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

Running Title: Sleep and obesity in children and adolescents.

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ABSTRACT

Study Objective: 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 25th September 2017). Included studies were prospective, had follow-up ≥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 (7 Studies, 14 738 participants, RR: 1.40; 95% CI 1.19 to 1.65; p<0.001), early childhood (8 Studies, 31 104 participants, RR: 1.57; 1.40 to 1.76; p<0.001), middle childhood (3 studies, 3 005 participants, RR: 2.23; 2.18 to 2.27; p<0.001) and adolescence (3 studies, 26 652 participants, RR: 1.30; 1.11 to 1.53; p<0.002). Sleep duration was also associated with a significant change in BMI z-score (14 studies, 18 cohorts, 31 665 participants) (mean difference -0.03; -0.04 to -0.01 per h sleep; P=0.001) and in BMI (16 studies, 24 cohorts, 24 894 participants) (mean difference -0.03 kg/m^2; -0.04 to -0.01 for every h of increase in sleep; P=0.001).

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

Keywords:

Sleep deprivation; obesity; overweight; body mass index; meta-analysis; prospective; infants; 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 programmes should be developed to aid parents and children to improve sleep.

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 westernised 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, behavioural, patho-physiological 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 behavioural 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 haemostatic 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 have 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 (i) to systematically review published prospective population-based studies of the association between sleep duration and overweight or obesity in infants, children and adolescents, (ii) 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, (iii) 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 PubMed, Medline, Embase Web of Science and Cochrane Central Register of Controlled Trials (from 1966 to 25th Sept 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: (a) original published article, (b) study in infants, children or adolescents (c) observational prospective design, (d) assessment of duration of sleep quantity as baseline exposure, (e) follow-up of $\geq$ 1 year for incident outcomes, (f) one of the following outcomes: i) incident cases of overweight and/or obesity ii) prospective changes in BMI z-score or iii) changes in BMI.

Studies were excluded if (a) case-control design was used; (b) cross-sectional associations were reported, (c) only meeting abstract or unpublished material available or, (d) 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 was not readily available from published reports, we wrote to the authors to ask for raw data.

Data extraction

Three reviewers (MAM, MK & FPC) independently extracted the data. Differences about inclusion of studies were resolved by arbitration with the co-authors. From a total of 4,683 search records, 2,569 studies were identified after duplicates had been removed (**Figure 1**). Full text evaluation of 127 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 relative risks of overweight/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 h).[12] The definition of "short sleep" was defined by age as stated in **Table 1**. For odds ratios, 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 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/m^2 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 sub-groups 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 (12-18 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 where appropriate,. However, in some cases of papers using BMI z-score as outcome, age and 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 & Black Quality Index score system using a validated checklist for assessing the quality of the studies.[13] For the assessment of non-randomized 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 odds ratios (OR) or hazard ratios (HR) with 95% confidence intervals 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, where 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/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 I^2-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] where 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 meta-regression 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 non-randomised studies, with the appropriate exclusion of non-relevant items.[19]

Results

Characteristics of Study Cohorts

Of a total of 4,683 studies identified from the searches (**Figure 1**), after exclusion of ineligible studies (**Supp 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 75,499 participants from 9 different countries, for BMI 24,894 from 9 countries and for BMI z-score 31,665 from 8 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<0.001). There was significant heterogeneity between studies (I^2 = 92%, p<0.001) with evidence of publication bias (**Supp Figure S1a)** (Egger's test p=0.005). 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 sub-group 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<0.001, with no statistical evidence of heterogeneity (I^2 = 40%; p=0.13). Eight cohorts included children 3 to <9 years at baseline. The pooled relative risk was 1.57 [1.40, 1.76], P<0.001, with no statistical evidence of heterogeneity (I^2 = 23%; p=0.25). Three cohorts included children 9 to <12 years at baseline. The pooled relative risk was 2.23 [2.18, 2.27], P<0.001 with no evidence of heterogeneity (I^2 = 0%; p=0.41). Three

cohorts included children 12-18 years at baseline. The pooled relative risk was 1.30 [1.11, 1.53], P=0.002 with no evidence of heterogeneity (I^2 = 0%; p=0.49) (**Figure 2**).

Sub group analysis by continent in the combined age groups

Sub-group analysis by continent yields risk ratios ranging from 1.26 to 2.19 across the three sub-groups; each with statistically significant results. Heterogeneity estimates ranged from 0% to 92%, with no evidence of heterogeneity in the Australia and Oceania sub-group (**Supp Table S2**).

