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ORIGINAL ARTICLE

Sleep duration and incidence of obesity in infants, children, and adolescents: a systematic review and meta-analysis of prospective studies

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Abstract

Study Objectives: To assess the prospective relationship between sleep and obesity in a paediatric population.

Methods: We performed a systematic search using PubMed, Embase, Web of Science, and Cochrane (up to September 25, 2017). Included studies were prospective, had follow-up of ≥1 year, had duration of sleep at baseline, and measures of incidence of overweight or obesity and/or changes in body mass index (BMI) z-score and BMI during follow-up. We extracted relative risks or changes in BMI z-score or BMI and 95% confidence intervals (CI) and pooled them using a random effect model.

Results: Forty-two studies were included but, as there was significant heterogeneity, results are presented by age strata. Short sleep was associated with a greater risk of developing overweight or obesity in infancy (seven studies, 14738 participants, risk ratio [RR]: 1.40; 95% CI 1.19 to 1.65; p < .001), early childhood (eight studies, 31104 participants, RR: 1.57; 1.40 to 1.76; p < .001), middle childhood (three studies, 3005 participants, RR: 2.23; 2.18 to 2.27; p < .001), and adolescence (three studies, 26652 participants, RR: 1.30; 1.11 to 1.53; p < .002). Sleep duration was also associated with a significant change in BMI z-score (14 studies, 18 cohorts, 31665 participants; mean difference -0.03; -0.04 to -0.01 per hour sleep; p = .001) and in BMI (16 studies, 24 cohorts, 24894 participants; mean difference -0.03 kg/m²; -0.04 to -0.01 for every hour of increase in sleep; p = .001)

Conclusions: Short sleep duration is a risk factor or marker of the development of obesity in infants, children, and adolescents.

Statement of Significance

This comprehensive systematic review of prospective studies shows that short sleep duration is a risk factor for weight gain and the development of obesity in infants, children, and adolescents. The findings suggest that parents, medical practitioner, and health care workers need to be aware of the importance of adequate sleep in children and that educational programs should be developed to aid parents and children to improve sleep.

Key words: sleep deprivation; obesity; overweight; body mass index; meta-analysis; prospective; infants; adolescents

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Introduction

Sufficient sleep is necessary for optimal daytime performance and wellbeing. Whilst babies and children spend more time asleep than adults, the amount of sleep that people get varies greatly [1]. A decrease in the average duration of sleep, alongside an increase in shift work and longer work hours, has been reported in westernized adult populations. Decreased sleep is associated with increased reporting of fatigue, tiredness, and excessive daytime sleepiness [1]. Too little sleep is also associated with adverse health outcomes, including total mortality [2], stroke and coronary heart disease [3], type 2 diabetes, hypertension [5, 6], and poor self-rated health [2]. Usual sleep duration in children and adolescents is affected by age and a number of different cultural, social, psychological, behavioral, pathophysiological, and environmental factors. Insufficient and disturbed sleep in children has been shown to be associated with performance deficits, including reduced school grades, and mood and behavioral disruption, including hyperactivity and depression [7].

The prevalence of obesity has increased worldwide in the last few decades and the World Health Organization has now declared it a global epidemic. In childhood, obesity can cause a number of psychosocial problems including low self-esteem and it has been suggested that it may be associated with the increased prevalence of type 2 diabetes seen in children [8]. Furthermore, if continued into adulthood, it is likely to be associated with an increased risk of cardiovascular disease. Sleep deprivation also has major effects on metabolism, endocrine function, and immune and hemostatic pathways [9].

Early cross-sectional studies reported associations between short duration of sleep and the risk of obesity in children [10]. New evidence from prospective longitudinal studies in children has now shown that short duration of sleep may precede the development of overweight or obesity [11]. If causal, the potential public health implications would be far reaching.

The aims of this article are as follows: (1) to systematically review published prospective population-based studies of the association between sleep duration and overweight or obesity in infants, children, and adolescents; (2) to carry out a meta-analysis to assess whether the evidence supports the presence of a prospective relationship between short sleep duration and obesity in children of different ages; and (3) to obtain a quantitative estimate of the risk.

Methods

Search strategy and selection criteria

We performed a systematic search to identify studies that reported the longitudinal association between sleep duration and overweight, obesity, and body mass index. We searched the electronic databases such as PubMed, Medline, Embase Web of Science, and Cochrane Central Register of Controlled Trials (from 1966 to September 25, 2017). We used "Sleep terms" (sleep OR sleep-disordered breathing OR bed time) in combination with "Obesity terms" (BMI OR body mass index OR weight OR waist circumference OR waist OR WHR OR waist hip ratio OR obese OR overweight OR adiposity OR adipose tissue OR anthropometry OR body composition OR body constitution) and "Study Population terms" (children OR adolescents OR pediatrics OR

pediatric OR paediatric OR paediatrics OR infant OR preschool) with "Study type terms" (prospective OR cohort OR longitudinal). Search strategies used subject headings and key words. Articles resulting from these searches and relevant references cited in those articles were reviewed. We did not use language restrictions.

Inclusion and exclusion criteria

For inclusion, studies had to fulfil the following criteria: (1) original published article; (2) study in infants, children, or adolescents; (3) observational prospective design; (4) assessment of duration of sleep quantity as baseline exposure; (5) follow-up of ≥1 year for incident outcomes; and (6) one of the following outcomes: (1) incident cases of overweight and/or obesity, (2) prospective changes in BMI z-score, or (3) changes in BMI.

Studies were excluded if (1) case—control design was used, (2) cross-sectional associations were reported, (3) only meeting abstract or unpublished material available, or (4) if all individuals had sleep-disordered breathing. If multiple published reports from the same study were available, we included only the one with the most detailed information for both exposure and outcome. When data were not readily available from published reports, we wrote to the authors to ask for raw data.

