Fatima, Y., Doi, S.A.R., and Mamun, A.A. (2016) *Sleep quality and obesity in young subjects: a meta-analysis.* Obesity Reviews, 17. pp. 1154-1166

http://dx.doi.org/10.1111/obr.12444

Abstract

Objectives: To assess the impact of poor sleep quality on Overweight/Obesity (Ow/Ob) in young subjects, and explore if this association is independent of sleep duration.

Methods: Pubmed, EMBASE, and MEDLINE databases were searched for papers on sleep quality and overweight/obesity, focusing on children, adolescents, and young adults. Studies based on subjects with medical/psychological problems or published in languages other than English were excluded. Quality effects model was used to pool studies with regression coefficient (β) or odds ratio (OR) for meta-analysis.

Results: Findings from the systematic review suggest a link between poor sleep quality and Ow/Ob in young subjects. Pooled estimate (from 26,553 subjects) suggest a role of inadequate sleep (including both short duration and poor quality) in Ow/Ob (OR: 1.27 95% CI: 1.05-1.53). Sub-group-analyses suggest considerably higher odds of Ow/Ob (OR=1.46, 95% CI: 1.24-1.72) in young subjects with poor sleep quality (independent of duration).

Conclusions: Poor sleep quality seems to have an impact on Ow/Ob, and some studies indicate this association to be independent of duration. Therefore, considering only sleep duration might not help in disentangling sleep-obesity association. However, this review is mostly composed of cross-sectional studies. Therefore, causal link and stability of sleep quality and Ow/Ob association could not be established.

Keywords: adolescents; children; inadequate sleep; obesity; overweight; sleep quality; young adults

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Introduction

Results from numerous epidemiological and experimental studies have established the role of inadequate sleep in Ow/Ob outcome (302, 303). However, sleep inadequacy has been defined inconsistently across these studies. Overall satisfaction with sleep experience requires both an optimal duration and a good quality of sleep (341). Therefore, inadequate sleep can broadly be defined as either sleep of insufficient quantity, i.e., short duration, or of poor quality or both. Intriguingly, the majority of the existing epidemiological literature on sleep-Ow/Ob association has used short duration as the benchmark for sleep inadequacy and does not provide as much information on the role of sleep quality in Ow/Ob outcome.

The lack of epidemiological evidence on sleep quality-obesity association can be partly attributed to the notion, strengthened by some experimental studies, that suppression of slow-wave sleep (SWS), a marker of sleep quality, has implications for daytime sleepiness and cognitive performance, but not much for glucose kinetics per se (342). Moreover, epidemiological inferences on sleep quality and glucose metabolism are often obscured by confounding factors and provide limited insight into pathophysiologic mechanisms (343). Nonetheless, some clinical and epidemiological studies provide evidence that poor sleep characterized by sleep fragmentation are associated with altered glucose metabolism, independent of sleep duration (344, 345). Another clinical study demonstrated poor sleep has cardiovascular repercussions for young adults where selective suppression of SWS, without changing sleep duration, resulted in decreased insulin sensitivity without an adequate compensatory increase in insulin release(346). Therefore, it seems that not only sleep deprivation, i.e., short sleep duration but sleep fragmentation, i.e., sleep quality also plays important roles in the biochemical pathways related glucose metabolism. Hence, a broader approach considering both quality and quantity aspects is essential when attempting to investigate the sleep-obesity relationship.

For young subjects, where extensive use of electronic media devices, academic and professional demands, and lifestyle changes is reported to make them more vulnerable for both shortened sleep duration and poor sleep quality(347), soliciting information on both sleep duration and quality is even more desirable for decoding sleep-obesity association.

It seems that a critical evaluation of all epidemiological evidence on the role of sleep quality in Ow/Ob will support future studies by providing an explicit understanding of the current evidence

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base and the gaps in existing literature. However, unlike sleep duration where some studies have critically evaluated the available evidence(18, 348, 349), there is a lack of studies assessing the evidence for sleep quality and Ow/Ob association. Therefore, the aim of this study is to review the existing evidence for the association between sleep quality and Ow/Ob in young subjects critically and see if this association, if present, is independent of sleep duration.

Methods

Literature search

A systematic search using the keywords: sleep problems, sleep disturbances, sleep quality, sleep efficiency, and sleep latency was conducted to identify articles available on Pubmed, EMBASE, and MEDLINE databases (Appendix-E). A detailed search algorithm for PubMed is given in the supplementary material. All English language articles, focusing on children, adolescents, and young adults, published until November 2015 were included. Along with this, reference lists of relevant articles were checked for any missing study.

Inclusion/exclusion criteria

Original research studies with sleep issues, i.e., sleep problems, sleep disturbances, poor quality, poor efficiency, or longer latency as the exposure were included. Inclusion was restricted to children, adolescents or young adults as subjects, and continuous or a categorical body mass index (BMI) as the outcome. Conference abstracts were included if the study was a part of a bigger study and methodological features of the study could be retrieved.

Studies were excluded if they were published in languages other than English, were based solely on overweight or obese subjects, or subjects with medical/psychological problems. Additionally, studies focusing solely on sleep duration and case reports, letters to the editor were also excluded.