Sensitivity analysis

Sensitivity analysis by deleting one study at a time yields risk ratios that are still statistically significant for each sub-group (**Supp Table S3a**). The heterogeneity estimates range from 0% to 49%. 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 (see **Supp Table S3a**). Removal of two studies[27,39] with quality scores <15 has no major effect on the estimates (see **Supp Table S4**). Follow-up time was not significantly associated with heterogeneity (p=0.878 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 [-0.04, -0.01]; P=0.0001) (**Figure 3**). In the pooled analysis there was significant heterogeneity between studies ((I^2 = 54%, p< 0·003) (Eggers test p=0.054)) (**Supp Figure S1b**). In a sub-group analysis by age group, there was no overall statistical heterogeneity, yet whilst the risk estimates were statistically significant in infants and early childhood they were not statistically significant in middle childhood or adolescents. (p=0.45) (**Figure 3**). The 'trim and fill' method did not produce any correction to the original estimates.

Sensitivity analysis by deleting one study in the sub-groups at a time is shown in the online supplement. In middle childhood the heterogeneity was reduced to 0% 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] Supp **Table S3b**). The removal of two studies with quality scores <15 has no major effect on the results (**Table A4**). Follow-up time was not significantly associated with heterogeneity (p=0.837 by meta-regression).

Short sleep and BMI

Data on the relationship between sleep and change in BMI are shown in the online supplement (**Supp 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=0.001), with significant heterogeneity between studies (I^2 = 80%, P<0·001) and evidence of publication bias; Eggers test p 0.001) (**Supp Figure S1c**). The 'trim and fill' method did not produce any correction to the original estimates. In a sub-group analysis by age groups, there was some heterogeneity of effect (p=0.03) with the effect being greater in children aged 3 to <9 years (**Supp Figure S2**). Sensitivity analysis is shown in the online supplement. In middle childhood the heterogeneity was reduced to zero by the removal of Seegers et al[35] (**Supp Table S3c**). The removal of eight cohorts (5 studies)[27,42,51,57,58] with quality scores <15 has no major effect on the results (**Supp Table S4**). Follow-up time was not significantly associated with heterogeneity (p=0.836 by meta-regression).

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. Sub-group 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, whilst 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 hours; infant (4-11 months), 12-15 hours; toddler (1-2 years), 11-14 hours; preschool-age (3-5 years), 10-13 hours; school-age (6-13 years), 9-11 hours; and teenage (14-17 years), 8-10 hours.[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 <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 self-reported (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 whilst 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 the methods section, 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. Whilst 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 led 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 behaviours, 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 pre-scan hunger ratings. These results suggest that sleep loss enhances hedonic stimulus processing in the brain underlying the drive to consume food.[80]

Whilst the results of a clinical trial to assess the feasibility of increasing sleep duration to a healthy length (approximately 7½ h 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 programmes 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.

Abbreviations list.

CI Confidence intervals

BMI Body mass index

WHR Waist hip ratio

S.d. Standard deviation

RR Risk ratio

OR Odds ratios

HR Hazard ratios

NSF National Sleep Foundation

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Conflict statement:

None

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Figure Captions

Figure 1. PRISMA flow chart

(†Studies contribute to more than one meta-analysis).

Figure 2. Incidence of overweight or obesity in short sleeper by age group.

Results are expressed as risk ratio (95% Confidence Intervals).

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).

Table 1. Description of the 42 studies included in the meta-analyses for i) Overweight/obesity ii) BMI Z-score iii) BMI.