Data extraction

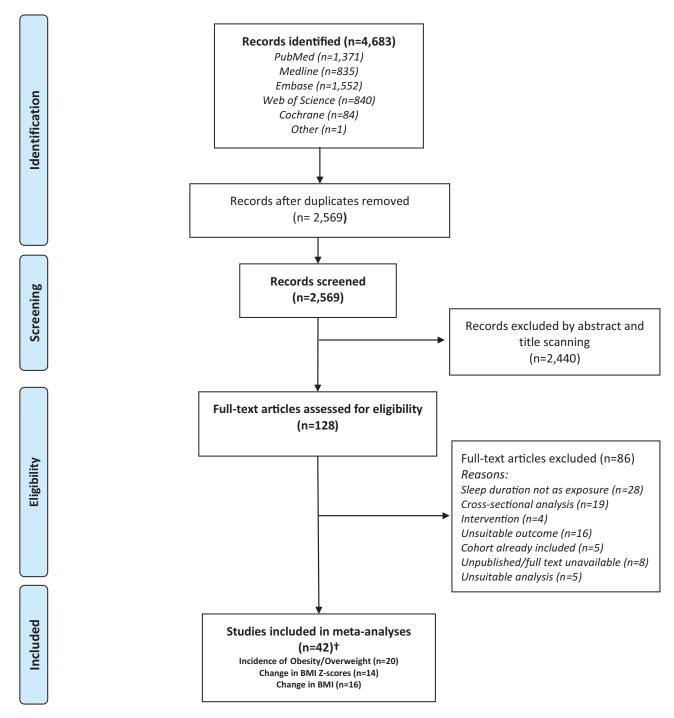
Three reviewers (M.A.M., M.K., and F.P.C.) independently extracted the data. Differences about inclusion of studies were resolved by arbitration with the co-authors. From a total of 4683 search records, 2569 studies were identified after duplicates had been removed (Figure 1). Full text evaluation of 128 studies identified 42 studies that had data suitable for meta-analysis (20 for overweight/obesity, 14 for BMI z-score, and 16 for BMI). Relevant data included the first authors surname, year of publication, country of origin and details of the population studied (including the number of participants), recruitment year, number of recoded cases of obesity, BMI, participants' age, method used to determine sleep, category for "short" sleep, outcome assessment method, odds ratios (OR) or relative risks of overweight or obesity, change in BMI z-score or in BMI, corresponding 95% CI, and covariates adjusted in the statistical analysis.

Exposure

Sleep in children and adolescent is different from that of adults and although by age 10 sleep is similar to that of adults, the total time is longer (10 hr) [12]. The definition of "short sleep" was defined by age as stated in Table 1. For OR, short sleepers were compared to both middle and long sleepers, although in some studies they were compared to a reference category.

Outcome

Unless stated otherwise in Table 1, obesity in children was defined either as BMI > 95th percentile and overweight as >85th percentile according to local national growth charts or by international growth charts where the thresholds for obesity is defined as the percentile which passes through BMI > 30 kg/m²



 $\textbf{Figure 1.} \ \ \textbf{PRISMA flow chart.} \ \ ^{\dagger} \textbf{Studies contribute to more than one meta-analysis.}$

at age 18 years. Both BMI z-scores also called BMI standard deviation (s.d.) scores, and changes in BMI, were also used for outcome data. The former are measures of relative weight adjusted for child age and sex. BMI z-scores are calculated relative to an external reference.

Populations

For the purpose of this study, children were categorized into four subgroups according to the average age at the time of the baseline

assessment: infants (0 to <3 years); early childhood (3 to <9 years); middle childhood (9 to <12 years), and adolescents (12 to 18 years).

Confounders

Studies adjusted for various confounders including age, sex, ethnicity, income, exercise, etc. (Table 1). With consideration to the causal pathway, estimates from the most adjusted model were used, for the meta-analysis wherever appropriate. However, in some cases of papers using BMI z-score as outcome, age and

Table 1. Description of 42 studies included in the meta-analyses for (1) overweight/obesity, (2) BMI z-score, and (3) BMI

Author	Year Published	Country	Cohort	Quality Score	Recruitment year(s)	Age at baseline sleep measurement(s)	Duration of follow-up
Agras [27]	2004	USA	Recruited from well newborn nurseries in San Francisco (n = 150)	12	Unreported	3 years	5.5 years
Reilly [20]	2005	UK	Avon longitudinal study (ALSPAC) (n = 5493)	17	1991–1992 (mothers)	2.5 years	4.5 years
Lumeng [34]	2007	USA	National Institute of Child Health & Human Development Study in early Child Care & Youth Development (NICHD_SECCYD).	17	1991	Mean age (SD): 9.02 (0.31) years	Average 2.6 years.
Snell [44]	2007	USA	(n = 785) Longitudinal Child Development Supplement of the Panel Survey of Income Dynamics (n = 1441)	16	1997	Young: 3–7.9 years Older: 8–12.9 years	5.5 years
Taveras [22]	2008	USA	Project Viva (n = 915)	18	1999–2002†	0.5 years	2.5 years
Landhuis [28]	2008	New Zealand	Prospective birth cohort (n = 1037)	16	1972–1973	5 years	27 years
Berkey [58]	2008	USA	Growing up today Study of children of Nurses health study II participants (n = 5036)	13	2001	14-21 years	1 year
Touchette [21]	2008	Canada	Quebec longitudinal study of child development ($n = 1138$)	17	1997–1998	2.5 years	4.5 year

Table 1. Continued

Author	Sleep exposure	Sleep exposure categories Short sleep (SS) refer- ence (RS)	Exposure assessment	Outcome	Outcome assessment	Adjusted variables
Agras [27]	Sleep duration (average of sleep time at age 3 and 4, not reported if it includes naps)	SS: <11.25 hr RS: >11.25 Continuous (hours)	Parental report (unreported)	Analyzed as OW/OB: OW: BMI > 85th percentile for age and sex. Ref: (charts unreported). Analyzed For BMI: Changes in BMI kg/m² at end of follow-up	Height and weight measured by researchers	No adjustments mentioned in correspondence
Reilly [20]	Sleep duration (not reported if it includes naps)	SS: Lowest quar- ter; <10.5 (<i>n</i> = 1831) RS: highest quar- ter; >12 hr	Parental report (questionnaire)	Analyzed as OW/OB: BMI ≥95th centile Ref: UK population 1990	Height and weight measured by researchers	Maternal education, energy intake at age 3 years (food groups), sex
Lumeng [34]	Total daily sleep duration (includ- ing naps)	SS: Lowest percentile Continuous (hours)	Maternal report (questionnaire)	Analyzed as OW/OB: OW: ≥ 95th percentile for age and gender. Ref: National Center for Health statistics norms	Height and weight measured by researchers	Gender, race, maternal edu- cation, child BMI z-score at 3rd grade, change in sleep duration between 3rd and 6th grade
Snell [44]	Nighttime sleep duration (weighted aver- age of week and weekend)	Continuous (hours)	Mixed- child and parent reported sleep duration (time diary)	Analyzed for BMI Z-score: Changes in BMI z-score standardized for age and sex at end of follow up Ref: CDC OW: age and gender spe- cific IOTF cut-offs, similar to adult ≥ 25.	Height and weight measured by researchers	Family income, parent education, child race, child age at time 1, child age at time 2 sex, BMI at time 1
Taveras [22]	Weighted average of sleep duration (weekend + week) from 6 months to 2 years (including naps)	SS: <12hr (n = 329) RS: ≥12 hr Continuous (hours)	Parental report (questionnaire)	Analyzed as OW/OB: OW: BMI ≥ 95th percentile or greater for age and sex, analyzed as OB: Ref: CDC Analyzed for BMI Z-score: Difference in BMI z-scores at end of follow up	Height and weight measured by researchers	Maternal education, income, pre-pregnancy BMI, marital status, prenatal smoking his tory, breastfeeding duration, child's race/ethnicity, child's birth weight and 6 month weight for length 2 score, daily television viewing, daily active play
Landhuis [28]	Nighttime sleep duration (Average of sleep duration at 5, 7, 9 and 11 years)	SS: <11 hr (n = 301) Mod: 11–11.5 hr (n = 400) Long >11.5 (n = 311). Continuous (hours)	Parental report (bedtimes and rising times)	Analyzed as OW/OB: OB: BMI ≥ 30 kg/m². Analyzed For BMI: Changes in BMI kg/m² at end of follow up	Height and weight measured by researchers	Sex, SES, early BMI, parental BMI, physical activity, smok- ing, level of parental control and television watching, sleep time at age 32
Berkey [58]	Typical nighttime sleep duration on a school or work day	Continuous (hours)	Self-reported (questionnaire)	Analyzed For BMI: change in BMI kg/m² over one year change in BMI kg/m² over one year compared to reference group	Self-reported height and weight	Internet, coffee, alcohol, past year physical activity, tv/ videos, games, age, age [2], menarche, height growth and baseline BMI
Touchette [21]	Nighttime sleep duration (on average) Based on sleep duration on age 2.5, 3.5, 4 and 5	SS: short persist- ent (<10) RS: 11-hour persistent	Maternal report (questionnaire)	Analyzed as OW/OB: Overweight or obesity Ref: age and sex specific cut-offs from IOTF	Height and weight measured by researchers	Birth weight, prematurity, low birth weight, sex of child, maternal smoking during pregnancy, weight at 5 months, low parental education, modified family structure, late cereal introduction, not breast-fed, immigrant mother, naptime at 2.5 years, watching TV at 6 years, doing physical activities, overeating at 6 years, snacking at 6 years, eating sweets at 6 years, snoring at 6 years, low income status at 6 years