Data extraction and reporting

Two reviewers extracted relevant information from each study, e.g. subject characteristics, study design, exposure and outcome assessment, covariates and results (YF, AM) and a dataset was created. The study was conducted in accordance with the Meta-analysis of Observational Studies in Epidemiology (MOOSE) statement for reporting systematic reviews and meta-analysis (350).

Quality assessment

The quality of the studies included in the systematic review was assessed through a quality assessment tool derived from the guidelines of Methodological Evaluation of Observational Research (MEVORECH)-Observational Studies of Risk Factors of Chronic Diseases and the quality assessment tool for observational cohort and cross-sectional studies developed by National Institutes of Health (NIH) (309, 351). The validity of this instrument is comparable to other available tools, as attention is given to biases related to design, selection, information, confounding, and analysis. All studies were individually scored for safeguards against potential bias in their protocols. These points were then summed into a score that had a possible maximum of 17 points (Appendix-F). While an attempt has been made to consider important safeguards in the five areas mentioned above, the choice is indeed indicative only, and, of course, superior to no assessment at all. Thus, a study with a maximum score will not be devoid of bias, but will have the highest rank (in quality) amongst the list of studies. Disagreements regarding quality items were discussed and resolved through consensus.

Classification of Inadequate sleep

There was considerable variation across the studies in defining inadequate sleep. Review of the approaches used in all studies to defining inadequate sleep suggested that a broad classification can be applied. In this review, the following approach was utilized to categorize inadequate sleep.

1. Inadequate sleep predominantly measured as insufficient duration, e.g., short duration of sleep.
2. Inadequate sleep predominantly measured as poor quality irrespective of sleep duration. These include problems associated with sleep initiation (e.g., higher latency) and maintenance (e.g., sleep disturbances, recurrent awakenings, poor efficiency)
3. Inadequate sleep as an overall measurement of sleep including both duration and quality, e.g., using the Pittsburgh Sleep Quality Index (PSQI).

Since inadequate sleep due to insufficient duration has already been explored in some systematic reviews and meta-analysis (18, 348), studies focusing solely on sleep duration were not included in this review.

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Statistical analysis

Studies were included in the meta-analysis if the exposure variable was: inadequate sleep due to poor quality or inadequate sleep due to both short duration and poor quality. The outcome variable was BMI category, and the reported measure of association was either the regression coefficient (β) or the odds ratio (OR). Results from the studies with continuous BMI results were not pooled, as the outcome variable was not measured in a similar fashion across the studies, e.g., some studies reported raw BMI, whereas others reported BMI z-scores. To adjust for bias pooled estimates were calculated using the quality effects (QE) model (314, 352). Heterogeneity was determined to be present when the value of τ^2 was greater than zero, or if the Q-statistic was significant at a $P < 0.10$. (315). The robustness of meta-analyses was explored by conducting sensitivity analyses. All analyses were done using MetaXL version 3.0 (352).

Results

Study characteristics

A total of 18 studies discussed the association between sleep quality and BMI in children, adolescents, and young adults (Table 14) (23, 82, 103, 187, 197, 353-365). Among these, three were longitudinal studies (23, 103, 354), one was case-control (362), and remaining were cross-sectional. The majority of studies were conducted in the USA (n=6), followed by Canada (n=3), the UK(n=2), and the remaining were each from Brazil, Portugal, Norway, Taiwan, KSA, Belgium, and Malaysia. The study participants ages ranged from <2 years to 34 years, and they came from diverse socioeconomic and ethnic backgrounds. Most of the studies explored the impact only of the quality of sleep (23, 82, 103, 187, 197, 353, 355, 356, 358-360, 364, 365) while the remaining examined the combined effects of both quantity and quality of sleep on Ow/Ob outcome (361-363). Though most of the studies used validated questionnaires to explore sleep quality, some relied on parent or self-reports (103, 197, 360). The objective methods for sleep assessment were rarely used, with just three studies reporting the use of actigraphy (354, 356, 365).

For assessing the Ow/Ob outcome, BMI was mostly computed from height and weight, measured by trained persons, except four studies, where self-reported height and weight was used (355, 358, 361, 363). Some of the studies also used additional adiposity indicators, e.g., neck circumference, waist to hip ratio and body fat (82, 197, 353, 354, 362). The commonly

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controlled confounders were socio-demographic attributes, media hours, and extent of physical activity.

Study Quality

Each study included in the systematic review was evaluated for relative (to the scale) risk of bias (Appendix-F). The lowest scoring study had 12 points deducted while the highest scoring study had no points deducted resulting in a score of 17. There were ten studies comprising the middle two quartiles (scores 9 – 11) (187, 353, 355-358, 361, 363-365), two studies in the lowermost quartile (scores 5 – 7) (197, 360) and six studies in the uppermost quartile (scores 12 – 17) (23, 82, 103, 354, 359, 362).

Of the deficits in bias safeguards, the most common was a lack of clarity about eligibility criteria, but a few studies (23, 82, 103, 357-359, 361) did provide this information. Other deficits included not adjusting for the role of potential confounders (197, 360) However; all longitudinal studies accounted for missing data and compared the sample with complete data with the sample without complete data.

