Short duration of sleep and incidence of overweight or obesity in Chinese children and adolescents: a systematic review and meta-analysis of prospective studies.

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SHORT TITLE: Sleep and obesity in Chinese children

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Abstract

Background and Aims. Overweight and obesity in children have become a global public health problem. Epidemiological studies suggest that sleep duration may contribute to the incidence of overweight and obesity in all stages of life. China has an increasing prevalence of overweight and obesity, and sleep deprivation is common among Chinese children. The aim of this study was to assess the prospective relationship between short sleep duration and overweight or obesity in Chinese children and to gain an estimate of the risk.

Methods and Results. A systematic search was performed on 28/04/2020 by using Medline, PubMed and Web of Science. The exposure was the duration of sleep, and the outcome measures the incidence of overweight or obesity. The odds ratios (OR) and hazard ratios (HR) and 95% confidence intervals (C.I.) were extracted to calculate the pooled relative risk (RR) by a random effect model. Heterogeneity and publication bias of the studies were checked by sensitivity analysis. Seven studies fulfilled the criteria for a systematic review, and 5 studies for a meta-analysis. The total of 33,206 participants included boys and girls, aged 6 to 17 years old. In Chinese children the pooled RR for short sleep duration and overweight or obesity combined was 1.47 (95% C.I. 1.26, 1.71, p<0.00001, n=32,607), and for obesity alone 1.40 (95% C.I. 1.01, 1.95, p=0.04, n=17,038). There was no significant heterogeneity or publication bias between studies.

Conclusion. Short sleep duration is associated with the development of overweight and obesity in Chinese children.

KEY WORDS: Sleep duration; obesity; overweight; meta-analysis; Chinese; children; adolescents

INTRODUCTION

During the last few decades, overweight and obesity in children and adolescent have become a serious global public health issue, which contribute to the development of chronic diseases, low cognitive development and psychological disorders, and impose serious socio-economic burden (1-2). When obesity persists into adulthood, it can result in several serious consequences, including metabolic syndrome and cardiovascular symptoms, as well as an increased risk of high blood pressure, diabetes, stroke and coronary heart disease (2-3). In 2016, the estimated number of overweight and obese children worldwide was nearly 216 and 124 million, respectively (4). According to the survey of World Health Organization, nearly half of all overweight children under five live in Asia (5). According to a systematic analysis from 1980 to 2013, the prevalence of overweight and obese for boys and girls in the world was over 22%. During the same period, the rate of incresase of obesity in children was higher than in adults. Also, this health problem is particularly acute in developing countries, where more than 60% of the world's obese people reside (6). China is the largest developing country in the world. In recent decades, the rapid development of China's social economy and the gradual improvement of residents' living standards have led to a significant increase in the prevalence of overweight and obesity, especially in urban areas (7). In 2012, the prevalence of overweight and obesity among children and adolescents aged 6 to 17 years was 9.6% and 6.4%, respectively (8).

Dietary habits and unhealthy lifestyle, such as high consumption of high-calorie foods and reduced physical activity, are the main environmental factors that explain the occurrence of obesity (7,9). Recent research shows that sleep may be a new modifiable factor contributing to weight gain at a young age (10). Sleep deprivation would alter levels of hormones such as leptin and ghrelin, which can lead to increase appetite and facilitate obesity (11). At the same time, many studies show that sleep deprivation is common among Chinese children and adolescents (12-13). In 2010, an epidemiological sampling survey of Chinese primary and secondary school students aged 9 to 18 years, in 30 provinces across China, showed that less than 40% of respondents had an average sleep time of more than 8 hours per day. Sleep deprivation

was most common among adolescents aged 16 to 18 years, reaching 91.1% (14). The association between sleep and obesity has been confirmed in previous epidemiological studies of many western countries; most cross-sectional studies have found negative linear relationship between sleep duration and obesity (15). An exploratory survey using an anonymous questionnaire probing self-reported sleep and ill-health in over 17,000 college students, aged 17-30 years, from 27 non-health-related universities from 24 countries, showed that short duration of sleep (<7 hours per night) were associated with poorer self-rated ill-health both in men and in women (16). Countries with the shortest sleep duration and the worst associated ill-health were all in the Far East Asia, stimulating interest in studying the possible underlying reasons for such excess. Prospective longitudinal studies have reported that sleep deprivation may occur before the development of overweight or obesity (10, 17-18). Many cross-sectional studies have been conducted in China on the relationship between sleep duration and the risk of obesity. In a survey of Chinese children, aged 3 to 4 years, the risk of obesity in those who slept less than 9 hours per day was raised by 3.8 folds compared to those sleeping 11 hours or longer (19). Due to the nature of the study design, cross-sectional associations cannot be interpreted as an expression of a cause-effect relationship. Therefore, it is important to find evidence from prospective longitudinal studies to establish a temporal sequence and point towards a causality effect. Until recently, such studies from China were not available.