Table 1. Continued

Author	Year Published	Country	Cohort	Quality Score	Recruitment year(s)	Age at baseline sleep measurement(s)	Duration of follow-up
Bell [23]	2010	USA	Longitudinal analysis of Panel Survey of Income Dynamics (PSID Chid Development Supplements (CDS) (0-4 years n = 822) (5-13 years n = 983)	16	1997	Younger cohort: mean (SD): 2.67 (1.42) Older cohort: mean (SD): 8.58 (2.17) years	5 years
Silva [36]	2011	USA	Tucson Children's assessment of Sleep Apnea Study (n = 304)	17	1999–2003	6–12 years	4.7 years
Storfer-Isser [47]	2011	USA	Longitudinal Cleveland Children's Sleep and Health Study (boys n = 157)	15	1998-2001	8–11 years	8 years
Carter [29]	2011	New Zealand	(girls n = 156) Birth cohort (n = 244)	16	2001–2002	3 years	4 years
Hiscock [40]	2011	Australia	Longitudinal study of Australian children a) ≤ 1 year ($n = 3857$) b) 4–5 years ($n = 3844$)	18	2004	a) mean (sd): 8.7 (2.5), 0.725 years b) mean (s.d.): 56.8 (2.6), 4.73 years	2 years
Diethelm [24]	2011	Germany	Dortmund Nutritional and Anthropometric Longitudinally Designed (DONALD) Study (n = 481)	15	Ongoing since 1985	1.5 years	5.5 years
Seegers [35]	2011	Canada	Quebec Longitudinal Study of Kindergarten Children (n = 1916)	16	1986–1987	10 years	3 years
Lytle [59]	2012	USA	Longitudinal IDEA study and ECHO study (boys $n = 320$) (girls $n = 328$)	16	IDEA: 2006-2007 ECHO: 2007-2008	7 14.7 years	2 years
Araújo [4 9]	2012	Portugal	Urban population based cohort (EPITeen) (boys $n = 545$) (girls $n = 626$)	18	2003–2004	13 years	4 years
Lee [54]	2012	South Korea	Prospective Obesity and Metabolic Disorders Cohort (Grade 1 $n = 474$) (Grade 4 $n = 1030$)	17	2008	1st (7.3 years) and 4th graders (10.0 years)	2 years

Table 1. Continued

Author	Sleep exposure	Sleep exposure categories Short sleep (SS) refer- ence (RS)	Exposure assessment	Outcome	Outcome assessment	Adjusted variables
Bell [23]	Duration of nighttime sleep (average of one weekend and one week day)	SS: Low nighttime sleep at baseline (age specific sleep score below the 25th percentile for sleep for age) RS: age specific sleep score above the 25th percentile for sleep for age	Parental report (Time diaries of a week and week- end day)	Analyzed as OW/OB: OW: BMI >85th to <95th percentile for age and sex Ref: CDC	Parental report of height and weight	Age, sex, birth weight, father present, hours per day of television viewing, birth order and urban residence, race/ethnicity, family income, maternal education, parents' BMI. For older cohort additionally adjusted for child BMI z-score at baseline and physical activity.
Silva [36]	Nighttime sleep duration	SS: <7.5 hr sleep per night Ref: ≥9 hr sleep per night	Polysomngraphy (PSG)	Analyzed as OW/OB: OW/OB: ≥85th age and sex specific BMI percentile OB: ≥95th age and sex specific BMI percentile Ref: CDC growth charts.	Height and weight measured by researchers	BMI, ethnicity, SDB, age, caf- feine use, baseline values where appropriate
Storfer-Isser [47]	Sleep duration (weighted aver- age of week and weekend days)	Continuous (hours)	parental report (questionnaire)	Analyzed For BMI: Changes in age and sex specific BMI-z-scores at end of follow up Ref: CDC data	Height and weight measured by researchers	Age, time to follow up, African-American, low birth- weight, low SES, BMI z-score at age 8–11
Carter [29]	Sleep duration (average of week and weekend sleep, average over age 3, 4 and 5)	Continuous (hours)	Accelerometry and parental sleep logs of week and week- end days	Analyzed as OW/OB: OW: ≥ 85th age and sex specific percentile Ref: CDC Analyzed for BMI: Changes in BMI kg/m² at end of follow up	Height and weight measured by researchers	BMI at age 3, sex, maternal education, maternal BMI, income, ethnicity, birth weight, smoking during pregnancy, physical activity, TV viewing, fruit-vegetable intake, non-core foods intake
Hiscock [40]	Sleep duration (average of one week and one weekend day), including daytime	Continuous (min- utes), converted to hours	Parental report (time diary of a week and week- end day)	Analyzed for BMI Z-score: Changes in BMI z-scores at end of follow up Ref: CDC	Height and weight measured by researchers	Wave 1 sex and BMI (or weight-for-age adjusted for birth length for infants)
Diethelm [24]	naps Usual daily sleep duration (day and nighttime sleep)1	SS: Consistent short sleep duration: <13hr at 1.5 and 2 years (n = 122). RS: consistent long sleep duration: > 13 hr at 1.5 and 2 years	Parental report (interview)	Analyzed as OW/OB: OW: IOTF BMI cut-offs for children.	Height and weight measured by researchers	Sex, gestational age, birth year, birth weight, fully breastfeeding, rapid weight gain, SES family, maternal education status, maternal overweight, smoking in the household. Maternal age at birth of child, birth order of participating child.
Seegers [35]	Weekday sleep duration	SS: <10.5 hours trajectory RS: 11 hour sleep- ers trajectory Continuous (hours), not for sensitivity	Parent-reported (questionnaire of bed and wake times)	Analyzed as OW/OB: OW and OB Ref: age and sex specific BMI curves IOTF. Analyzed for BMI: Changes in BMI kg/m² at end of follow up	Parental report	Sex, immigrant status, familial income, birth weight, maternal and paternal education, pubertal status at ages 11–13, time spent watching television and physical activity out of school at age 13 years
Lytle [59]	Changes in usual nighttime sleep duration (average of a week and weekend day)	Continuous (hours)	Self-report (questionnaire of bedtime and time getting out of bed)	Analyzed for BMI: Change in BMI kg/m² over two years	Height and weight were measured by researchers	Race, grade, parent educa- tion, school lunch, puberty, study, screen time/sedentary behavior, depression, activity and energy intake
Araújo [49]	Usual nighttime sleep duration	Continuous (hours)	Self-reported (from bed and wake up times)	Analyzed for BMI z-score: Change in age and sex specific BMI z-scores from age 13 to 17 Change in age and sex specific BMI z-scores at end of follow up Ref. CDC	Weight and height measured by researchers	Parental education, KIDMED index, BMI-Z score at age 13
Lee [54]	Average daily sleep duration (average of one week)	SS: ≤8.5hr RS: ≥9.5hr	Self-report (questionnaire)	Analyzed for BMI: Change in BMI kg/m² compared to ref over 2 years	Height and weight measured by researchers	Age, sex, sexual maturation, baseline BMI, exercise frequency, weekly screen time, household income, maternal and paternal education, maternal job, family structure, energy intake, fat % of energy intake, meal skipping, snacking

