

## Observational Study

## Interaction between adolescent sleep rhythms and gender in an obese population

Nan-Nan Wu, Guo-Li Yan, Hong-Yu Zhang, Ling Sun, Min Hou, Guang-Ming Xu

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The obesity rate of adolescents is gradually increasing, which seriously affects their mental health, and sleep plays an important role in adolescent obesity.

**AIM**

To investigate the relationship between sleep rhythm and obesity among adolescents and further explores the interactive effect of sleep rhythm and gender on adolescent obesity, providing a theoretical basis for developing interventions for adolescent obesity.

**METHODS**

Research data source Tianjin Mental Health Promotion Program for Students. From April to June 2022, this study selected 14201 students from 13 middle schools in a certain district of Tianjin as the research subject using the convenient cluster sampling method. Among these students, 13374 accepted and completed the survey, with an effective rate of 94.2%. The demographic data and basic information of adolescents, such as height and weight, were collected through a general situation questionnaire. The sleep rhythm of adolescents was evaluated using the reduced version of the morningness-eveningness questionnaire.

**RESULTS**

A total of 13374 participants (6629 females, accounting for 49.56%; the average age is  $15.21 \pm 1.433$  years) were analyzed. Among them, the survey showed that 2942 adolescent were obesity, accounting for 22% and 2104 adolescent were

overweight, accounting for 15.7%. Among them, 1692 male adolescents are obese, with an obesity rate of 25.1%, higher than 18.9% of female adolescents. There is a statistically significant difference between the three groups ( $\chi^2 = 231.522$ ,  $P < 0.000$ ). The obesity group has the smallest age ( $14.94 \pm 1.442$  years), and there is a statistical difference in age among the three groups ( $F = 69.996$ ,  $P < 0.000$ ). Obesity rates are higher among individuals who are not-only-child, have residential experience within six months, have family economic poverty, and have evening-type sleep ( $P < 0.05$ ). Logistic regression analysis shows a correlation between sleep rhythm and adolescent obesity. Evening-type sleep rhythm can increase the risk of obesity in male adolescents [1.250 (1.067-1.468)], but the effect on female obesity is not remarkable. Further logistic regression analysis in the overall population demonstrates that the interaction between evening-type sleep rhythm and the male gender poses a risk of adolescent obesity [1.122 (1.043-1.208)].

## CONCLUSION

Among adolescents, the incidence of obesity in males is higher than in females. Evening-type sleep rhythm plays an important role in male obesity but has no significant effect on female obesity. Progressive analysis suggests an interactive effect of sleep rhythm and gender on adolescent obesity, and the combination of evening-type sleep and the male gender promotes the development of adolescent obesity. In formulating precautions against adolescent obesity, obesity in male adolescents with evening-type sleep should be a critical concern.

**Key Words:** Adolescent; Obesity; Sleep rhythm; Gender; Interaction

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**Core Tip:** The obesity rates of male adolescents is higher than that of female adolescents, and older adolescents have a protective effect on obesity of different genders. The study shows that sleep rhythm and gender have an interactive effect on adolescent obesity, and the combination of evening-type sleep and male sexuality promotes the development of adolescent obesity. In formulating measures to prevent adolescent obesity, attention should be paid to the obesity problem of male adolescents with evening-type sleep.

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## INTRODUCTION

With the rapid development of the economy and the improvement of people's living standards, the increasing obesity among global teenagers[1] has become one of the most important public health issues of the 21<sup>st</sup> century[2], posing significant physical and psychological risks to adolescents[3]. Gutiérrez-Cuevas *et al*[4] concluded that obesity is strongly associated with some serious physical illness, which pose serious health risks. The incidence of obesity among Chinese adolescents is also gradually rising[5,6]. According to the Report on Nutrition and Chronic Diseases of Chinese Residents (2020), the obesity rates among adolescents aged 6-17 in China is 19.0%. Moreover, childhood obesity is closely related to gender[7]. The obesity rates of boys in the general population, urban areas, and rural areas are all higher than those of girls[8,9]. Meanwhile, some research confirmed that obesity in adolescents had genetic susceptibility. Many genetic markers associated with obesity have been identified, such as melanocortin-4 receptor mutations, leptin deficiency, anterior epithelial layer deficiency, and the *FTO* gene variant rs9939609[4].

