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Association between Depression and Overweight or Obesity in Chinese Adolescents: A Cross-sectional Study

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3	Association between Depression and Overweight or Obesity in Chinese
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Abstract

Objective: Based on a nationally representative adolescent sample, we sought to examine the effect of depression on the prevalence of overweight or obesity and whether this effect was moderated by gender.

Methods: One thousand and eighty-one adolescents from the China Family Panel Studies (CFPS) participated in our study. Depression in adolescents was assessed using the Center for Epidemiologic Studies Depression Scale (CES-D). An ordered logistic regression model was used to quantify its association with overweight or obesity. Analyses were performed for the total group, and separately for males and females.

Results: The prevalence of depression in Chinese adolescents was 23.22%. Depression (CES-D≥16) was significantly associated with overweight or obesity (OR=1.47, 95%CI: 1.14-1.91) after adjustment for personal, household, and regional confounders. Among four sub-dimensions of depression, depressed affect and lack of positive affect were significantly associated with increases in the odds of overweight or obesity. In females, only lack of positive affect was significantly associated with overweight or obesity, whereas, the estimated effects of all the other measures of depression on overweight or obesity were positive in males.

Conclusions: These findings provide evidence that depression is associated with overweight or obesity among adolescents in China, especially among males.

Key words: Depression; Overweight or obesity; China

Strengths and limitations of this study

- Based on a nationally representative sample, we demonstrated the association between depression and obesity in Chinese adolescents the gender differences in these associations additionally
- Our results provide additional evidence from different cultures for the relationship between depression and obesity among adolescents
- The cross-sectional nature of the dataset used in the present study did not allow us to explore of the causal relationship between depression and obesity

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Overweight and obesity in adolescents have become a major public health concern worldwide since the prevalence of overweight and obesity in adolescents has increased substantially over the last decades^{1,2}, especially in the developing world³. For example, in China, there is a significant and continuous increase in the prevalence of obesity in adolescents, with an approximate 9% increase per year between 1985 and 2010⁴. In another large developing country, India, the overall prevalence of overweight or obesity in children is as high as 23.9% according to the WHO classification⁵. Considering the facts that overweight or obese adolescents are more likely to remain overweight or obese after growing up ⁶ and that obesity is associated with many poor health outcomes including cardiovascular disease and metabolic syndrome ^{7 8}, studies identifying risk factors of adolescent obesity will contribute to developing effective and efficient intervention strategies.

Recently, besides physical inactivity and excessive food intake ⁹, many researchers started investigating the effects of psychological features such as depression on the development of obesity ¹⁰⁻¹⁷. Although symptoms of depression might lead to obesity theoretically because they were closely related to several key obesogenic risk factors such as physical activity, daily screen time, and dietary intake ¹⁸, the empirical studies failed to reach a consensus. For example, depressed adolescents are at increased risk for the development and persistence of obesity in the United States ¹⁴, while for Korean adolescents, overweight or obesity is not related to high levels of depressive symptoms ¹⁹.

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One possible reason is that depression is multifaceted, including somatic ²⁰, cognitive, and affective dimensions ²¹. Dimensions of depression might affect adolescent obesity in different ways, and their effects possibly differ across different populations. Another reason could be the mediation role of cultural factors ²². The arguments above have not been confirmed in other studies and therefore cannot be generalized to the present study as existent studies were conducted in Western countries ^{11 14 16 17}. So far, in China, several studies have been conducted to confirm the role of overweight or obesity in the development of depressive symptoms among young adolescents ^{23 24}. However, the effect of depression on the prevalence of overweight or obesity and whether this effect was moderated by gender is still unclear. Therefore, more investigations using valid and reliable measures of depression based on well-representative data from Asian countries are needed.

The association between depression and obesity in adolescents was of particular interest in the present study. By using a nationally representative sample of Chinese adolescents and a standardized self-reported scale of depression, we aimed to examine 1) whether depression was associated with overweight or obesity; 2) whether dimensions of depression differed in their association with overweight or obesity; and 3) gender differences in these associations additionally.

Methods

Data source

The data used in this study was obtained from the China Family Panel Studies

(CFPS), which was a general-purpose, nationally representative, longitudinal social survey conducted by the Institute of Social Science Survey (ISSS) at Peking University in collaboration with the Survey Research Center at the University of Michigan²⁵. The study was approved by the Biomedical Ethics Committee of Peking University (Ref. IRB00001052-14010). Extensive information on not only economic characteristics, but also health status was collected ²⁶. In the second wave in 2012, the Center for Epidemiologic Studies Depression Scales (CES-D) was introduced into questionnaires for assessing depression among adolescents aged 10 to 12 years, which was the interest of the present study. All relevant variables were extracted from three databases of CFPS. For instance, variables of age, gender, height, weight, ethnicity, duration of breastfeeding, birth weight, and region were from the child database; maternal height, weight and education level were from the adult database; and household income level was from the family database. Then, we matched the three kinds of variables with a unique ID code for each family. Those 1,081 ten- to 12-year-old adolescents with complete information on CES-D and overweight or obesity status formed our sample.

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Measures Overweight and Obesity

Based on caregiver-reported height and weight, body mass index (BMI, kg/m²) was calculated. Then, according to the criteria of Working Group on Obesity in China, adolescents were categorized as being obese if the BMI was greater than or equal to the 95th percentile for age and gender or as being overweight if BMI was greater than or equal to the 85th percentile but less than the 95th percentile ²⁷.

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Depressive symptoms

Ten- to 12-year-old CFPS participants were investigated with the help of the Center for Epidemiologic Studies Depression Scales (CES-D), which was designed to assess the frequency of depressive symptoms in the previous week and has been used extensively with adolescents ²⁸. CES-D contains 20 Likert-type items (on a four-point scale ranging from 0=Never to 3= Usually). The total scores, ranging from 0 to 60, was the sum of all the responses to 20, items among which four items (Item 4, 8, 12 and 16) were reversely scored. Higher values represented higher frequency of symptoms of depression. Additionally, the findings of factor analysis implemented by the CFPS group, consistent with Western studies ²⁶⁻³⁰, showed that the four sub-dimensions of depressive symptoms (depressed affect, lack of positive affect, somatic symptoms and interpersonal problems) can be identified. We therefore had three measures of psychological depression: subjects who meet the cutoff point for depression (CES-D≥16) ³⁰; total CES-D scores; and four sub-dimensions of CES-D.