Table 1. Continued

Author	Year Published	Country	Cohort	Quality Score	Recruitment year(s)	Age at baseline sleep measurement(s)	Duration of follow-up
Klingenberg [41]	2012	Denmark	SKOT cohort (n = 211)	16	2006–2007	0.75 years (9 months)	2.25 years (2 years 3 months)
Magee [30]	2013	Australia	Wave 2 and 3 of 4–5 years old cohort Longitudinal Study of Australian Children (n = 1833)	17	2006	6–7 years	2 years
Mitchell [60]	2013	USA	Cohort of 4 suburban high schools in Philadelphia (n = 1390)	15	Unreported	14 years	4 years
Suglia [37]	2014	USA	Add Health Longitudinal Study, Waves 2 and 3 (n = 8718)	16	1994–1995	Mean (SE): 16 (0.03) years	5 years
Miller [46]	2014	USA	Participants in Headstart, low income families in midwest $(n = 273)$	16	Unreported	mean (s.d.): 4.11 (0.54) years	1 year
Michels [48]	2014	Belgium	Belgium longitudinal Children's Body composition and Stress study (n = 193)	15	2010	6–12 years at baseline	2 years
Magee [55]	2014	Australia	Waves 1 to 3 of 4–5 years old cohort Longitudinal Study of Australian Children (n = 2984)	18	2004	4 years	4 years
Speirs [51]	2014	USA	STRONG Kids (n = 247)	13	Unreported	2–3 years	1 year
Martinez [45]	2014	USA (Mexican descent)	Longitudinal cohort stud in Mexican-American children (n = 229)	16	2007–2009	8–10 years	2 years
Scharf [31]	2014	USA	Early childhood Longitudinal Study-Birth Cohort (n = 8950)	15	2001	4 years	1 year

Table 1. Continued

Author	Sleep exposure	Sleep exposure categories Short sleep (SS) refer- ence (RS)	Exposure assessment	Outcome	Outcome assessment	Adjusted variables
Klingenberg [41]	Total sleep dur- ation (nighttime sleep + daytime napping)	Continuous (hours)	Parental report (TSD-Q questionnaire)	Analyzed for BMI z-score: Changes in sex and age adjusted BMI z-score at end of follow up Ref: WHO standard	Height and weight measured by researchers	Birth weight, gestational age duration of breast feeding, maternal smoking during pregnancy, maternal BMI at 9 months, household income, highest education
Magee [30]	Weighted average of week and weekend Sleep duration (including napping)	SS: <10hr combined with unhealthy eating (as a health profile) (n = 237) Ref: healthy profile (lowest rates of short sleep and screen time, high levels of PA)	Parental report (time use diary)	Analyzed as OW/OB: OB Ref: age and sex specific cut-offs from IOTF	Height and weight measured by researchers	level of both parents Child gender, country of birth, household income, place of residence/ remoteness
Mitchell [60]	Typical nighttime sleep duration (weighted aver- age of week and weekend night)	Continuous (hours)	Self-reported	Analyzed for BMI: Changes in BMI from age 14 to 18	Self-reported	Gender, race, maternal edu- cation, MVPA and screen time
Suglia [37]	Usual nighttime sleep duration	SS <6 hr RS >8 hr	Self-reported (questionnaire)	Analyzed as OW/OB: OB: BMI ≥30 kg/m²	Height and weight measured by research- ers and by self-report	Age, sex, race/ethnicity, parental education, further adjusted for watching tv more than 2 hr per day and physical activity
Miller [46]	Nightly sleep dur- ation (average of week and week- end days)	Continuous (hours)	Parental report (interview)	Analyzed for BMI z-score: Change in age and sex specific BMI z-score over one year Ref: CDC	Height and weight measured by researchers	Baseline BMI z-score, SDB, soda consumption, home chaos
Michels [48]	Nighttime sleep duration (weighted aver- age of week and weekend days)	Continuous (hours)	Actigraphy and parental report (sleep diary)	Analyzed for BMI z-score: Changes in age and sex specific BMI z-scores over 2 years, Ref: IOTF	Height and weight measured by researchers	Age, sex, parental educa- tion, physical activity and reported snacking frequency, reported sleep duration
Magee [55]	Sleep duration (including nap- ping, weighted average of week and weekend sleep)	Continuous (hours)	Parental report (time use diary)	Analyzed for BMI: Changes in BMI kg/m² at end of follow up	Height and weight measured by researchers	Child gender, child sleep problems, household income, maternal education and maternal weight status
Speirs [51]	Night-time sleep duration (Average over the past week)	Continuous (hours)	Mother's/par- ental report (questionnaire)	Analyzed for BMI: Changes in BMI kg/m² at end of follow up Ref: CDC	Height and weight measured by researchers	Gender of child, child age, maternal BMI, maternal age, maternal education, marital status, annual household income, maternal race/ethni- city, maternal employment Additional data from Author
Martinez [45]	Nighttime sleep duration (Average from two week- days and one weekend day)	Continuous (hours)	Accelerometry for 3 days	Analyzed for BMI z-score: Changes in age and gen- der specific BMI z-scores at end of follow up Ref: National Child Health Statistics growth charts Weight change from baseline to 24 month fol- low up	Height and weight measured by researchers	BMI z-score at baseline, maternal occupation. For weight gain, adjustments for maternal occupation and BMI, sleep duration at 12 months, height gain (baseline to 24 months)
Scharf [31]	Usual nighttime sleep duration	SS:<9.48 hr RS: ≥ 9.48 hr Continuous (hours)	Parental report (Computer assisted inter- view admin- istered by assessors)	Analyzed as OW/OB: OW ≥85-95th percentile for age and sex OB ≥ 95th percentile for age and sex Ref: CDC Analyzed for BMI z-score: Changes in age and gen- der specific BMI-z score over one year	Height and weight measured by researchers	Sex, race/ethnicity, SES, television viewing