However, over-nutrition and lack of exercise are not all the causes of obesity in adolescents. Over the past two decades, inadequate sleep duration and abnormal sleep rhythms have emerged as new risk factors for obesity and metabolism-related diseases in adolescents[10-12]. Sleep is increasingly recognized as a critical component of cognitive, emotional, and physical health. Healthy sleep possesses the characteristics of adequate duration, good quality, appropriate timing, and the absence of sleep disorders[13]. Sleep problems often occur in childhood and adolescence[14,15]. Children transitioning from late childhood into adolescence undergo rapid biological and emotional changes[16,17], including changes in sleep[18]. Sleep rhythm, also known as chronotype, is a specific sleep-wake cycle regulated by endogenous (such as the biological clock gene) and exogenous factors (such as light). There are usually three types: Morning-type, evening-type, and no-preference-type or intermediate-type. Some studies found that sleep rhythm disorders could cause metabolic and endocrine disorders in the body, with the symptoms of hyperglycemia, obesity, and poor sleep quality [19]. Tse *et al*[20] demonstrated a specific relationship between changes in night sleep time and obesity in adults. Participants staying up late, especially from 2 to 6 a.m., tended to develop obesity. Yu *et al*[21] concluded that in men, evening-type was associated with diabetes and obesity, and only metabolic syndrome was associated with evening-type in women[21]. Rensen *et al*[22] suggested that the sleep rhythm of adolescents could be more easily altered than that of

young children.

Previous studies on the relationship between sleep rhythm and obesity in adolescents mainly focus on sleep time, awake time and sleep duration. Research on the overall station of adolescent sleep rhythm and gender is rare. This study aims to explore the relationship between sleep rhythm and obesity in adolescents. The reduced version of the morningness-eveningness scale (rMEQ) was adopted to evaluate sleep rhythm from the perspective of their physical and mental state. Moreover, a questionnaire survey was conducted among middle school students in Tianjin to further analyze the relationship between sleep rhythm and obesity among adolescents of different genders. This study provides a theoretical basis for formulating interventions for adolescent obesity.

## MATERIALS AND METHODS

### **Subject and methods**

**Subject:** Research data source Tianjin Mental Health Promotion Program for Students. From April to June 2022, this study selected 14201 students from 13 middle schools in a certain district of Tianjin as the research subject using the convenient cluster sampling method. Among these students, 13374 accepted and completed the survey, with an effective rate of 94.2%. Schoolboys were 6745, accounting for 50.4%, and schoolgirls 6629, accounting for 49.6%. The average age is  $15.21 \pm 1.433$ . The project team distributed informed consent forms about the project and what to expect from this survey to students and parents. After being signed by students and guardians, the informed consent forms were given to the project team for joint custody. This study was reviewed and approved by the Ethics Committee of Anding Hospital in Tianjin (2021-42).

### **Research tools**

**General condition questionnaire:** The general condition questionnaire is a self-made scale filled out by students through the Internet. The survey includes demography data, such as age, gender, only child or not, self-evaluation of the family's economic situation, parent's marital status, residential experience within six months, height, and weight. Students' height and weight are used to calculate body mass index (BMI). The assessment of adolescent obesity is based on the "Overweight and Obesity Screening Standards for School-Age Children and Adolescents" released by the National Health Department in 2018[23]. Research has shown that self-reported height and weight have a high predictive ability in identifying subjects' obesity and can be used confidently in research[24].

**Sleep rhythm:** The rMEQ is used to evaluate sleep rhythm types. This scale consists of five items (items 1, 7, 10, 18, and 19 in the original MEQ questionnaire), filled out by students based on their actual situations in the past month. It is used to assess the degree of activity and wakefulness (sleep rhythm) of subjects during specific periods in the morning and evening. The lower the score, the later the sleep rhythm. According to the scores on this scale, the population can be divided into "absolute morning type" (22-25 points), "moderate morning type" (18-21 points), "intermediate type" (12-17 points), "moderate evening type" (8-11 points), and "absolute evening type" (4-7 points)[25]. This study amalgamated the "absolute morning type" and "moderate morning type" into the "morning-type", and the "moderate evening type" and "absolute evening type" into the "evening-type". For the Chinese version of the scale, the Cronbach's- $\alpha$  coefficient is 0.74, indicating high reliability and validity[26].