Statistical analysis

Only the adolescents aged between 10 and 12 years with complete information on BMI and CES-D were included in the current study. Further exclusion of those with extreme values in BMI (>40 kg/m² or <10 kg/m²) formed the final sample of 1,081 adolescents. The missing values on confounders were imputed by using the multiple imputation technique ³¹.

We ran separate ordered logistic regression models for each measure of depression.

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We first ran the regression models without controlling for any confounders (Model 1). Model 2 controlled for a series of personal characteristic covariates of adolescents: gender (reference group: females) and age (in years), ethnicity (reference group: Han ethic), duration of breastfeeding (reference group=None breastfeeding), and birthweight (reference group: normal birthweight). In Model 3, we further adjusted for three covariates on the household level—maternal BMI (kg/m²), maternal education level (reference group: no schooling), and household income per capita (in 10³ RMB Yuan). In Model 4, we additionally introduced the interaction term between two confounders indicating where the adolescents were from-rural areas (reference group: urban areas) and regions (reference group: West). Finally, in order to examine the gender difference in the association between depressive symptoms and weight status, we reran all models after additionally introducing the interaction term between primary predictor variables and gender. Standard errors were clustered at the region level. Non-significance of test statistics of the parallel regression assumption for each model suggested that ordered logistic models might be appropriate. A two-sided P < 0.05 was considered statistically significant. All analyses were performed using Stata 13³².

Patient and Public Involvement

Patients were not involved in the development of the study. The results will be published in a peer-reviewed journal, but there is no plan to specifically disseminate the findings to study participants.

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Results

Descriptive statistics of 1,081 adolescents aged between 10 and 12 years from China in Table 1 shows that nearly one-fourth (23.22%) of adolescents were depressed. In this special group, the prevalence of overweight and obesity were 13.15% and 11.95% respectively, which were significantly higher than those in the non-depression group (9.88% and 6.75% respectively; $\chi^2(2)=10.20$, p=0.006). As seen in table 1, the summary statistics also indicated that those from ethnic minority groups, rural areas, and Western China were more likely to be depressed. Although maternal educational level was significantly associated with depression symptoms, duration of breastfeeding, birthweight, maternal BMI, and household income per capita were irrelevant.

As the results of Model 1 in Table 2 shows, the presence of depressive symptoms (CES-D \geq 16) was significantly associated with overweight or obesity (OR = 1.70; 95% CI = 1.57-1.85). Even after controlling for personal, household, and regional confounders, the odds ratio (=1.47, 95%CI=1.14-1.91) was still significant on the 0.01 level (Model 4). When depression was measured by the CES-D scores, the mean scores of adolescents who were overweight or obese were 32.0±6.50 and 33.57±7.33, respectively. After introducing the confounders on the household level, the association between depression and overweight or obesity became non-significant. Among the four sub-dimensions of the depression, the estimated effect of depressed affect was the largest (Model 1, OR=1.07, 95% CI=1.05-1.10; Model 4, OR=1.06, 95% CI=1.02-1.10), followed by lack of positive affect (Model 1, OR=1.07, 95% CI=1.05-1.10; Model 4, OR=1.06, 95% CI=1.02-1.10), followed by lack of positive affect (Model 1, OR=1.07, 95% CI=1.05-1.10; Model 4, OR=1.04, 95% CI=1.02-1.05). However, somatic symptoms and interpersonal difficulties did not affect overweight or

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obesity significantly in adolescents.

The results in Table 3 demonstrated the gender difference in the association between depression and weight status. Only male adolescents with depression, but not females, had a higher risk of overweight or obesity irrespective of whether depression was measured with a binary variable (CES-D \geq 16) or a continuous one (the CES-D scores), and irrespective of which confounders were controlled for. Specifically, compared with non-depressed male adolescents, the odds ratio of overweight or obesity versus normal weight (or obesity versus over- or normal-weight) for the depressed group was 1.48 (95% CI: 1.24-1.76). When depression was measured using the CES-D scores, a one-unit increase in CES-D scores was correlated with a 2% increase in the odds of overweight or obesity (OR=1.02, 95% CI: 1.01-1.04), which corresponded to each standard deviation increase in CES-D scores (31.45±6.61), resulting in a 13.22% increase in the risk of overweight or obesity. Additionally, the detailed analysis showed that the estimated effect of the depressed affect on obesity was the same for male and female adolescents in the magnitude, but only significant for males (OR=1.06, 95% CI: 1.01-1.11). Similarly, somatic symptoms and interpersonal difficulties were only associated with males' obesity (OR=1.04, 95% CI: 1.01-1.07 and OR=1.14, 95% CI: 1.02-1.27), although marginally significant. The results of the fully adjusted model (Model 4) showed that the effect of lack of positive affect on obesity was only significant for female adolescents on the 0.01 level.

Discussion

In this study, with the help of a nationally representative dataset, we demonstrated

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that depression (CES-D≥16) was a significant risk factor of overweight or obesity among adolescents in China independent of a wide array of confounding variables. Dimensions of depressed affect and lack of positive affect, rather than somatic symptoms or interpersonal difficulties, were significantly associated with overweight or obesity. Moreover, the association were gendered-Whether depressed, depressed affect, somatic symptoms and interpersonal difficulties were all significantly correlated with obesity among male adolescents, whereas lack of positive affect was only significant among female adolescents.