Table 1. Continued

Author	Year Published	Country	Cohort	Quality Score	Recruitment year(s)	Age at baseline sleep measurement(s)	Duration of follow-up
Bonuck [32]	2015	UK	Avon Longitudinal study of parents and children ($n = 1899$)	18	1991–1992	4.75 years	10.25 years
Roberts [38]	2015	USA	Teen Health 2000 cohort (n = 3134)	16	2000	11-17 years	1 year
Bolijn [25]	2015	The Netherlands	KOALA study (n = 1658)	16	2000‡	2 years	7 years
de Souza [61]	2015	Portugal	Oporto Growth, Health and Performance Study, Longitudinal study of adolescents (boys <i>n</i> = 3476)	18	Unreported	10, 12, 14, and 16 years at baseline (4 age cohorts)	3 years
Krueger [39]	2015	USA	(girls n = 3418) National Longitudinal Study of Adolescent to Adult Health (n = 14800)	14	1994–1995	Mean: 15.9 years	Max 15 years
Zhou [52]	2015	Singapore	Growing Up in Singapore Towards healthy Outcomes (GUSTO) birth cohort (n = 799)	16	2009–2011	0.25 years (3 months)	1.75 years (21 months)
Küpers [42]	2015	The Netherlands	GECKO Drenthe Birth Cohort (n = 2475)	14	2006–2007	0.33 years (4 months)	1.67 years (20 months)

Table 1. Continued

Author	Sleep exposure	Sleep exposure categories Short sleep (SS) refer- ence (RS)	Exposure assessment	Outcome	Outcome assessment	Adjusted variables
Bonuck [32]	Weekday night- time sleep duration	SS <10.5 hr RS >10.5 - <12.08 hr	Parental report (typical weekday bed and wake times)	Analyzed as OW/OB: OB: BMI > 95th percentile for age and sex Ref: IOTF	Weight and height measured by researchers	Childs sex, age at BMI/height assessment and birth weight, child's estimated weight and height at 6 months, maternal education, age, parity and pre-pregnancy BMI, T&A, SDB cluster
Roberts [38]	Nighttime sleep duration (on aver- age past 4 weeks)	SS: sleep restric- tion, sleeping 6 hr or less on weeknights and weekends RS: no sleep restriction,	Self-reported (interview)	Analyzed as OW/OB: OB: ≥95th age and sex specific percentile Ref: CDC	Height and weight measured by researchers	Age, gender, family income, major depression and weight status at wave 1
Bolijn [25]	Night-time sleep duration	Continuous (hours)	Parental report (questionnaire)	Analyzed as OW/OB: OW: > 85th percentile BMI z-score Ref: (charts not mentioned) Analyzed for BMI z-score: Changes in BMI Z-score at age 5 through 9	Parental report	Daytime sleep duration, recruitment group, pre- pregnancy BMI, maternal smoking during pregnancy, pregnancy, weight gain, maternal age at birth, country of birth, educational level, hours/week of paid work by mother, age of child at BMI measurement, child gender, time at kindergarten, tv time, computer time, time playing
de Souza [61]	Usual sleep dur- ation (weekly average)	Continuous (hours)	Self-reported (questionnaire)	Analyzed for BMI: Annual Change in BMI kg/m²	Height and weight measured by researchers	outside Peak height velocity, physical fitness components, total pa, sleep habits, fruit/vegetable intake
Krueger [39]	Usual nighttime sleep duration (weighted aver- age of week and weekend days)	SS: <7 hr in all 4 waves RS: <7 hr in none of the waves	Self-reported (questionnaire)	Analyzed as OW/OB: OB: kg/m2 ≥30	Measured weights and heights	Age, sex, race/ethnicity, excluded obese in wave 1
Zhou [52]	Total daily sleep duration on aver- age (sum of night- time sleep and daytime sleep)	Continuous (hours)	Parental report (Brief Infant Sleep Questionnaire)	Analyzed for BMI: Changes in BMI kg/m² over 21 months	Height and weight measured by researchers	Ethnicity, maternal education, household income, maternal height and BMI at 26 weeks of gestation, age, sex, gestational age, birth weight and length, pregnancy smoking status, maternal gestational diabetes, breast-feeding duration, total media use and outdoor physical activity at
Küpers [42]	Total sleep duration (including naps)	Continuous (hours)	Parental report (questionnaire)	Analyzed for BMI: Changes in BMI kg/m² from 6 to 24 months. Analyzed for BMI z-score: Changes in age and gender specific BMI z-scores from 6 to 24 months Ref: Dutch growth references from 1997	Height and weight measured by researchers	24 months Gestational age, birth weight, gender, paternal BMI, maternal pre-pregnancy BMI, gestational weight gain mother, smoking during pregnancy, maternal age at date of birth, maternal diabetes, maternal hypertension, Dutch ethnicity, type of feeding at 3 months, complementary feeding at 4 months, family screen time at 6 months, time of possible unrestricted moving at 9 months, multiparity, maternal education level, household income, one-parent family, childcare by family or friends at 3 months, mother working at 3 months after delivery Additional data provided by author

Table 1. Continued

Author	Year Published	Country	Cohort	Quality Score	Recruitment year(s)	Age at baseline sleep measurement(s)	Duration of follow-up
Ames [57]	2016	Canada	Victoria Healthy Youth Survey (V-HYS) (n = 662)	13	2003	Mean (SD): 15.5 (1.9) years	11 years
Butte [56]	2016	USA	Pre-school age cohort (n = 111)	17	2010–2012	Mean (SD): 4.6 (0.9) years	1 year
Halal [26]	2016	Brazil	2004 Pelotas Birth Cohort (n = 4231)	16	2004	1 year	3 years
Baird [53]	2016	UK	Children of the women included in the Southampton Women's Survey (SWS) ($n = 587$)	15	1998–2002 (of mothers)	3 years	1 year
Wang [33]	2016	China	Jiaxing Birth Cohort (n = 16028)	16	1999–2009	3 years	2 years
Derks [43]	2017	Netherlands	Embedded in Generation R $(n = 5161)$	14	2002–2006	2–6 months	5–6 years
Maume [50]	2017	USA	Study of Early Child Care and Youth Development (SECCYD) $(n = 974)$	15	1991	12 years	3 years