### **Survey methods**

The project team organized online training sessions for the teachers from each school participating in the survey to explain the content, requirements for questionnaire filling, and precautions. Electronic survey links were sent to the psychological teachers of each school. They organized training meetings for their homeroom teachers to explain the requirements for filling out questionnaires. Schools issued letters to students' parents to inform them of this survey's project content and precautions. The informed consent was returned to the school for safekeeping after being signed by students and guardians. Homeroom teachers provided training sessions about the requirements and precautions for filling out the questionnaire to participating students. Electronic survey links were sent to the students for them to complete the survey questions using their mobile phones.

### **Quality control**

An electronic questionnaire platform was constructed. All questions were set compulsory to avoid being missed out. A normal value range for the blank-filling questions was set to prevent outliers. All personnel involved received unified training before the project. Students were explained the survey content, requirements, and precautions and were required to fill out the questionnaire independently. Each student had a specific questionnaire code to ensure correct filling. Only after completing all the questions could they submit.

### **Statistical analysis**

Statistical analysis of survey data was conducted using SPSS 26.0. Descriptive analysis was conducted using frequency and percentage or mean and standard deviation. The enumeration data was expressed as a percentage or rate. Comparisons of rates between different groups were conducted using the  $\chi^2$  test. The measurement data was represented by the mean plus/minus standard deviation, and the measurement data between different groups were compared using the independent sample T-test or analysis of variance. Logistic regression was used to analyze the influencing factors of adolescent obesity. Multiple logistic regression analysis was conducted by incorporating relevant variables, and  $P < 0.05$

was statistically significant. In the logistic regression model, the assignment of independent variables was as follows: Gender: Female = 1, male = 2; sleep rhythm: Intermediate-type sleep = 1, morning-type sleep = 2, evening-type sleep = 3; residential experience within six months: Yes = 1, no = 2; family economic situation: Wealthy = 1, average = 2, poverty = 3; dependent variables: Obesity = 1, non-obesity = 0.

## RESULTS

### **Comparison of demography data on adolescents objectivity**

The survey showed that 2942 adolescent were obesity, accounting for 22% and 2104 adolescent were overweight, accounting for 15.7%. Among them, 1692 male adolescents are obese, with an obesity rate of 25.1%, higher than 18.9% of female adolescents. There is a statistically significant difference between the three groups ( $\chi^2 = 231.522$ ,  $P < 0.000$ ). The obesity group has the smallest age ( $14.94 \pm 1.442$  years), and there is a statistical difference in age among the three groups ( $F = 69.996$ ,  $P < 0.000$ ) (Table 1).

Adolescents being the only child of the family, having no residential experience within six months, having family economic poverty, and having evening-type sleep have higher obesity rates, and there are statistical differences ( $P < 0.05$ ). Among female adolescents, the obesity rates are higher among those who have no residential experience within six months, have family economic poverty, and have remarried or single-parent families, and there are statistical differences ( $P < 0.05$ ). For male adolescents, there are higher obesity rates among those who have no residential experience within six months and have evening-type sleep, and there are statistical differences ( $P < 0.05$ ) (Table 2).

### **Comparison of sleep rhythm in age, gender, and BMI**

This study shows that 1674 adolescents have evening-type sleep, accounting for 12.3%, and 11729 adolescents belong to non-nocturnal sleep, accounting for 87.7%. The evening-type sleep group has more males, with a younger average age and a higher BMI (Table 3).

### **Multi-element analysis of obesity in adolescents of different sexes**

In this study, the obesity rate of males is higher than that of females, and there are differences in the influencing factors of obesity between male and female adolescents. According to the regression analysis on obese male and female adolescents, it is found that self-assessment family poverty is a risk factor of 1.280 (1.125-1.456) in female obesity, while the age is a protective factor of 0.818 (0.783-0.854). Among male obesity, having no resident experience within six months is a risk factor of 1.337 (1.153-1.550), and evening-type sleep is a risk factor of 1.250 (1.067-1.468). The age is a protective factor of 0.903 (0.863-0.944) (Table 4).

### **Interaction of adolescent sleep rhythms and gender on obesity**

The univariate analysis results in this study indicate that adolescent obesity has statistically significant differences in age, gender, only child status, residential experience within six months, family economic status, and sleep rhythm ( $P < 0.05$ ). To further investigate the role of sleep rhythm and gender in obesity, taking into account the collinearity between variables, this study selected age, only child status, family marital status, residential experience within six months, and family economic status as adjusting factors and incorporated them into the logistic regression model along with sleep rhythm, gender, and the interaction of the multiplication of sleep rhythm and gender. The results show that the interaction between gender and evening-type sleep has a significant impact on adolescent obesity by 1.222 (1.043-1.208) (Table 5).