In the present study, the increased odds of overweight or obesity with depression among Chinese adolescents was consistent with the cross-sectional results of an earlier study of American adolescents indicating that depression and obesity with onsets by early adolescence (by age 14) were concurrently associated³³. Another cross-sectional study of adults also suggested that depression was a strong and statistically significant predictor of BMI in the Supplemental Nutrition Assistance Program (SNAP)¹³. However, some studies failed to document any significant association¹⁶ ¹⁹ ²². The possible reason for the inconsistencies between depression and obesity might be due to differences in sociodemographic characteristics of the samples, assessments of depression and measurements of height and weight. For example, the analysis of present study suggested that only depressed affect and lack of positive affect were significantly associated with overweight or obesity. Therefore, the estimated results were prone to be significant if the instrument of depression emphasizing these two dimensions was

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Consistent with our findings, a cross-sectional study in 4150 US adolescents indicated that depression was significant associated with obesity among males rather than females ¹⁶. However, several studies demonstrated that the association between depression and obesity was only significant among female adolescents, which needs further scientific attention. For example, a meta-analysis indicated that female adolescents with depression were 2.57 times more likely to have obesity status or weight gain at follow-up measurements ¹². Another community-based study found that for females, a history of depression was associated with greater yearly gains in body mass index z score (BMIz) compared with females without a history of depression, whereas this association was not observed in males ¹¹. Again, the reason could be that the association between each dimension of depression and obesity was also affected by gender. When the instrument of depression focused more on dimensions of depressed affect, somatic symptoms, or interpersonal difficulties, the results obtained were likely to be significant among male adolescents. In contrast, the estimates were prone to be significant among females if the instrument mainly emphasized the dimension of lack of positive affect. In addition, considering the fact that positive affect could occur even if elevated levels of negative affect presented ³⁴, future studies on the relationship between depression and obesity should comprehensively evaluate the obesity effect of all dimensions of depression.

Our findings were similar to those reported in studies conducted in some Western countries ¹¹ ¹³ ¹⁶ ¹⁷ ³³. However, among Asian adolescents, the association between depression and overweight or obesity had not been consistently confirmed, and cultural factors were considered to be one of the possible reasons argued by researchers ¹⁹ ²²⁻²⁴. However, the present study suggests that the mediation effect of culture on the association between depression and obesity was little, if any, in contemporary China. After China embraced an economic reform and open door policy in 1978, Chinese people started to be exposed to a multicultural environment. As a result, the cultural gap between China and Western countries narrowed due to adapting behaviors and reshaping in preference. For example, new generations in China do not give as much preference sons to males as their ancestors did. Thus, it is not surprising that the findings of the present study are consistent with those of studies in Western countries.

We conducted a nationally representative investigation of depression and overweight or obesity among Chinese adolescents independent of a wide array of confounding variables. However, several major limitations needed to be acknowledged. First, the cross-sectional nature of the dataset used in the present study did not allow us to address the issue of causality. Second, we have focused on the effects of depression on the development of obesity in the present study. However, we admit that the possible reverse causality might bias our estimation because of, as recent longitudinal studies highlighted, the bidirectional association between depression and obesity ³⁵⁻³⁷. The clarification of whether psychiatric disorders and psychological problems are a cause or a consequence

of childhood obesity among Chinese adolescent needs future longitudinal studies, which could address the reverse causality problem. Third, the measurement of overweight or obesity was calculated based on the caregiver-reported height and weight, which might not be accurate. However, studies confirmed that the errors in these measurements were limited and did not lead to misclassification with regard to overweight or obesity in adolescent samples ¹⁴ ³⁸⁻⁴⁰. Nevertheless, we have applied appropriate analytic procedures to collect data comprehensively from a large, nationally representative cohort study and demonstrated that depression, particularly dimensions of depressed affect and lack of positive affect , might be a risk factor of obesity among Chinese adolescents and these influences could be modified by gender.

Conclusions

If depression is indeed a risk factor for being overweight or obese, then interventions aimed at improving mental health in Chinese adolescents could have major public health implications if they help prevent becoming overweight or obese. Considering the increasing prevalence of obesity among adolescents worldwide, it is critical to recognize not only the physiological but also the psychological characteristics among overweight and obese adolescents and to design corresponding interventions to promote both their physical and mental well-being in the current obesogenic environment.

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University.

Conflict of Interest

The authors declared no potential conflicts of interest with respect to the research,

authorship and publication of this article.

Authors' Contribution

Study design: Deliang Wen; Zhongyi Zhao

Analysis of data: Ning Ding, Yang Liu

Interpretation of data: Zhongyi Zhao, Shenzhi Song

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	Depressed	Non-depressed	
	(CES-D≥16)	(CES-D<16)	p- values
	n(%)	n(%)	
Weight status			0.006
Normal weight	188(74.90)	692(83.37)	
Overweight	33(13.15)	82(9.88)	
Obese	30(11.95)	56(6.75)	
Male	128(51.00)	432(52.05)	0.770
Age (year)			0.041
10	83(33.07)	257(30.96)	
11	95(37.85)	262(31.57)	
12	73(29.08)	311(37.47)	
Ethnic minorities ^a	51(20.32)	65(7.86)	0.000
Duration of breastfeeding ^b			0.411
None	14(5.58)	54(6.15)	
0-6 months	34(13.55)	100(12.06)	
6-12 months	113(45.02)	370(44.63)	
12-18 months	47(18.73)	192(23.16)	
>18 months	43(17.13)	113(13.63)	
Birthweight ^c			0.249
Low (≤2.5 kg)	8(4.79)	56(8.10)	
Normal (2.5-4 kg)	154(92.22)	606(87.70)	
High (≥4 kg)	5(2.99)	29(4.20)	
Maternal educational level ^d			0.000
No school	99(45.83)	186(25.10)	
Primary school	57(26.39)	197(26.59)	
Middle school	57(17.59)	223(30.09)	
High school or higher	22(10.19)	135(18.22)	
Rural areas	185(73.71)	478(57.59)	0.000
Region			0.000
West	128(51.00)	236(28.43)	
East	69(27.49)	254(30.60)	
Central	43(17.13)	223(26.87)	
Northeast	11(4.38)	117(14.10)	
Total	251(23.22)	830(76.78)	

Note: BMI = body mass index; ^a Sample size is 1078; ^b Sample size is 1080; ^c Sample size is 858; ^d Sample size is 957.