Table 1. Continued

Author	Sleep exposure	Sleep exposure categories Short sleep (SS) refer- ence (RS)	Exposure assessment	Outcome	Outcome assessment	Adjusted variables
Ames [57]	Nighttime sleep duration (on average)	Continuous (hours)	Self-report (interview)	Analyzed for BMI: Changes in BMI kg/m² over 11 year period	Height and weight measured by researchers	Physical activity, internalizing symptoms, age group (12–15 or 16–18)
Butte [56]	Total sleep dur- ation (Nighttime sleep and nap time)	Continuous (min/day), converted to per hour	Accelerometry for 7 consecutive days	Analyzed for BMI: Annual Changes in BMI kg/m² Annual Weight gain (kg)	Height and weight measured by researchers	Age, sex, race/ethnicity, day- care hours, household size, household income, mother's age, BMI and education
Halal [26]	Usual nighttime sleep duration	SS: <10 hr in at least one of the follow up visits (at age 1,2,3,4) RS: ≥ 10 hr in each of the follow up visits.	Annual parental report (interview)	Analyzed as OW/OB: OW (BMI Z-scores between 2–2.99 SD's) or OB: (BMI Z-scores ≥3 SD's) Ref: WHO charts	Height and weight measured by researchers	Mother's skin color and schooling, sleep character- istics measured at 1 y of age (sleep latency, number of night awakenings, duration of daytime naps)
Baird [53]	Usual nighttime sleep duration	Continuous (hours)	Maternal report (interview)	Analyzed for BMI: Changes in BMI at end of follow up	Height and weight measured by researchers	Age at DXA measurement, gestational age at birth, sex, maternal pre-pregnancy BMI maternal educational attainment and smoking during pregnancy, age last breastfed child's television watching and level of activity, dietary quality, highest social class of parents
Wang [33]	Average sleep duration during a 'typical' week.	Categorized ≤ 10 hr, 11–12 hr, and ≥ 13 hr	Parental report (questionnaire)	Analyzed as OW/OB: Overweight and obesity were defined by age and gender-specific cut-off points according to the latest Chinese criteria (overweight:, 16.5, and 16.6 for 5-year old boys, and 5-year old girls; obesity: 17.9, and 18.2 for 5-year-old boys, and 5-year-old girls	Height and weight measured by trained nurses.	Age, gender, birth weight, breastfeeding status, appetite, physical activity, maternal age at delivery, maternal body mass index, education and occupation.
Derks [43]	Usual bedtimes and wake times, Daytime sleep (naps) assessed.	Continuous (hours)	Parental report (questionnaire)	Analyzed for BMI z-score:BMI (kg/m²) standard deviation (SD) scores calculated by adjusting BMI for age and sex using Dutch reference growth curves.	Height and weight measured by trained staff.	Ethnicity, birth weight, duration of television watching, duration of breastfeeding, maternal education level, maternal BMI, maternal psychopathology symptoms, baseline BMI SD score.
Maume [50]	Usual bedtimes and arise times (week days)	Continuous (hours)	Self-reported (questionnaire)	Analyzed for BMI z-score: Standardized to percentile scores.	Height and weight measured by trained staff.	

†Not mentioned in paper. From Maternal age and other predictors of newborn blood pressure by Gillman et al. http://www.ncbi.nlm.nih.gov/pubmed/14760269. ‡Not mentioned in paper. From Etiology of atopy in infancy: the KOALA Birth Cohort Study by Kummeling et al. http://www.ncbi.nlm.nih.gov/pubmed/16343090.

BMI were also adjusted for, suggesting possible overadjustment. Mean age of the populations, country, and sample size were collected and used in stratified analyses of heterogeneity, publication bias, and sensitivity.

Statistical analysis

The quality of the studies included in the meta-analysis was evaluated by the Downs and Black Quality Index score system using a validated checklist for assessing the quality of the studies [13]. For the assessment of nonrandomized studies, the maximum score is 20. To estimate the quantitative relation between short sleep duration and overweight or obesity, we calculated an estimate of relative risk (risk ratio [RR]) from either OR or hazard ratios (HR) with 95% confidence intervals (CI) or regression coefficient β (95% CIs) for changes in BMI z-score or BMI as a continuous outcome. When studies did not report the necessary data, we requested them from the authors. If the SE of either the RR or β were not supplied, it was algebraically computed from the 95% CIs, wherever possible. We used a random effect model weighted by the inverse of the variance [14], and by comparison with the reference category, we estimated the pooled risk and 95% CI of risk of development of overweight or obesity or the mean difference in BMI z-score or BMI with each additional hour of sleep. The heterogeneity among studies was tested by Q-statistic and quantified by H-statistic and I2-statistic [15]. Funnel plot asymmetry was used to detect publication bias, and Egger's regression test was applied to measure funnel plot asymmetry [16, 17] wherever appropriate. "Trim and fill" method was used to attempt to correct for publication bias [18]. The influence of individual studies, from which the meta-analysis estimates are derived, was examined by omitting one study at a time to see the extent to which inferences depend on a particular study or group of studies (sensitivity analysis). Subgroup analysis was carried out to assess possible sources of heterogeneity and to check for the potential impact of geographic location on the relationship between sleep and obesity. Egger's test and "trim and fill" were performed using Stata version 14 (Stata corporation, College Station, TX, USA). Random effects metaregression was used to determine if follow-up was significantly associated with heterogeneity. Other statistical analyses were performed using Review Manager software version 5. The systematic review and the meta-analysis were carried out in line with the PRISMA guidelines for nonrandomized studies, with the appropriate exclusion of nonrelevant items [19].

Results

Characteristics of study cohorts

Of a total of 4683 studies identified from the searches (Figure 1), after exclusion of ineligible studies (Supplementary Table S1 for details of the studies and the reason for exclusion), 42 studies (63 cohorts) met the inclusion criteria for the qualitative synthesis and had data suitable for the different sets of analyses. Studies that reported data for boys and girls, for different age groups, or for different nationalities were treated as separate cohorts. Ages at the start of the study ranged from 0 to 12 years (Table 1). There were 20 studies for obesity (21 cohorts across the different age groups) [20–39], 14 studies for BMI z-score (18 cohorts

across the age groups) [22, 25, 40–50], and 16 studies for BMI (24 cohorts across the different age groups) [27–29, 35, 42, 51–61]. Overall, for sleep and obesity, the meta-analysis included 75499 participants from nine different countries, for BMI 24894 from nine countries, and for BMI z-score 31665 from eight countries.

