohort studies**

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Key words: short sleep, obesity, meta-analyses, systematic review.

**Abstract**

**Context:** The literature has explored a possible association between short sleep duration and risk of obesity. **Objective:** To analyze the association between sleep duration and obesity. **Methods:** LILACS, Medline, Central, Embase and Opengrey were searched until July 2020. Two authors screened the studies independently in Rayyan software according to PECO strategy (P: participants over 18 years old, E: short sleep duration, C: regular sleep, O: obesity). Only cohort studies were included. 3 286 studies were retrieved with the search strategy, but only 36 were included and disagreements were resolved by a third author. **Results:** Thirty-six studies were included, and twenty-two contributed with quantitative data. The quality of studies was assessed with Newcastle-Ottawa. The certainty of evidence was assessed using GRADE. The meta-analysis showed a significant association between short sleep and development of obesity (RR = 1.18, 95% CI, 1.15, 1.26; GRADE moderate), and the chances of developing obesity increased when sleep duration decreased. **Conclusions:** Short sleep duration may be associated with obesity. An increased odd of becoming obese may be associated to a sleep duration decreased. **PROSPERO registration number:** CRD42019130143.

**Keywords:** sleep, obesity, short sleep, sleep deprivation, overweight,

## INTRODUCTION

Short sleep duration has increased dramatically in the last decades[1] both in developed[2] and developing countries[3]. At the same time there has been a significant increase in the prevalence of obesity worldwide.[4] According to the World Health Organization, obesity is a global epidemic[5] and is a cause of major morbidity and mortality, including risk of cardiovascular disease and type 2 diabetes[6–8]. Nowadays, 39% of people around the world are considered overweight[9] and 12% are obese.[4]

Studies conducted since 1970 have proposed an association between short sleep duration and development of obesity,[10] which was demonstrated firstly in adults,[11–23] and after in children[24–32] and adolescents.[25,33–35] The possible mechanisms proposed since then to explain this association include the effect of lack of sleep on increasing plasma concentrations of the orexigenic hormone ghrelin and decreasing the anorexigenic hormone leptin, which would lead to the increase of energy intake by the increased hunger and appetite and reduced satiety.[36,37] This metabolic pattern was also found in epidemiologic studies.[37,38] In addition, sleep deprivation is associated with impaired insulin sensitivity and insulin resistance,[39,40] which is associated with obesity. Finally, more awake time may allow more time to eat[41], and greater fatigue,[41,42] which can reduce the willingness to perform physical activities and lead to the best energy expenditure.[41] All of these factors together could lead to weight gain and obesity in sleep-deprived individuals.

Some original studies[15–19,21–23] and also reviews[42–45] have found an association between short sleep duration and obesity. Current studies have proposed an association of short sleep duration not only with obesity, but also with comorbidities associated with this disease – such as systemic arterial hypertension,[46,47] type 2 diabetes,[43,48] risk of cardiovascular disease, and[43,49] metabolic syndrome[50,51]. However these studies analyzed data from cross-sectional studies or analyzed it by pooled effect measures, and in some of them the association between sleep duration and development of obesity was not observed.[42,44] Furthermore, other studies did not assess the degree of evidence of each results[43,52], this raises the need to study the topic systematically, notably including cohort studies to increase the strength of the evidence and the methodologic rigor to avoid bias. In addition, the scientific production on this topic has increased rapidly, which justifies the need to update the results.

This study aimed to carry out a systematic review of cohort studies that assessed the association between sleep duration and development of obesity and, subsequently, with available pooling data, perform a meta-analysis. It was also assessed comorbidities related to obesity. We hypothesized that short sleep duration increases the risk of obesity and its related diseases, quality of life and mortality.

## METHODS

The review was registered in the PROSPERO database under the number CRD42019130143. This review was reported according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement[53] and following the recommendations described in the Cochrane Handbook for Systematic Reviews of Interventions.[54]

### Literature search

A systematic search in the literature was performed up to July 2020 using LILACS (Literatura Latino-Americana e do Caribe em Ciências da Saúde) via Biblioteca Virtual em Saúde (BVS), MEDLINE via PubMed, CENTRAL via Wiley, and Embase via Elsevier electronic databases. Additionally, grey literature was consulted (http://opengrey.eu). There was no data, status (abstracts, full-text or on-going studies), and study publication language limits. The reference lists from retrieved articles were searched for further additional studies. The search strategy includes the following terms with their own similar words (e.g. for Medline): “sleep deprivation"[MeSH] AND (“overweight” OR “obesity”). The complete search strategy is available on Table S1 in the Supporting Information online.

**Selection criteria**

The PECO strategy (Population; Exposure; Comparison; Outcome) was used to define search strategies and the selection criteria, established by the inclusion criteria (Table 1). Only cohort studies, these studies had to be performed with participants over 18 years and evaluated at least one of the associations between sleep duration and development of overweight/obesity available by BMI ≥25kg/m² and ≥ 30kg/m², respectively;[55] or abdominal obesity, with waist circumference values ≥88cm for women and ≥102cm for men;[56] type 2 diabetes, with glucose levels ≥126mg/dL or a glycated hemoglobin value ≥6.5%;[57] systemic arterial hypertension, considering systolic blood pressure ≥140mmHg and diastolic blood pressure ≥90mmHg;[58] metabolic syndrome, with the presence of three or more of the following criteria: blood pressure ≥130/85mm/hg, waist circumference >88cm for women and >102cm for men, HDL-c <50mg/dL for women and <40mg/dL for men, triglycerides ≥150mg/dL and fasting blood glucose ≥110mg/dL;[59] risk factors for cardiovascular disease, including obesity, sedentary lifestyle, family history of coronary heart disease and/or stroke, triglycerides >180mg/dl and HDL-c <50mg/dl for women and <40mg/dl for men;[60] quality of life through a validated questionnaire, considering physical,

psychosocial aspects, social and environmental relations;[56] and overall mortality.

The cohort studies that included pregnant, lactating, or physically disabled participants that preclude routine activities, such as osteoarthritis, amputations were excluded. Potential eligible studies for data extraction were identified after the full-text screening.

The Rayyan software[61] was used to select studies, according to inclusion and exclusion criteria. This was performed by two authors independently, double-blind (K.C.G. and C.M.S.), and disagreements were resolved by a third author (C.A.C.).

**Data extraction and quality assessment**

Two authors (K.C.G. and C.M.S.) extracted data from the selected cohort studies according to: data source, eligibility criteria, methods (assessment of exposure and outcomes), total of participants (exposed, non-exposed, with and without outcomes), time of exposure to the risk factor, results, and conclusions. The disagreements were resolved by a third author (C.A.C.). Missing or incomplete data was requested by the main reviewer from the authors of the studies via e-mail.

The Newcastle-Ottawa Quality Assessment Form for Cohort Studies instrument[62] was used to evaluate and assess the risk of bias of the cohort

studies, according to: selection, evaluating representativeness of the exposed cohort, selection of the non-exposed cohort, ascertainment of exposure, demonstration that outcome of interest was not present at the start of the study, comparability of cohorts on the basis of the design or analysis and outcome, time to follow-up long enough for outcomes to occur and adequacy of follow-up of cohorts. Studies were classified as "good quality" (if it presented 6 to 9 aspects favorable), "fair quality" (if it presented 5 to 7 aspects favorable), or "poor quality" (if it presented no aspect or less than two aspects favorable). The quality of the selected cohort studies was assessed by two authors (K.C.G. and C.M.S.) independently, and a third author (C.A.C.) was included in case of discrepancy.

The overall certainty of evidence was assessed using the Grading of Recommendations Assessment, Development, and Evaluation (GRADEpro GDT)[63], which contemplate study design, risk of bias, inconsistency, indirectness, imprecision, the precision of effect estimates and the possibility of publication bias.[63] The general certainty of evidence ranged from "high" that indicates a high degree of certainty that the estimated effect lies on truth effect, and "very low" that indicates substantial uncertainty about the estimated effect.[64]

**Data synthesis**

The meta-analysis was carried out using the Cochrane Review Manager 5.3 Software.[65] We have made a descriptive and quantitative analysis. The heterogeneity between studies was assessed using $I^2$ statistics. We considered an important heterogeneity if there was an $I^2$ of at least 50%. The risk ratio (RR) was measured for dichotomous data. We used odds ratio (OR) for pooled data of chances analysis from the studies and we made a sensitivity analysis with the RR. The RR and OR, analyses were estimate separately according to data of the primary studies related to the main and if possible related to the comorbidities related to obesity. We performed a sensitivity analysis calculating risk ratio (RR) and odds ratio (OR), excluding all studies that were classified as "poor quality" by the NewCastle-Ottawa Assessment for Cohort Studies, to avoid bias in measured effect size. The sensitivity analysis was performed for random effects since imbalances, given that it is expected in cohort studies due to lack of randomization. However, when the inconsistencies found were large, the study was not included in the meta-analysis, while studies with similar population and analysis were included.

## RESULTS

A total of 3 286 studies were screened with Rayyan software.[61] Duplicate studies (n=174) were excluded. Of the 3 112 studies, 3 069 studies were excluded due to wrong study design or, different population, different outcome of interest, and insufficient information on the measure of the outcome. Therefore, 43 studies were considered eligible (Figure 1).

After reading the full text, twelve studies were excluded –five cross-sectional studies,[66–70] four studies with outcome different from the interest,[71–74] two studies with adolescents[75,76], and one that included pregnant women.[77] Four studies was included by hand search and 36 studies were included in this systematic review[11–13,15–23,66–74,77–88,88–98]. Twenty-two studies had comparable data and were pooled in the meta-analysis[13,15–19,21–23,79,80,82,86,88–90,94–97,99,100] , and 15 studies were not included due to insufficient or incompatible data information on the measures in the association of interest to perform a meta-analysis (Figure 1).[11,12,14,20,78,81,83–85,87,91–93,98] Most authors who were contacted by email did not answer.

The characteristics of the 36 included studies are presented on Table 2. Twelve studies were conducted in the United States,[14,23,83–85,87,89,94,95,98–100] eight in Japan,[16–20,22,88,90] two in Canada,[12,79] two in Korea,[80,91] three in Spain,[15,82,97] two in Sweden,[21,78] two in Taiwan,[13,81] one in England,[96] one in the United Kingdom,[86] one in Brazil,[92] one in China,[93] and one in Italy.[11] Self-reported sleep duration was provided in 27 studies.[11–23,78,79,81,86–

[91,93,96,97,99,100], four studies by polysomnography,[83–85,95] two studies by actigraphy,[92,94] two studies by interview[80,98] and in one study this information was not described.[82] The reference categories for short sleep were the following: ≤5 hours of sleep in 14 studies;[16,17,19,20,23,78,83,84,87,88,90,91,99,100] ≤6 hours of sleep in 15 studies,[11–13,18,21,22,79–81,85,86,89,92,94,95] ≤7 hours of sleep in six studies,[14,15,82,96–98] and in one study this information was not described.[93] Obesity was defined as BMI ≥30 kg/m² in European and American studies,[11,12,14,15,21,23,78,79,82–87,89,92,94–100] and BMI ≥25 kg/m² in Asian studies.[13,16–20,22,80,81,88,90,91,93] In eight studies only the abstract was available.[13,78,82,83,85,91,92] Results from four studies were presented according to sex and were separated in the data analysis.[16,22,23,80] Of the 36 studies included, a meta-analysis was performed to evaluate the association between short sleep duration and development of obesity in six studies,[17,19,22,23,96,97] metabolic syndrome in four studies,[13,79,80,90] type 2 diabetes in three studies,[13,86,89]

The effect measures data available was used to confirm the association between short sleep duration and the outcomes. We were able to pool data for development of obesity in eleven studies;[15–19,21–23,94–96] metabolic syndrome in four studies;[13,80,88,90] type 2 diabetes in four studies;[15,18,86,100] risk of cardiovascular disease in two studies,[18,82] systemic arterial hypertension in four studies.[13,18,88,99] The meta-analysis could not be performed for the

abdominal obesity, quality of life and mortality outcomes due to the lack of information.

**Quality of the included studies (Risk of bias)**

The quality score was assessed by Newcastle-Ottawa Scale and is shown in Table 3. Twenty-one studies were classified as "good quality",[11–20,22,79,80,84,86,88,90,92,96,99,100] three studies were classified as "fair quality"[87,89,94], and five studies were classified as "poor quality"[21,23,95,97,98]. Only studies classified as poor quality were excluded in the sensitivity analysis.

**Quality of evidence**

The overall grading of evidence of the association between short sleep duration and obesity using GRADEpro GDT is presented in the Table 4. This software analyzes the quality of evidence basing on eight domains: study design, risk of bias, inconsistency, indirectness, imprecision, publication bias, dose-response gradient and magnitude of effect. All studies of that association were observational studies. The risk of bias was serious considering that two studies were classified as poor quality by NewCastle-Ottawa. Rating inconsistency in the result was also not serious due to 31% of heterogeneity in $I^2$ statistical test. That evidence answers directly the question about the association between short sleep duration and obesity. So,

this result is precise enough to do not downgrade the quality of evidence in this criterion.