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Table 2 The association between depressive symptoms and weight status

	Model 1	Model 2	Model 3	Model 4
Variable	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Whether depressed	1.70(1.57,1.85)***	1.63(1.35,1.97)***	1.48(1.11,1.97)**	1.47(1.14,1.91)**
CES-D scores	1.04(1.02,1.05)***	1.03(1.01,1.05)**	1.02(0.99,1.05)	1.02(1.00,1.05)
Depressed affect	1.07(1.05,1.10)**	1.07(1.04,1.10)***	1.06(1.01,1.10)*	1.06(1.02,1.10)**
Lack of positive affect	1.07(1.05,1.10)***	1.06(1.04,1.07)***	1.04(1.03,1.06)***	1.04(1.02,1.05)***
Somatic symptoms	1.04(0.99,1.10)	1.03(0.96,1.10)	1.02(0.94,1.11)	1.02(0.95,1.10)
Interpersonal difficulties	1.17(1.04,1.32)**	1.14(0.98,1.33)	1.11(0.92,1.33)	1.11(0.92,1.33)

1. 1.02 <u>3.02° 1.14(0.92</u> . Depression Scates, No. ation of breastfeeding and bin. .ation and household income per cal. interaction between regions and urban .oti Note: CES-D = Epidemiologic Studies Depression Scales; Model 1: no adjustments; Model 2: adjusted for age, gender, ethnic minority, duration of breastfeeding and birthweight; Model 3: additionally adjusted for maternal BMI, maternal education and household income per capita on the base of Model 2; Model 4: additionally adjusted for the interaction between regions and urban areas on the base of Model 3; * p<0.05; ** p<0.01; ***p<0.001.

Table 3 Gendered difference in the association of CES-D scores and weight status

Veriable	Conder	Model 1	Model 2	Model 3	Model 4
Variable	Gender	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Whether depressed	Male	1.69(1.35,2.13)***	1.64(1.36,1.97)***	1.49(1.25, 1.76)***	1.48(1.24,1.76)***
	Female	1.81(1.21,2.70)**	1.63(0.95,2.81)	1.47(0.76,2.85)	1.46(0.76,2.80)
CES-D scores	Male	1.04(1.03,1.06)***	1.03(1.01,1.04)***	1.02(1.00,1.04)*	1.02(1.01,1.04)**
	Female	1.02(1.00,1.04)*	1.03(0.99,1.08)	1.02(0.97,1.08)	1.02(0.97,1.08)
Depressed affect	Male	1.10(1.07,1.12)***	1.07(1.03,1.11)***	1.06(1.01,1.10)**	1.06(1.01,1.11)**
	Female	1.03(0,98,1.07)	1.07(0.98,1.16)	1.06(0.95,1.17)	1.06(0.96,1.16)
Lack of positive affect	Male	1.10(1.08,1.13)***	1.03(1.01,1.05)**	1.02(0.98,1.06)	1.02(0.98,1.06)
	Female	1.03(0.98,1.09)	1.09(1.04,1.15)***	1.08(1.03,1.13)***	1.08(1.03,1.13)**
Somatic symptoms	Male	1.06(1.01,1.12)*	1.04(1.02,1.07)***	1.04(1.00,1.07)	1.04(1.01,1.07)*
	Female	0.99(0.94,1.05)	1.01(0.87,1.16)	1.00(0.85,1.16)	1.00(0.86,1.16)
Interpersonal difficulties	Male	1.27(1.10,1.46)**	1.25(1.04,1.49)*	1.13(1.02,1.25)*	1.14(1.02,1.27)*
	Female	0.99(0.89,1.11)	1.15(1.06,1.26)	1.07(0.75,1.51)	1.05(0.74,1.49)

Note: CES-D = Epidemiologic Studies Depression Scales; Model 1: no adjustments; Model 2: adjusted for age, gender, ethnic minority, duration of breastfeeding and birthweight; Model 3: additionally adjusted for maternal BMI, maternal education and household income per capita on the base of Model 2; Model 4: additionally adjusted for the interaction between regions and urban areas on the base of Model 3; * p<0.05; ** p<0.01; ***p<0.001.

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Association between Depression and Overweight in Chinese Adolescents: A Cross-sectional Study

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Abstract

Objective: Based on a nationally representative adolescent sample, we examined the association of depression on the prevalence of overweight or obesity and whether this association was moderated by gender.

Methods: There were 1081 adolescents from the China Family Panel Studies that participated in our study. Depression in adolescents was assessed using the Center for Epidemiologic Studies Depression Scale (CES-D). Ordered logistic regression model was used to quantify its association with overweight or obesity. Analyses were performed for the total group, and separately for males and females.

Results: The prevalence of depression in Chinese adolescents was 23.22%. Depression (CES-D \ge 16) was significantly associated with overweight or obesity (OR = 1.47, 95% CI: 1.14–1.91, p=0.004) after adjustment for personal, household, and regional confounders. Among four sub-dimensions of depression, depressed affect and lack of positive affect were significantly associated with increases in the odds of overweight or obesity. In females, only lack of positive affect was significantly associated with overweight or obesity, whereas the estimated associations of all other measures of depression on overweight or obesity or obesity were positive in males.

Conclusions: These findings provide evidence that depression is associated with overweight or obesity among adolescents in China, especially among males.

Key words: Depression; Overweight or obesity; China

Strengths and limitations of this study

- Our study was based on a nationally representative sample of Chinese adolescents, with adjustment of a wide range of important confounders, which makes the results relatively robust.
- Our study is one of the few studies that tend to clarify the association between depression and overweight or obesity and the gender differences in these associations additionally.
- The cross-sectional design of our study limits the value in supporting causal effects and generalisability of the results.
- Information on height and weight was obtained from subjective report, which, to some extent, resulted in response bias.

Introduction

Overweight and obesity in adolescents have become major public health concerns worldwide since their prevalence has increased substantially over recent decades ^{1 2}, especially in the developing world ³. For example, in China, there has been a significant and continuous increase in prevalence of obesity in adolescents, with an approximate 9% annual increase during 1985–2010 ⁴. In another large developing country, India, the overall prevalence of overweight or obesity in children is as high as 23.9% according to the WHO classification ⁵. Considering that overweight or obese adolescents are more likely to remain overweight or obese after maturing ⁶ and that obesity is associated with many poor health outcomes, including cardiovascular disease and metabolic syndrome ⁷⁸, studies identifying risk factors of adolescent obesity will contribute to developing effective and efficient intervention strategies.