Systematic Review Findings

Inadequate sleep due to poor sleep quality was assessed in individual studies as perceptions about sleep quality (360), sleep disturbances (23, 82, 103, 187, 197, 355, 358, 359) and sleep efficiency and latency (353, 354, 356, 364, 365). There was some discrepancy in the results depending upon the criteria used to define sleep quality.

Studies based on validated questionnaires reported a significant association between inadequate sleep and Ow/Ob (82, 359). However, studies that used non-validated tools, or separately explored the effect of problems with sleep initiation, maintenance, or efficiency produced inconsistent results (187, 354, 355). Alamian et al. raised a similar issue., suggesting that the reported outcome for sleep problems and overweight association varied depending upon the criteria used to define sleep problems (103).

Some studies exploring poor sleep due to sleep efficiency issues found a significant impact on Ow/Ob, though one of the studies concluded that the effect was moderated by familial risk factors (353, 356). Likewise, sleep latency was also found to be negatively associated with BMI z-scores in a group of adolescents (364). Since the majority of the studies were cross-sectional in nature not much is known about the causal association between sleep quality and Ow/Ob. Only two longitudinal studies explored sleep quality and Ow/Ob link and found no significant relationship (23, 354).

Inadequate sleep measured through a combination of quality and quantity was reported in a few studies, using either the PSQI or Children's Sleep Habits Questionnaire (CSHQ) (361-363). Where two of the studies reported higher odds of Ow/Ob in subjects with inadequate sleep (361, 362) but one of the cross-sectional studies did not find any significant association (OR=1.11, 95%CI: 0.74-1.65)(363).

Gender difference in inadequate sleep and impact on obesity was explored in only one study where a strong U-shaped association was seen between sleep quality and BMI for girls, whereas the relationships seemed linear for boys (358). The studies included in this reviewed varied regarding adjusting for potential confounders, e.g., diet, physical activity, however, the majority of the studies that adjusted for these variables found that the association between sleep quality and Ow/Ob was robust to adjustment for these variables (187, 359, 362, 364).

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Table 1: Summary of observational studies assessing the association between inadequate sleep and BMI score/category in young subjects

(References: (23, 82, 103, 187, 197, 353-365)

Author (year)	Country	Study design	Data source	Sample size	Age group	Sleep variable	Outcome variable	Covariates	Results β(SE)/OR(95%CI)
Lumeng at al (2007)	USA	Longitudinal (FU after 3 years)	National Institute of Child Health and Human Development Study of Early Child Care and Youth Development	785	9.02 (±0.31 years)	Short sleep duration, sleep problems (based on Children's Sleep Habits Questionnaire)	BMI, overweight (using CDC reference)	Gender, maternal education, race	Sleep duration, not sleep problems, is a significant predictor of overweight later in life Overweight Long sleep duration: OR= 0.60 (95%CI: 0.36–0.99) Sleep Problems: OR= 1.59 (95%CI:0.71–3.59)
Bawazeer et al. (2009)	KSA	Cross sectional	Riyadh Childhood Obesity Study	5,877	10-19 years	Parent reported sleep duration and sleep disturbances	BMI, waist and hip ratio, overweight/ obesity (using CDC reference)	NI	Short sleep duration and intermittent sleep are associated with significantly higher prevalence of overweight and obesity Overweight/obesity Intermittent sleep :7.9%-24.6% Continuous sleep: 6.5%-23.6% (p=0.024)

Mota et al. (2010)	Portugal	Cross sectional	Middle and high school students	1,726	10-18 years	Self-reported Quality of sleeping time (QST)	Body mass index (BMI), obese (IOTF reference)	Cardiorespiratory fitness	Sleep quality is not associated with obesity OR: 1.19 (95%CI:0.134–1.67)
Liu et al (2011)	Canada	Cross sectional	Physical Health Activity Study Team	2,200	8-9 years	Sleep duration and sleep difficulties using a short Sleep Behaviour Questionnaire (SBQ)	Overweight/ Obesity (using IOTF reference)	Age, gender, total physical activity, and total calories intake maternal education, sleep duration	Even after adjusting for sleep duration, sleep problems are significantly associated with higher odds of overweight and obesity Overweight/ Obesity in subjects reporting waking up at night, snoring and restless sleep OR: 3.53 (95%CI:1.87-6.66)
Narang et al. (2012)	Canada	Cross sectional	Healthy Heart Schools' Program	4,104	14.6 (± 0.5) years	Sleep disturbance using the sleep disturbance score derived from the Pittsburgh Sleep Quality Index (PSQI), Sleep duration	Cardiovascular risk (CVR) factor (based on non–HDL cholesterol > 3.10 mmol/L, BMI > 85th percentile or BP > 90th percentile)	Sleep duration, screen time, CV in first degree relative, gender, caffeine, snack, screen hour, exercise soft drink	Even after adjusting for sleep duration, sleep disturbances are significantly associated with CVR. Short sleep duration is not significantly associated with CVR CVR Sleep disturbances OR:1.43 (95% CI: 1.16–1.77) Sleep duration: OR:1.03 (95% CI: 0.81–1.30)
Arora et al. (2013)	UK	Cross sectional	Six randomly selected schools across the Midlands region of the UK	1,043	11-18 years	Sleep duration, sleep onset latency (SOL), night-time awakening (assessed using School Sleep Habits Survey)	BMI *z*-score	Age, sex, and ethnicity; quantity of weekday technology, activity, school, snacking, depression, potential OSA, bedroom sharing, chronotype,	Negative linear relationship was observed between weekday sleep duration weekday SOL (min) and BMI *z*-score, but not night time awakenings Sleep duration β =--0.24 (p<0.001)