Author	Year Published	Country	Cohort	Quality Score	Recruit-ment year(s)	Age at baseline sleep measure-ment (s)	Duration of follow-up	Sleep exposure	Sleep exposure categories Short sleep (SS) Reference (RS)	Exposure Assessment	Outcome	Outcome assessment	Adjusted variables
Agras[27]	2004	USA	Recruited from well newborn nurseries in San Francisco (n=150)	12	Unreported	3 years	5.5 years	Sleep duration (average of sleep time at age 3 and 4, not reported if it includes naps)	SS: <=11.25hr RS: >11.25 Continuous (hours)	Parental report (unreported)	**Analysed as OW/OB:** OW: BMI > 85th percentile for age and sex. Ref: (charts unreported). **Analysed 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]	2005	UK	Avon longitudinal study (ALSPAC) (n= 5493)	17	1991-1992 (mothers)	2.5 years	4.5 years	Sleep duration (not reported if it includes naps**)**	SS: Lowest quarter; <10.5 (n=1831) RS: highest quarter; >12 hours	Parental report (questionnaire)	**Analysed 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]	2007	USA	National Institute of Child Health & Human Development Study in early Child Care & Youth Development (NICHD_SECCYD). (n=785)	17	1991	Mean age (SD): 9.02 (0.31) years	Average 2.6 years.	Total daily sleep duration (including naps)	SS: Lowest tertile Continuous (hours)	Maternal report (questionnaire)	**Analysed 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 education, child BMI z-score at 3rd grade, change in sleep duration between 3rd and 6th grade
Snell[44]	2007	USA	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	Nighttime sleep duration (weighted average of week and weekend)	Continuous (hours)	Mixed- child and parent reported sleep duration (time diary)	**Analysed for BMI Z-score:** Changes in BMI z-score standardised for age and sex at end of follow up Ref: CDC OW: age and gender specific 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]	2008	USA	Project Viva (n= 915)	18	1999-2002*[1]	0.5 years	2.5 years	Weighted average of sleep duration (weekend + week) from 6 months to 2 years (including naps)	SS: <12hr (n=329) RS: ≥12 hrs Continuous (hours)	Parental report (questionnaire)	**Analysed as OW/OB:** OW: BMI ≥ 95th percentile or greater for age and sex, **analysed as OB:** Ref: CDC **Analysed 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 history, breastfeeding duration, child's race/ethnicity, child's birth weight and 6-mo weight for length z score, daily television viewing, daily active play
Landhuis[28]	2008	New Zealand	Prospective birth cohort (n=1037)	16	1972-1973	5 years	27 years	Nighttime sleep duration (Average of sleep duration at 5, 7, 9 and 11 years)	SS: <11 hrs (n=301) Mod: 11-11.5 hrs (n=400) Long >11.5 (n= 311). Continuous (hours)	Parental report (bedtimes and rising times)	**Analysed as OW/OB:** OB: BMI ≥ 30 kg/m2. **Analysed 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, smoking, level of parental control and television watching, sleep time at age 32
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	Typical nighttime sleep duration on a school or work day	Continuous (hours)	Self-reported (questionnaire)	**Analysed 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]	2008	Canada	Quebec longitudinal study of child development (n=1138)	17	1997-1998	2.5 years	4.5 year	Nighttime sleep duration (on average) Based on sleep duration on age 2.5, 3.5, 4 and 5	SS: short persistent (<10) RS: 11-hour persistent	Maternal report (questionnaire)	**Analysed 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

*[1] 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

Bell[23]	2010	USA	Longitudinal analysis of Panel Survey of Income Dynamics (PSID Chid Development Supplements (CDS) (0-4years 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	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 weekend day)	**Analysed 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]	2011	USA	Tucson Children's assessment of Sleep Apnea Study (n=304)	17	1999-2003	6-12 years	4.7 years	Nighttime sleep duration	SS: <7.5 hours sleep per night Ref: ≥9 hours sleep per night	Polysomngraphy (PSG)	**Analysed 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, caffeine use, baseline values where appropriate
Storfer-Isser[47]	2011	USA	Longitudinal Cleveland Children's Sleep and Health Study (boys n=157) (girls n=156)	15	1998-2001	8-11 years	8 years	Sleep duration (weighted average of week and weekend days)	Continuous (hours)	parental report (questionnaire)	**Analysed 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]	2011	New Zealand	Birth cohort (n=244)	16	2001-2002	3 years	4 years	Sleep duration (average of week and weekend sleep, average over age 3, 4 and 5)	Continuous (hours)	Accelerometry & parental sleep logs of week and weekend days	**Analysed as OW/OB:** OW: ≥ 85th age and sex specific percentile Ref: CDC **Analysed 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]	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 (sd): 56.8 (2.6), 4.73 years	2 years	Sleep duration (average of one week and one weekend day), including daytime naps	Continuous (minutes), converted to hours	Parental report (time diary of a week and weekend day)	**Analysed 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]	2011	Germany	Dortmund Nutritional and Anthropometric Longitudinally Designed (DONALD) Study (n=481)	15	Ongoing since 1985	1.5 years	5.5 years	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 hrs at 1.5 and 2 years	Parental report (interview)	**Analysed 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]	2011	Canada	Quebec Longitudinal Study of Kindergarten Children (n=1916)	16	1986-1987	10 years	3 yers	Weekday sleep duration	SS: <10.5 hours trajectory RS: 11 hour sleepers trajectory Continuous (hours), not for sensitivity	Parent-reported (questionnaire of bed and wake times)	**Analysed as OW/OB:** OW and OB Ref: age and sex specific BMI curves IOTF . **Analysed 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]	2012	USA	Longitudinal IDEA study and ECHO study (boys n=320) (girls n=328)	16	IDEA: 2006-2007 ECHO: 2007-2008	14.7 years	2 years	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)	**Analysed For BMI:** Change in BMI kg/m2 over two years	Height and weight were measured by researchers	Race, grade, parent education, school lunch, puberty , study, screen time/sedentary behaviour, depression, activity and energy intake

