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BMJ Open Association of low birth weight with thinness and severe obesity in children aged 3-12 years: a large-scale population-based cross-sectional study in Shanghai, China

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ABSTRACT

Objectives Low birth weight (BW) is a general symbol of inadequate intrauterine conditions that elicit abnormal fetal growth and development. The aim of current study is to investigate the relationship between low BW and thinness or severe obesity during maturation.

Design A large-scale cross-sectional population-based survey.

Setting 134 kindergartens and 70 elementary schools. **Participants** 70 284 Chinese children aged 3–12 years. Outcome measures International Obesity Task Force body mass index (BMI) cut-offs were used to define grade 1, grade 2 and grade 3 thinness, overweight, obesity and severe obesity. Multinomial logistic regression was used to estimate the association between BW and BMI category. Results A total of 70 284 children participated in the survey. The percentage of grade 1 thinness and severe obesity in children with low BW is significantly higher than that in children with normal BW (p<0.05). Low BW was associated with an increased risk of grade 1 thinness (OR 1.56, 95% CI 1.38 to 1.75), grade 2 thinness (OR 1.34, 95% CI 1.10 to 1.64), grade 3 thinness (OR 1.99, 95% CI 1.63 to 2.42) and severe obesity (OR 1.27, 95% CI 1.03 to 1.55) but was not associated with obesity (OR 0.85, 95% CI 0.67 to 1.06).

Conclusion There is a positive association between low BW and thinness or severe obesity risk.



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INTRODUCTION

Childhood obesity is one of the most serious global public health challenges. Furthermore, obesity in childhood may lead to short-term morbidity and to subsequent adverse consequences across the individual's lifespan and his or her subsequent generation. 1 Growing evidence indicates that perinatal characteristics have been recognised as contributing factors to the obesity epidemic.² Birth weight (BW) is frequently used as an indicator of the conditions experienced in utero, which contribute

Strengths and limitations of this study

- ► This study is a large population-based cross-sectional survey with a representative, multistage proportional cluster sampling.
- Low birth weight (BW) was found to be associated with an increased risk of grade 1 thinness, grade 2 thinness, grade 3 thinness and severe obesity, rather than overweight or obesity.
- Height/weight and BW data were collected by self-reported questionnaires in a cross-sectional study.

to the newborn baby's survival, health, growth and development. 3'4 Lower BW is a general symbol of inadequate intrauterine conditions that elicit abnormal fetal growth and development.⁵ Based on the findings of numerous studies, low BW (BW <2500g) has been shown to trigger various short-term and longterm health issues, especially for birth injuries, delayed motor development, delayed cognitive and social skills, obesity and chronic diseases.46

A great number of studies have indicated that high BW is associated with an increased risk of childhood obesity. 6-9 Nevertheless, the conclusions drawn by studies evaluating the associations between low BW and obesity appear to be controversial. Some studies suggest that low BW correlates with a significantly elevated risk of obesity, 10 11 while some other studies contradict this result, reporting that low BW is unrelated to or protective against overweight and/or obesity.⁶ 12 13 However, these studies only assess the effect of BW on childhood overweight or obesity but ignored childhood thinness.

Because of the absence of evidence regarding the relationship between BW and thinness and the inconsistent conclusions regarding the relationship between BW and overweight or obesity, in this large population-based observational study, we aimed to examine the relationship between BW and the risk of obesity and placed extra emphasis on the effect of thinness in children aged 3–12 years from seven districts of Shanghai.

METHODS

Study design and quality control

Our study was a school-based cross-sectional population study and was part of a governmental population survey of autism spectrum disorders. Multistage, stratified clustered random sampling was conducted in children aged 3-12 years in Shanghai, China, and related baseline data were collected from 134 kindergartens and 70 elementary schools in June 2014. Details of the sample size, sampling and quality control process have been described previously. 14 15 The 17 districts of Shanghai were stratified into eight urban districts in the central area and in nine suburban areas according to the geographical and social population distributions; people living in urban and suburban districts were defined as urban and suburban residents. EpiData V.3.1 (EpiData Association, Odense, Denmark) was used for data inputting, and a logical error check was applied. We also repeated data entry by randomly sampling 15% of the questionnaires to ensure consistency. The study was approved by the institutional review boards of the Shanghai Municipal Commission of Health and Family Planning.