Our study aims to (1) systematically review published prospective longitudinal studies of the relationship between sleep duration and overweight or obesity in Chinese children and adolescents; (2) perform a meta-analysis to identify whether the evidence supports the presence of a prospective relationship between short sleep duration and overweight or obesity in Chinese children and adolescents, and (3) obtain a quantitative estimate of the risk of overweight and obesity in short sleepers.

METHODS

Literature Search

A systematic search was performed on 28th April 2020 to identify the longitudinal

studies that related with the association between sleep duration and overweight or obesity in Chinese children and adolescents. The selected electronic databases included Medline (from 1946), PubMed (from 2002), and Web of Science (from 1900). The key words were searched for all fields included subject headings. Keywords related to "sleep" (sleep or sleep-disordered breathing or bed time) and "weight" (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" (children or adolescents or pediatrics or pediatric or paediatric or paediatrics or preschool) and "ethnicity" (China or Chinese) were combined and searched. The search did not use language restrictions (**APPENDIX**). The results from these searches were reviewed and screened. Other relevant studies were also obtained from review articles.

Inclusion and exclusion criteria

Studies were included if they met the following criteria: (1) the research object related to the relationship between sleep duration (exposure) and overweight, obesity, or change in body mass index (BMI)(outcome); (2) Chinese children, and adolescents (aged 0-18 years at baseline) were the study population; (3) observational longitudinal study design was used; (4) exposure was reported as duration of sleep and outcomes as incidence of overweight or obesity, or changes in BMI.

The exclusion criteria were: (1) sleep duration was not measured; (2) no data of Chinese people was available; (3) no related indicators or indices for overweight or obesity; (4) cross-sectional, case-control or case series study designs, or other meta-analysis.

Data extraction

Through independent review by two researchers (Y.G and F.P.C), the data of the studies were extracted. The systematic searches identified 516 records, of which 362 papers were identified after duplicates removed (**FIGURE 1**).

After exclusions from title and abstract perusals, 49 full texts articles were

analysed for inclusion and exclusion criteria. Finally, 5 studies (6 groups) were deemed suitable for meta-analysis, and 2 studies were used for a qualitative description (**TABLE 1**). The extracted data included the surname of first authors, publication year, demographic characteristics of study populations, follow-up time, year and areas of recruitment, sample size, measurement methods of sleep exposure, categories of sleep duration, methods of exposure assessment, definition of outcomes, odds ratios (OR) or hazard ratios (HR) of overweight or obesity and corresponding 95% confidence intervals (C.I.), and adjusted variables in the studies.

Exposure and Outcome

The total average sleep duration of children and adolescents, and their reference categories, are different at all ages of life (20); therefore, the classification method used in the original papers were used to define "short sleep". The definitions of short sleep are showed in **TABLE 1** as the exposure, according to different papers, and the relative risk (RR) of short sleepers were calculated by comparing with middle or long sleepers. If the paper compared long sleepers with middle sleepers, the reciprocal of RR was used to estimate the RR of short sleepers. The definitions of overweight and obesity are listed in **TABLE 1** as the outcomes, and the one paper that used BMI as outcome instead of overweight and obesity was referenced in support of the result of meta-analysis.

Confounders

Many confounders were adjusted for in these studies, such as child age, sex, dietary intake, physical activity, maternal education level, household income, etc (**TABLE 1**). Sample size were collected for analyses of heterogeneity and sensitivity.