Araújo[49]	2012	Portugal	Urban population based cohort (EPITeen) (boys n=545) (girls n=626)	18	2003-2004	13 years	4 years	Usual nighttime sleep duration	Continuous (hours)	Self-reported (from bed and wake up times)	**Analysed 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]	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	Average daily sleep duration (average of one week)	SS: ≤8.5h RS: ≥9.5h	Self-report (questionnaire)	**Analysed 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 BMI, maternal and paternal education, maternal job, family structure, energy intake, fat % of energy intake, meal skipping, snacking
Klingenberg[41]	2012	Denmark	SKOT cohort (n=211)	16	2006-2007	0.75 years (9 months)	2.25 years (2 years 3 mo)	Total sleep duration (nighttime sleep + daytime napping)	Continuous (hours)	Parental report (TSD-Q questionnaire)	**Analysed 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 level of both parents
Magee[30]	2013	Australia	Wave 2 and 3 of 4-5yr old cohort Longitudinal Study of Australian Children (n=1833)	17	2006	6-7 years	2 years	Weighted average of week and weekend Sleep duration (including napping)	SS: <10hrs 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)	**Analysed as OW/OB:** OB Ref: age and sex specific cut-offs from IOTF	Height and weight measured by researchers	Child gender, country of birth, household income, place of residence/remoteness

Mitchell[60]	2013	USA	Cohort of 4 suburban high schools in Philadelphia (n=1390)	15	Unreported	14 years	4 years	Typical nighttime sleep duration (weighted average of week and weekend night)	Continuous (hours)	Self-reported	**Analysed For BMI:** Changes in BMI from age 14 to 18	Self-reported	Gender, race, maternal education, MVPA and screen time
Suglia[37]	2014	USA	Add Health Longitudinal Study, Waves 2 and 3 (n8718)	16	1994-1995	Mean (SE): 16 (0.03) years	5 years	Usual nighttime sleep duration	SS <6 hrs RS >8hrs	Self-reported (questionnaire)	**Analysed as OW/OB:** OB: BMI ≥30kg/m^2	Height and weight measured by researchers and by self-report	Age, sex, race/ethnicity, parental education, further adjusted for watching tv more than 2 h per day and physical activity
Miller[46]	2014	USA	Participants in Headstart, low income families in midwest (n=273)	16	Unreported	mean (sd): 4.11 (0.54) years	1 year	Nightly sleep duration (average of week and weekend days)	Continuous (hours)	Parental report (interview)	**Analysed 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]	2014	Belgium	Belgium longitudinal Children's Body composition and Stress study (n=193)	15	2010	6-12 years at baseline	2 years	Nighttime sleep duration (weighted average of week and weekend days)	Continuous (hours)	Actigraphy and parental report (sleep diary)	**Analysed 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 education, physical activity and reported snacking frequency, reported sleep duration
Magee[55]	2014	Australia	Waves 1 to 3 of 4-5yr old cohort Longitudinal Study of Australian Children (n=2984)	18	2004	4 years	4 years	Sleep duration (including napping, weighted average of week and weekend sleep)	Continuous (hours)	Parental report (time use diary)	**Analysed 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]	2014	USA	STRONG Kids (n=247)	13	Unreported	2-3 years	1 year	Night-time sleep duration (Average over the past week)	Continuous (hours)	Mother's/parental report (questionnaire)	**Analysed 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/ethnicity, maternal employment Additional data from Author

Martinez[45]	2014	USA (Mexican descent)	Longitudinal cohort stud in Mexican-American children (n=229)	16	2007-2009	8-10 years	2 years	NIghttime sleep duration (Average from two weekdays and one weekend day)	Continuous (hours)	Accelerometry for three days	**Analysed for BMI Z-score**: Changes in age and gender specific BMI z-scores at end of follow up Ref: National Child Health Statistics growth charts Weight change from baseline to 24 month follow 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]	2014	USA	Early childhood Longitudinal Study-Birth Cohort (n=8950)	15	2001	4 years	1 year	Usual nighttime sleep duration	SS:<9.48 hrs RS: ≥ 9.48 hrs Continuous (hours)	Parental report (Computer assisted interview administered by assessors)	**Analysed as OW/OB:** OW ≥85-95th percentile for age and sex OB ≥ 95th percentile for age and sex Ref: CDC **Analysed for BMI Z-score**: Changes in age and gender specific BMI-z score over one year	Height and weight measured by researchers	Sex, race/ethnicity, SES, television viewing
Bonuck[32]	2015	UK	Avon Longitudinal study of parents and children (n=1899)	18	1991-1992	4.75 years	10.25 years	Weekday nighttime sleep duration	SS ≤10.5hrs RS >10.5 - <12.08 hrs	Parental report (typical weekday bed and wake times)	**Analysed 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]	2015	USA	Teen Health 2000 cohort (n=3134)	16	2000	11-17 years	1 year	Nighttime sleep duration (on average past 4 weeks)	SS: sleep restriction, sleeping 6hrs or less on weeknights and weekends RS: no sleep restriction,	Self-reported (interview)	**Analysed 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