## DISCUSSION

According to the "Report on the Nutrition and Chronic Disease Status of Chinese Residents (2020)," the obesity rate among teenagers aged 6-17 in China is 19.0%. This study calculated the BMI based on the self-reported height and weight of adolescents and used common Chinese standards to judge adolescent obesity. In contrast, the results of this study show that the obesity rate among adolescents is 22%, slightly higher than the national data on adolescent obesity. It may be because previous studies exhibit a high incidence of obesity among adolescents in developed regions or cities[7], while this paper focuses on Tianjin, a developed coastal city in eastern China. It is recommended to pay further attention to the issue of urban adolescent obesity and develop corresponding interventions, thus maintaining adolescent physical health.

In this study, the obesity rate of male adolescents is 25.1%, significantly higher than that of female adolescents, 18.9%. It is consistent with the studies of Fang *et al*[8] and Spinelli *et al*[9]. The reasons why female adolescents are less prone to obesity may be: (1) Male adolescents have exercise habits with a higher intensity level than female adolescents. High physical energy consumption can easily cause voracious appetites[27]; (2) Male adolescents have extroverted personalities, and their satiety center cannot receive timely feedback, leading to excessive energy intake[28]; and (3) In current Chinese social cognition, a slender body shape of females is regarded as beauty. Female adolescents pay high attention to their body shape and image and control their diet. Moreover, parents have higher requirements for female adolescents than male adolescents. They supervise female adolescents to prevent obesity while being tolerant of male adolescents. These factors decrease the risk of obesity in female adolescents. It indicates that male adolescents are a high-risk group for overweight and obesity. The issue of obesity among male adolescents should be emphasized, and corresponding

**Table 1 Comparison of obesity, overweight, and normal weight among adolescents by gender and age (n = 2942)**

Characteristic	Obesity	Overweight	Normal	P value	F/ $\chi^2$
Age (years), mean $\pm$ SD	14.94 (1.442)	15.22 (1.454)	15.30 (1.412)	0.000	69.996
Sex				0.000	231.522
Boy, n (%)	1692 (25.1)	1275 (18.9)	3778 (56.0)		
Girl, n (%)	1250 (18.9)	829 (12.5)	4550 (68.6)		
Sum, n (%)	2942 (22.0)	2104 (15.7)	8328 (62.3)		

**Table 2 Comparison of demographic information on obesity in adolescents of different gender (n = 2942)**

Characteristic		Sum obesity	Girl obesity	Boy obesity
One-child family	Yes, n (%)	925 (23.1) <sup>a</sup>	278 (18.5)	647 (25.8)
	No, n (%)	2017 (21.5)	972 (19.0)	1045 (24.6)
School residential experience within 6 mo	Yes, n (%)	695 (17.3) <sup>c</sup>	317 (15.4) <sup>c</sup>	378 (19.38) <sup>c</sup>
	No, n (%)	2247 (24.0)	933 (20.4)	1314 (27.5)
Parents' marital status	Normal, n (%)	2560 (21.8)	1061 (18.4) <sup>a</sup>	1499 (25.1)
	Single parent or remarriage, n (%)	382 (23.3)	189 (22.0)	193 (24.8)
Family economic situation	Family economic prosperity, n (%)	235 (21.3) <sup>a</sup>	89 (17.1) <sup>a</sup>	146 (25.0)
	No family economic pressure, n (%)	2189 (21.6)	924 (18.4)	1265 (24.9)
	High family economic pressure, n (%)	518 (24.0)	237 (21.9)	281 (26.1)
Sleep rhythm	ITs, n (%)	2327 (21.4) <sup>b</sup>	1012 (18.6)	1315 (24.3) <sup>a</sup>
	MTs, n (%)	200 (22.9)	76 (18.4)	124 (27.0)
	ETs, n (%)	415 (25.2)	162 (21.2)	253 (28.7)

<sup>a</sup>P < 0.05.

<sup>b</sup>P < 0.01.

<sup>c</sup>P < 0.001.

MTs: Morning-type sleep; ETs: Evening-type sleep; ITs: Intermediate-type sleep.