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								academic performance	SOL β =- -0.01 (p<0.001)
Bagley et al (2013)	USA	Cross sectional	Auburn University Sleep Study	228	10.41 (±0.67) years	Sleep duration (actigraphy), sleep efficiency	BMI-z score	Sex, pubertal status, race, asthma	Sleep duration and sleep efficiency are significantly associated with BMI Sleep efficiency β= -0.02, p<.0.01 Sleep duration β= -0.01, p<.0.001
Chen et al. (2013)	Taiwan	Cross sectional	Social Development Trend Survey	2,113	15-17 years	Difficulty in initiating and maintaining sleep, non-restorative sleep assessed by insomnia Self-assessment Inventory	BMI	Household income, parent/guardian level of education, disability status, work night shift, and smoking, age, sex, regular exercise, smoking, employment, and feeling secure in the neighbourhood	Difficulty initiating sleep is associated with BMI Linear regression: 0.76* (P<0.05)
Jarrin et al. (2013)	Canada	Cross sectional	Healthy Heart Project	240	12.6 (±1.98) years	Self-reported sleep duration, quality, pattern (based on self-reported bed- and wake time during school and weekends) and sleep disturbances	BMI, waist and hip circumference Hip circumference, Percent body fat	Age, sex, pubertal status, physical activity, screen time and socioeconomic status	Even after adjusting for sleep duration, sleep pattern, sleep disturbances, and sleep quality are associated with adiposity and body composition measures. Impact of sleep duration became non-significant in adjusted models

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						(assessed using Children's Sleep Habits Questionnaire)			Sleep disturbances: β= 0.12, p<0.09 Weekend delay: : β= 0.14, p<0.05 Poor sleep quality: : β= -0.15,p<0.05
Vasconcelos et al. (2013)	Brazil	Cross sectional	Survey of college students	702	21.5 (±4.5) Years	Sleep quality (assessed by Pittsburgh Sleep Quality Index)	BMI, neck circumference (NC), abdominal circumference (AC)	NI	Anthropometric measurement doesn't have statistically significant correlation with PSQI scores Correlation between AC and poor sleep quality ρ=-.033; p=.382 Correlation between NC and poor sleep quality ρ=-.070; p=.070
Alamian (2014)	USA	Longitudinal	NICH study of Early Child Care and Youth Development	895	Infants (age <24 months)	Sleep problems assessed by three different definitions	Overweight/obese (CDC reference)	Birth weight, race, sex, breastfeeding, maternal poverty, family structure, maternal education	Sleep problems in infancy lead to overweight in grade 6th, though, associations varied according to the definition Zukerman's Definition: OR = 1.68; (95% CI: 1.11-2.55) Richman's definition OR = 1.76; (95% CI = 1.05-2.97) Lozoff's Definition: non-significant association

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Arora et al (2014)	UK	Cross sectional	Midlands Adolescent Schools Sleep Education Study	511	11-13 years	Sleepiness (based on Cleveland Adolescent Sleepiness Questionnaire), Sleep efficiency, Chronotype, sleep duration (actigraphy)	BMI *z*-score	Age, sex and ethnicity school, dietary behaviours, parental obesity, daytime sleepiness, depression and anxiety	In adjusted models, definitely evening chronotype was positively associated with BMI z-score, while sleep duration had an inverse association. However, sleep efficiency was not, with BMI z-score after adjustment Evening chronotype $\beta = 0.51$ ($p<0.001$), Sleep duration $\beta = -0.36$ ($p<0.001$)
Bailey et al. (2014)	USA	Cross Sectional	Subjects from two Mountain West region universities	330	17-26 years	Sleep pattern inconsistency sleep efficiency	BMI, body fat	Age, season of assessment, PA	Sleep pattern inconsistency and sleep efficiency are associated with body fat, but only sleep efficiency is associated, negatively, with BMI: 1 SD increase in sleep pattern inconsistency and sleep efficiency was associated with 0.15 SD increase in percent body fat
Firouzi et al (2014)	Malaysia	Case control	Students from 10 randomly selected schools	164	6-12 years	Sleep duration, sleep disorder score (based on Children Sleep Habit Questionnaire)	BMI, overweight/ obesity (WHO reference), waist circumference, and body fat percentage	Age, sex, food intake, physical activity level and sedentary time	Sleeping for less than normal duration, and poor sleep quality is associated with higher risk of overweight/obesity Overweight/obesity Poor sleep quality: OR=2.17 (95%CI: 1.02-4.73) Short sleep duration: OR= 4.54 (95% CI:1.92-8.90)