Incidence of overweight and/or obesity in short sleepers

Data on the relationship between sleep and overweight and/ or obesity by age groups are shown in Figure 2. In the pooled analysis, short sleep was associated with an increased risk of overweight or obesity in the combined group (RR: 1.58 [95% CI 1.35, 1.85]; p < .001). There was significant heterogeneity between studies (I^2 = 92%, p < .001) with evidence of publication bias (Supplementary Figure S1a; Egger's test, p = .005). The addition of seven point estimates identified by the "trim and fill" method resulted in a revised pooled estimate of 1.42 [1.12, 1.81] but still remained significant. In a subgroup analysis by age group, seven cohorts included infants 0 to <3 years at baseline. The pooled relative risk was 1.40 [1.19, 1.65], p < .001, with no statistical evidence of heterogeneity ($I^2 = 40\%$; p = .13). Eight cohorts included children 3 to <9 years at baseline. The pooled relative risk was 1.57 [1.40, 1.76], p < .001, with no statistical evidence of heterogeneity ($I^2 = 23\%$; p = .25). Three cohorts included children 9 to <12 years at baseline. The pooled relative risk was 2.23 [2.18, 2.27], p < .001 with no evidence of heterogeneity ($I^2 = 0\%$; p = .41). Three cohorts included children 12-18 years at baseline. The pooled relative risk was 1.30 [1.11, 1.53], p = .002 with no evidence of heterogeneity ($I^2 = 0\%$; p = .49; Figure 2).

Subgroup analysis by continent in the combined age groups

Subgroup analysis by continent yields risk ratios ranging from 1.26 to 2.19 across the three subgroups, each with statistically significant results. Heterogeneity estimates ranged from 0 to 92 per cent, with no evidence of heterogeneity in the Australia and Oceania subgroups (Supplementary Table S2).

Sensitivity analysis

Sensitivity analysis by deleting one study at a time yields risk ratios that are still statistically significant for each subgroup (Supplementary Table S3a). The heterogeneity estimates range from 0 to 49 per cent. In infants, the heterogeneity was reduced to zero by the removal of the study of Bolijn et al. [25]. In early childhood, the heterogeneity was reduced to zero by the removal of the study of Scharf et al. [31]. In middle childhood and in adolescents, there was no overall heterogeneity (Supplementary Table S3a). Removal of two studies [27, 39] with quality scores of <15 has no major effect on the estimates (Supplementary Table S4). Follow-up time was not significantly associated with heterogeneity (p = .878 by meta-regression).

Short sleep and BMI z-score

In the pooled analysis, short sleep was associated with a decrease in BMI z-score per hour of increase in sleep (RR: -0.03

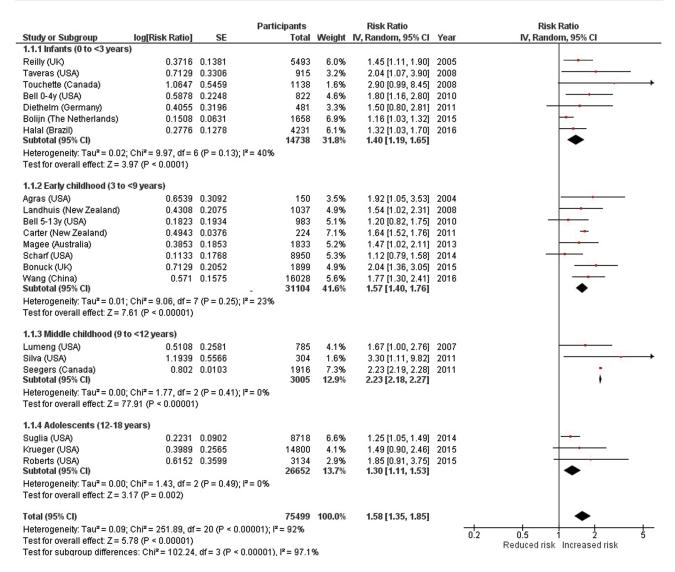


Figure 2. Incidence of overweight or obesity in short sleeper by age group. Results are expressed as risk ratio (95% confidence intervals).

[-0.04, -0.01]; p = .0001; Figure 3). In the pooled analysis, there was significant heterogeneity between studies ($[I^2 = 54\%, p < .003;$ Eggers test, p = .054]; Supplementary Figure S1b). In a subgroup analysis by age group, there was no overall statistical heterogeneity; yet, although the risk estimates were statistically significant in infants and early childhood, they were not statistically significant in middle childhood or adolescents (p = .45; Figure 3). The "trim and fill" method did not produce any correction to the original estimates.

Sensitivity analysis by deleting one study in the subgroups at a time is shown in Supplementary Material. In middle childhood, the heterogeneity was reduced to 0 per cent by the removal of either Michels et al. [48] or Storfer-Isser et al. (girls) [47]. Likewise, in adolescents, it was reduced to zero by the removal of Maume et al. [50] (Supplementary Table S3b). The removal of two studies with quality scores of <15 has no major effect on the results (Supplementary Table S4). Follow-up time was not significantly associated with heterogeneity (p = .837 by meta-regression).

Short sleep and BMI

Data on the relationship between sleep and change in BMI are shown in Supplementary Figure S2. In the pooled analysis, short sleep was associated with a decrease in BMI per hour of increase in sleep (RR: -0.03 [-0.04, -0.01]; p = .001), with significant heterogeneity between studies ($I^2 = 80\%$, p < .001) and evidence of publication bias (Eggers test, p = .001; Supplementary Figure S1c). The "trim and fill" method did not produce any correction to the original estimates. In a subgroup analysis by age groups, there was some heterogeneity of effect (p = .03) with the effect being greater in children aged 3 to <9 years (Supplementary Figure S2). Sensitivity analysis is shown in Supplementary Material. In middle childhood, the heterogeneity was reduced to zero by the removal of Seegers et al. [35] (Supplementary Table S3c). The removal of eight cohorts (five studies) [27, 42, 51, 57, 58] with quality scores of <15 has no major effect on the results (Supplementary Table S4). Follow-up time was not significantly associated with heterogeneity (p = .836 by meta-regression).