It was not possible to rating the publication bias owing to that analyzes does not have enough studies to include on funnel plot. The effect was not large enough to upgrade the quality of evidence in this item (RR between 0.5 and 2.0). In these analyses it may have plausible confounding that would reduce demonstrated effect, for example, the difference between population (age, occupation, marital status, physical activity, medications, lifestyle), and the lack of food pattern describing in each study. At last, it was possible to notice a dose-response gradient in Figure 3, where it was shown the association between short sleep duration and obesity in analyzes by subgroup of sleep duration. It could observe the greater chances of being obesity when sleep duration decrease, with a high quality of that evidence.

**Data synthesis**

**Short sleep duration and obesity**

Figure 2 shows the results of the number of patients who developed obesity and association with short sleep duration (≤ 7 hours). This association was found in six studies,[17,19,22,23,96,97] with a total of 154 859 participants (RR = 1.18, 95% CI, 1.15, 1.26; GRADE moderate certainty of evidence; $I^2$ = 31%; *P* for heterogeneity 0.18). A sensitivity analysis

removing studies due to high risk of bias (poor quality[23,97]) remained the statistical significance (RR = 1.15, 95%CI, 1.02, 1.29; $I^2$ = 50%; *P* for heterogeneity 0.09). Figure 3 shows that nine studies were included in the meta-analysis for the association between short sleep and obesity by subgroup analysis,[15–19,21–23,94–96] with a total of 226 915 participants analyzing with pooled *Odds Ratio*. The association between short sleep duration (≤ 7 hours) and development of obesity remained significant with according to the main analysis (OR = 1.26, 95%CI: 1.17, 1.36; $I^2$ = 61%; *P* for heterogeneity < 0.0001). After removing three studies in a sensitivity analysis due to low[21,23,95] risk of bias the association also remained significant (OR = 1.28, 95%CI, 1.16, 1,41; $I^2$ = 64%; *P* for heterogeneity < 0.0001).

In the meta-analysis performed using subgroups of different sleep duration, the rates of obesity decreased when sleep duration was increased (four studies[16,22,23,95] with 143 241 participants, < 5 hours of sleep, OR = 1.38, 95%CI. 1.11, 1.71; $I^2$ = 57%; *P* for heterogeneity 0.03; eight studies[17–19,21–23,95,96] with 201 578 participants, 5.0-5.9 hours of sleep, OR = 1.30, 95%CI, 1.14, 1.48, $I^2$ = 75%; *P* for heterogeneity <0.0001; eight studies[15,17–19,22,94–96] with 114 833 participants, 6-7 hours of sleep, OR = 1.16, 95%CI, 1.06, 1.26; $I^2$ = 28%; *P* for heterogeneity 0.19) (Figure 3). A sensitivity analysis removing three studies classified as poor quality[21,23,95] showed that the association lost significance between < 5 hours of sleep duration and development obesity (OR = 1.41, 95%CI. 0.91, 2.18; $I^2$ = 76%; *P* for

heterogeneity 0.006), a possible explanation for this might be the insufficient number of evidence and participants in this association. However, the associations remained significant with sleep time between 5-5.9 hours (OR = 1.45, 95%CI. 1.29, 1.62; $I^2$ = 22%; *P* for heterogeneity 0.27) and 6-7 hours (OR = 1.16, 95%CI. 1.05, 1.27; $I^2$ = 37%; *P* for heterogeneity 0.13).

Figure 4 shows analysis stratified by sex (female and male) and geographic location (America, Europe and Asia). The association between short sleep duration and obesity was found in both female and male, (female OR = 1.42; 95%CI, 1.10, 1.81; $I^2$ = 14%; *P* for heterogeneity 0.32 and male (OR = 1.31; 95%CI, 1.04, 1.66; $I^2$ = 75%; *P* for heterogeneity 0.02). The association between short sleep and obesity stratifying by geographic location was also significant (America and Europe OR = 1.54; 95%CI, 1.31, 1.81; $I^2$ = 4%; *P* for heterogeneity 0.39; Asia OR = 1.33, 95%CI, 1.13, 1.55; $I^2$ = 64%; *P* for heterogeneity 0.010)

Some studies were not included in the meta-analysis due to lack of compatible data, such as dichotomous data or when the analyses from the primary study do not directly answer the question in this review.[11,12,14,20] Bo et al.[11] concluded that every hour of sleep has a protective effect on obesity development (OR = 0.70 per hour of sleep; 95%CI, 0.57, 0.86; $P \leq 0.001$). Gangwisch et al.[14] analyzed 6 981 individuals aged between 32 and 49 years and found that higher BMI among participants with short sleep duration (< 7 hours of sleep) were more likely to become obese than individuals with

regular sleep duration (7 hours of sleep). Finally, Patel et al.[98] the association between sleep duration and the incident obesity in 68 183 women followed for 16 years were 1.15 (95%CI, 1.04, 1.26) for who slept 5 hours and 1.06 (95%CI, 1.01, 1.11) for 6 hours of sleep duration.

Two studies assessed the association between short sleep and weight gain.[12,20] Chaput et al,[12] evaluated 283 participants for six years and observed that sleep duration and weight gain were associated. Participants with short sleep duration (< 6 hours) gained 1.65kg (95%CI, 1.05, 2.31) compared to participants with seven or more hours of sleep. To identify if sleep duration and weight gain were associated, Nishiura et al,[20] followed for four years 3 803 middle-aged Japanese white-collar workers (47.8 ± 5.3 years) and found that short sleepers (≤ 5 hours of sleep) gained 0.15 kg/m² in BMI (95%CI, 0.03, 0.27) compared with regular sleepers (7 hours of sleep) in 6 years.

**Short sleep duration and comorbidities related to obesity**

Figure 5 shows the Risk Ratio between short sleep duration (< 7 hours) and the metabolic syndrome and type 2 diabetes rates. Four studies[13,79,80,90] with 149 753 participants showed that individuals who had short sleep duration (< 7 hours) presented an increased risk of developing metabolic syndrome (RR = 1.54, 95%CI, 1.13, 2.11; $I^2$ = 61%; *P* for heterogeneity 0.04). For this outcome no study was removed for the sensitivity analysis. The

association between short sleep duration (< 7 hours of sleep) and type 2 diabetes was also evaluated in with a total of 152 822 individuals in three studies.[13,86,89] Short sleep duration increased the risk to develop type 2 diabetes (RR = 1.13, 95%CI, 1.02, 1.25; $I^2$ = 46%; *P* for heterogeneity 0.16). For this outcome, no study was removed for the sensitive analysis.

The meta-analysis assessing the association between sleep duration and risk of cardiovascular disease, metabolic syndrome, hypertension and type 2 diabetes by pooling adjusted effect measures is shown in Figure 6. The relationship between sleep duration and metabolic syndrome was performed using the natural form of OR with data from four studies,[13,80,88,90] including 202 358 participants and the chances to short sleepers (< 7 hours) to develop metabolic syndrome compared to regular sleepers was not significative (OR = 1.27, 95% CI: 1.00, 1.60; $I^2$ = 71%; *P* for heterogeneity 0.007). The association between sleep duration and type 2 diabetes using pooled measures was performed with four studies[15,18,86,100] with 46 205 individuals remained significant comparing with the main analyses. Available data shows there is a higher risk of developing type 2 diabetes among short sleepers (mean: <7 hours of sleep) compared to regular sleepers (7 – 8 hours of sleep) (OR = 1.25, 95%CI, 1.08, 1.45; $I^2$ = 0%; *P* for heterogeneity 0.78). No sensitivity analysis was necessary, given that all studies in these analysis were classified as “good quality”.

Two studies evaluated risk of cardiovascular diseases,[18,82] with a total of 35 804 participants. Cardiovascular disease risk was not significantly higher in short sleepers (< 7 hours of sleep) compared to regular sleepers in a (7 - 8 hours of sleep) (OR = 1.36, 95% CI, 0.94, 1.97; $I^2$ = 37%; *P* for heterogeneity 0.21). A sensitivity analysis was performed removing one study,[82] and the association became significant (OR = 1.78, 95%CI, 1.03, 3.08; $I^2$ = not applicable; *P* for heterogeneity not applicable)[18]. One study[78] that associated short sleep with risk of cardiovascular disease was not included in this meta-analysis because this was the only study using HR values, different from the others that used OR values. Bengtsson et al.[78] investigated whether short sleep duration is associated with increased risk of major adverse cardiovascular events (MACE) during 21 years of follow-up. Patients with short sleep duration (< 5 hours) had almost twice the risk of developing MACE (HR = 1.93, 95%, 1.15 – 3.25) compared to the group set as reference (7-8 hours).

The association between short sleep duration and systemic arterial hypertension was analyzed with three studies,[13,88,99] with 35 804 participants. No significant association was found in the comparison of short (< 7 hours of sleep) and regular sleepers (7-8 hours of sleep) (OR = 1.05, 95%, 0.91, 1.22; $I^2$ = 94%; *P* for heterogeneity < 0.00001).

One study[81] that investigated the association between short sleep and metabolic syndrome was not included in the meta-analysis since it is a

duplication of a study previously reported.[13] The association between short sleep and abdominal fat was available in one study.[13] Thus, it was not possible to evaluate this association. There were no sufficient data to analyze the association between short sleep duration and overall mortality due these studies is evaluate with the same population.[83–85] Cohort studies analyzing the association between sleep duration and quality of life were not found.

## DISCUSSION

The present systematic review found a negative association between short sleep duration (7 hours or less) and the development of obesity, which confirms our initial hypothesis. It is also possible to observe that a progression in this association, that is, the greater chance of developing obesity increases as the sleep duration decreases. It was also observed a possible association between comorbidities related to obesity, as the obesity the central focus of this review and others health parameters are naturally affected by it.

Previous systematic reviews and meta-analysis that studied the association between short sleep duration and obesity in adults.[43,44,101] showed similar findings current study current study. The association between subgroups of sleep duration and obesity was also assessed in another systematic review[43] that included different study designs. Different from our

findings, short sleep duration (< 5, 6 and 7 hours of sleep) was associated with obesity compared to regular sleep duration, decreasing according to the hours of sleep (7 hours: RR = 1.73, 95%, 1.13, 2.64; 6 hours: RR = 1.66, 95%, 1.19, 2.31; 5 hours: RR = 1.27, 95%, 1.17, 1.38).[43] However, we highlight that previous reviews[43,44,101] calculated the analysis by pooling adjusted effect measures from the original studies, different from ours, that performed the analysis by dichotomous data from the primary studies, as recommended by *Cochrane Handbook for Systematic Reviews*,[54] . In addition, the present review was performed rating the quality of the body of evidence in systematic reviews.[63] Our study, as in previous systematic review,[52] reported the relationship between short sleep duration and obesity by subgroup analyses and by stratification, although, they were limited to include studies only in English, the last search was 2 years before the publication, at this time primary studies on this relationship were published that could change the effect of the evidence, they did not use dichotomous data in theirs analysis, and the study did not grade the evidence.

A large set of mechanisms have been proposed to explain the association between short sleep and obesity, among which the changes in leptin and ghrelin after sleep deprivation stand out[36,37,40,102,103]. Both hormones are part of the orexin system, which is responsible for the control of feeding, wakefulness, and energy expenditure in the body.[36] These changes in the level of leptin and ghrelin are likely to increase appetite and

may explain the increase in BMI observed in short sleepers.[36] In addition, individuals who sleep less have more opportunities to consume calories, mainly from unhealthy food, with high carbohydrate, sugar, fat, and sodium content,[40,42,104,105] Beside the unhealthy food consumption, short sleepers are more likely to have meals late evening,[40] considered as an inappropriate time for eating due to the deterioration in the metabolism of nutrients compared to the early day, which can lead to obesity.[106,107] Short sleepers also experience more fatigue which reduces physical exercise, practice increasing sedentary lifestyle which also contributes to obesity development.[1,42]

It is well known that metabolic syndrome involves components such as obesity, central obesity, systemic arterial hypertension, dyslipidemias, hyperglycemia, and type 2 diabetes.[108] The association between short sleep duration and metabolic syndrome found in the present study was similar to other studies[109,110] and may be suggested by the change in the main component of energy homeostasis, such as glucose tolerance, food cravings for calorie-dense and carbohydrate-rich food and hormones critical to appetite regulation.[37–39]

The short sleep duration was also associated with type 2 diabetes in the present study, similar to the findings of other evidence.[43,111] It is documented in the literature that sleep restriction leads to decreased insulin sensitivity,[40,42,104,105,112] explaining the possible association between type 2 diabetes and lack of sleep. Other possible link between short sleep duration

and type 2 diabetes might be mediated through GH and cortisol, which can contribute to changes in glucose metabolism observed during sleep loss, increasing the insulin resistance and decreasing insulin sensitivity.[39,113] It is also suggested that short sleepers tend to deviate from traditional eating.[114] In this sense, late-time eating after dinner is common among short sleepers, as a result of being awake.[114] Thus, the carbohydrate intake at night -a time of decreased insulin sensitivity and lower efficiency of digestion and absorption of carbohydrates -can also be associated with type 2 diabetes. [113,115] Type 2 diabetes is a comorbidities related to obesity, which reinforce the main evidence, the association between short sleep duration and obesity.