**Table 3 Comparison of sleep rhythm in age, gender and body mass index (n = 13374)**

Characteristic	Sleep rhythm			P value
	ITs	MTs	ETs	
Age (years), mean $\pm$ SD	15.23 (1.433)	14.94 (1.461)	15.19 (1.403)	0.000
BMI (kg/m <sup>2</sup> ), mean $\pm$ SD	23.41 (7.022)	23.46 (7.160)	23.81 (7.504)	0.000
Sex				0.005
Boy, n (%)	5403 (80.1)	460 (6.8)	882 (13.1)	
Girl, n (%)	5454 (82.3)	412 (6.2)	763 (11.5)	
Sum, n (%)	10857 (81.2)	872 (6.5)	1674 (12.3)	

MTs: Morning-type sleep; ETs: Evening-type sleep; ITs: Intermediate-type sleep; BMI: Body mass index.

interventions should be taken.

From the regression analysis on the obesity of male and female adolescents, age is a protective factor in both males and females. The overall obesity rate shows a decreasing trend with age. Chen *et al*[29] proposed the same viewpoint in the survey on the prevalence of overweight and obesity in Chinese children and adolescents, believing that the obesity rate generally declined with age[29]. Wang *et al*[30] confirmed it by analyzing the trend of overweight and obesity among students aged 7-18 in Shanghai from 1985 to 2014. The possible reason is that as children grow older, they become

**Table 4 Multi-element analysis of obesity in adolescents of different sexes**

Characteristic	Characteristic	AOR (95%CI)	P value
Girl	Age	0.818 (0.783-0.854)	0.000
	Self-evaluation of family experience pressure	1.280 (1.125-1.456)	0.000
Boy	Age	0.903 (0.863-0.944)	0.000
	No school residential experience within 6 mo	1.337 (1.153-1.550)	0.000
	Sleep rhythm (ITs)		
	(MTs)	1.095 (0.882-1.360)	0.412
	(ETs)	1.250 (1.067-1.468)	0.006

MTs: Morning-type sleep; ETs: Evening-type sleep; ITs: Intermediate-type sleep.

**Table 5 Interaction of adolescent sleep rhythms and gender on obesity**

Characteristic	AOR (95%CI)	P value
Age	0.869 (0.841-0.898)	0.000
Self-evaluation of family experience pressure	1.173 (1.077-1.1.278)	0.000
Student's way of study	1.223 (1.095-1.368)	0.000
Sex	1.406 (1.292-1.530)	0.000
Sex*ITs		
Sex*MTs	1.028 (0.930-1.136)	0.590
Sex*ETs	1.122 (1.043-1.208)	0.002

MTs: Morning-type sleep; ETs: Evening-type sleep; ITs: Intermediate-type sleep.

conscious of their physical appearance and exercise more. It indicates that obesity in the young age group should be taken seriously.

The results of the univariate analysis show that in the obesity rate of female adolescents, there are statistically significant differences in residential experience within six months, parent's marital status, and family economic situation, while for the obesity rate of male adolescents, residential experience within six months and sleep rhythm have statistically significant differences. The results of the multivariate analysis show that family poverty is a risk factor for obesity in female adolescents, and evening-type sleep rhythm and no residential experience in the past six months are risk factors for obesity in male adolescents. There are significant differences in influencing factors between the two groups. Gutiérrez-Cuevas *et al*[4] comprehensively summarized the risk factors for obesity; low income, poverty, low educational attainment, unemployment, and socioeconomic status on the socioeconomic side; and sleep problems on the behavioral side are all relevant risk factors for obesity[4]. In China, the possible reason is that female adolescents are sensitive to economic pressure and prone to developing a sense of inferiority. They will take eating as a way to relieve stress, thus leading to obesity. On the contrary, male adolescents are different in terms of economic pressure sensitivity or stress management methods, and the incidence of obesity is relatively low. These explanations need to be verified in future research. Without residential experience in the past six months is a risk factor for male obesity, possibly due to the better living conditions and higher nutritional status of male adolescents living at home compared to those living in school. Female adolescents do not have a significant correlation with this factor in multivariate analysis, which may be related to the different attitudes of parents towards male and female adolescents' obesity mentioned earlier.

Previous studies have shown that inadequate sleep duration and abnormal sleep rhythms can be stressful to an individual's health and have adverse health consequences, such as an increased risk of developing obesity[31]. For example, it has been found that there is a strong correlation between less than six hours of sleep per day and the incidence of obesity[32]. One explanation is that individuals do not control their energy intake well during periods of sleep deprivation, and the increase in energy intake is greater than energy expenditure, which in turn contributes to the individual's weight gain[33]. A possible explanation for the lack of sleep leading to enhanced hedonic feeding is the activation of the underlying endogenous cannabinoid system[34,35].