Measurements

We used growth questionnaires for collecting information about children's families and social environments. Teachers distributed questionnaires to students, asked students to take the questionnaire home and have their parents fill in the information, then the teachers collected the completed questionnaires and returned them to the investigator. Parents provided the following information about their children: age, sex, weight, height, BW, education level, and so on, by self-report. Participants with complete BW, weight and height data constituted the final sample. Body mass index (BMI) was calculated as weight divided by the square of height (kg/m²) and classified as grade 3 thinness, grade 2 thinness, grade 1 thinness, overweight, obesity and severe obesity, according to the International Obesity Task Force age-specific and sex-specific cut-off points, of which BMI cut-offs equal to $16.0, 17.0, 18.5, 25.0, 30.0 \text{ and } 35.0 \text{ kg/m}^2$, respectively, at age 18 years. 16

BW was divided into the low BW group (neonates weighing <2500 g at birth, irrespective of gestational age), the normal BW group (neonates weighing 2500–4000 g at birth, irrespective of gestational age) and the high BW group (neonates weighing ≥4000 g at birth, irrespective of gestational age).

Neonatal characteristics, including gestational weeks $(<37, 37-42 \text{ and } \ge 42 \text{ weeks})$, normal delivery (yes or no), single-child family (yes or no), maternal history of abortion (yes or no), asphyxia (lack of oxygen at birth, yes or no) and infant feeding patterns (breast feeding exclusively, formula feeding exclusively and mixed feeding) were considered as potential prenatal confounding factors. 6 17 Moreover, parental socioeconomic characteristics were considered as follows: family income was divided into three categories (low: <\footnote{150,000} per year, middle: ¥50 000–2 00 000 per year and high: ≥¥200 000 per year) according to the definitions of social science, ¹⁸ parental education (low: illiterate, primary school and junior school; middle: high school, technical school and college; high: undergraduate, master and doctor) and residence location (urban districts: Yangpu, Xuhui and Jing'an; suburban districts: Minhang, Pudong, Fengxian and Chongming).

Statistical analysis

Continuous variables were presented as mean values with SDs, and Student's t-test was carried out for group comparisons. Categorical variables were presented as absolute numbers with relative frequencies (%). The linear-by-linear trend test was performed to detect the distribution of different BMI categories between low BW and normal BW, and intersubgroup differences were examined using Pearson's χ^2 test. Multinomial logistic regression was used to estimate the relationship between BW and the risk of childhood thinness and obesity with normal weight as a reference group. Model 1 adjusted for the basic characteristics, age and gender, which were all influence factors of BMI category. Also, neonatal characteristics were reported to be associated with both BW and BMI category and thus were adjusted as a confounder in model 2. Socioeconomic characteristics could reflect the environment and nutritional status to some extent and were further adjusted in model 3. All confounding variables enter into the multinomial regression model. OR and 95% CI were obtained by using the multiple models. All statistical analyses were performed with IBM SPSS Statistics V.22. The criterion for statistical significance was 0.05 by two-tailed test.

Patient and public involvement

Parents were informed about questions and data of the survey before filling in the questionnaires, and were not involved the design, recruitment and conduct of the study; the results will be disseminated to participants as required.

RESULTS

In total, 84 075 questionnaires were distributed and 81 384 completed questionnaires were returned with a response rate of 96.80%. Complete data regarding weight, height and BW were available for 70 284 children. A total of 3359 children were born with low BW and 59 356 children were