In addition to physical inactivity and excessive food intake ⁹, many researchers have begun investigating the effects of psychological features such as depression on the development of obesity ¹⁰⁻¹⁸. Although symptoms of depression might lead to obesity theoretically because they are closely related to several key obesogenic risk factors – such as physical activity, daily screen time, and dietary intake ¹⁹, – empirical studies have not reached a consensus. For example, whether in clinical or non-clinical adolescent samples, depressed adolescents are at increased risk for development and persistence of obesity in the United States ¹⁴ ²⁰, but for Korean ²¹ and Island Puerto Rican adolescents²², overweight or obesity is not related to high levels of depressive symptoms. One possible reason is that depression is multifaceted, including somatic ²³, cognitive, and affective

dimensions ²⁴. Dimensions of depression might affect adolescent obesity in different ways, and their effects possibly differ across different populations. Another reason could be the mediation role of cultural factors ²⁵. The arguments above have not been confirmed and therefore cannot easily be generalized to China as the existing studies were mostly conducted in Western countries ^{11 14 16 17}. There have been several studies in China to confirm the role of overweight or obesity in the development of depressive symptoms among young adolescents ^{26 27}. However, the association of depression on the prevalence of overweight or obesity and whether this association is moderated by gender remains unclear. Therefore, more investigations using valid and reliable measures of depression based on representative data from Asian countries are needed.

The association between depression and obesity in adolescents is of particular interest in the present study. By using a nationally representative sample of Chinese adolescents and a standardized self-reported scale of depression, we aimed to examine whether (1) depression was associated with overweight or obesity; (2) dimensions of depression differed in their association with overweight or obesity; and (3) there were gender differences in these associations.

Methods Data source

The data used in this study were obtained from the China Family Panel Studies (CFPS), which was a general-purpose, nationally representative, longitudinal social survey conducted by the Institute of Social Science Survey at Peking University in collaboration with the Survey Research Center at the University of Michigan ²⁸. Extensive information on not only economic characteristics, but also health status was collected ²⁹. In the second

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wave in 2012, the Center for Epidemiologic Studies Depression Scale (CES-D) was introduced into questionnaires for assessing depression among adolescents aged 10–12 years, which was the area of interest of the present study. All relevant variables were extracted from three CFPS databases: variables of age, gender, height, weight, ethnicity, duration of breastfeeding, birth weight, and region were from the child database; maternal height, weight, and education level were from the adult database; and household income level was from the family database. Then, we matched the three kinds of variables with a unique ID code for each family and 1081 10–12-year-old adolescents with complete information on CES-D and overweight or obesity status formed our sample.

Written informed consent was obtained from all participants and their parents prior to the study, and our analysis did not involve personal privacy information for adolescents and their parents. Ethical approval for the study was granted by the Biomedical Ethics Committee of Peking University (Ref. IRB00001052-14010). All research data is publicly available (http://www.isss.pku.edu.cn/cfps/index.htm).

Measures Overweight and obesity

Based on caregiver-reported height and weight, body mass index (BMI, kg/m²) was calculated. Then, according to the criteria of the Working Group on Obesity in China, adolescents were categorized as obese if BMI was greater than or equal to the 95th percentile for age and gender or as overweight if BMI was greater than or equal to the 85th percentile but less than the 95th percentile ³⁰.

Depressive symptoms

The Chinese version of the Center for Epidemiology Scale for Depression (CES-D),

which was previously validated ³¹ and is widely used in studies on Chinese adolescents ³², was used to determine if individuals had symptoms of depression. Participants were asked to indicate the frequency of each depressive symptom experienced in the past week. This self-report scale comprises 20 items, which are answered on a four-point Likert scale (0– 3 points). Among them, four items (Items 4, 8, 12 and 16) were reversely scored, which means the higher raw score they obtain, the less indicative of depression. The total score ranges from 0 to 60 with higher scores indicating higher levels of depression ³³ and a score of 16 represents the optimal cutoff point for identifying major depressive disorder ³⁴. Additionally, the findings of factor analysis implemented by the CFPS group, showed that the four sub-dimensions of depressive symptoms (depressed affect, lack of positive affect, somatic symptoms and interpersonal problems) can be identified. Therefore, we had three measures of psychological depression: subjects who meet the cutoff point for depression (CES-D≥16); total CES-D scores; and four sub-dimensions of CES-D.

Statistical analysis

Only adolescents aged 10–12 years with complete information on BMI and CES-D were included in the current study. Further exclusion of those with extreme BMI values (>40 or <10 kg/m²) formed the final sample of 1081 adolescents. The missing values on confounders were imputed by using the multiple imputation technique ³⁵. The convergence and dispersion trends for quantitative variables were expressed as mean ± standard deviation and qualitative variables were expressed as frequencies and percentages. The prevalence of depression was calculated and the sociodemographic variables were compared between adolescents with and without depressive symptoms. Continuous variables were compared using the independent-samples t test. Categorical variables were

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compared using Pearson's chi-square test or Fisher's exact test, as appropriate. A comparison of the total CES-D scores and the four sub-dimensions scores between different weight status groups was performed using one-way ANOVA.

We ran separate ordered logistic regression models for each measure of depression, where the cut-off for CES-D was used as a binary variable, and the total CES-D scores and the four sub-dimensions scores were regarded as continuous variables in the model input. In our ordered logistic regression model, the weight status as the dependent variable was grouped by normal BMI, overweight and obesity. We ran separate ordered logistic regression models for each measure of depression. We first ran the regression models without controlling for any confounders (Model 1). Model 2 controlled for a series of personal characteristic covariates of adolescents: gender (reference group: females) and age (in years), ethnicity (reference group: Han ethnic), duration of breastfeeding (reference group: no breastfeeding), and birthweight (reference group: normal birthweight). In Model 3, we further adjusted for three covariates at the household level: maternal BMI, maternal education level (reference group: no schooling), and household income per capita (in 10³ RMB Yuan). In Model 4, we additionally introduced the interaction term between two confounders indicating where the adolescents were from: rural areas (reference group: urban areas) and regions (reference group: West). Finally, to determine the gender difference in any association between depressive symptoms and weight status, we reran all models after additionally introducing the interaction term between primary predictor variables and gender. Standard errors were clustered at the region level. Non-significance of test statistics of the parallel regression assumption for each model suggested that

ordered logistic models might be appropriate. Two-sided p < 0.05 was considered significant. All analyses were performed using Stata 13 ³⁶.