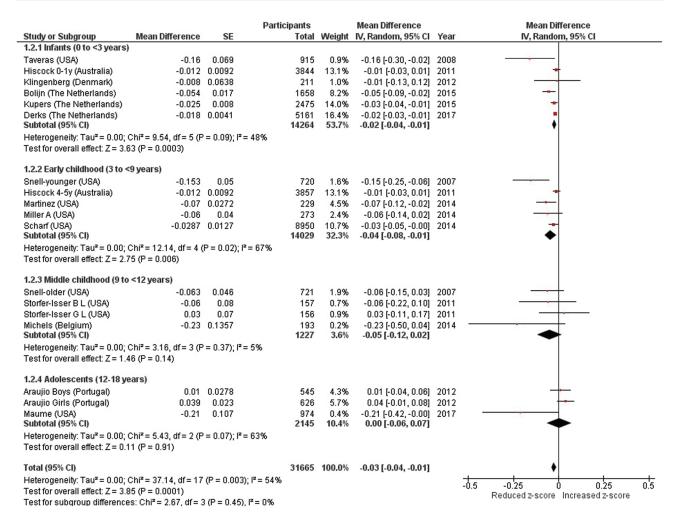


Figure 3. Change in BMI z-score per hour of increase in sleep by age group. Results are expressed as mean difference (95% confidence intervals).

Discussion

This study provides a comprehensive and systematic review of the literature and quantitative estimates of the longitudinal associations between short sleep and overweight or obesity, change in BMI z-scores, or change in BMI. For sleep and overweight or obesity, the pooled effect is strong. The association is supported by the significant relationships between hours of sleep and changes in both BMI z-scores and BMI. Subgroup analyses show that the effect of short sleep on risk of overweight or obesity was significant for each age group.

Strengths and limitations

The results are of interest for a number of reasons. Firstly, although our previous meta-analysis showed that obese children were more likely to be short sleepers [10], it only reported evidence from cross-sectional studies and could not rule out reverse causality [62]; these results extend those previous observations. Secondly, the association is consistent in different populations. Thirdly, they demonstrate that the effect on the risk of overweight or obesity appears to be consistent across all age groups. Although the meta-analysis detected significant heterogeneity between studies for both infants and early childhood,

this was reduced to zero by the removal of one study from each group. Furthermore, when we attempted to correct for publication bias by using the "trim and fill" method, the pooled estimate was only marginally reduced and maintained statistical significance. Finally, the categorical results were corroborated by the meta-analysis of regression coefficients from studies looking at both change in BMI z-score and change in BMI. These show that longer sleep duration in children is associated with a reduced age-related weight gain.

These results are important as studies suggest that there has been a worldwide decrease in night time sleep duration [63] and a study conducted in 2004 suggested that children got less sleep than was recommended at the time [64]. The National Sleep Foundation (NSF) in America recommends different sleep durations for different age groups. The recommendations, as stated on their website, are as follows: newborn (0–3 months), 14–17 hr; infant (4–11 months), 12–15 hr; toddler (1–2 years), 11–14 hor; preschool-age (3–5 years), 10–13 hr; school-age (6–13 years), 9–11 hr; and teenage (14–17 years), 8–10 hr [65]. However, whether "an hour" of sleep reduction or extension has the same effect on metabolic outcomes at different ages of development from infancy to adolescence is not known.

There are some limitations. The quality of the data cannot go beyond the quality of the individual studies included. However, the removal of studies with quality scores of <15 out of a maximum of 20 had no appreciable effect on the results. The results can only be representative of the studies that have been included and are unable to provide a representative inference of all studies published. There are limitations associated with the measurement of the variables of interest. The majority of the included studies have assessed sleep by means of selfreported (child or parental) questionnaires. Only one used the gold-standard polysomnography [36] and three used accelerometry [29, 45, 56]. Furthermore, in many of the studies, it is the parents who reported children's sleep duration, and although this is necessary for young children, it does require that the parent has a good level of awareness of their child's sleep schedule. As described in Methods, the diagnostic classification of overweight and obesity varied across studies. A meta-analysis of observational studies is open to important fallacies in that it cannot directly control for confounding and therefore may be open to biased estimates. Some papers adjusted for age and sex in BMI z-score models. The adjustment was unnecessary as both variables were used for BMI standardization (although continuous age might slightly improve the estimation). However, we are unable to derive estimates by excluding age and sex from the models. Although this is an inextricable problem, any overadjustment would result in an underestimation of the true effect, hence indicating that the relationship we describe might be conservative and even stronger, had overadjustment been avoided.

Potential mechanisms

This meta-analysis of prospective studies supports a causal relationship between short sleep and subsequent weight gain and obesity in children. There are several lines of evidence to suggest plausible mechanisms. Sleep deprivation is associated with various hormonal responses which may lead to appetite dysregulation, affecting both hunger and satiety. These include lower leptin and higher ghrelin levels [66, 67], which would increase appetite. Sleep restriction has effects on endocannabinoids which regulate a variety of central nervous system processes including appetite [68]. Changes in factors which would affect metabolism, including insulin and glucose metabolism, cortisol, growth hormone, and thyroid-stimulating hormone are also important [69–74]. Sleeping less would give more time to eat and to engage in other sedentary activities, as exemplified by children and adolescents who like to stay up late to play on their computer or watch TV or to interact with social networks whilst snacking [69]. More opportunities to eat energy dense foods and concomitant tiredness may lead us to less engagement in physical activity [69].

Activation of inflammatory pathways by short sleep may be implicated in the development of obesity [75] and it can up- and down-regulate the expression of genes involved in oxidative stress and metabolism [76]. Finally, insufficient sleep is associated with alterations in mood, attention, impulse control, motivation, and judgment, all of these factors could potentially influence eating behaviors, energy intake, and ultimately BMI in children [77].

Short-term, acute, laboratory, and cross-sectional observational studies indicate that adverse changes in sleep are associated with adverse changes in insulin and glucose response but can be reversed when sleep quantity and quality are restored [78]. The detrimental effects of sustained and prolonged chronic sleep, however, may not be reversible leading to long-term adverse health and safety consequences [79].

An fMRI study has shown that acute sleep deprivation enhances the brain's response to hedonic food stimuli [80]. Compared with sleep, total sleep deprivation was associated with an increased activation in the right anterior cingulate cortex in response to food images, which was independent of calorie content and prescan hunger ratings. These results suggest that sleep loss enhances hedonic stimulus processing in the brain underlying the drive to consume food [80].

Although the results of a clinical trial to assess the feasibility of increasing sleep duration to a healthy length (approximately 7½ hr in an adult population) and the effect of sleep extension on body weight are still awaited [81], studies in adults have shown that insufficient sleep can impair one's ability to lose fat mass-associated weight [82].

Implications

Sleep is not a passive state but is an active process in which memory consolidation, tissue restoration, metabolic, and haemostatic processes occur [83]. The findings from this study suggests that sleep may be an important and potentially modifiable risk factor (or marker) of future obesity and ensuing type 2 diabetes in early life. Our study highlights the need for a greater awareness of the importance of adequate sleep in children both for parents and for medical practitioners. Educational programs could be used to empower parents and children to improve sleep quality and maximize quantity.

Conclusion

Short sleep duration is a risk factor or marker of the development of obesity in infants, children, and adolescents.

Supplementary Material

Supplementary material is available at SLEEP online.

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Notes

Conflict of interest statement. None declared.

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