Statistical Analysis

The quality of the studies included in the meta-analysis was evaluated by the Downs and Black Quality Index score system using a validated checklist for assessing the quality of the studies (21). For the assessment of nonrandomized studies, the

maximum score is 20. The aim of this study was to estimate the quantitative relationship between short sleep duration and the prospective risk overweight or obesity, so the estimated values of relative risk (RR) as the effect measure were calculated by the OR or HR with their 95% C.I. from each study. Also, if the OR or HR was not reported in the original papers, the estimated RR would be calculated by regression coefficient β (95% C.I.) for changes of BMI as a continuous outcome (only one study in **TABLE 1**). When standard error (SE) was not supplied, it was algebraically computed by the 95% C.I. of estimated RR, or by the sample size (N) and standard deviation (SD). We used a random effect analysis model and selected inverse variance as the statistical method (22). The pooled analysis was conducted by calculating pooled RR of overweight or obesity, and its 95% C.I.. The possible heterogeneity between these studies was tested by Cochran's Q statistic, and H-statistic and I^2-statistic would be used to correct the influence of the number of studies on the Q-statistic (23-24). Funnel plot asymmetry to detect publication bias, and the Egger's and Begg's tests to judge symmetry of the funnel plots (25-26) were not used due to the small numbers of data points (less than 10) in each of the two datasets (27). Sensitivity analysis was performed to examine the effects of individual studies on the overall meta-analysis, which omitted one study at a time to understand how much the inferences of the results depended on a particular study or group of studies (**APPENDIX**). The systematic review and meta-analysis processes were conducted based on the PRISMA 2009 checklist and flow diagram for literature screening, with the appropriate inclusion and exclusion criteria (28). The statistical analyses were performed by using Review Manager version 5.2.

RESULTS

Characteristics of studies

Five longitudinal studies (providing six groups) were included in the meta-analysis (29-33). In the study of Cao et al. (30), the author grouped the children participants by sex and reported the results separately. These two groups have been analysed independently. They include a total of 33,206 participanys from 10 provincial regions

of China. Two additional studies were described in support of the results (34-35), although the data reported were not suitable for a meta-analysis. The studies covered boys and girls, and their age ranged from 6 to 17 years old. The study sample size ranged from 411 to 16,028. All data was extracted from the published papers. Most studies reported RR for overweight and obesity combined; the study by Huang et al. (33) only reported the risk for obesity, whilst the studies of Wang et al. (29) and Lim et al. (31) reported both RR for overweight and obesity combined and for obesity only. Two meta-analyses were carried out where the outcome was either incidence of overweight and obesity combined (5 groups from 4 studies, n=32,607) or of obesity only (3 studies, n=17,038). Various sensitivity analyses are reported in the text to test possible differences in estimations due to different criteria used to define the outcome. Details of the studies are shown in **TABLE 1**.

Short sleep and overweight or obesity in Chinese children

FIGURE 2a shows the Forest plot of longitudinal prospective associations between short sleep and overweight and obesity combined. The pooled analysis shows significant direct relationship between short sleep and the risk of overweight and obesity with an RR of 1.47 (95% C.I. 1.26, 1.71; p＜0.001). The heterogeneity between groups was not statistically significant (I^2 = 1%; P=0.40). Publication bias was not tested due to small numbers (36). In further sensitivity analyses, after omitting the groups one by one, the change of estimated RR was narrow, ranging from 1.42 to 1.50, and the estimated heterogeneity varied between 0% and 25% (**APPENDIX**).

　　FIGURE 2b shows the Forest plot of longitudinal prospective associations between short sleep and obesity only. The pooled RR was 1.40 (95% C.I. 1.01, 1.95; p=0.04). The heterogeneity was not statistically significant (I^2 = 59%; P=0.09). Publication bias was not tested due to small numbers (27). Further sensitivity analyses by excluding any one of these studies shows that the changes in estimated RR varied between 1.19 and 1.75, and the estimated heterogeneity varied from 0% to 80%. The latter was detected when the study by Lim et al. (31) was excluded (**APPENDIX**).

Qualitative analysis

Two studies were not included in the meta-analysis due to lack of suitable data (34-35). They focus on Chinese infants aged 1 to 24 months, and provide useful information (**TABLE 1**). The result of Sha et al. (35) found an inverse relationship between infant sleep duration (hours) and their weight gain (kg). In this retrospective birth cohort study, 519 infants (1-12 months at baseline) were followed up for 12 months. Sleep quality and duration was obtained from maternal self-report. Sleep duration was inversely associated with weight gain (measured by Z-score) (beta = -0.258; SE 0.013; p<0.001). In a similar the study by Zhou et al. (34), in 150 Chinese infants in a birth cohort from Singapore, aged 3-24 months at baseline, short sleep duration ($\leq$12h per night) was inversely associated with body mass index (beta = -0.044; p<0.05). After algebraic calculations, the estimated RRs of the relationship between short sleep and overweight or obesity of these two studies were 1.29 (95% C.I. 1.26, 1.33) and 1.04 (95% C.I. 0.57, 1.93), respectively.