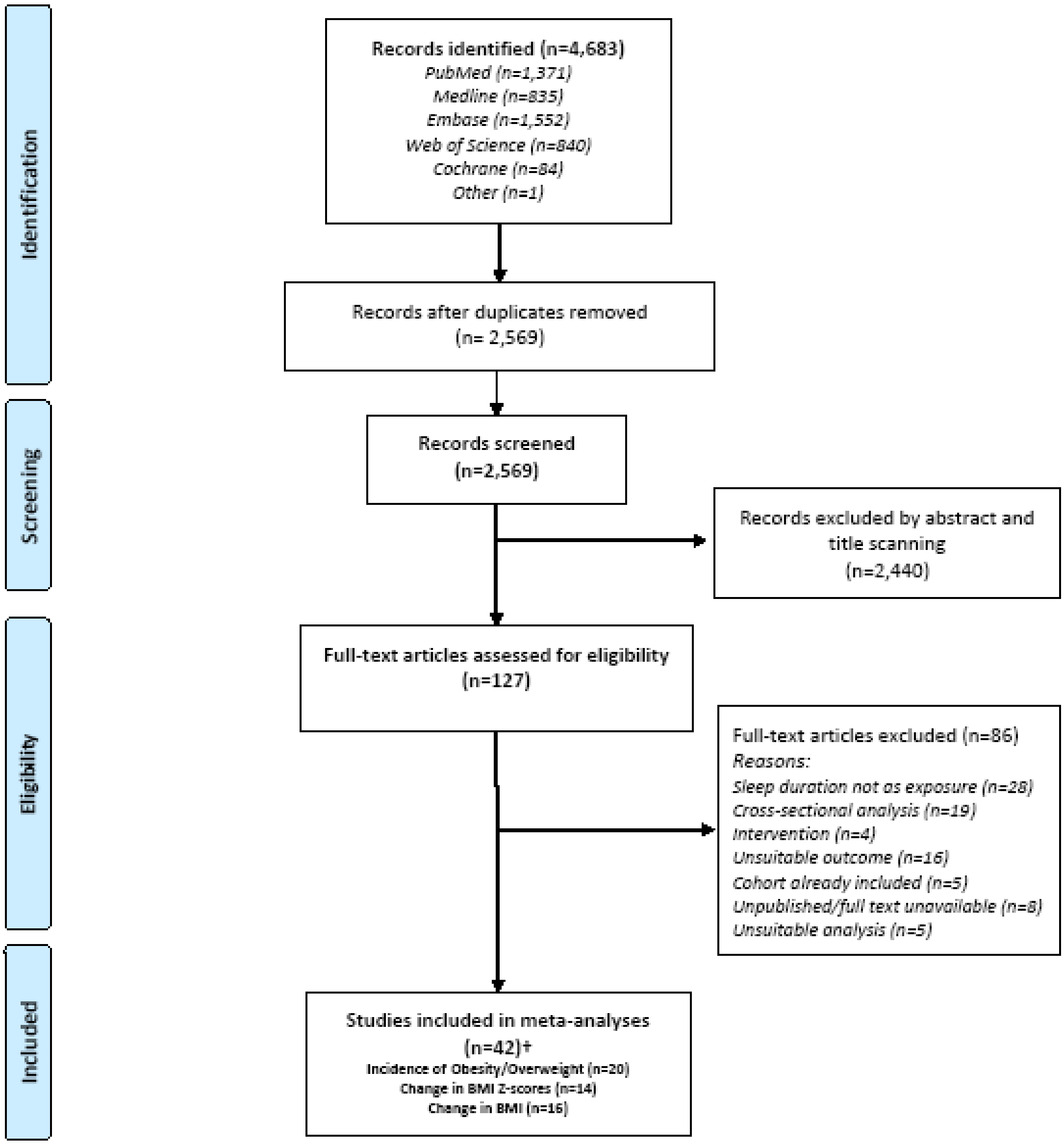
Bolijn[25]	2015	The Netherlands	KOALA study (n=1658)	16	2000*[2]	2 years	7 years	Night-time sleep duration	Continuous (hours)	Parental report (questionnaire)	**Analysed as OW/OB:** OW: > 85th percentile BMI z-score Ref: (charts not mentioned) **Analysed for BMI Z-score:** Changes in BMI Z-score at age 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 outside
de Souza[61]	2015	Portugal	Oporto Growth, Health and Performance Study, Longitudinal study of adolescents (boys n=3476) (girls n=3418)	18	Unreported	10, 12, 14 and 16 years at baseline (4 age cohorts)	3 years	Usual sleep duration (weekly average)	Continuous (hours)	Self-reported (questionnaire)	**Analysed For BMI:** Annual Change in BMI kg/m2	Height and weight measured by researchers	Peak height velocity, physical fitness components, total pa, sleep habits, fruit/vegetable intake
Krueger[39]	2015	USA	National Longitudinal Study of Adolescent to Adult Health (n=14800)	14	1994-95	Mean: 15.9 years	Max 15 years	Usual nighttime sleep duration (weighted average of week and weekend days)	SS: <7 hours in all 4 waves RS: <7 hours in none of the waves	Self-reported (questionnaire)	**Analysed as OW/OB:** OB: kg/m2 ≥30	Measured weights and heights	Age, sex, race/ethnicity, excluded obese in wave 1
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)	Total daily sleep duration on average (sum of nighttime sleep and daytime sleep)	Continuous (hours)	Parental report (Brief Infant Sleep Questionnaire)	**Analysed For BMI:** Changes in BMI kg/m2 over 21 monts	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 24 months