Variables	No	Boys, n (%)	Girls, n (%)	χ^2	P value
Number	62715	32 629 (52.0)	30 086 (48.0)	κ	. varac
Age (year)	02713	32 029 (32.0)	30 000 (40.0)	2.76	0.948
3	2006	1023 (3.1)	983 (3.3)	2.7.0	0.010
4	8186	4250 (13.0)	3936 (13.1)		
5	8481	4434 (13.6)	4047 (13.5)		
6	8237	4286 (13.1)	3951 (13.3)		
7	8133	4260 (13.1)	3873 (12.9)		
8	8540	4431 (13.6)	4109 (13.7)		
9	7494	3876 (11.9)	3618 (12.0)		
10	6477	3402 (10.4)	3075 (10.2)		
11	5161	2667 (8.2)	2494 (8.3)		
BMI category		(, ,	()	803.87	<0.001
Grade 3 thinness	1637	752 (2.3)	885 (2.9)		
Grade 2 thinness	2071	938 (2.9)	1133 (3.8)		
Grade 1 thinness	6568	3001 (9.2)	3567 (11.9)		
Normal	38 831	19502 (59.8)	19329 (64.3)		
Overweight	8614	5292 (16.2)	3322 (11.0)		
Obesity	2514	1696 (5.2)	818 (2.7)		
Severe obesity	2480	1448 (4.4)	1032 (3.4)		
Birth weight category (g)		- ()	(* (*)	19.88	<0.001
<2500	3359	1622 (5.0)	1737 (5.8)		
2500–4000	59356	31 007 (95.0)	28349 (94.2)		
Neonatal characteristics		, ,			
Pregnancy term (weeks)				19.22	<0.001
<37	3854	2135 (6.5)	1719 (5.7)		
37–42	56238	29 106 (89.2)	27 132 (90.2)		
≥42	2035	1063 (3.3)	972 (3.2)		
Missing	588	325 (1.0)	263 (0.9)		
eeding patterns (<4 months)			, ,	4.59	0.101
Breast feeding	30716	15 925 (48.8)	14791 (49.2)		
Formula feeding	9959	5119 (15.7)	4840 (16.1)		
Mixed feeding	21612	11 363 (34.8)	10249 (34.1)		
Missing	428	222 (0.7)	206 (0.7)		
Normal delivery		(- /		1.23	0.267
Yes	30 054	15 563 (47.7)	14491 (48.2)		
No	32 226	16831 (51.6)	15 395 (51.2)		
Missing	435	235 (0.7)	200 (0.7)		
One-child family		,	,	34.94	<0.001
Yes	43207	22 748 (69.7)	20 459 (68.0)		
No	15 665	7816 (24.0)	7849 (21.6)		
Missing	3843	2065 (6.3)	1778 (5.9)		
Abortion		()	, -,	3.16	0.076
Yes	14849	7818 (24.0)	7031 (23.4)		
No	47 401	24561 (75.3)	22 840 (75.9)		
Missing	465	250 (0.8)	215 (0.7)		
Asphyxia		(3.2)	(211)	45.15	<0.001
Yes	2146	1269 (3.9)	877 (2.9)		

Continued

Table 1 Continued								
Variables	No	Boys, n (%)	Girls, n (%)	χ²	P value			
No	59732	30 916 (94.8)	28 816 (95.8)					
Missing	837	444 (1.4)	393 (1.3)					
Socioeconomic characteristics								
Area				3.20	0.074			
Suburban	49231	25 709 (78.8)	23 522 (78.2)					
Urban	13371	6866 (21.0)	6505 (21.6)					
Missing	113	54 (0.2)	59 (0.2)					
Income				4.92	0.086			
Low	16762	8811 (27.0)	7951 (26.4)					
Middle	34 442	17 898 (54.9)	16544 (55.0)					
High	10279	5261 (16.1)	5018 (16.7)					
Missing	1232	659 (2.0)	573 (1.9)					
Mother's education level				48.07	<0.001			
Low	17541	9485 (29.1)	8056 (26.8)					
Middle	24365	12 435 (38.1)	11 930 (39.7)					
High	16972	8629 (26.4)	8343 (27.7)					
Missing	3837	2080 (6.4)	1757 (5.8)					
Father's education level				33.79	<0.001			
Low	15357	8280 (25.4)	7077 (23.5)					
Middle	24305	12 467 (38.2)	11 838 (39.3)					
High	19196	9805 (30.0)	9391 (31.2)					
Missing	3857	2077 (6.4)	1780 (5.9)					

The boldfaced number means P<0.05 for chi-square test. BMI, body mass index.

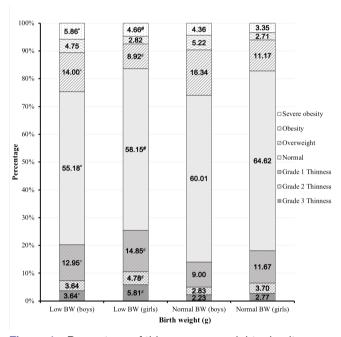


Figure 1 Percentage of thinness, overweight, obesity and severe obesity between low BW and normal BW. *Statistically significant difference between low BW and normal BW in boys (χ^2 test, p<0.05); *Statistically significant difference between low BW and normal BW in girls (χ^2 test, p<0.05). BW, birth weight.

born with normal BW: 32629 boys (52.03%) and 30086 girls (47.97%) aged 3–12 years. Sex-specific variables, such as growth (age, BMI category and BW), neonatal characteristics (pregnancy term, breast feeding, normal delivery, number of children, abortion and asphyxia) and parental socioeconomic characteristics (residence, family income and parental education), are described in detail in table 1.