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Michels et al (2014)	Belgium	Longitudinal (FU after 2 years)	Children's Body composition and Stress study	239	6-12 years	Sleep duration (actigraphy and sleep diary) Sleep quality (based on sleep efficiency, sleep latency and wake after sleep onset)	BMI , overweight/obese (IOTF reference) % fat, WC	Age, sex, parental education, physical activity, weekly snacking frequency	The association between sleep duration and BMI remained robust to adjustment for sleep quality variable (sleep efficiency, sleep latency and WASO). Sleep quality variables were not associated with BMI in models with and without adjusting for sleep duration Sleep duration β =-- 0.381 (p<0.03) Sleep latency β =--0.001 (p=0.830) Sleep efficiency β =-0.008 (p=0.589) WASO β =0.001 (p=0.868)
Quick et al (2014)	USA	Cross sectional	Students enrolled at nine US universities	1,252	18-24 years	Sleep quality (assessed by Pittsburgh Sleep Quality Index)	Overweight/obesity (CDC reference)	Age, sex, race, eating competence total score, and emotional eating	Sleep quality is significantly associated with overweight/obesity Overweight/obesity OR= 1.07 (95% CI: 1.01–1.13)
Silverstein et al. (2014)	Norway	Cross sectional	youth@hordaland survey	9,875	16-19 years	Insomnia , Obstructive sleep apnoea and sleep duration (short sleep duration <5 hours/day)	BMI, Overweight Obesity (IOTF reference)	Demographics, physical activity, depression and two other sleep variables (sleep duration, insomnia or OSA symptoms	In adjusted models only short sleep duration and OSA were linked with BMI, Subjects with non-compensated sleep on weekends had a high risk of overweight Short sleep OR= 1.51 (95% CI 1.10-2.08) Insomnia OR=1.14(95% CI 0.83-1.58) OSA symptoms

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									OR = 3.52(95% CI 2.35-5.26)
Vargas et al (2014)	USA	Cross sectional	Online survey response from college students	515	18 -34 years	Sleep quality (assessed by Pittsburgh Sleep Quality Index)	BMI (self-reported height and weight) overweight/obesity (based on the recommendations of the Clinical Guidelines)	Age, sex (sleep disturbances)	Overall poor quality of sleep was not associated with overweight/obesity. only sleep disturbances component of PSQI had a significant impact Overweight/obesity Global PSQI OR= 1.11 (95% CI: 0.74–1.65) Sleep disturbances OR= 1.66 (95% CI: 1.08–2.57)

BMI: body mass index, WC: waist circumference, OR: odds ratio, CI: confidence interval,SD: standard deviation, SEM: structural equation modelling, CDC: Centers for Disease Control and Prevention, IOTF: international obesity task force, WHO: world health organization NI: no information, PA: physical activity,SES: socioeconomic status, SOL: sleep onset latency

Table 2: List of studies concomitantly assessing the role of sleep quality and sleep quantity on overweight and obesity in young subjects

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(Reference: 20, 26-28)

Author	Sleep Dimensions	Results	Findings
Narang et al. (2012)	Sleep disturbance, Sleep duration	Sleep disturbance: OR: 1.43 (95%CI:1.16-1.77) Short Sleep duration: OR:1.03 (95%CI:0.81-1.30)	After adjusting for sleep duration and confounders (sex, caffeine, family history, snack, screen time, physical activity, and soft drink), higher sleep disturbance score was associated with increased odds of being at high cardiovascular risk.
Liu et al (2011)	Sleep problems, Sleep duration	Sleep problems: : OR: 3.52 (95%CI:1.42-8.70)	After adjusting for sleep duration and confounders (age, gender, total physical activity, total calories intake, maternal education), sleep problems were associated with higher odds of Ow/Ob.
Jarrin et al. (2013)	Sleep quality, sleep disturbances, sleep timing sleep duration	Poor sleep quality: β=-0.14 (p<0.01) Sleep disturbances: β=-0.13 (p<0.05) Delayed sleeping: β= 0.15 (p<0.05)	After adjusting for sleep duration and confounders (age, sex, pubertal status, physical activity, screen time, socioeconomic status) sleep disturbances, and delayed sleeping were positively associated with obesity, sleep quality was negatively linked with obesity. After adjustment for covariates, sleep duration was no longer associated with any obesity.
Silverstein et al (2014)	Insomnia, Obstructive sleep apnoea (OSA), short sleep duration (weekday & weekend),	Short sleep duration (weekday): OR = 1.51(95% CI: 1.10-2.08) Short sleep duration (weekend): OR = 1.42(95% CI: 0.87-2.31) Insomnia: OR = 1.14(95% CI: 0.83-1.58) OSA: OR = 3.52(95% CI: 2.35-5.26)	After adjusting for remaining other sleep variables (sleep duration/insomnia/ OSA symptoms) and confounders (socio-demographics, physical activity, and depressive symptoms), Short sleep duration and OSA were associated with higher odds of obesity.