Contrary to the results of other reviews,[43,116] there was not enough evidences to estimate an association between short sleep duration and risk of cardiovascular disease and systemic arterial hypertension, so it was not significant in this systematic review. This could be explained because, this is comorbidities related to obesity, our main outcome, and these evidences were analyzed within the studies raised by the primary outcomes. This review highlights the need for future studies to better evaluate whether short sleep duration is negatively associated with health outcomes separately.

It was conducted subgroup analyses by sleep duration, and stratification by sex and geographic location among studies to lead with the high heterogeneity found in some analysis. The heterogeneity was higher in analysis with pooled effect measures data, and it decreases in stratified

analyses, except for male and Asia group. This inconsistency may be due the differences in groups such as the cutoff point for defining short sleep duration and obesity, differences in ages, socioeconomic status, and dietary pattern.

A strength part of this study was the large number of included studies and a large number of participants from the prospective cohorts. This review had a strong differential since we have used dichotomous data in order to measure effect size for clinically relevant outcomes and the overall certainty of evidence for the primary outcome. However, there were some limitations to consider. High heterogeneity in three meta-analysis should not be ignored, to deal with this, we used random-effect model to perform meta-analysis considering worst scenario to estimate effect size. Time point for measuring outcomes need to be greater ensuring that the effect could effectively happen. Finally, the design of this review was directed to answer primary outcome, so search strategy.

## CONCLUSION

This systematic review of cohort studies provides evidence that short sleep duration is significantly associated with a higher incidence of obesity, with moderate quality of evidence, metabolic syndrome and type 2 diabetes.

Short sleep duration was not associated and risk of cardiovascular disease. Lastly, as a small number of studies found evaluate the relationship between short sleep duration and mortality, abdominal obesity and quality of life, we could not perform the meta-analysis about these outcomes and further studies are needed to confirm these associations.

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**Supporting Information**

The following Supporting Information is available through the online version of the article at the publisher's website.

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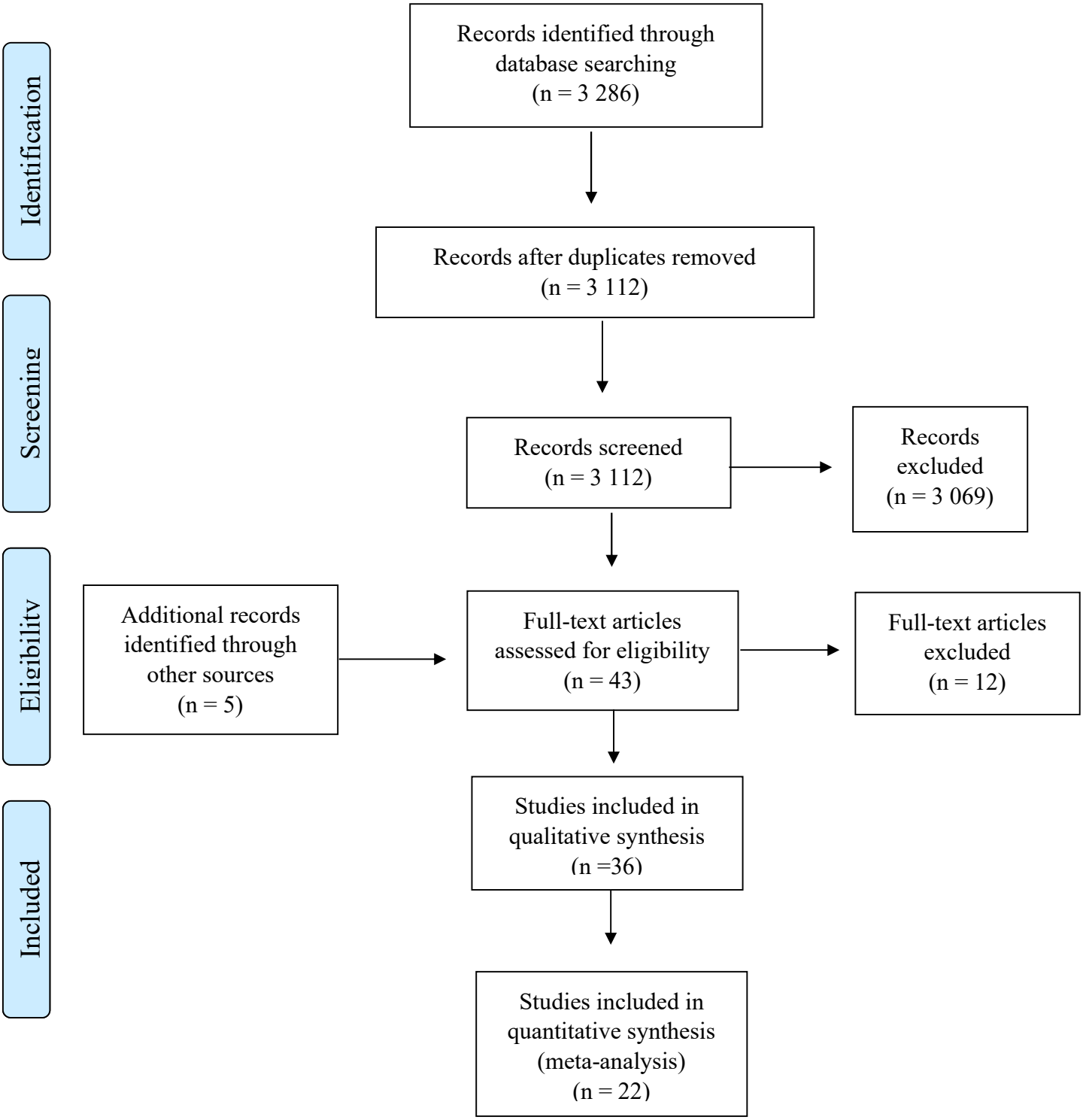


*Figure 1* **Flow diagram of the literature search process.**

*Table 1* **PECO worksheet.**

| | |
|---|---|
| **Population** | Adults over 18 years old |
| **Exposure** | Short sleep (< 7 hours) |
| **Control** | Regular sleep duration (7 – 8 hours) |
| **Primary Outcome** | Overweight (BMI ≥ 25 kg/m²)<br>Obesity identified by body mass index (BMI) - Eastern (BMI ≥ 25 kg/m²); Western (BMI ≥ 30 kg/m²) |
| **Secondary outcome** | Type 2 diabetes; hypertension; dyslipidemia; metabolic syndrome; cardiovascular risk; quality of life; overall mortality. |

*Table 2* **Study design, population characteristics and results of included studies.**

**Obesity**

| Authors | Location | Follow-up period (years) | Sample (n) | Age at baseline (years) | Exposure* (hours of sleep) | Control** (hours of sleep) | Outcome | Results |
|---|---|---|---|---|---|---|---|---|
| Gangwisch et al.[14] | United States | 10 | 1987: 8 073<br>1992: 6 981 | 32-49 | < 7 | 7-7.9 | Obesity (BMI ≥ 30kg/m²) | Short sleep duration was associated with obesity |
| Patel et al.[98] | United States | 16 | 68 183 | 30-55 | < 7 | 7-7.9 | Obesity (BMI ≥ 30kg/m²) | The association between sleep duration and the incident obesity in 68 183 women followed for 16 years were 1.15 (95%CI, 1.04, 1.26) for who slept 5 hours and 1.06 (95%CI, 1.01, 1.11) for 6 hours of sleep duration. |
| Stranges et al.[96] | England | 10 | 10308 | 35-55 | < 7 | 7-7.9 | Obesity (BMI ≥ 30kg/m²) | Short sleep duration was associated with obesity (≤ 5 hours: OR = 1.65, 95%CI, 1.22, 2.24 and 6 hours: OR = 1.23, 95%CI, 1.01, 1.50) comparing to regular sleep durantion. |
| Chaput et al.[12] | Canada | 6 | 283 | 18-64 | < 6 | ≥ 7 | Overweight/obesity (BMI ≥ 25kg/m²) | Short sleepers gained 1.65 kg (95%CI, 1.05, 2.31) compared to regular sleepers |
| Nishiura et al.[20] | Japan | 4 | 3 803 | 47.8±5.3 | ≤ 5 | 7-7.9 | Changes in BMI | Participants with ≤ 5h of sleep gained 0.15 kg/m² in BMI (95%CI, 0.03, 0.27). |
| Watanabe et al.[22] | Japan | 1 | 35 247 | Male: 40.0±9.6<br>Female: 38.0±9.0 | < 6 | 7-8 | Obesity (BMI ≥ 25kg/m²) | Higher incidence of obesity only among male participants with 5h and 5-6h of sleep (OR = 1.91; 95%CI, 1.36, 2.67 and OR = 1.50; 95%CI, 1.24-1.80 respectively) |
| Bo et al.[11] | Italy | 6 | 1 597 | 45-60 | < 6.5 | 7-7.9 | Obesity (BMI ≥ 30kg/m²) | Sleep duration was associated with obesity incidence (OR = 0.70 per hour; 95%CI, 0.57, 0.86; p:< 0.001) |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Itani et al.[16] | Japan | 7 | 23 802 | NS | <5 | 5-7 | Obesity (BMI ≥ 25 kg/m²) | Short sleep was associated with obesity only in female (OR = 1.82; 95%CI, 1.02, 3.25; *P* = 0.44). Male shift workers with < 5h of sleep had greater chance of become obese (OR = 1.30; 95%CI, 1.14, 1.49; *P* < 0.01) |
| Kobayashi et al.[17] | Japan | 3 | 21 469 | ≥ 20 | < 5 | 7-7.9 | Weight gain and obesity (BMI ≥ 25 kg/m²) | Participants with < 5h of sleep were more likely to experience weight gain (β = 0.03; 95%CI, 0.03, 1.1) and greater chance to become obese (OR = 1.5; 95%CI, 1.1, 2.0; *P*: < 0.01) |
| Nagai et al.[19] | Japan | 11 | 13 629 | 40-79 | ≤ 5 | 7-7.9 | ≥5 kg of weight gain and BMI ≥ 25 kg/m² | The multivariate OR for obesity was 0.96 in short sleepers (95%CI, 0.59, 1.57). |
| Sayón-Orea et al.[97] | Spain | 6.5 | 10 532 | 20-90 | < 7 | 7-7.9 | Obesity (BMI ≥ 30 kg/m²) | Sleep less than 5 hours per night was associated with higher risk of becoming obese (HR = 1.94, 95%CI, 1.19, 3.18) comparing with who sleep between 7 and 7.9 hours. |
| Xiao et al.[23] | United States | 7.5 | 83 377 | 51-72 | < 5 | 7-8 | Obesity (BMI ≥ 30 kg/m²) | Association inversely linear between short sleep duration (< 5h and 5-6h of sleep) and obesity in women (OR = 1.37; 95%CI, 1.04, 1.79 and OR = 1.15; 95%CI, 1.05, 1.28; respectively). Male with < 5h of sleep had greater chance of becoming obese (OR = 1.45; 95%CI, 1.06, 1.99). |
| Gutiérrez-Repiso et al.[15] | Spain | 11 | 1 145 | 18-65 | ≤ 7 | 7-8 | Obesity (BMI ≥ 30kg/m²) | Becoming obese was significantly higher among short sleepers (OR = 2.73; 95%CI, 1.47, 5.04). |
| Theorell-Haglöw et al.[21] | Sweden | 10 | 4 903 | 46±17.5 | <6 | 6-9 | Obesity (BMI ≥ 30kg/m²) | Short sleep presented a greater chance of general obesity in women (< 40 years) (OR = 6.78; 95%CI, 2.71, 17.0) |
| Vgontzas et al.[95] | United States | 7.5 | 815 | ≥ 20 | < 6 | 7-7.9 | Obesity (BMI ≥ 30kg/m²) | Short sleep duration was not associated with incident obesity (≤ 5 hours: OR = 1.08, 95%CI, 0.48, 2.41; 5-6 hours: OR = 1.27, 95%CI, 0.89, 2.76; 6-7 hours: OR = 1.03, 95%CI, 0.46, 2.34). |
| Deng et al.[13] | Taiwan | 18 | 162 121 | 20-80 | < 6 | 6-8 | Overweight/obesity (BMI ≥ 25kg/m²) | Short sleep duration was associated with an increase of 18% of overweight and obesity risk (95%CI, 1.12,1.23; *P* < 0.001). |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Kobayashi et al.[18] | Japan | 5 | 31 830 | ≥ 20 | < 6 | 7-8 | Obesity (BMI ≥ 25kg/m²) | Sleep duration < 6h and 6-7h were associated with overweight or obesity (OR = 1.49; 95%CI, 1.32, 1.69 and OR = 1.19; 95%CI, 1.07, 1.32, respectively) |
| McMahon et al.[94] | United States | 2 | 390 | 21-35 | < 6 | 6-<7 | Overweight/Obesity (BMI ≥ 25kg/m²) | Sleep duration (< 6 hours) was not significantly associated with overweight or obesity (OR = 1.30 95%CI 0.77,2.19). |