Patient and Public Involvement

Patients were not involved in the development of the study. The results were intended for publication in a peer-reviewed journal, but there is no plan to specifically disseminate the findings to study participants.

Results

The descriptive statistics for the 1081 adolescents aged 10–12 years showed that nearly one-fourth (23.22%) of adolescents were depressed (Table 1). In this special group, the prevalence of overweight and obesity were 13.15% and 11.95%, respectively, which were significantly higher than those in the non-depression group (9.88% and 6.75% respectively; $\chi^2(2) = 10.20$, p = 0.006). The summary statistics also indicated that those from ethnic minority groups, rural areas, and Western China were more likely to be depressed (Table 1). Although maternal educational level was significantly associated with depression symptoms, duration of breastfeeding, birthweight, maternal BMI, and household income per capita were irrelevant. Table 2 shows the distribution of the total CES-D scores and the four sub-dimensions scores between different weight status groups (normal weight, overweight and obesity). We found an increasing trend for the CES-D scores by increasing weight status, although only the depressed affect and the interpersonal difficulties had significant associations with weight status (F_(2,1078) = 4.92, p = 0.001; F_(2,1078) = 3.16, p = 0.040, respectively).

The results of Model 1 (Table 3) showed that the presence of depressive symptoms

(CES-D \ge 16) was significantly associated with overweight or obesity (OR = 1.70, 95% CI: 1.57-1.85, p < 0.001). Even after controlling for personal, household, and regional confounders, the OR of 1.47 (95% CI: 1.14–1.91) was still significant at p < 0.01 (Model 4). The mean CES-D scores of adolescents who were overweight or obese were 32.0 ± 6.50 and 33.57 ± 7.33, respectively. After introducing the confounders at the household level, the association between depression and overweight or obesity became non-significant. Among the four sub-dimensions of depression, the estimated effect of depressed affect was the largest (Model 1, OR = 1.07, 95% CI: 1.05–1.10, p < 0.001; Model 4, OR = 1.06, 95% CI: 1.02–1.10, p = 0.003), followed by lack of positive affect (Model 1, OR = 1.08, 95% CI: 1.05–1.10, p < 0.001; Model 4, OR = 1.04, 95% CI: 1.03–1.05, p < 0.001). However, somatic symptoms and interpersonal difficulties did not affect overweight or obesity significantly in adolescents.

There was a gender difference in the association between depression and weight status (Table 4). Only male adolescents with depression, but not females, had a higher risk of overweight or obesity irrespective of whether depression was measured with a binary (CES-D \geq 16) or a continuous variable (CES-D scores), and irrespective of which confounders were controlled for. Specifically, compared with non-depressed male adolescents, the overweight or obesity versus normal weight (or obesity versus over- or normal-weight) for the depressed group had OR of 1.48 (95% CI: 1.24–1.76, p<0.001). When depression was measured using CES-D scores, a one-unit increase in score was correlated with a 2% increase in the OR of overweight or obesity (OR = 1.02, 95% CI: 1.01–1.04, p=0.004), which corresponded to each standard deviation increase in CES-D

scores (31.45 ± 6.61), resulting in a 13.22% increase in the risk of overweight or obesity. Additionally, detailed analysis showed that the estimated effect of the depressed affect on obesity was the same for male and female adolescents in magnitude, but only significant for males (OR = 1.06, 95% CI: 1.01–1.11, p=0.009). Similarly, somatic symptoms and interpersonal difficulties were only associated with male obesity (OR = 1.04, 95% CI: 1.01–1.07, p=0.013 and OR = 1.14, 95% CI: 1.02–1.27, p=0.020, respectively), although marginally significant. The fully adjusted model (Model 4) showed that the lack of positive affect only had a significant effect on obesity for female adolescents at p < 0.01.

Discussion

 Using a nationally representative dataset, we demonstrated that depression (CES-D ≥ 16) was a significant risk factor of overweight or obesity among adolescents in China independent of a wide array of confounding variables. Dimensions of depressed affect and lack of positive affect, rather than somatic symptoms or interpersonal difficulties, were significantly associated with overweight or obesity. Moreover, the association was gendered – whether depressed, depressed affect, somatic symptoms, and interpersonal difficulties were all significantly associated with obesity among male adolescents, but for female adolescents only lack of positive affect was significant.

In the present study, the increased odds of overweight or obesity with depression among Chinese adolescents was consistent with the cross-sectional results of an earlier study of American adolescents indicating that depression and obesity with onsets by early adolescence (by age 14) were concurrently associated ³⁷. Another cross-sectional study of adults also suggested that depression was a strong and significant predictor of BMI in Page 11 of 23

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the Supplemental Nutrition Assistance Program ¹³. However, some studies failed to document any significant association ¹⁶ ²¹ ²² ²⁵. The inconsistencies between depression and obesity might be due to differences in sociodemographic characteristics of samples, assessments of depression, and measurements of height and weight. For example, only depressed affect and lack of positive affect were significantly associated with overweight or obesity in the present study. Therefore, the estimated results were prone to be significant if an instrument of depression emphasizing these two dimensions was employed.

Consistent with our findings, a cross-sectional study in 4150 US adolescents indicated that depression was significantly associated with obesity among males rather than females ¹⁶. However, several studies demonstrated that the association between depression and obesity was only significant among female adolescents, which needs further scientific attention. For example, a meta-analysis indicated that female adolescents with depression were 2.57 times more likely to have obesity status or weight gain at follow-up measurements ¹². Another community-based study found that, for females, a history of depression was associated with greater yearly gains in BMI z-score compared to without a history of depression, whereas this association was not observed in males ¹¹. Again, the reason could be that the association between each dimension of depression and obesity was also affected by gender. When the instrument of depression focused more on dimensions of depressed affect, somatic symptoms, or interpersonal difficulties, the results were likely to be significant among male adolescents. In contrast, the estimates were prone to be significant among females if the instrument mainly emphasized the dimension of lack of positive affect. In addition, considering that positive affect could occur even if elevated

 levels of negative affect are present ³⁸, future studies on the relationship between depression and obesity should comprehensively evaluate the obesity effect of all dimensions of depression.