DISCUSSION

This study presents a systematic review and meta-analysis of the longitudinal relationship between short sleep duration and the incidence of overweight and/or obesity in Chinese children and adolescents. The result shows that shorter sleep duration than it is the norm for age would increase the risk of becoming overweight or obese in Chinese children and adolescents.

There are many reasons why our results are valuable. First, this is the first systematic review and meta-analysis of longitudinal cohort studies carried out in Chinese children to examine the prospective relationship between sleep duration and overweight and obesity. The studies were all published in the last 5 years and were never represented in previous meta-analyses. The pooled results show that short sleep duration is prospectively associated with an increased risk of developing overweight or obesity by 35% to 41% in Chinese children and adolescents. Our results are consistent with previous meta-analyses of both cross-sectional and prospective cohort studies based on Western populations with little or no representations of samples from

China (15, 17-18, 36). Second, the size of effect estimate is large enough to be of significant public health impact if treatment tools to prevent sleep deprivation became applicable to China. Third, the analyses did not show evidence of significant heterogeneity between studies. Fourth, the results appeared robust both when considering incidence of overweight and obesity, as sensitivity analyses did not alter substantially the estimates of effect. Fifth, additional perusal of two studies in infants suggests that the effects of short sleep duration on weight gain may be present since birth, as shown convincingly in Western populations (17-18).

There are some limitations in this study. First, the quality of the data cannot exceed that of the individual studies included. Second, the results of this meta-analysis represent only the included studies and are unable to provide representative inferences from all other published studies. Third, the degree of control for confounding factors were different in the included studies, most of them set age, sex, and physical activity as the adjusted variables. However, we could not directly adjust for the confounders that existed in the original papers. Fourth, the method to assess sleep exposure by questionnaires of parental self-report, contains uncertainties regarding accuracy and risk of recall bias. Fifth, the definitions of sleep exposure categories and of overweight and obesity across studies were different, possibly introducing inaccuracies. Sixth, other potential sleep factors, such as sleep habit, sleep quality and sleep patterns, were not included in the study. They may increase the risk of overweight and obesity in children and adolescents (36) or interact with quantity in determining their risk. Finally, due to the small number of studies, we could not statistically rule out publication bias. Even though many limitations are inevitable, the results of this study provide supportive evidence for further developments of public health strategies in pediatric age, regarding protection of sleeping patterns in Chinese children and adolescents.

The articles of this pooled analysis are all prospective longitudinal studies, therefore, because of clear time sequences, causality between short sleep and the incidence of overweight or obesity in Chinese children and adolescents can be supported. However, the potential mechanisms implicated in this relationship cannot

be determined from our study.

Some short term experiments in adults show that sleep deprivation affects several hormonal responses and energy balance in body, which result in increasing level of the orexigenic factor ghrelin, decreasing level of the anorexigenic hormone leptin, and increasing of hunger and appetite, and eventually lead to overweight or obesity (37-38). Sleep restriction is also associated with decreased insulin sensitivity and glucose tolerance (39). Moreover, the inflammatory pathways activated by sleep loss may be related to the occurrence of obesity (40).

There is evidence that chronically sleep-deprived adolescents would have a change in nutritional behaviour, that is, making them more likely to choose sweets with a higher glycemic index and glycemic load (41). Sleep deprivation enhances hedonic stimulus processing in the cerebral cortex, like orbital frontal cortex, and result in food consumption. In addition, sleep-deprived people consume more food than usual to maintain the physiological need for additional wakefulness (38, 42-43). All of these factors mentioned above would finally affect children's dietary pattern or energy intake, result in increased BMI or weight gain.

Fatigue and tiredness due to sleep deprivation are additional factors that could lead to increased sedentary time, reduced physical activity, and decreased energy expenditure (43). The excessive use of electronic devices in children and adolescents leads to poor sleep habits and disturbances in normal sleep, including decreased sleep quality and inhibition of melatonin secretion (44-45). Moreover, comorbidities, such as depression, mental health conditions, chronic illnesses, physical and psychological illnesses, would decrease sleep duration or sleep quality, and reduce the number of times of physical activities, which result in limited energy expenditure and weight gain (15, 46).