**Type 2 Diabetes**

| Author | Location | Follow-up period (years) | Sample (n) | Age at Baseline (years) | Exposure* (hours of sleep) | Control** (hours of sleep) | Outcome | Results |
|---|---|---|---|---|---|---|---|---|
| Gangwisch et al.[100] | United States | 10 | 8 992 | 32-86 | ≤ 5 | 7-7.9 | Type 2 diabetes | Short sleepers were significantly more likely to develop type 2 diabetes (OR = 1.47; 95%CI, 1.03, 2.09). |
| Gutiérrez - Repiso et al.[15] | Spain | 6 and 11 | 1 145 | 18-65 | ≤ 7 | 7-8 | Type 2 diabetes | Type 2 diabetes incidence at the 6-year follow-up was higher in the participants who slept ≤ 7h (OR = 1.96; 95%CI, 1.10, 3.50). |
| Ferrie et al.[86] | United Kingdom | 5 | Cycle 1: 5 545<br>Cycle 2: 4 117<br>Cycle 3: 3 878<br>Cycle 4: 4 238 | 35-55 | < 6 | 7-7.9 | Type 2 diabetes | Short sleep was associated with incidence type 2 diabetes (OR = 1.35; 95%CI, 1.04, 1.76). |
| Deng et al.[81] | Taiwan | 16 | 146 454 | ≥ 20 | < 6 | 6-8 | Type 2 diabetes | Short sleepers presented HR of 6% higher for impaired fasting glucose and diabetes (95%CI,1.03, 1.10) |
| Nuyujukian et al.[89] | United States | 3 | 1 899 | ≤ 6h: 48.1<br>7h: 46.7<br>≥ 8h: 47.1 | ≤ 6 | 7-7.9 | Type 2 diabetes | Short sleep duration was associated with increased diabetes risk in 32% (95%CI, 0.92, 1.89). |
| Yu et al.[91] | Korea | 12 | 7 378 | NS | < 5 | 7-9 | Type 2 diabetes | Short sleep duration increased the risk of diabetes (HR = 1.46; 95%CI, 1.04, 2.04). |
| Deng et al.[13] | Taiwan | 18 | 162 121 | 20-80 | < 6 | 6-8 | Type 2 diabetes | Short sleep significantly increased the type 2 diabetes risk in 6% (95%CI, 1.03, 1.09; *P* < 0.001). |

**Metabolic Sydrome**

| Author | Location | Follow-up period (years) | Sample (n) | Age at Baseline (years) | Exposure*(hours of sleep) | Control** (hours of sleep) | Outcome | Results |
|---|---|---|---|---|---|---|---|---|
| Choi et al.[80] | Korea | 4 | 1 107 | 40-70 | < 6 | 6-7.9 | Metabolic syndrome (central obesity, triglyceride, high density lipoprotein, blood pressure, fasting plasma glucose) | Short sleepers' women were significantly more likely to experience metabolic syndrome (HR = 1.798; 95%CI, 1.06, 3.05). |
| Otsuka et al.[90] | Japan | 3.7 | 948 | 44±6 | ≤ 5 | > 5 and ≤ 6 | Metabolic syndrome (abdominal obesity, elevated blood pressure, dyslipidemia, and elevated fasting glucose) | The metabolic syndrome risk for who slept ≤ 5 h of sleep was 3.18 (95%CI, 1.52, 6.64; *P*: 0.002). |
| Chaput et al.[79] | Canada | 6 | 293 | 18-65 | ≤ 6 | 7-8 | Metabolic syndrome (the presence of three or more of the following risk factors: central obesity, dyslipidemia; elevated blood pressure, elevated fasting glucose) | Short sleepers presented greater risk of developing metabolic syndrome (RR = 1.74; 95%CI, 1.05, 2.72). |
| Deng et al.[81] | Taiwan | 16 | 146 454 | ≥ 20 | < 6 | 6-8 | NS | Short sleepers had greater HR for metabolic syndrome: 10% higher central obesity (95%CI, 1.05, 1.16), 6% higher for impaired fasting glucose and diabetes (95%CI, 1.03, 1.10), 8% higher for hypertension (95%CI, 1.03, 1.13), 6% |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | | higher for hypercholesterolemia (95%CI, 1.01, 1.11), 15% higher for hypertriglyceridemia (95%CI, 1.09, 1.21). |
| Deng et al.[13] | Taiwan | 18 | 162 121 | 20 – 80 | < 6 | 6-8 | Metabolic syndrome (Central obesity, high blood pressure, elevated fasting glucose (IFG and diabetes), low HDL-C, high triglycerides and metabolic syndrome) | Short sleepers presented HR of 9% for metabolic syndrome (95%CI, 1.05, 1.13; $P <$ 0.001). |
| Itani et al.[88] | Japan | 7 | 39 182 | 18-65 | < 5 | ≥ 5 | Metabolic syndrome (obesity, high blood pressure, triglycerides, elevated fasting glucose). | The HR associated for the following numbers of high-risk lifestyle parameters were 1.22 (95%CI, 1.15, 1.29) for 2-3 of these parameters; and 1.43 (95%CI, 1.33, 1.54) for 4-7 parameters including sleep duration. Parameters: (1) <5 hours/day of sleep; (2) shift work; (3) insufficient days off work; (4) always eating until satiety; (5) not attempting to take every opportunity to walk; (6) consuming ≥60 g/day of pure alcohol (≥540 mL of Japanese sake); and (7) smoking. |
| Li et al.[93] | China | 4.5 | 5 845 | NS | NS | NS | Metabolic syndrome | Short sleep durations increased the incidence of metabolic síndrome in mixed-gender population (HR = 1.43). |

**Risk of Cardiovascular Diseases**

| Author | Location | Follow-up period (years) | Sample (n) | Age at Baseline (years) | Exposure* (hours of sleep) | Control** (hours of sleep) | Outcome | Results |
|---|---|---|---|---|---|---|---|---|
| Bengstsson et al.[78] | Sweden | 21 | 798 | NS | < 5 | 7-8 | MACE risk | Short sleepers were twice as likely to developing MACE in univariate and multivariate analysis (HR = 2.45; 95%CI, 1,34, |

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|---|---|---|---|---|---|---|---|---|
| | | | | | | | | 4,46 and HR = 2.39; 95%CI, 1,31, 4,35 respectively). |
| Dominguez et al.[82] | Spain | 1 week | 3 974 | 45.8 ± 4.3 | < 7 | 7-8 | Cardiovascular disease risk | Sleep duration < 6h of sleep was associated with a higher atherosclerotic burden (OR = 1.19; 95%CI, 1.00, 1.42; *P* = 0.05). |
| Kobayashi et al.[18] | Japan | 5 | 31 830 | ≥ 20 | < 6 | 7-8 | Non-fatal cardiovascular events | Participants < 6 h of sleep were significantly more likely to experience non-fatal cardiovascular events (OR = 1.78; 95%CI, 1.03, 3.07; *P* = 0.04). |
| Drager et al.[92] | Brazil | 2 | 2 064 | 49 ± 8 | < 6 | NS | Cardiovascular risk | Prevalent of cardiovascular risk as obesity, hypertension, type 2 diabetes and dyslipidemias, were not independently associated with short sleep duration (OR = 1.19; 0.93; .0.97 and 0.94 respectively). |

**Hypertension**

| Author | Location | Follow-up period (years) | Sample (n) | Age at Baseline (years) | Exposure* (hours of sleep) | Control (definition of normal sleep duration) | Outcome | Results |
|---|---|---|---|---|---|---|---|---|
| Gangwisch et al.[99] | United States | 10 | 4 810 | 32-59 | ≤ 5 | 7-8 | Hypertension | Short sleep was associated with an increased risk of hypertension (HR = 1.74 95%CI, 1.30, 2.32). The increased risk continued to be significant after controlling for obesity and diabetes (HR = 1.60; 95%CI, 1.19, 2.14). |
| Deng et al.[81] | Taiwan | 16 | 146 454 | ≥ 20 | < 6 | 6-8 | Hypertension | Short sleepers had a HR of 8% higher for hypertension (95%CI, 1.03, 1.13) |
| Deng et al.[13] | Taiwan | 18 | 162 121 | 20-80 | < 6 | 6-8 | Hypertension | Short sleepers had an increased risk of high blood pressure (HR =1.08; 95%CI, 1.04, 1.13; *P* < 0.001). |

**Mortality**

| Author | Location | Follow-up period (years) | Sample (n) | Age at Baseline (years) | Exposure* (hours of sleep) | Control** (hours of sleep) | Outcome | Results |
|---|---|---|---|---|---|---|---|---|
| Deng et al.[81] | Taiwan | 16 | 146 454 | ≥ 20 | < 6 | 6-8 | Death risk | Short sleepers had an increased risk of death (HR = 1.11; 95%CI, 1.06, 1.16). The association between short sleep and mortality was significant in participants with or without preexisting disease (HR = 1.09; 95% CI, 1.04, 1.14 and HR = 1.18; 95%CI, 1.05, 1.33, respectively). |
| Fernandez-Mendoza et al.[83] | United States | 15.5±4.1 | 1 741 | 48.7±13.5 | ≤ 5 | 5-6 | Cardiovascular disease risk on mortality | The impact of elevated glucose or blood pressure on increased in mortality was significantly modified by sleep duration ($P$ = 0.04 and $P$ = 0.01, respectively). |
| Fernandez-Mendoza et al.[85] | United States | 16.7±4.6 | 1 741 | 48.7±13.5 | < 6 | NS | Mortality | The hazard ratios (95%CI) of all-cause and cardiovascular / cerebrovascular mortality associated with metabolic syndrome were 1.99 (1.53-2.59) and 2.10 (1.39-3.16) for individuals who slept < 6 hours. |
| Fernadez-Mendoza et al.[84] | United States | 15.5±4.1 | 1 741 | 48.7±13.5 | ≤ 5 | 5-6 | Mortality | The greater chance of all-cause mortality associated with hypertension was found in participants who slept at least 6h (OR = 1.77; 95%CI, 1.07, 2.92; $P$ = 0.03), 5-6 h (OR = 2.78; 95%CI, 1.47, 5.24; $P$ < 0.01) and ≤ 5h (OR = 3.93; 95%CI, 2.22, 6.95; $P$ < 0.01) |

**Abdominal Obesity**

| Author | Location | Follow-up period (years) | Sample (n) | Age at Baseline (years) | Exposure*(hours of sleep) | Control* (hours of sleep) | Outcome | Results |
|---|---|---|---|---|---|---|---|---|
| Hairston et al.[87] | United States | 5 | 1 107 | 18-81 | ≤ 5 | 6-7 | VAT and SAT | Participants aged < 40 years with ≤ 5h of sleep was related to a greater accumulation of BMI |

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|---|---|---|---|---|---|---|---|---|
| | | | | | | | | (1.8 kg/m², $P < 0.001$), SAT (42 cm², $P < 0.001$) and VAT (13 cm², $P > 0.01$) |
| Theorell-Haglöw et al.[21] | Sweden | 10 | 4 903 | 46±17.5 | < 6 | 6-9 | Central obesity | Habitual short sleep duration was not a risk factor for central obesity (OR = 1.93; 95%CI, 0.87, 4.81) |
| Deng et al.[13] | Taiwan | 18 | 162 121 | 20-80 | < 6 | 6-8 | Central obesity | Short sleep significantly increased the risk for central obesity by 12% (95%CI, 1.07, 1.17; $P < 0.001$). |

*Short sleep duration; **Regular sleep duration; BMI: Body Mass Index; OR: Odds Ratio; h: hours; CI: Confidence Interval; HR: Hazard Ratio; ANOVA: Analysis of Variance; NS: No Stated; MACE: major adverse cardiovascular events; RR: Risk Ratio; VAT: visceral adipose tissue; SAT: subcutaneous adipose tissue WC: waist Circumference.