Our findings were similar to those reported in studies conducted in some Western countries ¹¹ ¹³ ¹⁶ ¹⁷ ³⁷. However, among Asian adolescents, an association between depression and overweight or obesity has not been consistently confirmed, and cultural factors were considered a possible reason ²¹ ²⁵⁻²⁷. However, the present study suggests little, if any, mediation effect of culture on the association between depression and obesity in contemporary China. After China embraced an economic reform and open door policy in 1978, the Chinese people began to be exposed to a multicultural environment. As a result, the cultural gap between China and Western countries narrowed due to adapting behaviors and reshaping preferences. For example, new generations in China do not give as much preference to male sons as their ancestors did. Thus, it is not surprising that the findings of the present study are consistent with those from Western countries.

We conducted a nationally representative investigation of depression and overweight or obesity among Chinese adolescents independent of a wide array of confounding variables. However, several major limitations need to be acknowledged. First, the crosssectional nature of the dataset used in the present study did not allow addressing the issue of causality. Second, we focused on the effects of depression on the development of obesity. However, the possible reverse causality might bias our estimation because, as recent longitudinal studies have highlighted, of the bidirectional association between depression and obesity ³⁹⁻⁴¹. The clarification of whether psychiatric disorders and

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psychological problems are a cause or a consequence of childhood obesity among Chinese adolescents requires future longitudinal studies, which could address the reverse causality problem. Third, the measurement of overweight or obesity was calculated based on caregiver-reported height and weight, which might be inaccurate. However, previous studies confirmed that errors in such measurements were limited and did not lead to misclassification with regard to overweight or obesity in adolescent samples ^{14 42-44}. Finally, due to the cross-sectional nature of our research data, we were unable to observe the short-term weight changes (including weight loss and gain) caused by depression, which was mediated by factors such as decreased appetite, sleep disorders, etc. Future studies with longitudinal design were needed to systematically observe the short-term and longterm associations between depressive symptoms and weight changes among Chinese adolescent. Nevertheless, we applied appropriate analytic procedures to collect data comprehensively from a large, nationally representative cohort study and demonstrated that depression, particularly dimensions of depressed affect and lack of positive affect, might be a risk factor of obesity among Chinese adolescents and these influences could be modified by gender.

Conclusions

If depression is indeed a risk factor for being overweight or obese, then interventions aimed at improving mental health in Chinese adolescents could have major public health implications if they help prevent adolescents becoming overweight or obese. Considering the increasing prevalence of obesity among adolescents worldwide, it is critical to recognize not only the physiological but also psychological characteristics among overweight and obese adolescents and to design corresponding interventions to promote both their physical and mental well-being in the current obesogenic environment.

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Conflict of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship and publication of this article.

Authors' Contribution

Study design: Deliang Wen; Zhongyi Zhao

Analysis of data: Ning Ding, Yang Liu

Interpretation of data: Zhongyi Zhao, Shenzhi Song

Data sharing

All research data is publicly available (http://www.isss.pku.edu.cn/cfps/index.htm).

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Table 1 Descriptive characteristics of the study subjects with and without depression

Depressed	Non-depressed	p-values

	(CES-D ≥ 16)	(CES-D < 16)	
	n (%)	n (%)	
Weight status			0.006
Normal weight	188 (74.90)	692 (83.37)	
Overweight	33 (13.15)	82 (9.88)	
Obese	30 (11.95)	56 (6.75)	
Male	128 (51.00)	432 (52.05)	0.770
Age (year)			0.041
10	83 (33.07)	257 (30.96)	
11	95 (37.85)	262 (31.57)	
12	73 (29.08)	311 (37.47)	
Ethnic minorities ^a	51 (20.32)	65 (7.86)	0.000
Duration of breastfeeding ^b			0.411
None	14 (5.58)	54 (6.15)	
0-6 months	34 (13.55)	100 (12.06)	
6-12 months	113 (45.02)	370 (44.63)	
12-18 months	47 (18.73)	192 (23.16)	
>18 months	43 (17.13)	113 (13.63)	
Birthweight ^c			0.249
Low (≤ 2.5 kg)	8 (4.79)	56 (8.10)	
Normal (2.5-4 kg)	154 (92.22)	606 (87.70)	
High (≥ 4 kg)	5 (2.99)	29 (4.20)	
Maternal educational leveld			0.000
No school	99 (45.83)	186 (25.10)	
Primary school	57 (26.39)	197 (26.59)	
Middle school	57 (17.59)	223 (30.09)	
High school or higher	22 (10.19)	135 (18.22)	
Rural areas	185 (73.71)	478 (57.59)	0.000
Region			0.000
West	128 (51.00)	236 (28.43)	
East	69 (27.49)	254 (30.60)	
Central	43 (17.13)	223 (26.87)	
Northeast	11 (4.38)	117 (14.10)	
Total	251 (23.22)	830 (76.78)	

Note: BMI = body mass index; ^a Sample size is 1078; ^b Sample size is 1080; ^c Sample size is 858; ^d Sample size is 957.

Normal weight Overweight Obesity <i>p-values</i>

(n = 880)	(n = 115)	(n = 86)	
31.17 ± 6.52	32.00 ± 6.50	33.57 ± 7.33	0.309
9.73 ± 2.76	9.97 ± 2.72	10.72 ± 3.66	0.001
8.83 ± 2.64	9.32 ± 2.80	9.40 ± 2.67	0.701
10.05 ± 2.75	10.11 ± 2.51	10.63 ± 2.82	0.408
2.56 ± 0.92	2.60 ± 0.94	2.83 ± 1.12	0.040
	31.17 ± 6.52 9.73 ± 2.76 8.83 ± 2.64 10.05 ± 2.75	31.17 ± 6.52 32.00 ± 6.50 9.73 ± 2.76 9.97 ± 2.72 8.83 ± 2.64 9.32 ± 2.80 10.05 ± 2.75 10.11 ± 2.51	31.17 ± 6.52 32.00 ± 6.50 33.57 ± 7.33 9.73 ± 2.76 9.97 ± 2.72 10.72 ± 3.66 8.83 ± 2.64 9.32 ± 2.80 9.40 ± 2.67 10.05 ± 2.75 10.11 ± 2.51 10.63 ± 2.82