A number of studies have demonstrated the association and causal relationship between sleep deprivation and overweight or obesity at all stages of life, as well as its potential public health impact. Future prospective studies need to add other measurements to determine overweight and obesity, such as waist circumference or waist hip ratio, rather than just the weight, height, and BMI. The definition and

measurement of sleep duration should be more precise and objective, such as considering naps, sleep quality and other factors that may affect sleep. At the same time, researchers should focus on the effects of other chronic or psychiatric diseases (47) on both sleep duration and obesity, identifying whether these factors are confounding factors or mediations and control if it is defined as a confounding factor (15).

CONCLUSION

Through systematic review and meta-analysis, the relationship between short sleep duration and development of overweight or obesity in Chinese children and adolescents is significant. The intervention studies in the future should focus on identifying methods to prevent children and adolescents from reducing their normative sleep requirement for their age and, where there is evidence of sleep deprivation, of increasing sleep duration to reduce the risk of gaining weight at an early stage of their lives (15). The Chinese public health departments should conduct health education for children and their parents and urge them to develop good living and eating habits, so as to promote physical health and reduce the incidence of obesity.

Contributors

YG and FPC were involved in each of the following points:1. Design. 2. Data Collection. 3. Analysis. 4. Writing manuscript. YG, MAM, and FPC were involved in each of the following points: 1. Manuscript revision.

Research involving human participants and/or animals

This article does not contain any studies with human participants or animals performed by any of the authors.

Declaration of Competing Interest

YG, MAM, and FPC have no relevant conflicts of interest to declare. All the authors approved the final version of this manuscript.

Appendix. Supplementary data to this article can be found online at https://doi.org/10.1016/xxxxx

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Author (Year)	City Baseline Sample size Follow-up	QS	Age	Sleep exposure: Definition & assessment	Obesity outcome: definition & assessment	Confounders
	Longitudinal studies included in the meta-analysis					
Wang (2016)	Jiaxing 1993 N=19,580 (of which 16,028 used in longitudinal analysis) 2 years	17	3 yrs	Average sleep duration ≤ 10h, 11–12h, ≥ 13h Parental Self-report	OW: BMI ≥ 16.8, 16.9, 16.5, and 16.6 for 3-year old boys and girls, 5-year old boys and girls. OB: BMI ≥ 18.1, 18.3, 17.9, and 18.2 for 3-year old boys and girls, 5-year old boys and girls[1] HT and WT measured by trained nurses	Age, gender, birth weight, breastfeeding, appetite, physical activity, maternal age at delivery, BMI, education, and occupation.
Cao (2018)	Beijing, Tianjing, Liaoning, Ningxia, Shanghai, Changsha, Guangzhou 2013 N=14,089 6-9 months	18	6-17 yrs	Sleep duration (hours per night) SS: ＜7h, MS: 7-9hLS: ≥9h Mixed: child and parent self-report	OW: BMI ≥ 24 kg/m². [1] HT and WT measured by researchers	Age, sex, physical activity, sedentary behaviour, dietary intake, mother's education, family income
Gong (2020)	Ningbo 2016 N=1,510 2 years	15	12-13 yrs	Average sleep duration(24h) SS:＜8h, MS:8-9h, LS:≥9h Self-reported	OW: BMI ≥ 25 kg/m². [2] HT and WT measured by researchers	Age, sex, diet, physical activity, sedentary behaviors, smoking, drinking
Huang (2019)	Hong Kong 2009-10 N=599 2 years	16	6-8 yrs	Average weekly sleep duration SS: catch-up＜1h MS: catch-up 1–2h LS: catch-up≥2h Parental Self-reported	IOTF criteria[2] HT and WT measured by researchers	Child age, sex, measurement time point, maternal education, parental BMI, siblings, sedentary time, accelerometer wear time, and school clustering
Lim (2019)	Hong Kong 2007-8 N=411 6 years	15	6-20 yrs	Average weekly sleep duration SS: <7h, LS: ≥7h Self-reported	OW: BMI ≥ age- and sex-specific 85th percentile or ≥23 kg/m² OB: BMI ≥ age- and sex-specific 95th percentile or ≥25 kg/m². [3] HT and WT measured by researchers	Age and sex
	Longitudinal studies not included in the meta-analysis					
Zhou (2015)	Singapore 2009-11 N=150 24 months	15	3 mo	Daily sleep duration (sum of daytime and nighttime hours.) SD≤ 12h, LD＞12h Parental Self-report	Change in BMI HT and WT by researchers	Ethnicity, maternal education, household income, parental anthropometry, child sex, gestational age, birth weight and length, smoking in pregnancy, gestational diabetes, breast-feeding, early lifestyle
Sha (2017)	Changsha 2013 N=519 12 months	16	1 mo	Average sleep duration (24-h period) Continuous (hours) Maternal Self-report	OW and OB according to weight-for-age Z-score[4] HT and WT by doctors	Maternal age, educational level, marital status, child sex, household income