*[2] 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

Küpers[42]	2015	The Netherlands	GECKO Drenthe Birth Cohort (n=2475)	14	2006-2007	0.33 years (4 months)	1.67 years (20 months)	Total sleep duration (including naps)	Continuous (hours)	Parental report (questionnaire)	**Analysed For BMI:** Changes in BMI kg/m2 from 6 to 24 months. **Analysed 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	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
Ames[57]	2016	Canada	Victoria Healthy Youth Survey (V-HYS) (n=662)	13	2003	Mean (SD): 15.5 (1.9) years	11 years	Nighttime sleep duration (on average)	Continuous (hours)	Self-report (interview)	**Analysed For BMI:** Changes in BMI kg/m2 over 11 year period	Height and weight measured by researchers	Physical activity, internalising symptoms, age group (12-15 or 16-18)
Butte[56]	2016	USA	Pre-school age cohort (n=111)	17	2010-2012	Mean (SD): 4.6 (0.9) years	1 year	Total sleep duration (Nighttime sleep and nap time)	Continuous (min/day), converted to per hour	Accelerometry for seven consecutive days	**Analysed For BMI:** Annual Changes in BMI kg/m2 Annual Weight gain (kg)	Height and weight measured by researchers	Age, sex, race/ethnicity, daycare hours, household size, household income, mother's age, BMI and education
Halal[26]	2016	Brazil	2004 Pelotas Birth Cohort (N=4231)	16	2004	1 year	3 years	Usual nighttime sleep duration	SS: <10 hrs in at least one of the follow up visits (at age 1,2,3,4) RS: ≥ 10 hrs in each of the follow up visits.	Annual parental report (interview)	**Analysed 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 colour and schooling, sleep characteristics measured at 1 y of age (sleep latency, number of night awakenings, duration of daytime naps)
Baird[53]	2016	UK	Children of the women	15	1998-2002 (of	3 years	1 year	Usual nighttime	Continuous (hours)	Maternal report (interview)	**Analysed For BMI:** Changes in BMI at	Height and weight	Age at DXA measurement, gestational age at birth, sex,

			included in the Southampton Women's Survey (SWS) (n=587)		mothers)			sleep duration			end of follow up	measured by researchers	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]	2016	China	Jiaxing Birth Cohort (n=16,028)	16	1999-2009	3 years	2 years	Average sleep duration during a 'typical' week.	Categorised $\leq$10h, 11-12h and $\geq$ 13 h	Parental report (questionnaire)	**Analysed 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]	2017	Netherlands	Embedded in Generation R (n=5,161)	14	2002-2006	2-6 months	5-6 years	Usual bedtimes and wake times, Daytime sleep (naps) assessed.	Continuous (hours)	Parental report (questionnaire)	**Analysed for BMI Z-score:** BMI (kg/m^2) 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]	2017	US	Study of Early Child Care and Youth Development (SECCYD) (n=974)	15	1991	12 years	3 years	Usual bedtimes and arise times (week days)	Continuous (hours)	Self-reported (questionnaire)	**Analysed for BMI Z-score:** Standardised to percentile scores.	Height and weight measured by trained staff.	

Figure 1.



Identification
Screening
Eligibility
Included
Records identified (n=4,683)
PubMed (n=1,371)
Medline (n=835)
Embase (n=1,552)
Web of Science (n=840)
Cochrane (n=84)
Other (n=1)
Records after duplicates removed
(n= 2,569)
Records screened
(n=2,569)
Records excluded by abstract and title scanning
(n=2,440)
Full-text articles assessed for eligibility
(n=127)
Full-text articles excluded (n=86)
Reasons:
Sleep duration not as exposure (n=28)
Cross-sectional analysis (n=19)
Intervention (n=4)
Unsuitable outcome (n=16)
Cohort already included (n=5)
Unpublished/full text unavailable (n=8)
Unsuitable analysis (n=5)
Studies included in meta-analyses
(n=42)†
Incidence of Obesity/Overweight (n=20)
Change in BMI Z-scores (n=14)
Change in BMI (n=16)

Figure 2.