*Table 3* **Risk of bias assessment using the Newcastle-Ottawa Quality Assessment Scale criteria.**

| Study | Selection | | | | Comparability | Outcome | | | Conclusion |
|---|---|---|---|---|---|---|---|---|---|
| | Representativeness of the exposed cohort | Selection of the non-exposed cohort | Ascertainment of exposure | Demonstration that outcome of interest was not present at start of study | Comparability of cohorts on the basis of the design or analysis controlled for confounders | Assessment of outcome | Was follow-up long enough for outcomes to occur? (> 1 year) | Adequacy of follow-up of cohorts | |
| **Bengtson et al.**[78] | All men living in Gothenburg, born in 1943★ | Yes ★ | Structured interview★ | Yes ★ | Diabetes, BMI and smoking status ★ | Independent blind assessment★ | Yes ★ | Indeterminate | Indeterminate |
| **Bo et al.**[11] | Adults of six family physicians ☆ | Yes★ | Structured interview★ | Yes ★ | Baseline fiber intake, saturated fat intake, metabolic syndrome, degrees centigrade of high temperature, hours of sleep, hours of TW, use and incident-obesity and incident hyperglycemia, after controlling for sex, baseline body mass index, education level and (in case of incident hyperglycemia) baseline glucose values and alcohol intake | Independent blind assessment★ | Yes ★ | Lost 11% of follow up ★ | Good quality |
| **Chaput et al.**[12] | Adults from the greater Quebec City area ★ | Yes ★ | Structured interview★ | No ☆ | Age, sex, socioeconomic status, baseline body mass index and length of follow-up | Independent blind assessment★ | Yes ★ | Complete follow up – all subject accounted for★ | Good quality |
| **Chaput et al.**[79] | Adults from the greater Quebec City area ★ | Yes ★ | Structured interview★ | No ☆ | Age, sex, smoking habits, total annual family income, alcohol | Independent blind assessment★ | Yes ★ | Complete follow up – all subject | Good quality |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | consumption, coffe intake daily caloric intake, and cardiorespiratory fitness. | | | accounted for ★ | |
| **Choi et al.[80]** | Adults from rural Korea ★ | Yes ★ | Structured interview★ | Yes ★ | Age, body mass index, smoking exposure (packs per year), alcohol intake (per day), physical activity, and menopausal status. | Independent blind assessment★ | Yes ★ | Complete follow up – all subject accounted for ★ | Good quality |
| **Deng et al.[81]** | Participants in a standard medical screening program in Taiwan ★ | Yes ★ | Written self-report ☆ | Yes ★ | Smoking and physical activity ★ | Self-report ☆ | Indeterminate | Indeterminate | Indeterminate |
| **Deng et al.[13]** | Adults who participated in a standart medical screening programme conducted by the MJ Health Management Instituition in Taiwan☆ | Yes ★ | Structured interview★ | Yes ★ | Sex, age, socioeconomic status, lifestyle factors (education levels, marital status, smoking, alcohol drinking and leisure-time physical activity), and biomedical risk factors. | Independent blind assessment★ | Yes ★ | Complete follow up – all subject accounted for ★ | Good quality |
| **Dominguez-Rodriguez et al.[82]** | PESA study participants ☆ | Yes ★ | Secure Record ★ | Indeterminate | Indeterminate | Independent blind assessment★ | Indeterminate | Indeterminate | Indeterminate |
| **Drager et al.[92]** | The Brazilian Longitudinal Study of Adult Health (ELSA-Brasil) ★ | Yes ★ | Structured interview and actigraphy ★ | No☆ | Age, sex, BMI, race, education beyond high school, in addition to income, excessive drinking, and insufficient physical activity ★ | No description ☆ | Yes ★ | Complete follow up- all subject accounted for ★ | Good quality |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Fernandez-Mendoza et al.**[83] | Penn State Adult Cohort participants underwent in lab PSG ☆ | Yes ★ | Secure Record ★ | Indeterminate | Sex, age, race, smoking, depression, sleep complaints, sleep apnea, heart disease, and stroke ★ | Independent blind assessment ★ | Yes ★ | Indeterminate | Indeterminate |
| **Fernandez-Mendoza et al.**[84] | Households from Penn State Cohort Study ☆ | Yes ★ | Secure record★ | Yes ★ | Sex, age, race, body mass index, smoking, sleep apnea, sleep difficulty, heart disease, stroke, TC levels, and depression. | Independent blind assessment★ | Yes ★ | Complete follow up – all subject accounted for ★ | Good quality |
| **Fernandez-Mendoza et al.** [85] | Penn State Adult Cohort, a random, general population☆ | Yes ★ | Secure Record ★ | Indeterminnate | Multiple potential confounders ★ | Independent blind assessment★ | Yes ★ | Lost more than 20% of follow up ☆ | |
| **Ferrie et al.**[86] | London-based office staff in 20 civil service departments ★ | Yes ★ | Structured interview★ | Yes ★ | Age, sex, ethnicity, employment grade, body mass index. | Independent blind assessment★ | Yes ★ | No statement☆ | Good quality |
| **Gangwisch et al.**[14] | Noninstitutionalized population of United States ★ | Yes ★ | Structured interview★ | No ☆ | Depression, physical activity, education, ethnicity, alcohol consumption, cigarette smoking, gender, waking during the night, daytime sleepiness, and age. | Self-reported☆ | Yes ★ | Lost 5% of follow-up ★ | Good quality |
| **Gangwisch et al.**[99] | Noninstitutionalized population of United States★ | Yes ★ | Structured interview★ | Yes ★ | Daytime sleepiness, depression, physical activity alcohol consumption salt per day, current smoking status, pulse rate, gender, demographic variables fo education, age, ethnicity, body mas | Independent blind assessment★ | Yes ★ | Complete follow up – all subject accounted for ★ | Good quality |

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|---|---|---|---|---|---|---|---|---|---|
| | | | | | index and history of diabetes. | | | | |
| **Gangwisch et al.**[100] | Noninstitutionalized population of United States ★ | Yes ★ | Structured interview★ | Yes ★ | Physical activity, depression, alcohol consumption, ethnicity, education marital status, body mass index, history of hypertension. | Independent blind assessment★ | Yes ★ | No statement☆ | Good quality |
| **Gutiérrez-respiso et al.**[15] | Adult population of Pizarra, a village in the province of Malaga (Spain) ★ | Yes ★ | Structured interview★ | No ☆ | Age, sex, obesity and abnormal glucose regulation. | Independent blind assessment★ | Yes ★ | Lost 42% of follow-up ☆ | Good quality |
| **Hairston et al.**[87] | Adults from three American communities ☆ | Yes ★ | Structured interview★ | No ☆ | Age, gender, race center, baseline fat measure, smoking status, physical activity, total calories, education and macronutrient intake or kcal energy expended per kg body weight per year. | Independent blind assessment★ | Yes ★ | Follow up rate less than 80% and no descritpion of those lost ☆ | Fair quality |
| **Itani et al.**[16] | Employees of a local government organization in Japan ★ | Yes ★ | Structured interview★ | No ☆ | Age class, eating habits, alcohol consumption, smoking habit, exercise habit, mental complaints, hypertension, hypertension, hyperglycemia, hypertriglyceridemia and hypo-HDL cholesterolemia. | Independent blind assessment★ | Yes ★ | No statement☆ | Good quality |
| **Itani et al.**[88] | Employees of a local government organization in Japan ★ | Yes ★ | Structured interview★ | No ☆ | Age class, hypertension, hyperglycemia, dyslipidemia and mental health complaints | Independent blind assessment★ | Yes ★ | No statement☆ | Good quality |

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|---|---|---|---|---|---|---|---|---|---|
| | | | | | (irritability, reduced concentration, and lethargy). | | | | |
| **Kobayashi et al.**[17] | Healthy adults (annual health check-up at the Center for Preventive Medicine) ★ | Yes ★ | Structured interview★ | Yes ★ | Age, gender, alcohol consumption, frequency of exercise, hypertension, dyslipidemia, diabetes, cerebral infarction, and myocardial infarction. | Independent blind assessment★ | Yes ★ | No statement☆ | Good quality |
| **Kobayashi et al.**[18] | Healthy adults (annual health check-up at the Center for Preventive Medicine) ★ | Yes ★ | Structured interview★ | Yes ★ | Age, gender, occupation, health habits, marital status, calorie intake treatment status. | Self-reported☆ | Yes ★ | Lost 18,9% of follow-up ★ | Good quality |
| **Li et al.**[93] | Indeterminate | Yes ★ | Written self-report ☆ | Yes ★ | Indeterminate | Independent blind assessment★ | Yes ★ | Indeterminate | Indeterminate |
| **McMahon et al.** [94] | Recruitment consistedof targeting participants across four demographic cells. ☆ | Yes ★ | Secure Record ★ | No☆ | Age, sex, race, education, annual income, employment, marital status, having children, physical activity, caffeine intake, napping, season, and current dieting. | Independent blind assessment★ | Yes ★ | Lost 49% of follow-up ☆ | Fair Quality |
| **Nagai et al.**[19] | Adults of Ohsaki Public Health Center ★ | Yes ★ | Written self report☆ | Yes ★ | Sex, age, body mass index, education, smoking status, alcohol drinking, time spent walking per day, sports and physical exercise time per week, job status, marital status, menopausal status, | Self-reported☆ | Yes ★ | Complete follow up – all subject accounted for ★ | Good quality |

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|---|---|---|---|---|---|---|---|---|---|
| | | | | | coffee consumption, and self-rated health. | | | | |
| **Nishimura et al.**[20] | Middle-aged Japanese male white-collar workers in a gas company in Tokyo ☆ | Yes ★ | Structured interview★ | Yes ★ | Age, baseline body mass index, lifestyle behavior, and medication. | Independent blind assessment★ | Yes ★ | Complete follow up – all subject accounted for ★ | Good quality |
| **Nuyujukian et al.**[89] | Participants of the Special Diabetes Program for Indians Diabetes Prevention Demonstration Project (SDPI-DP) of 8 tribes in 18 states and 11 Indian Health Service (HIS) administrative areas☆ | Drawn from a different source☆ | Secure record★ | No ☆ | Age, sex, socioeconomic characteristics, behavioral characteristics, self-reported health status, body mass index, and percent weight loss at postcurriculum assessment. | Independent blind assessment★ | Yes ★ | Lost 43% of follow-up ☆ | Fair quality |
| **Otsuka et al.**[90] | Male workers★ | Yes★ | Structured interview★ | Yes ★ | Sleep duration, smoking, alcohol intake, age. | Independent blind assessment★ | Yes ★ | Lost 18% of follow-up ★ | Good quality |
| **Patel et al.**[98] | Women participating in the Nurse's Health Study | Yes ★ | Written self-report | Yes ★ | Age, smoking status, alcohol consumption, caffeine consumption, spousal education, use of medications known to affect sleep and/or weight, menopausal status, snoring frequency, shift-working history. | Self-report | Yes (mean: 12 years) ★ | No statement | Poor Quality |

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|---|---|---|---|---|---|---|---|---|---|
| **Sayón-Orea et al.**[97] | All participants are university graduates ★ | Yes ★ | Structured Interview ★ | Yes ★ | Medical history (prevalence of chronic diseases such as cancer, diabetes and CVD), health-related habits (smoking status, physical activity durting leisure time), lifestyle and sociodemographic variables (sex, age, marital status and employment) and anthropometric (weight and height) ★ | Self-report | Yes (2 years) ★ | 52% | Poor Quality |
| **Stranges et al.**[96] | Selected group | Yes ★ | Structured Interview ★ | Yes ★ | Age, sex, employment, alcohol consumption, smoking, physical activity, cardio-vascular drugs, mental and physical scores, depressive symptoms and use of hypnotics ★ | Self-report | Yes (2 years) ★ | Complete follow-up ★ | Good quality |
| **Theorell-Haglöw et al.**[21] | Women, non-pregnant, randomly selected from the population registry of the City of Uppsala, Sweden ☆ | Yes★ | Structured interview★ | No ☆ | Age, snoring, smoking/nicotine use, alcohol dependence, physical activity, caffeine intake, shift work, anxiety, depression, diabetes medication, and baseline weight. | Self-reported☆ | Yes ★ | Lost 31% of follow-up ☆ | Poor quality |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Vgontzas et al.**[95] | Selected group | Yes ★ | Secure Record / interview ★ | Yes ★ | Gender, race, age, diabetes, hypertension, AHI, baseline BMI. ★ | Self-report | Yes (7,5 years) ★ | 26,5% to 25,9% | Poor Quality |
| **Watanabe et al.**[22] | Employees of an electric power company ★ | Yes★ | Written self report☆ | Yes ★ | Age, body mass index at baseline, shift workers, smoking, alcohol consumption, physical activity, and depressive symptoms. | Independent blind assessment★ | Yes ★ | Follow up rate less than 80% and no descritpion of those lost☆ | Good quality |
| **Xiao et al.**[23] | Members of the National Institutes of Health – AARP (NIH-AARP) Diet and Health Study and resided in 1 of 6 United States (California, Florida, Louisiana, New Jersey, North Carolina, and Pennsylvania) or 2 metropolitan areas (Atlanta, Georgia and Detroit, Michigan)★ | Yes★ | Structured interview★ | No ☆ | Age, baseline body mass index, race/ethnicity, marital status, educational level, self-reported health, smoking status, alcohol consumption, coffee consumption, physical activity level, overall time spent sitting, total caloric intake, and the intake of fruits and vegetables, whole grains, and total fat. | Self-reported☆ | Yes ★ | Follow up rate less than 80% and no description of those lost☆ | Poor quality |
| **Yu et al.**[91] | Korean Genome and Epidemiology Study in 2001-2002 ☆ | Yes ★ | Structured interview★ | Yes ★ | Several confounding factors ★ | Independent blind assessment★ | Yes ★ | Complete follow up- all subject accounted for ★ | Indeterminate |

★: When the question receives a star according to NewCastle-Ottawa

☆: When the question does not receive a star according to NewCastle-Ottawa

*Table 4* **Findings of the effect of short sleep duration in obesity**

| Certainty assessment | | | | | | | № of patients | | Effect | | Certainty | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **№ of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **Short sleep duration** | **Regular sleep duration** | **Relative (95% CI)** | **Absolute (95% CI)** | | |
| **Short sleep and obesity** | | | | | | | | | | | | |
| **4** | Observational studies | Serious[a] | Not serious | Not serious | Not serious | All plausible residual confounding would reduce the demonstrated effect<br>Dose response gradient | 3686/71215 (5.2%) | 4243/783574 (5.4%) | **RR 1.18** (1.12 to 1.26) | **9 more per 1.000** (from 5 more to 12 more) | ⨁⨁⨁◯ MODERATE | IMPORTANT |

**CI:** Confidence interval; **RR:** Risk ratio

*Explanations*

a. Two study in this analysis has poor quality.