BMI=body mass index; HT=height; OB=obesity; OW=overweight; QS=Quality Score; WT=weight
[1]Body mass index cut-offs for overweight and obesity in Chinese children and adolescents aged 2-18 years (2010).
[2]BMI cut-offs from the International Obesity Task Force (IOTF)
[3]Overweight or obesity was defined by Cook's criteria with percentile curves based on a local population survey.
[4]The principles of World Health Organization Growth Standard (2006).

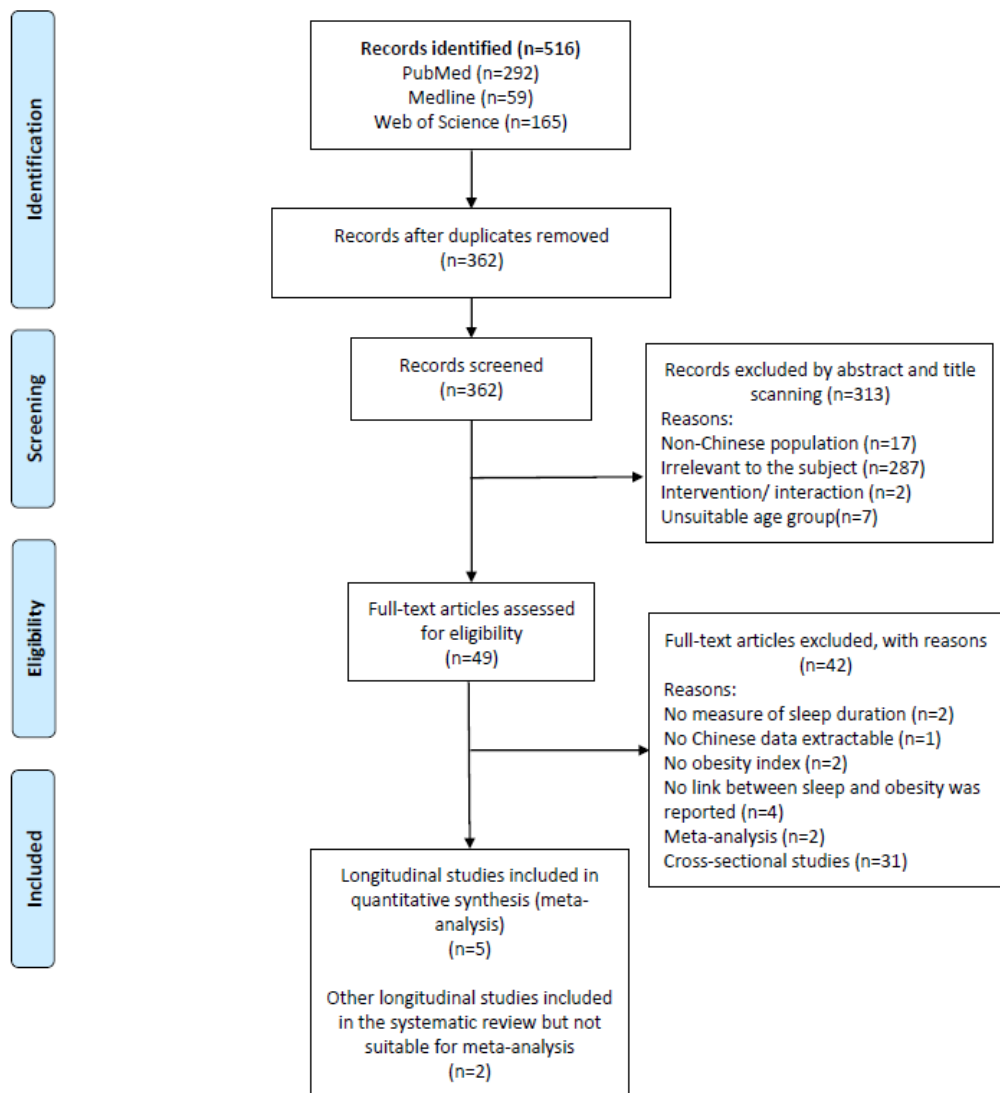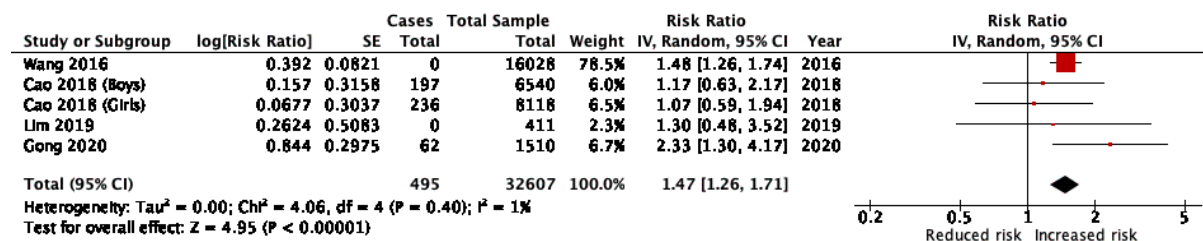**TABLE 1.** Longitudinal studies selected from the search.