Study or Subgroup	log[Risk Ratio]	SE	Participants Total	Weight	Risk Ratio IV, Random, 95% CI	Year
1.1.1 Infants (0 to <3 years)						
Reilly (UK)	0.3716	0.1381	5493	6.0%	1.45 [1.11, 1.90]	2005
Taveras (USA)	0.7129	0.3306	915	3.2%	2.04 [1.07, 3.90]	2008
Touchette (Canada)	1.0647	0.5459	1138	1.6%	2.90 [0.99, 8.45]	2008
Bell 0-4y (USA)	0.5878	0.2248	822	4.6%	1.80 [1.16, 2.80]	2010
Diethelm (Germany)	0.4055	0.3196	481	3.3%	1.50 [0.80, 2.81]	2011
Bolijn (The Netherlands)	0.1508	0.0631	1658	6.9%	1.16 [1.03, 1.32]	2015
Halal (Brazil)	0.2776	0.1278	4231	6.1%	1.32 [1.03, 1.70]	2016
Subtotal (95% CI)			**14738**	**31.8%**	**1.40 [1.19, 1.65]**	
Heterogeneity: Tau² = 0.02; Chi² = 9.97, df = 6 (P = 0.13); I² = 40%						
Test for overall effect: Z = 3.97 (P < 0.0001)						
1.1.2 Early childhood (3 to <9 years)						
Agras (USA)	0.6539	0.3092	150	3.5%	1.92 [1.05, 3.53]	2004
Landhuis (New Zealand)	0.4308	0.2075	1037	4.9%	1.54 [1.02, 2.31]	2008
Bell 5-13y (USA)	0.1823	0.1934	983	5.1%	1.20 [0.82, 1.75]	2010
Carter (New Zealand)	0.4943	0.0376	224	7.1%	1.64 [1.52, 1.76]	2011
Magee (Australia)	0.3853	0.1853	1833	5.2%	1.47 [1.02, 2.11]	2013
Scharf (USA)	0.1133	0.1768	8950	5.3%	1.12 [0.79, 1.58]	2014
Bonuck (UK)	0.7129	0.2052	1899	4.9%	2.04 [1.36, 3.05]	2015
Wang (China)	0.571	0.1575	16028	5.6%	1.77 [1.30, 2.41]	2016
Subtotal (95% CI)			**31104**	**41.6%**	**1.57 [1.40, 1.76]**	
Heterogeneity: Tau² = 0.01; Chi² = 9.06, df = 7 (P = 0.25); I² = 23%						
Test for overall effect: Z = 7.61 (P < 0.00001)						
1.1.3 Middle childhood (9 to <12 years)						
Lumeng (USA)	0.5108	0.2581	785	4.1%	1.67 [1.00, 2.76]	2007
Silva (USA)	1.1939	0.5566	304	1.6%	3.30 [1.11, 9.82]	2011
Seegers (Canada)	0.802	0.0103	1916	7.3%	2.23 [2.19, 2.28]	2011
Subtotal (95% CI)			**3005**	**12.9%**	**2.23 [2.18, 2.27]**	
Heterogeneity: Tau² = 0.00; Chi² = 1.77, df = 2 (P = 0.41); I² = 0%						
Test for overall effect: Z = 77.91 (P < 0.00001)						
1.1.4 Adolescents (12-18 years)						
Suglia (USA)	0.2231	0.0902	8718	6.6%	1.25 [1.05, 1.49]	2014
Krueger (USA)	0.3989	0.2565	14800	4.1%	1.49 [0.90, 2.46]	2015
Roberts (USA)	0.6152	0.3599	3134	2.9%	1.85 [0.91, 3.75]	2015
Subtotal (95% CI)			**26652**	**13.7%**	**1.30 [1.11, 1.53]**	
Heterogeneity: Tau² = 0.00; Chi² = 1.43, df = 2 (P = 0.49); I² = 0%						
Test for overall effect: Z = 3.17 (P = 0.002)						
Total (95% CI)			**75499**	**100.0%**	**1.58 [1.35, 1.85]**	
Heterogeneity: Tau² = 0.09; Chi² = 251.89, df = 20 (P < 0.00001); I² = 92%						
Test for overall effect: Z = 5.78 (P < 0.00001)						
Test for subgroup differences: Chi² = 102.24, df = 3 (P < 0.00001), I² = 97.1%						

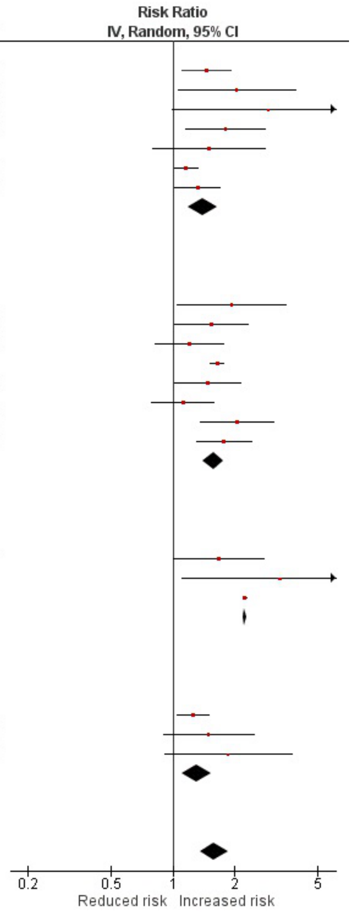


Figure 3.