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The impact of sleep duration on sleep quality-obesity association

Some of the studies are adjusted for sleep quantity to check if the association between sleep quality and Ow/Ob is independent of sleep duration (Table 15). The association remained significant even when sleep quality and duration were simultaneously considered in the regression analysis (82, 187, 359). Whereas, the same was not seen for sleep duration (359). Similar results were also seen when sleep duration and sleep quality were modeled as continuous variables (359). Additionally, unlike sleep duration, the association between sleep quality and adiposity and body composition indices was also robust to adjustment for various socio-demographic covariates (82).

Quantitative synthesis and sensitivity analysis

Meta-analysis was conducted on the 11 datasets related to the association between inadequate sleep and Ow/Ob (23, 103, 187, 358-363). The pooled OR for the association between inadequate sleep and Ow/Ob in young subjects was 1.27 (95% CI: 1.05-1.53), with considerable heterogeneity (I^2 = 60%) (Figure 7a). In the pooled analysis the study by Quick et, al. (361) was given the largest weight (53.7%). Sensitivity analysis was done to confirm if this study drives the meta-analysis results. It was seen that exclusion of this study did not have a considerable effect on the strength or direction of the association (OR=1.47, 95%CI: 1.26-1.71) (Figure 7b).

The subgroup analysis separating studies that focussed solely on poor sleep quality contained a total sample of 25,082 children, adolescents, and young adults (23, 103, 187, 358-360, 363) and was found to have a pooled OR of 1.46 (95% CI: 1.24-1.72), with non-significant heterogeneity across the eight datasets (I^2 = 30%). Studies that assessed combined sleep quantity and quality contained a total sample of 1,471 children, adolescents, and young adults (361-363), and was found to have a pooled OR of 1.10 (95% CI: 0.83-1.45), also without considerable heterogeneity across the three datasets (I^2 = 39%).

Sensitivity analyses were conducted by excluding studies based on the criteria of study design, age group, covariates selection, publication year and geographical location (Appendix-G). The association between poor sleep quality and Ow/Ob did not change for cross-sectional studies, based on adolescent subjects, conducted in countries other than the USA, and using non-validated questionnaires to explore inadequate sleep.

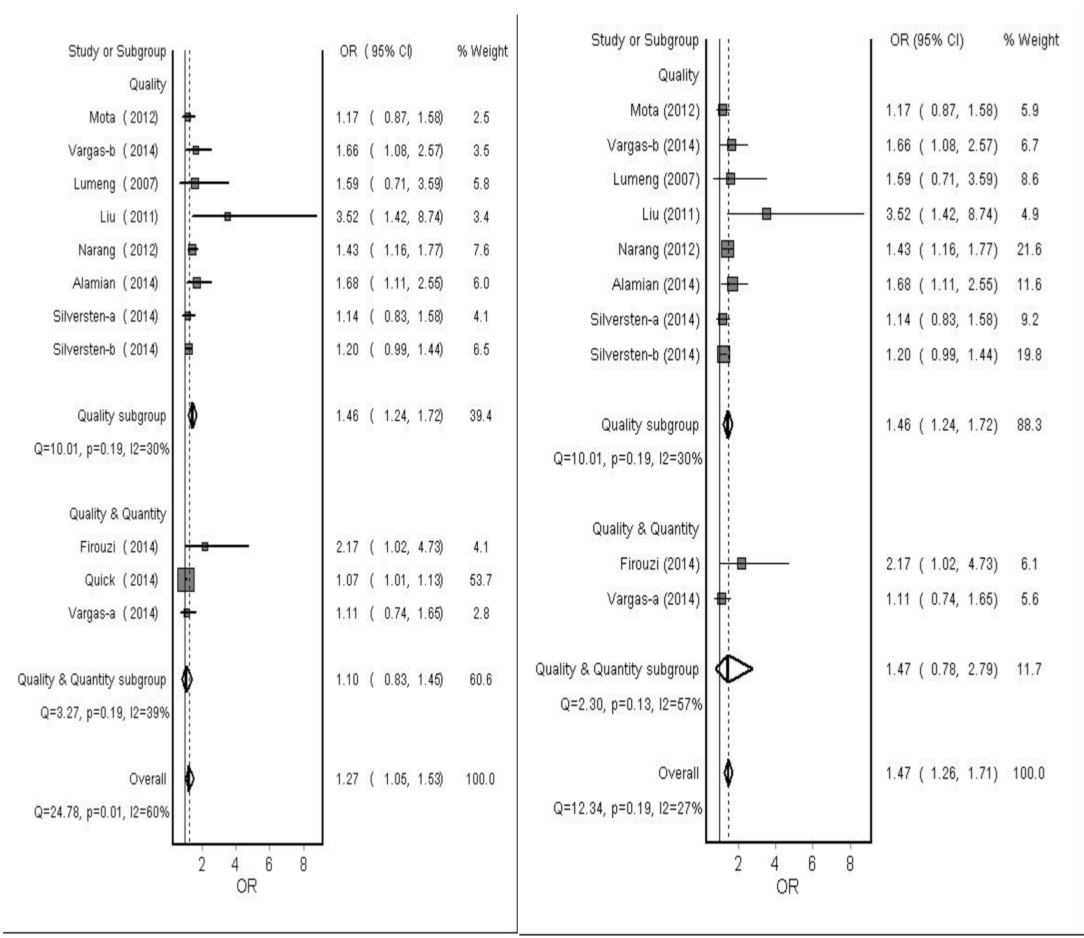

Figure 1: Quality effect model results for the association between inadequate sleep and overweight/obesity in young subjects

a) left: Quality effects model results for the association between inadequate sleep and overweight/obesity in young subjects b: (Right) The association between inadequate sleep and overweight/obesity in young subjects excluding the study by Quick et al.