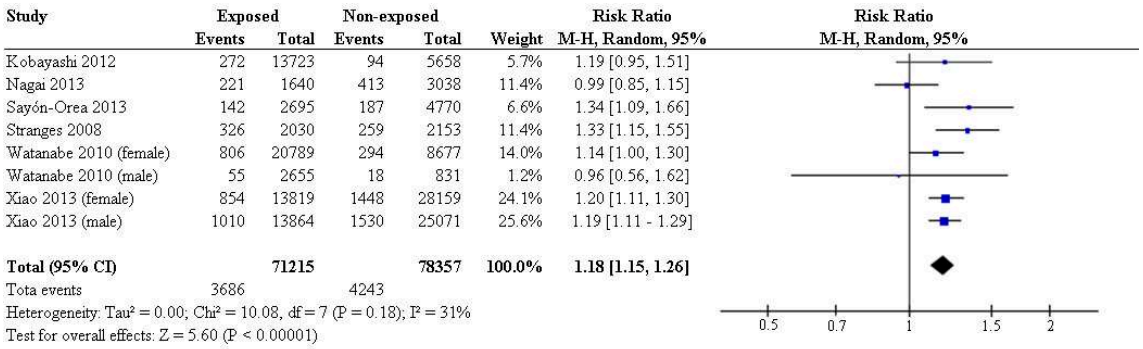


*Figure 2* **Forest plot of dichotomous data, risk ratio (RR) with 95% confidence interval (CI) of studies on short sleep duration and obesity.**

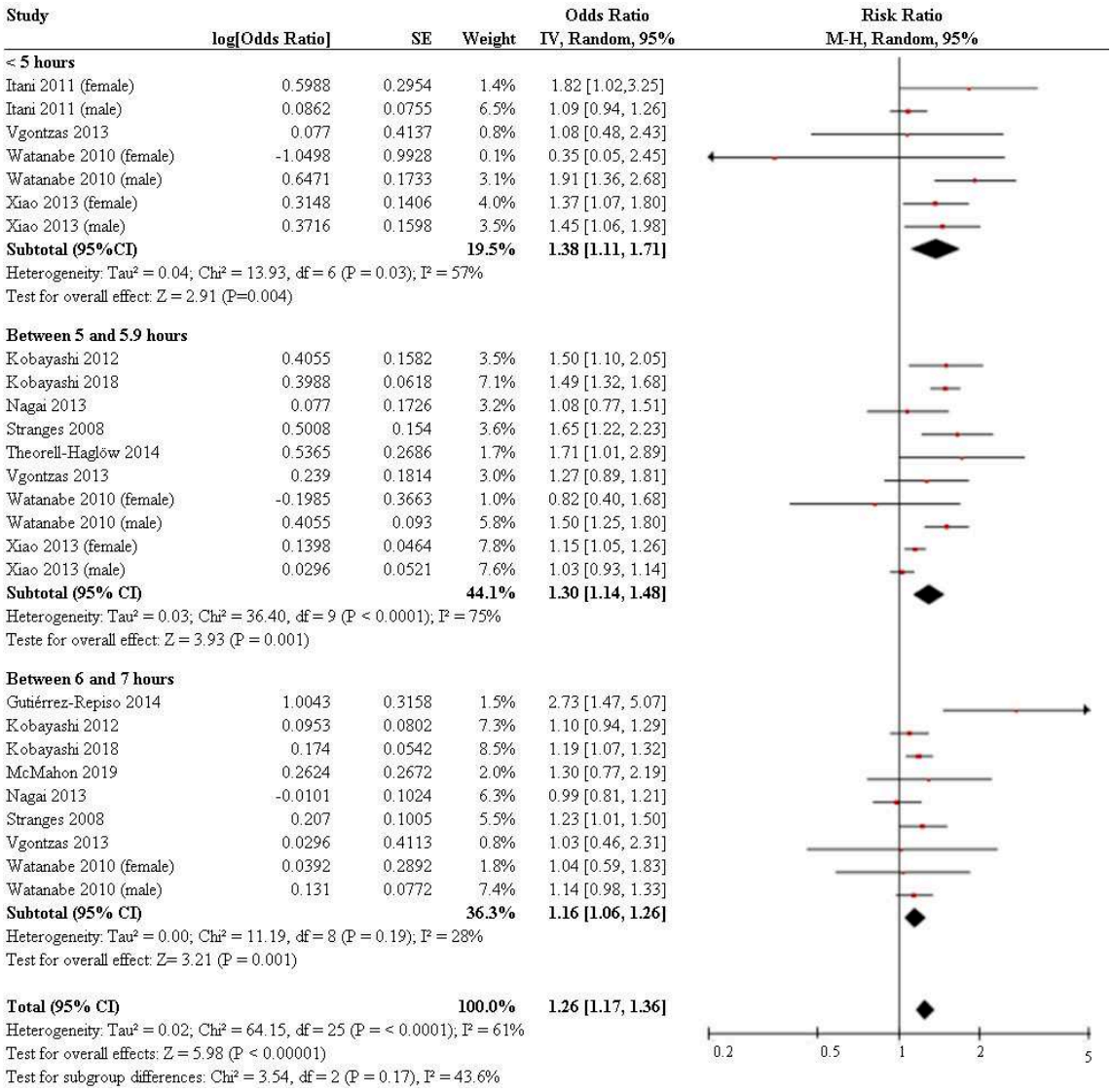


*Figure 3* **Forest plot of pooled Odds Ratio (OR) with 95% confidence interval (CI) of studies between short sleep duration and obesity.**

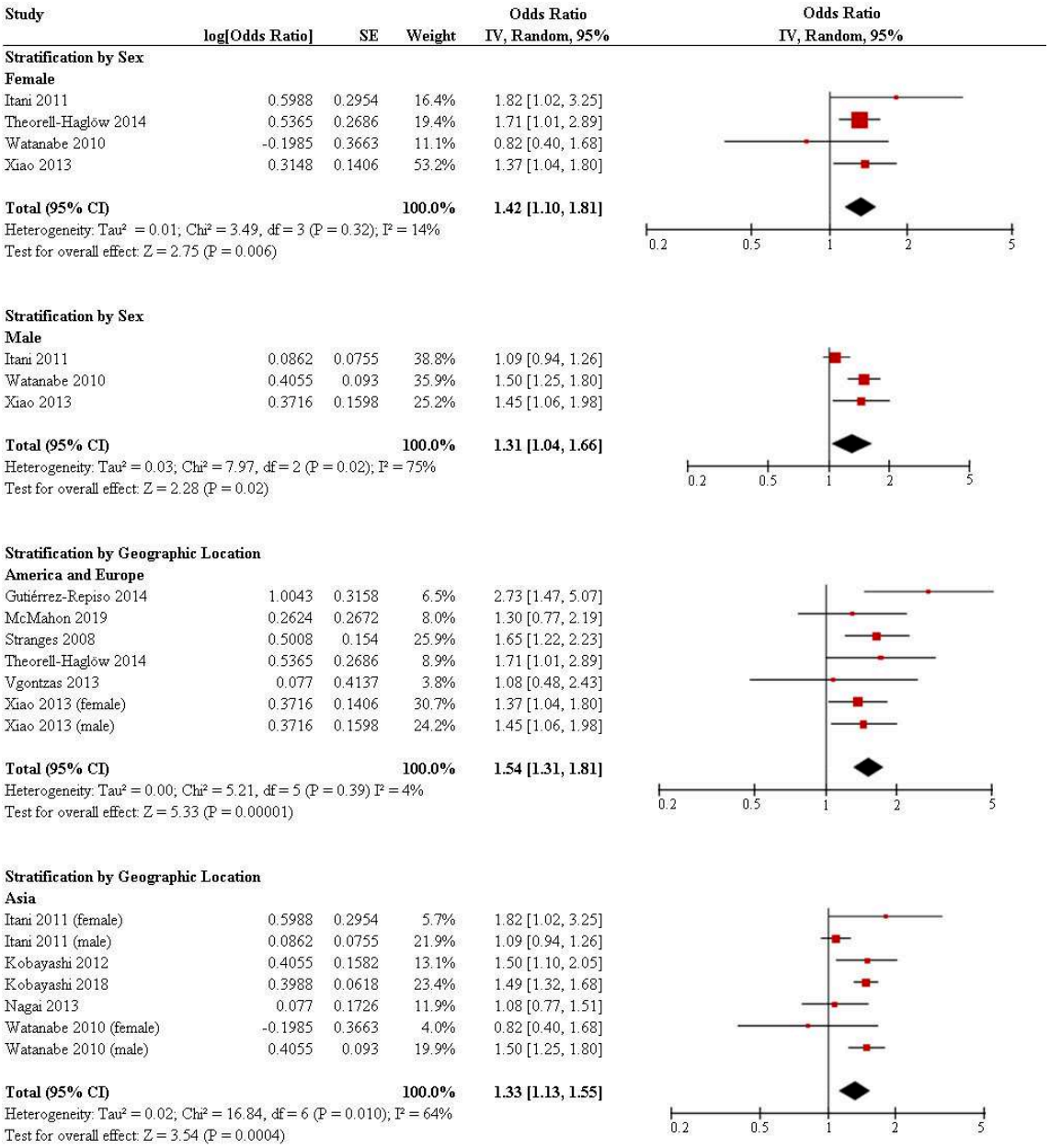


*Figure 4* **Odds Ratio (OR) with 95% confidence interval (CI) of studies between short sleep duration and obesity stratified by sex and geographic location.**

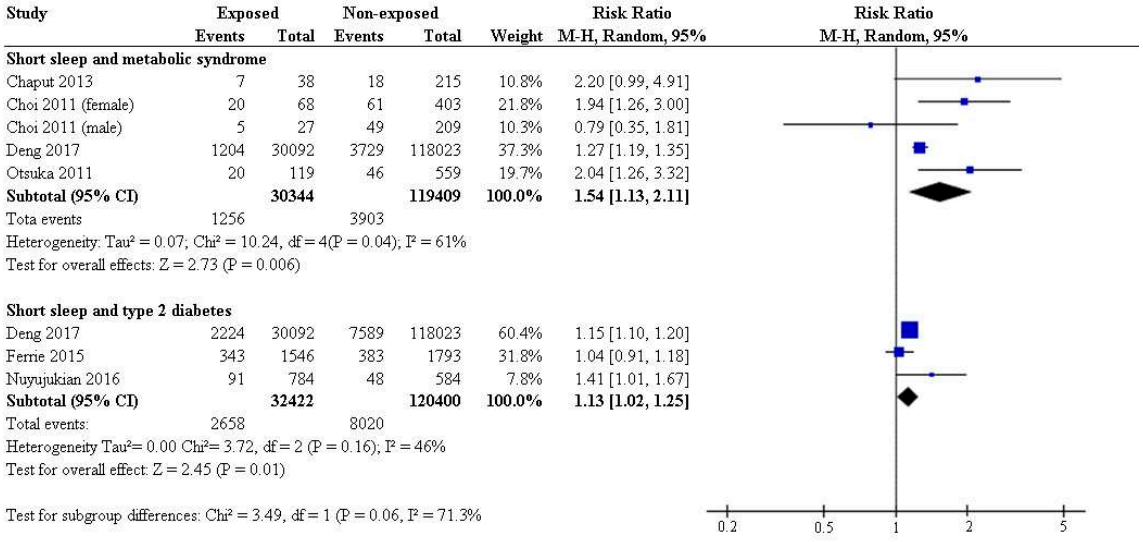


*Figure 5* **Forest plot of dichotomous data, risk ratio (RR) with 95% confidence interval (CI) of studies between short sleep duration and secondary outcomes.**