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Table 3 The association between depressive symptoms and weight status

	Variable	Model 1	Model 2	Model 3	Model 4	
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	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Whether depressed	1.70 (1.57,1.85)***	1.63 (1.35,1.97)***	1.48 (1.11,1.97)**	1.47 (1.14,1.91)**
CES-D scores	1.04 (1.02,1.05)***	1.03 (1.01,1.05)**	1.02 (0.99,1.05)	1.02 (1.00,1.05)
Depressed affect	1.07 (1.05,1.10)***	1.07 (1.04,1.10)***	1.06 (1.01,1.10)*	1.06 (1.02,1.10)**
Lack of positive affect	1.08 (1.05,1.10)***	1.06 (1.04,1.07)***	1.04 (1.03,1.06)***	1.04 (1.03,1.05)***
Somatic symptoms	1.04 (0.99,1.10)	1.03 (0.96,1.10)	1.02 (0.94,1.11)	1.02 (0.95,1.10)
Interpersonal difficulties	1.17 (1.04,1.32)**	1.14 (0.98,1.33)	1.11 (0.92,1.33)	1.11 (0.92,1.33)

Note: CES-D = Epidemiologic Studies Depression Scales; Model 1: no adjustments; Model 2: adjusted for age, gender, ethnic minority, duration of breastfeeding and birthweight; Model 3: additionally adjusted for maternal BMI, maternal education and household income per capita on the base of Model 2; Model 4: additionally adjusted for the interaction between regions and urban areas on the base of Model 3; * p<0.05; ** p<0.01; ***p<0.001.

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Table 4 Gendered difference in the association of CES-D scores and weight status

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Variable	Gend	Model 1	Model 2	Model 3	Model 4
Vallable	er	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Whathar depressed	Male	1.69	1.64	1.49 (1.25,	1.48
Whether depressed	wate	(1.35,2.13)***	(1.36,1.97)***	1.76)***	(1.24,1.76)***
	Fema	1.81	1.63	4 47 (0 70 0 0 0)	1.46
	le	(1.21,2.70)**	(0.95,2.81)	1.47 (0.76,2.85)	(0.76,2.80)
	Mala	1.04	1.03	1.02	1.02
CES-D scores	Male	(1.03,1.06)***	(1.01,1.04)***	(1.00,1.04)*	(1.01,1.04)**
	Fema	1.02	1.03	4 00 (0 07 4 00)	1.02
	le	(1.00,1.04)*	(0.99,1.08)	1.02 (0.97,1.08)	(0.97,1.08)
Democratic official	Mala	1.10	1.07	1.06	1.06
Depressed affect	Male	(1.07,1.12)***	(1.03,1.11)***	(1.01,1.10)**	(1.01,1.11)**
	Fema	1.03	1.07		1.06
	le	(0,98,1.07)	(0.98,1.16)	1.06 (0.95,1.17)	(0.96,1.16)
Lack of positive		1.10	1.03		1.02
affect	Male	(1.08,1.13)***	(1.01,1.05)**	1.02 (0.98,1.06)	(0.98,1.06)
	Fema	1.03	1.09	1.08	1.08
	le	(0.98,1.09)	(1.04,1.15)***	(1.03,1.13)***	(1.03,1.13)**
o		1.06	1.04		1.04
Somatic symptoms	Male	(1.01,1.12)*	(1.02,1.07)***	1.04 (1.00,1.07)	(1.01,1.07)*
	Fema	0.99	1.01		1.00
	le	(0.94,1.05)	(0.87,1.16)	1.00 (0.85,1.16)	(0.86,1.16)
Interpersonal		1.27	1.15	1.13	1.14
difficulties	Male	(1.10,1.46)**	(1.06,1.26)**	(1.02,1.25)*	(1.02,1.27)*
	Fema	0.99	1.12		1.05
	le	(0.89,1.11)	(0.83,1.51)	1.07 (0.75,1.51)	(0.74,1.49)

Note: CES-D = Epidemiologic Studies Depression Scales; Model 1: no adjustments; Model 2: adjusted for age, gender, ethnic minority, duration of breastfeeding and birthweight; Model 3: additionally adjusted for maternal BMI, maternal education and household income per capita on the base of Model 2; Model 4: additionally adjusted for the interaction between regions and urban areas on the base of Model 3; * p<0.05; ** p<0.01; ***p<0.001.

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		्रक् STROBE Statement—Checklist of items that should be included in reports of <i>cross-sectio</i> gal studies	
Section/Topic	ltem #	Recommendation 177 13	Reported on page #
Title and abstract	1	(<i>a</i>) Indicate the study's design with a commonly used term in the title or the abstract	1, 2
		(b) Provide in the abstract an informative and balanced summary of what was done and what was to und	2
Introduction	1		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3, 4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4, 5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4, 5
Participants	6	(<i>a</i>) Give the eligibility criteria, and the sources and methods of selection of participants	4, 5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5, 6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5, 6
Bias	9	Describe any efforts to address potential sources of bias	6
Study size	10	Explain how the study size was arrived at	5,6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	6, 7, 8
		(b) Describe any methods used to examine subgroups and interactions 고	7
		c) Explain how missing data were addressed	6
		(d) If applicable, describe analytical methods taking account of sampling strategy	4, 5
			N/A
Results			

23		BMJ Open 90, 2018	
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examine of for eligibility,	6, 8
Farticipants		confirmed eligible, included in the study, completing follow-up, and analysed	0,0
		(b) Give reasons for non-participation at each stage	6
		(c) Consider use of a flow diagram	N/A
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exaosumes and potential confounders	8
		(b) Indicate number of participants with missing data for each variable of interest	18, table 1 (note)
Outcome data	15*	Report numbers of outcome events or summary measures	8, 9, 10
Main results	16	(<i>a</i>) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision deg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	20, 21
		(b) Report category boundaries when continuous variables were categorized	18
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	N/A
Discussion		tt s	
Key results	18	Summarise key results with reference to study objectives	10, 11, 12
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	12, 13
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	13, 14
Generalisability	21	Discuss the generalisability (external validity) of the study results	14
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	14

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in c hort and cross-sectional studies.

checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine 🛱 rg/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.spote-statement.org.

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