The distribution of different BMI categories between low BW and normal BW was examined by linear-bylinear trend test and the chi-square tests value was 36.98 (p<0.001). Detailed information is shown in figure 1. For boys, the respective percentage of grade three thinness (3.64%, 95% CI 3.55% to 3.73%, vs 2.23%, 95% CI 2.21%to 2.25%, p<0.05), grade two thinness (3.64%, 95% CI 3.55% to 3.73%, vs 2.83%, 95% CI 2.81% to 2.85%, p<0.05), grade one thinness (12.95%, 95% CI 12.79% to 13.11%, vs 9.00%, 95% CI 8.97% to 9.03%, p<0.05) were higher in the low BW group than those in the normal BW group; in contrast, the respective percentage of overweight (14.00%, 95% CI 13.83% to 14.17%, vs 16.34%, 95% CI 16.30% to 16.38%, p>0.05), obesity (4.75%, 95% CI 4.65% to 4.85%, vs 5.22%–95% CI 5.20% to 5.24%, p>0.05) were not statistically significant but severe obesity (5.86%, 95% CI 5.75% to 5.97%, vs 4.36%, 95% CI 4.34% to 4.38%, p<0.05) was higher in low BW group compared with normal group (p<0.05). Meanwhile, the percentage of severe obesity and grade three thinness were relatively higher in low BW group compared with the normal BW group (p<0.05), which shows a U-shape. The pattern is similar in girls; the percentage of grade three thinness (5.81%, 95% CI 5.70% to 5.92% vs 2.77%–95% CI 2.75% to 2.79%, p<0.05), grade two thinness (4.78%, 95% CI 4.68% to 4.88% vs 3.70%, 95% CI 3.68% to 3.72%, p<0.05), grade one thinness (14.85%, 95% CI 14.68% to 15.02% vs 11.67%, 95% CI 11.63% to 11.71%, p<0.05) were higher, but severe obesity (4.66%, 95% CI 4.56% to 4.76% vs 3.35%, 95% CI 3.33 to 3.37, p<0.05) was lower in the low BW group. However, overweight (8.92%, 95% CI 8.79% to 9.05%, vs 11.17%, 95% CI 11.13% to 11.21%, p<0.05) and obesity (2.82%, 95% CI 2.74% to 2.90%, vs 2.71%, 95% CI 2.69 to 2.73, p>0.05) showed no statistical difference between the groups.

Multinomial logistic regression was used to further determine the relationship between BW and thinness, overweight and obesity after adjusting for potential confounders. As shown in table 2, an initial analysis was performed in model 1, adjusting for only age and gender variables. The results showed that low BW is significantly associated with a higher risk of both thinness (grade 3 thinness: OR 2.16, 95% CI 1.82 to 2.56; grade 2 thinness: OR 1.43, 95% CI 1.20 to 1.70; grade 1 thinness: OR 1.49, 95% CI 1.34 to 1.65) and severe obesity (OR 1.62, 95% CI 1.38 to 1.90), but was not associated with overweight (OR 0.89, 95% CI 0.80 to 1.00) or obesity (OR 1.05, 95% CI 0.87 to 1.26). In addition, model 2 is further adjusted for neonatal characteristics based on model 1, and model 3 is characterised by additional adjustments for socioeconomic variables based on model 2. Still, children with low BW are more likely to have grade 1 thinness (OR 1.56, 95% CI 1.38 to 1.75), grade 2 thinness (OR 1.34, 95% CI 1.10 to 1.64) and especially grade 3 thinness (OR 1.99, 95% CI 1.63 to 2.42); the pattern is consistent in the three models. Low BW remained a statistically significant

predictor of severe obesity (OR 1.27, 95% CI 1.03 to 1.55) but was not associated with obesity (OR 0.85, 95% CI 0.67 to 1.06).

DISCUSSION

In the present study, we reported a bidirectional effect of low BW, increasing the risk of grade 3 thinness and severe obesity.

Some studies have assessed the relationship between low BW and the risk of childhood obesity, but the results were controversial. 6 19-23 In a systematic review and meta-analysis involving 11 studies, pooled estimates for low BW (<2500g) revealed no association with obesity (pooled OR 0.87, 95% CI 0.69 to 1.08) using normal BW (2500-4000 g) as the reference category. Another systematic review and meta-analysis of 30 studies found that low BW was associated with a reduced risk of childhood obesity (pooled OR 0.67, 95% CI 0.59 to 0.76). 19 With regard to long-term risk of overweight and obesity, two previous papers have suggested a positive association with low BW, including a population-based cross-sectional survey among Chinese adults (obesity: OR 1.99, 95% CI 1.15 to 3.43) 11 and an observational study among older women in Sweden (obesity: OR 1.14, 95% CI 1.03 to 1.26). 10 On the contrary, a large, full-range BW study reported that children with a BW of <2500g were protected against overweight or obesity from 6 months to 3 years of life, but this association disappeared among boys at 2 years of age.²¹ Our study highlighted the association between low BW and increased risk of severe obesity rather than overweight or obesity among Chinese children aged between 3 and 12 years. An age-specific effect of low BW on obesity might address some of the primary reasons why previous studies have drawn contrasting conclusions. In a Swedish cohort with 285 children with marginally low BW (2000-2500 g) and 95 children with normal BW, no increased risk of overweight or obesity was observed