FIGURE 1. PRISMA flow chart. Studies contribute to the meta-analysis

(a)

Study or Subgroup	log[Risk Ratio]	SE	Cases Total	Total Sample Total	Weight	Risk Ratio IV, Random, 95% CI	Year	Risk Ratio IV, Random, 95% CI
Wang 2016	0.392	0.0821	0	16028	78.5%	1.48 [1.26, 1.74]	2016	
Cao 2018 (Boys)	0.157	0.3158	197	6540	6.0%	1.17 [0.63, 2.17]	2018	
Cao 2018 (Girls)	0.0677	0.3037	236	8118	6.5%	1.07 [0.59, 1.94]	2018	
Lim 2019	0.2624	0.5083	0	411	2.3%	1.30 [0.48, 3.52]	2019	
Gong 2020	0.844	0.2975	62	1510	6.7%	2.33 [1.30, 4.17]	2020	
Total (95% CI)			495	32607	100.0%	1.47 [1.26, 1.71]		

Heterogeneity: Tau² = 0.00; Chi² = 4.06, df = 4 (P = 0.40); I² = 1%
Test for overall effect: Z = 4.95 (P < 0.00001)

Reduced risk Increased risk

(b)

Study or Subgroup	log[Risk Ratio]	SE	Cases Total	Total Sample Total	Weight	Risk Ratio IV, Random, 95% CI	Year	Risk Ratio IV, Random, 95% CI
Wang 2016	0.571	0.1575	0	16028	40.9%	1.77 [1.30, 2.41]	2016	
Huang 2019	0.1732	0.0871	0	599	54.4%	1.19 [1.00, 1.41]	2019	
Lim 2019	0.239	0.7535	0	411	4.6%	1.27 [0.29, 5.56]	2019	
Total (95% CI)			0	17038	100.0%	1.40 [1.01, 1.95]		

Heterogeneity: Tau² = 0.04; Chi² = 4.89, df = 2 (P = 0.09); I² = 59%
Test for overall effect: Z = 2.01 (P = 0.04)
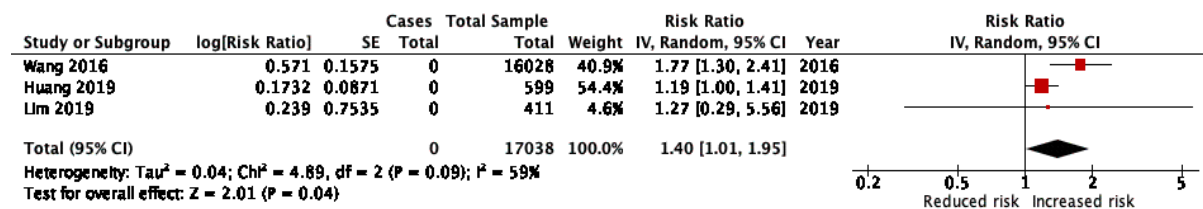
Reduced risk Increased risk

FIGURE 2. Forest plot of prospective observational studies on the effect of short sleep duration on the incidence of overweight and obesity combined (a) and obesity alone (b) in Chinese children and adolescents. Results are relative risks (and 95% confidence intervals).