Study or Subgroup	Mean Difference	SE	Participants Total	Weight	Mean Difference IV, Random, 95% CI	Year
1.2.1 Infants (0 to <3 years)						
Taveras (USA)	-0.16	0.069	915	0.9%	-0.16 [-0.30, -0.02]	2008
Hiscock 0-1y (Australia)	-0.012	0.0092	3844	13.1%	-0.01 [-0.03, 0.01]	2011
Klingenberg (Denmark)	-0.008	0.0638	211	1.0%	-0.01 [-0.13, 0.12]	2012
Bolijn (The Netherlands)	-0.054	0.017	1658	8.2%	-0.05 [-0.09, -0.02]	2015
Kupers (The Netherlands)	-0.025	0.008	2475	14.0%	-0.03 [-0.04, -0.01]	2015
Derks (The Netherlands)	-0.018	0.0041	5161	16.4%	-0.02 [-0.03, -0.01]	2017
Subtotal (95% CI)			**14264**	**53.7%**	**-0.02 [-0.04, -0.01]**	
Heterogeneity: Tau² = 0.00; Chi² = 9.54, df = 5 (P = 0.09); I² = 48%						
Test for overall effect: Z = 3.63 (P = 0.0003)						
1.2.2 Early childhood (3 to <9 years)						
Snell-younger (USA)	-0.153	0.05	720	1.6%	-0.15 [-0.25, -0.06]	2007
Hiscock 4-5y (Australia)	-0.012	0.0092	3857	13.1%	-0.01 [-0.03, 0.01]	2011
Martinez (USA)	-0.07	0.0272	229	4.5%	-0.07 [-0.12, -0.02]	2014
Miller A (USA)	-0.06	0.04	273	2.4%	-0.06 [-0.14, 0.02]	2014
Scharf (USA)	-0.0287	0.0127	8950	10.7%	-0.03 [-0.05, -0.00]	2014
Subtotal (95% CI)			**14029**	**32.3%**	**-0.04 [-0.08, -0.01]**	
Heterogeneity: Tau² = 0.00; Chi² = 12.14, df = 4 (P = 0.02); I² = 67%						
Test for overall effect: Z = 2.75 (P = 0.006)						
1.2.3 Middle childhood (9 to <12 years)						
Snell-older (USA)	-0.063	0.046	721	1.9%	-0.06 [-0.15, 0.03]	2007
Storfer-Isser B L (USA)	-0.06	0.08	157	0.7%	-0.06 [-0.22, 0.10]	2011
Storfer-Isser G L (USA)	0.03	0.07	156	0.9%	0.03 [-0.11, 0.17]	2011
Michels (Belgium)	-0.23	0.1357	193	0.2%	-0.23 [-0.50, 0.04]	2014
Subtotal (95% CI)			**1227**	**3.6%**	**-0.05 [-0.12, 0.02]**	
Heterogeneity: Tau² = 0.00; Chi² = 3.16, df = 3 (P = 0.37); I² = 5%						
Test for overall effect: Z = 1.46 (P = 0.14)						
1.2.4 Adolescents (12-18 years)						
Araujio Boys (Portugal)	0.01	0.0278	545	4.3%	0.01 [-0.04, 0.06]	2012
Araujio Girls (Portugal)	0.039	0.023	626	5.7%	0.04 [-0.01, 0.08]	2012
Maume (USA)	-0.21	0.107	974	0.4%	-0.21 [-0.42, -0.00]	2017
Subtotal (95% CI)			**2145**	**10.4%**	**0.00 [-0.06, 0.07]**	
Heterogeneity: Tau² = 0.00; Chi² = 5.43, df = 2 (P = 0.07); I² = 63%						
Test for overall effect: Z = 0.11 (P = 0.91)						
Total (95% CI)			**31665**	**100.0%**	**-0.03 [-0.04, -0.01]**	
Heterogeneity: Tau² = 0.00; Chi² = 37.14, df = 17 (P = 0.003); I² = 54%						
Test for overall effect: Z = 3.85 (P = 0.0001)						
Test for subgroup differences: Chi² = 2.67, df = 3 (P = 0.45), I² = 0%