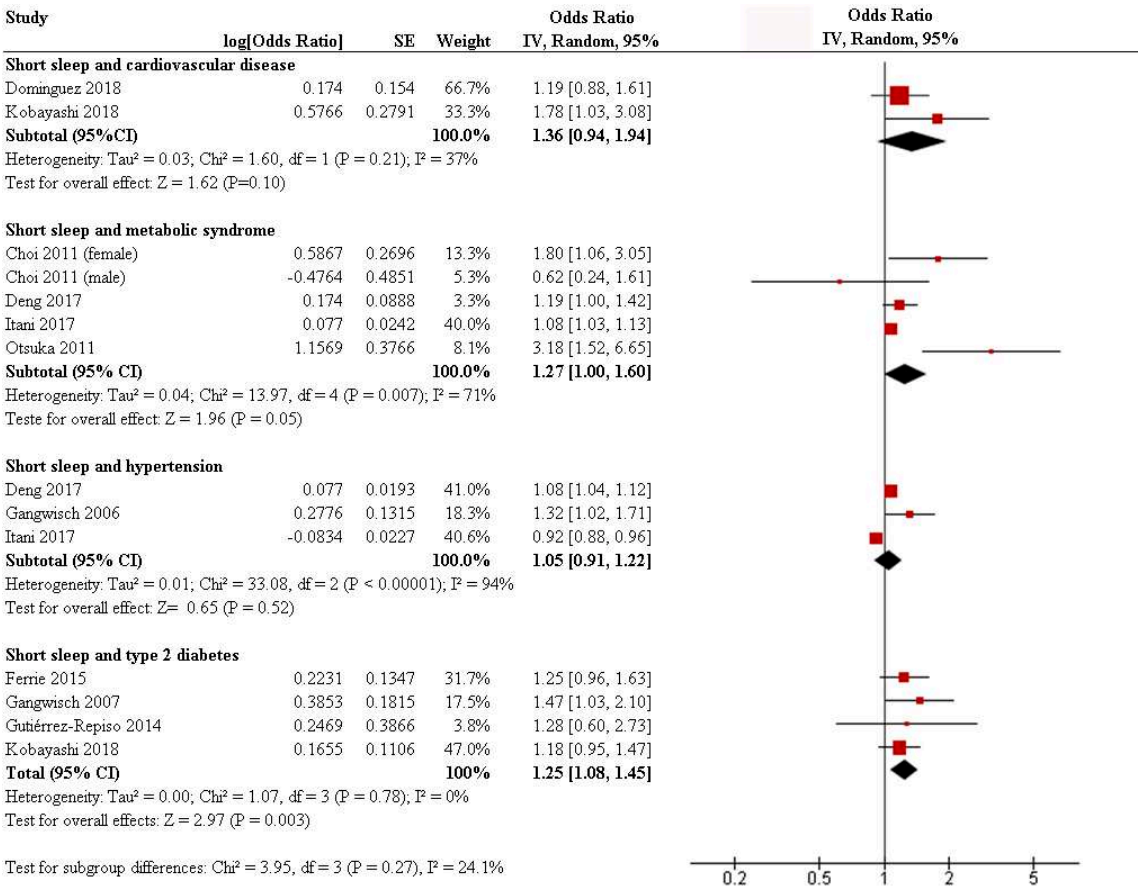


*Figure 6* **Forest plot of pooled Odds Ratio (OR) with 95% confidence interval (CI) of studies on short sleep duration and secondary outcomes.**

*Table S1* **Search strategy.**

| Base de dados | Estratégia de busca |
|---|---|
| **Medline via Pubmed** | #1 "Sleep Deprivation"[Mesh] OR (Sleep Deprivation) OR (Deprivation, Sleep) OR (Deprivations, Sleep) OR (Sleep Deprivations) OR (REM Sleep Deprivation) OR (Deprivation, REM Sleep) OR (Deprivations, REM Sleep) OR (REM Sleep Deprivations) OR (Sleep Deprivation, REM) OR (Sleep Deprivations, REM) OR (Sleep Fragmentation) OR (Fragmentation, Sleep) OR (Fragmentations, Sleep) OR (Sleep Fragmentations) OR (Insufficient Sleep Syndrome) OR (Insufficient Sleep Syndromes) OR (Syndrome, Insufficient Sleep) OR (Syndromes, Insufficient Sleep)<br><br>#l2 "Sleep Disorders, Circadian Rhythm"[Mesh] OR (Sleep Disorders, Circadian Rhythm) OR (Disturbed Nyctohemeral Rhythm) OR (Disturbed Nyctohemeral Rhythms) OR (Nyctohemeral Rhythm, Disturbed) OR (Nyctohemeral Rhythms, Disturbed) OR (Circadian Rhythm Sleep Disorders) OR (Sleep-Wake Schedule Disorders) OR (Sleep Wake Schedule Disorders) OR (Sleep-Wake Schedule Disorder) OR (Sleep-Wake Cycle Disorders) OR (Sleep Wake Cycle Disorders) OR (Sleep-Wake Cycle Disorder) OR (Shift-Work Sleep Disorder) OR (Shift Work Sleep Disorder) OR (Shift-Work Sleep Disorders) OR (Sleep Disorders, Shift-Work) OR (Sleep Disorder, Shift-Work) OR (Sleep Disorder, Shift Work) OR (Non-24 Hour Sleep-Wake Disorder) OR (Non 24 Hour Sleep Wake Disorder) OR (Sleep-Wake Disorder, Non-24 Hour) OR (Sleep Wake Disorder, Non 24 Hour) OR (Nonorganic Sleep Wake Cycle Disorders) OR (Advanced Sleep Phase |

Syndrome) OR (Delayed Sleep Phase Syndrome) OR (Delayed Sleep-Phase Syndrome) OR (Delayed Sleep-Phase Syndromes)

#3 #1 OR #2

#4 "Overweight"[Mesh] OR Overweight

#5 "Obesity"[Mesh] OR Obesity

#6 "Obesity Hypoventilation Syndrome"[Mesh] OR (Obesity Hypoventilation Syndrome) OR (Hypoventilation Syndrome, Obesity) OR (Syndrome, Obesity Hypoventilation) OR (Pickwickian Syndrome) OR (Syndrome, Pickwickian) OR (Obesity-Hypoventilation Syndrome)

#7 "Obesity, Abdominal"[Mesh] OR (Obesity, Abdominal) OR (Abdominal Obesities) OR (Obesities, Abdominal) OR (Abdominal Obesity) OR (Central Obesity) OR (Central Obesities) OR (Obesities, Central) OR (Obesity, Central) OR (Obesity, Visceral) OR (Visceral Obesity) OR (Obesities, Visceral) OR (Visceral Obesities)

#8 "Obesity, Metabolically Benign"[Mesh] OR (Obesity, Metabolically Benign) OR (Benign Obesity, Metabolically) OR (Metabolically Healthy Obesity) OR (Healthy Obesity, Metabolically) OR (Obesity, Metabolically Healthy) OR (Metabolically Benign Obesity)

#9 "Obesity, Morbid"[Mesh] OR (Obesity, Morbid) OR (Morbid Obesities) OR (Obesities, Morbid) OR (Obesity, Severe) OR (Obesities, Severe) OR (Severe Obesities) OR (Severe Obesity) OR (Morbid Obesity)

| | |
|---|---|
| | #10 "Body Weight"[Mesh] OR (Body Weight) OR (Body Weights) OR (Weight, Body) OR (Weights, Body)<br><br>#11 "Weight Gain"[Mesh] OR (Weight Gain) OR (Gain, Weight) OR (Gains, Weight) OR (Weight Gains)<br><br>#12 #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11<br><br>#13 #3 AND #12 |
| **LILACS via BVS** | #1 MH:"Privación de Sueño" OR<br>MH:"Sleep Deprivation" OR<br>MH:"Privação do Sono" OR<br>(Privación de Sueño) OR<br>(Sleep Deprivation) OR<br>(Privação do Sono) OR<br>(Síndrome de Sueño Insuficiente) OR<br>(Privación de Sueño REM) OR<br>(Fragmentación del Sueño) OR<br>(Insufficient Sleep Syndromes) OR<br>(REM Sleep Deprivations) OR<br>(Sleep Deprivations) OR<br>(Sleep Fragmentations) OR<br>(Insufficient Sleep Syndrome) OR<br>(REM Sleep Deprivation) OR |