It is found in this study that among adolescents, evening-type sleep rhythm significantly affects male obesity but has no apparent impact on female obesity. First, evening-type sleep can alter the timing and frequency of food intake[36] while reducing physical activity during the day[37], which may cause adolescent obesity. This study shows that the male gender and evening-type sleep rhythm have an interactive effect on adolescent obesity. The combination of the two

factors can easily promote adolescent obesity. The possible reasons are that, on the one hand, male adolescents are more resistant to parental constraints and less willing to listen to their parents' opinions. They may insist on some unhealthy lifestyle they prefer, such as using their phones for entertainment for a long time in the evening and eating a large amount of food. On the other hand, unlike that of female adolescents, parents' management of male adolescents adopts a permissive attitude. The combined effect of the two promotes the occurrence of obesity. In the intervention of adolescent obesity, attention should be paid to the development of plans for male adolescent evening-type sleep groups.

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## CONCLUSION

From this study, the obesity rate of male adolescents is higher than that of female adolescents, and older adolescents have a protective effect on obesity of different genders. Family poverty plays a vital role in the obesity of female adolescents. In contrast, it slightly affects male adolescent obesity. The absence of residential experience within six months and evening-type sleep rhythm significantly influence male adolescent obesity but have no remarkable effect on the obesity of female adolescents. Further analysis suggests that sleep rhythm and gender have an interactive effect on adolescent obesity, and the combination of evening-type sleep and male sexuality promotes the development of adolescent obesity. In formulating measures to prevent adolescent obesity, attention should be paid to the obesity problem of male adolescents with evening-type sleep.

### **Limitations**

Firstly, this study was a cross-sectional survey study and could not draw a clear causal relationship between sleep rhythms and obesity. Secondly, this study is a questionnaire survey, which is not precise enough to investigate sleep rhythms and obesity, and wearable devices can be used to investigate sleep rhythms in future surveys.

## ARTICLE HIGHLIGHTS

### **Research background**

The obesity rate of adolescents is gradually increasing, which seriously affects their mental health, and sleep plays an important role in adolescent obesity.

### **Research motivation**

This study provides a theoretical basis for formulating interventions for adolescent obesity.

### **Research objectives**

This paper investigates the relationship between sleep rhythm and obesity among adolescents and further explores the interactive effect of sleep rhythm and gender on adolescent obesity, providing a theoretical basis for developing interventions for adolescent obesity.

### **Research methods**

Questionnaire on the current situation.

### **Research results**

Logistic regression analysis shows a correlation between sleep rhythm and adolescent obesity. Evening-type sleep rhythm can increase the risk of obesity in male adolescents [1.250 (1.067-1.468)], but the effect on female obesity is not remarkable. Further logistic regression analysis in the overall population demonstrates that the interaction between evening-type sleep rhythm and the male gender poses a risk of adolescent obesity [1.122 (1.043-1.208)].

### **Research conclusions**

The study suggests an interactive effect of sleep rhythm and gender on adolescent obesity, and the combination of evening-type sleep and the male gender promotes the development of adolescent obesity.

### **Research perspectives**

Future research should carry out the longitudinal tracking of sleep rhythm and obesity to determine the causal relationship between adolescent sleep rhythm and obesity. Physical measurements of adolescent sleep rhythm can be conducted for accurate investigation. Furthermore, the characteristics of adolescent night activities and the impact of eating late on obesity should be explored.

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## FOOTNOTES

**Co-first authors:** Nan-Nan Wu and Guo-Li Yan.

**Author contributions:** Wu NN and Yan GL contribute equally; Wu NN and Yan GL was responsible for literature design of the study, acquiring and analyzing data from the survey, and writing of the actual manuscript; Zhang HY was responsible for article review and article writing; Zhang HY were responsible for data statistics; Sun L, Hou M and Xu GM were responsible for article revision.

**Institutional review board statement:** This study was reviewed and approved by the Ethics Committee of Anding Hospital in Tianjin, No. 2021-42.

**Informed consent statement:** All study participants, or their legal guardian, provided informed written consent prior to study enrollment.

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**Country/Territory of origin:** China

**ORCID number:** Nan-Nan Wu [0000-0002-8754-9367](https://orcid.org/0000-0002-8754-9367); Guang-Ming Xu [0000-0001-5116-9656](https://orcid.org/0000-0001-5116-9656).

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**L-Editor:** A

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