(Results shown are the pooled odds ratios (OR) and 95% confidence intervals (95% CI))

Publication bias

Eggers's regression (slope: 0.784, p <0.001) as well as the LFK index (major asymmetry, index =6.07) suggested asymmetry(366). The Doi and funnel plots also indicated the

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presence of asymmetry with a paucity of studies on the left-hand side (weaker effects) of the plot (Figure 8). The exclusion of study by Quick et al. fixed some of the asymmetry issues, nonetheless, gross asymmetry was still evident, as quantified by LFK index (major asymmetry, index=3.68) (Appendix-H). The assessment suggests an excess of studies with positive effect sizes, therefore, it could have affected the meta-analytic pooled estimate.

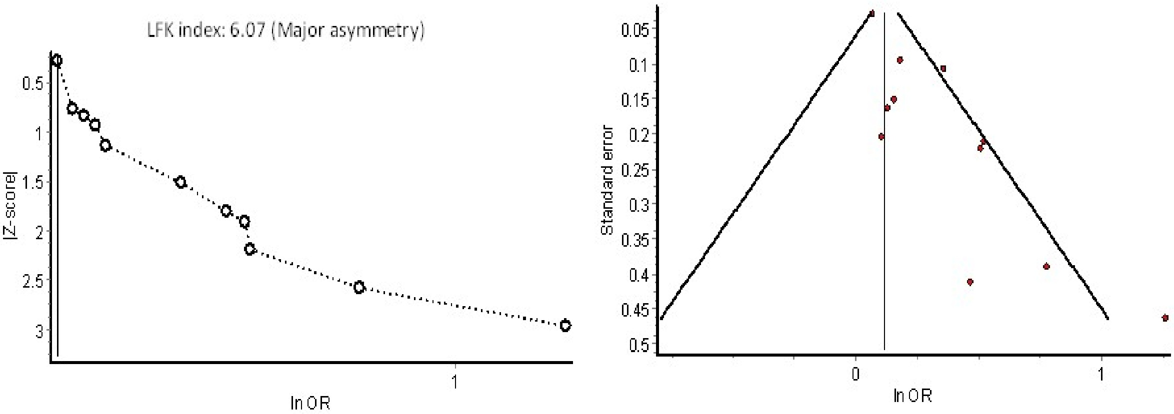

Figure 2: Funnel plot (right) and Doi plot (left) for the meta-analysis of studies exploring the association between inadequate sleep and overweight/obesity in young subjects.

(Both plots demonstrate severe positive asymmetry, favoring studies with positive results, and suggesting that the meta-analytic point estimates may be spuriously positive. The LFK index value of 6.07 concurs with positive asymmetry).

Discussion

This is the first systematic review and meta-analysis to establish the role of sleep quality in Ow/Ob outcome. Our finding suggests that sleep quality seems to have a considerable role in Ow/Ob, and this association is perhaps independent of sleep duration. Therefore, relying on only sleep duration to define inadequate sleep may not reveal the real association between sleep and Ow/Ob. However, due to the cross-sectional nature of the majority of the studies, the temporal sequence between poor sleep quality and Ow/Ob could not be determined. Therefore, the results of this study should be interpreted in the light of study limitations, and evidence from longitudinal studies should be solicited to establish the causal link between sleep quality and Ow/Ob.

Though the majority of the studies consistently reported a significant impact of sleep quality on Ow/Ob, there was considerable variation across the studies for defining key

*This is the Accepted Version of a paper published in the journal Obesity Reviews

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terms. For example, studies exploring sleep problems varied in their approach in considering the prevalence period, number, and type of sleep problems to classify sleep quality issues (197, 355, 358). Considering that the validity of findings depends greatly on the tools used to assess sleep quality, inconsistency in defining sleep quality, or the vague use of terminology, e.g., "sleep satisfaction" or "depth of sleep" is seen to lead variability in the results (103, 367). These findings highlight the complexity of sleep quality and the importance of understanding the different constructs of sleep quality (91, 367). It was also interesting to see that separately exploring the specific aspects of sleep quality did not demonstrate any significant impact, but when a broader context based on the co-occurrence of sleep problems was used the association became significant (187, 354, 355). Thus, indicating that using inadequate tools or exploring sleep quality constructs in isolation may not reveal the true impact of sleep on Ow/Ob. Therefore, the recommend best practice would be using validated tools, e.g., PSQI, for assessing poor sleep quality. Sleep quality assessment instruments such as the PSQI are quick and easy to use, have adequate reliability and good validity and therefore can help in obtaining valid findings (368).