(Sleep Fragmentation) OR

(Síndrome do Sono Insuficiente) OR

(Privação do Sono REM) OR

(Fragmentação do Sono) OR

MH:C10.886.425.175$ OR

MH:C23.888.592.796.772$ OR

MH:F02.830.855.671$ OR

MH:F03.870.400.099$ OR

MH:"Trastornos del Sueño del Ritmo Circadiano" OR

MH:"Sleep Disorders, Circadian Rhythm" OR

MH:"Transtornos do Sono do Ritmo Circadiano" OR

(Trastornos del Sueño del Ritmo Circadiano) OR

(Sleep Disorders, Circadian Rhythm) OR

(Transtornos do Sono do Ritmo Circadiano) OR

(Trastornos del Ritmo Circadiano del Sueño) OR

(Trastorno del Sueño Producido por el Trabajo en Turnos) OR

(Trastornos del Ciclo Sueño-Vigilia) OR

(Advanced Sleep Phase Syndrome) OR

(Delayed Sleep Phase Syndrome) OR

(Delayed Sleep-Phase Syndrome) OR

(Disturbed Nyctohemeral Rhythm) OR

(Non-24 Hour Sleep-Wake Disorder) OR

(Nonorganic Sleep Wake Cycle Disorders) OR

(Sleep-Wake Schedule Disorders) OR

(Delayed Sleep-Phase Syndromes) OR

(Disturbed Nyctohemeral Rhythms) OR

(Non 24 Hour Sleep Wake Disorder) OR

(Shift Work Sleep Disorder) OR

(Shift-Work Sleep Disorders) OR

(Sleep Wake Cycle Disorders) OR

(Sleep Wake Schedule Disorders) OR

(Sleep-Wake Cycle Disorder) OR

(Sleep-Wake Schedule Disorder) OR

(Circadian Rhythm Sleep Disorders) OR

(Shift-Work Sleep Disorder) OR

(Sleep-Wake Cycle Disorders) OR

(Transtornos do Ritmo Circadiano do Sono) OR

(Transtornos do Sono do Trabalho em Turnos) OR

(Transtornos do Ciclo Sono-Vigília) OR

MH:C10.281.800$ OR

MH:C10.886.425.200$ OR

MH:C24.900$ OR

MH:F03.870.400.200$

#2

MH:Sobrepeso OR

MH:Overweight OR

Sobrepeso OR

Overweight OR

MH:C23.888.144.699$ OR

MH:E01.370.600.115.100.160.120.699$ OR

MH:G07.100.100.160.120.699$ OR

MH:Obesidad OR

MH:Obesity OR

MH:Obesidade OR

Obesidad OR

Obesity OR

Obesidade OR

(Tratamiento de la Obesidad) OR

(Tratamento da Obesidade) OR

MH:C18.654.726.500$ OR

MH:C23.888.144.699.500$ OR

MH:E01.370.600.115.100.160.120.699.500$ OR

MH:G07.100.100.160.120.699.500$ OR

MH:SP6.016.047$ OR

MH:"Síndrome de Hipoventilación por Obesidad" OR

MH:"Obesity Hypoventilation Syndrome" OR

MH:"Síndrome de Hipoventilação por Obesidade" OR

(Síndrome de Hipoventilación por Obesidad) OR

(Obesity Hypoventilation Syndrome) OR

(Síndrome de Hipoventilação por Obesidade) OR

(Síndrome de Pickwick) OR

(Síndrome de Hipoventilación de la Obesidad) OR

(Obesity-Hypoventilation Syndrome) OR

(Pickwickian Syndrome) OR

(Síndrome de Pickwick) OR

(Síndrome de Hipoventilação da Obesidade) OR

MH:C08.618.085.852.850.500$ OR

MH:C08.618.846.565.500$ OR

MH:C10.886.425.800.750.850.500$ OR

MH:C18.654.726.500.695$ OR

MH:"Obesidad Abdominal" OR

MH:"Obesity, Abdominal" OR

MH:"Obesidade Abdominal" OR

(Obesidad Abdominal) OR

(Obesity, Abdominal) OR

(Obesidade Abdominal) OR

(Obesidad Central) OR

(Abdominal Obesity) OR

(Visceral Obesity) OR

(Abdominal Obesities) OR

(Central Obesities) OR

(Visceral Obesities) OR

(Central Obesity) OR

(Obesidade Central) OR

(Adiposidade Central) OR

(Adiposidade Abdominal) OR

MH:C18.654.726.500.697$ OR

MH:E01.370.600.115.100.160.120.699.500.249$ OR

MH:G07.100.100.160.120.699.500.249$ OR

MH:"Obesidad Metabólica Benigna" OR

MH:"Obesity, Metabolically Benign" OR

MH:"Obesidade Metabolicamente Benigna" OR

(Obesidad Metabólica Benigna) OR

(Obesity, Metabolically Benign) OR

(Obesidade Metabolicamente Benigna) OR

(Metabolically Benign Obesity) OR

(Metabolically Healthy Obesity) OR

MH:C18.654.726.500.698$ OR

MH:C23.888.144.699.500.250$ OR

MH:E01.370.600.115.100.160.120.699.500.375$ OR

MH:G07.100.100.160.120.699.500.375$ OR

MH:"Obesidad Mórbida" OR

MH:"Obesity, Morbid" OR

MH:"Obesidade Mórbida" OR

(Obesidad Mórbida) OR

(Obesity, Morbid) OR

(Obesidade Mórbida) OR

(Morbid Obesities) OR

(Severe Obesities) OR

(Severe Obesity) OR

(Morbid Obesity) OR

(Obesidade Grau III) OR

(Obesidade Grau 3) OR

MH:C18.654.726.500.700$ OR

MH:C23.888.144.699.500.500$ OR

MH:E01.370.600.115.100.160.120.699.500.500$ OR

MH:G07.100.100.160.120.699.500.500$ OR

MH:"Peso Corporal" OR

MH:"Body Weight" OR

(Peso Corporal) OR

(Body Weight) OR

(Body Weights) OR

MH:C23.888.144$ OR

MH:E01.370.600.115.100.160.120$ OR

MH:E05.041.124.160.750$ OR

MH:G07.100.100.160.120$ OR

MH:G07.345.249.314.120$ OR

MH:SP6.011.042.048.024$ OR

MH:"Aumento de Peso" OR

MH:"Weight Gain" OR

MH:"Ganho de Peso" OR

(Aumento de Peso) OR

(Weight Gain) OR

(Ganho de Peso) OR

(Weight Gains) OR

MH:C23.888.144.243.926$ OR

| | |
|---|---|
| | MH:G07.345.249.314.120.200.926$ OR<br><br>MH:SP6.011.042.048.054$ |
| **Cochrane Library** | #1 MeSH descriptor: [Sleep Deprivation] explode all trees 668<br><br>#2 (Sleep Deprivation) OR (Deprivation, Sleep) OR (Deprivations, Sleep) OR (Sleep Deprivations) OR (REM Sleep Deprivation) OR (Deprivation, REM Sleep) OR (Deprivations, REM Sleep) OR (REM Sleep Deprivations) OR (Sleep Deprivation, REM) OR (Sleep Deprivations, REM) OR (Sleep Fragmentation) OR (Fragmentation, Sleep) OR (Fragmentations, Sleep) OR (Sleep Fragmentations) OR (Insufficient Sleep Syndrome) OR (Insufficient Sleep Syndromes) OR (Syndrome, Insufficient Sleep) OR (Syndromes, Insufficient Sleep) 2217<br><br>#3 MeSH descriptor: [Sleep Disorders, Circadian Rhythm] explode all trees 167<br><br>#4 (Sleep Disorders, Circadian Rhythm) OR (Disturbed Nyctohemeral Rhythm) OR (Disturbed Nyctohemeral Rhythms) OR (Nyctohemeral Rhythm, Disturbed) OR (Nyctohemeral Rhythms, Disturbed) OR (Circadian Rhythm Sleep Disorders) OR (Sleep-Wake Schedule Disorders) OR (Sleep Wake Schedule Disorders) OR (Sleep-Wake Schedule Disorder) OR (Sleep-Wake Cycle Disorders) OR (Sleep Wake Cycle Disorders) OR (Sleep-Wake Cycle Disorder) OR (Shift-Work Sleep Disorder) OR (Shift Work Sleep Disorder) OR (Shift-Work Sleep Disorders) OR (Sleep Disorders, Shift-Work) OR (Sleep Disorder, Shift-Work) OR (Sleep Disorder, Shift Work) OR (Non-24 Hour Sleep-Wake Disorder) OR (Non 24 Hour Sleep Wake Disorder) OR (Sleep-Wake Disorder, Non-24 Hour) OR (Sleep Wake Disorder, |

Non 24 Hour) OR (Nonorganic Sleep Wake Cycle Disorders) OR (Advanced Sleep Phase Syndrome) OR (Delayed Sleep Phase Syndrome) OR (Delayed Sleep-Phase Syndrome) OR (Delayed Sleep-Phase Syndromes) 1170

#5 #1 OR #2 OR #3 OR #4 3169

#6 MeSH descriptor: [Overweight] explode all trees 14101

#7 MeSH descriptor: [Obesity] explode all trees 12101

#8 MeSH descriptor: [Obesity Hypoventilation Syndrome] explode all trees 35

#9 MeSH descriptor: [Obesity, Abdominal] explode all trees 286

#10 MeSH descriptor: [Obesity, Metabolically Benign] explode all trees 7

#11 MeSH descriptor: [Obesity, Morbid] explode all trees 996

#12 MeSH descriptor: [Body Weight] explode all trees24793

#13 MeSH descriptor: [Weight Gain] explode all trees 2310

#14 Overweight OR Obesity OR (Obesity Hypoventilation Syndrome) OR (Hypoventilation Syndrome, Obesity) OR (Syndrome, Obesity Hypoventilation) OR (Pickwickian Syndrome) OR (Syndrome, Pickwickian) OR (Obesity-Hypoventilation Syndrome) OR (Obesity, Abdominal) OR (Abdominal Obesities) OR (Obesities, Abdominal) OR (Abdominal Obesity) OR (Central Obesity) OR (Central Obesities) OR

| | |
|---|---|
| | (Obesities, Central) OR (Obesity, Central) OR (Obesity, Visceral) OR (Visceral Obesity) OR (Obesities, Visceral) OR (Visceral Obesities) OR (Obesity, Metabolically Benign) OR (Benign Obesity, Metabolically) OR (Metabolically Healthy Obesity) OR (Healthy Obesity, Metabolically) OR (Obesity, Metabolically Healthy) OR (Metabolically Benign Obesity) OR (Obesity, Morbid) OR (Morbid Obesities) OR (Obesities, Morbid) OR (Obesity, Severe) OR (Obesities, Severe) OR (Severe Obesities) OR (Severe Obesity) OR (Morbid Obesity) OR (Body Weight) OR (Body Weights) OR (Weight, Body) OR (Weights, Body) OR (Weight Gain) OR (Gain, Weight) OR (Gains, Weight) OR (Weight Gains) 83536<br><br>#15 #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 85323<br><br>#16 #5 AND #15 502 |
| **Embase** | #1 'sleep deprivation'/exp OR 'sleep deprivation' OR 'deprivation, sleep'/exp OR 'deprivation, sleep' OR 'induced sleep loss'/exp OR 'induced sleep loss' OR 'sleep deprivation procedure'/exp OR 'sleep deprivation procedure' OR 'sleep loss (procedure)'/exp OR 'sleep loss (procedure)' OR 'therapeutic sleep deprivation'/exp OR 'therapeutic sleep deprivation'<br><br>#2 'circadian rhythm sleep disorder'/exp OR 'circadian rhythm sleep disorder' OR 'sleep disorders, circadian rhythm'/exp OR 'sleep disorders, circadian rhythm'<br><br>#3 #1 OR #2<br><br>#4 'obesity'/exp OR 'obesity' OR 'adipose tissue hyperplasia'/exp OR 'adipose tissue hyperplasia' OR 'adipositas'/exp OR 'adipositas' OR 'adiposity'/exp OR 'adiposity' OR 'alimentary obesity'/exp OR 'alimentary obesity' OR 'body weight, excess'/exp OR 'body weight, excess' OR 'corpulency'/exp OR 'corpulency' OR 'fat overload syndrome'/exp OR 'fat overload syndrome' OR 'nutritional obesity'/exp OR 'nutritional |

| | |
|---|---|
| | obesity' OR 'obesitas'/exp OR 'obesitas' OR 'overweight'/exp OR 'overweight' |
| | #5 'obesity hypoventilation syndrome'/exp OR 'obesity hypoventilation syndrome' OR 'pickwick syndrome'/exp OR 'pickwick syndrome' OR 'pickwickian syndrome'/exp OR 'pickwickian syndrome' |
| | #6 'abdominal obesity'/exp OR 'abdominal obesity' OR 'abdominal adiposity'/exp OR 'abdominal adiposity' OR 'obesity, abdominal'/exp OR 'obesity, abdominal' |
| | #7 'metabolically benign obesity'/exp OR 'metabolically benign obesity' OR 'obesity, metabolically benign'/exp OR 'obesity, metabolically benign’ |
| | #8 'morbid obesity'/exp OR 'morbid obesity' OR 'obesity, morbid'/exp OR 'obesity, morbid' |
| | #9 'body weight'/exp OR 'body weight' OR 'total body weight'/exp OR 'total body weight' OR 'weight, body'/exp OR 'weight, body' |
| | #10 'body weight gain'/exp OR 'body weight gain' OR 'body weight increase'/exp OR 'body weight increase' OR 'weight gain'/exp OR 'weight gain' OR 'weight increase'/exp OR 'weight increase' |
| | #11 #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 |
| | #12 #3 AND #11 |
| | #13 #12 AND [embase]/lim NOT ([embase]/lim AND [medline]/lim) |

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## ANEXO A – NEWCASTLE OTTAWA ASSESSMENT FORM FOR COHORT STUDIES

Note: A study can be awarded a maximum of one star for each numbered item within the Selection and Outcome categories. A maximum of two stars can be given for Comparability

**Selection**

1) Representativeness of the exposed cohort

a) truly representative of the average _____ (describe) in the community ★

b) somewhat representative of the average _____ in the community ★

c) selected group of users eg nurses, volunteers

d) no description of the derivation of the cohort

2) Selection of the non exposed cohort

a) drawn from the same community as the exposed cohort ★

b) drawn from a different source

c) no description of the derivation of the non exposed cohort

3) Ascertainment of exposure

a) secure record (eg surgical records) ★

b) structured interview ★

c) written self report

d) no description

4) Demonstration that outcome of interest was not present at start of study

a) yes ★

b) no

**Comparability**

1) Comparability of cohorts on the basis of the design or analysis

a) study controls for _____ (select the most important factor) ★

b) study controls for any additional factor ★ (This criteria could be modified to indicate specific control for a second important factor.)

**Outcome**

1) Assessment of outcome

a) independent blind assessment ★

b) record linkage ★

c) self report

d) no description

2) Was follow-up long enough for outcomes to occur

a) yes (select an adequate follow up period for outcome of interest) ★

b) no

3) Adequacy of follow up of cohorts

a) complete follow up - all subjects accounted for ★

b) subjects lost to follow up unlikely to introduce bias - small number lost - > ____ % (select an adequate %) follow up, or description provided of those lost) ★

c) follow up rate < ____% (select an adequate %) and no description of those lost

d) no statement

## ANEXO B – PRISMA 2009 CHECKLIST

| Section/topic | # | Checklist item | Reported on page # |
|---|---|---|---|
| **TITLE** | | | |
| Title | 1 | Identify the report as a systematic review, meta-analysis, or both. | |
| **ABSTRACT** | | | |
| Structured summary | 2 | Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number. | |
| **INTRODUCTION** | | | |
| Rationale | 3 | Describe the rationale for the review in the context of what is already known. | |
| Objectives | 4 | Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS). | |
| **METHODS** | | | |
| Protocol and registration | 5 | Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number. | |
| Eligibility criteria | 6 | Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale. | |
| Information sources | 7 | Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched. | |
| Search | 8 | Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated. | |
| Study selection | 9 | State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis). | |

| | | | |
|---|---|---|---|
| Data collection process | 10 | Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators. | |
| Data items | 11 | List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made. | |
| Risk of bias in individual studies | 12 | Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis. | |
| Summary measures | 13 | State the principal summary measures (e.g., risk ratio, difference in means). | |
| Synthesis of results | 14 | Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., $I^2$) for each meta-analysis. | |
| Risk of bias across studies | 15 | Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies). | |
| Additional analyses | 16 | Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified. | |
| **RESULTS** | | | |
| Study selection | 17 | Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram. | |
| Study characteristics | 18 | For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations. | |
| Risk of bias within studies | 19 | Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12). | |
| Results of individual studies | 20 | For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot. | |
| Synthesis of results | 21 | Present results of each meta-analysis done, including confidence intervals and measures of consistency. | |
| Risk of bias across studies | 22 | Present results of any assessment of risk of bias across studies (see Item 15). | |
| Additional analysis | 23 | Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item | |

| | | | |
|---|---|---|---|
| | | 16]). | |
| **DISCUSSION** | | | |
| Summary of evidence | 24 | Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers). | |
| Limitations | 25 | Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias). | |
| Conclusions | 26 | Provide a general interpretation of the results in the context of other evidence, and implications for future research. | |
| **FUNDING** | | | |
| Funding | 27 | Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review. | |