Unfortunately, the association between objectively assessed indicators of poor sleep, e.g., efficiency, latency, and BMI in young subjects is relatively less explored. In this study we found only three studies that used objective methods for assessing poor sleep, though, these studies provided conflicting results (354, 356, 365). Therefore, further evidence is needed to establish the role of sleep efficiency and latency in obesity outcome. Nonetheless, the fact that only three studies used objective tools to measure sleep problems will not have a considerable impact on the findings of this meta-analysis since most of the studies included in the review used validated tools that probed for both objective and subjective components of sleep quality.

Previous studies report poor correlations between sleep duration and sleep quality for children and adolescents (369), suggesting that sleep quality and sleep duration are two separate dimensions of sleep. While, sleep quality refers to the subjective experience including satisfaction with sleep, sleep duration, on the other hand, is a more objective aspect of sleep, representing the actual time during which the individual is asleep (341). It is seen both sleep quality and sleep duration influence behavioural functions, but sleep quality was seen to have a stronger effect than sleep duration on emotional state, behaviour and cognitive function (370). Therefore, it can be argued that the effect of sleep duration cannot be used as a proxy for sleep quality and studies assessing sleep-obesity should look for the cumulative effect of sleep quality and sleep duration to get a true estimate of the inadequate sleep on obesity. Although, in this review, there were not many studies that explored inadequate sleep as a result of both sleep quality and quantity, yet most of these consistently reported a significant association between inadequate sleep due as a combined measure of poor quality and short duration, and Ow/Ob outcome(361, 362).

Due to the fewer number of studies we could not conduct a separate meta-analysis for subjects belonging to different developmental stages, but the results from sensitivity analysis suggest that association between poor sleep and Ow/Ob is stronger for children than adolescents and young adults (Table S-2). Similarly, some studies also found a gender difference in the prevalence of inadequate sleep suggesting that gender could be a moderating factor in sleep-obesity association (358). Therefore, it as suggested that future studies on sleep quality-obesity link should also consider the potential moderation by developmental stages and gender.

Emerging evidence from epidemiological and clinical studies highlight the role of SWS in the maintenance of normal glucose homeostasis, independent of total sleep duration (371, 372). The association between sleep quality and Ow/Ob can be explored by considering the link between energy balance and the specific parts of the sleep cycle, i.e., SWS and rapid eye movement (REM) sleep (373). While a study by Tasali et al. found a strong correlation between the magnitude of the decrease in insulin sensitivity with the magnitude of the reduction in SWS (346). Some studies also found an association between SWS and decreased secretion of cortisol and increased secretion of growth hormone, suggesting that poor sleep quality induces hormonal changes due to less time spent in SWS and alterations in REM sleep; eventually leading to obesity (374).

Our meta-analysis pooled estimate for the association between poor sleep quality and Ow/Ob is comparable to the pooled estimate for the association between short sleep duration and Ob/Ob (349). However, unlike the latter, this study is based on mainly cross-sectional studies. Therefore, the causal link and stability of the association between sleep dimensions and Ow/Ob could not be confirmed. Additionally, visual inspection of forest plot for pooled estimate suggested that the study by Quick et al. was assigned the highest weight. Review of this study reveals that to maximize sample size, data from two contemporaneous studies with same variables were combined. That perhaps had affected the overall OR for Ow/Ob and led to a narrow confidence interval, explaining the higher weight allocation. It was seen that the removal of this study had a minor effect on the pooled estimate, but did not change the direction of association or statistical significance. Considering that the quality of this study was also better than some other studies included in the review, we decided to keep this study in the meta-analysis since the results of this study might reflect the magnitude of the real effect of poor sleep quality.

Despite these limitations mentioned above, one of the strengths of our study is that we used quality effects model for meta-analyses that use adjustment based on measured methodological heterogeneity between studies (314). It has also been demonstrated to be more reliable than the use of the random effects model that requires strong assumptions that are unlikely to be valid in practice (335) and is known to produce spuriously positive results (336). Additionally, lack of practical heterogeneity as indicated by I^2 estimate imparts considerable generalizability of the findings of the meta-analysis(375).

Conclusion

In conclusion, the findings of this systematic review and meta-analysis indicate a potential role of sleep quality in sleep-obesity association in children, adolescents, and young adults, with some evidence for this association to be independent of sleep duration. Therefore, it is suggested that short sleep duration should not be used as the only benchmark of inadequate sleep, rather considering the cumulative effect of both poor quality and short duration would provide a reliable assessment of sleep-obesity link. Although the existing evidence for sleep quality and obesity association is weak, the preliminary findings are interesting enough not to dissuade future research in this area. Considering that the bulk of existing evidence is coming from cross-sectional studies further evidence from longitudinal studies is required to establish whether improving sleep quality can help in preventing obesity. Future epidemiological studies based on a longitudinal design using validated tools to explore both quantitative and quantitative aspects of sleep can help in better understanding of the causal association between sleep and obesity.