Table 2 Association between low birth weight and thinness, overweight, obesity and severe obesity by multinomial logistic regression models

	n	Grade 3 thinness	Grade 2 thinness	Grade 1 thinness	Overweight	Obesity	Severe obesity
Model 1	62715	2.16 (1.82 to 2.56)*	1.43 (1.20 to 1.70)*	1.49 (1.34 to 1.65)*	0.89 (0.80 to 1.00)	1.05 (0.87 to 1.26)	1.62 (1.38 to 1.90)*
Model 2	56909	2.12 (1.74 to 2.59)*	1.35 (1.10 to 1.65)*	1.52 (1.35 to 1.72)*	0.88 (0.77 to 1.00)	1.00 (0.81 to 1.25)	1.43 (1.18 to 1.75)*
Model 3	55 600	1.99 (1.63 to 2.42)*	1.34 (1.10 to 1.64)*	1.56 (1.38 to 1.75)*	0.87 (0.76 to 0.99)*	0.85 (0.67 to 1.06)	1.27 (1.03 to 1.55)*

Normal BMI as the reference group.

Model 1: adjusted for age and gender.

Model 2: adjusted for age, gender and neonatal characteristics (pregnant term, feeding pattern, delivery mode, one child, abortion and asphyxia).

Model 3: adjusted for age, gender, neonatal characteristics (pregnant term, feeding pattern, delivery mode, one child, abortion and asphyxia) and socioeconomic characteristics (urbanicity, parental education and family income).

*P value < 0.05.

BMI, body mass index.

by up to 7 years (BMI 0.47 kg/m² (95% CI 0.17 to 0.76) lower compared with controls). Another possible explanation might be the potential of growth have not been fully developed among those children with low BW. Not all children with low BW undergo catch-up growth, and different growth patterns might exist. Special attention should be payed among those children with low BW in future cohort studies.

It was difficult to explain the particular pattern between grade 1, grade 2 and grade 3 thinness and various BW groups. In a follow-up study in two rural Shaanxi counties of Northwest China, low BW was not related with boys' obesity or thinness rates (adjusted OR 2.91, 95% CI 0.95 to 8.93) but was significantly correlated with increased risk of thinness among girls (adjusted OR 4.41, 95% CI 1.77 to 10.97). Our study confirmed the association and further demonstrated that low BW is associated with an increased risk of subsequent grade 3 thinness, followed by grade 1 thinness and then grade 2 thinness after adjusting for confounding variables. On the other hand, high BW exerted a protective effect on grade 2 thinness, followed by grade 1 thinness, then grade 3 thinness. Most notably, low BW was a risk factor for grade three thinness, as well as severe obesity. We hypothesised that the relationship between BW and thinness, overweight or obesity risk was not directly linear, whereas the relationship between low BW and BMI was U-shaped. Low BW was an adverse perinatal environment factor that predicts changes to the central regulatory mechanism linked with negative influences on metabolism and BMI. 26 Thus, children with low BW, accompanied by poor childhood weight outcomes, should receive more public health attention.

Several studies have indicated that abnormal BW was an important risk factor for metabolic disease occurrence, especially for hypertension, type 2 diabetes, abdominal obesity and other chronic diseases later in life. 11 27-29 A proposed explanation for the relationship between BW and postnatal growth was through the concept of 'developmental origins of health and disease', which stated that environmental cues during critical periods of life lead to predictive adaptive responses that shape tissue development and metabolic pathways, thereby permanently affecting long-term health and disease risk. 30 Our epidemiological observations might have implications for understanding intrauterine environmental influences during early development and the relationship of BW with later risk of thinness and obesity.

Strengths and limitations

Our study recruited children from low-income to high-income families across seven districts of the Shanghai area by a large, representative, multistage proportional cluster sampling. We were able to assess the relationship between low BW and risk of childhood thinness, obesity or severe obesity using a large sample size (n=70 284) of children with low BW (4.61%). What's more, we provided a comprehensive profile of the distribution of overall BMI status, including grade 1, grade 2 and grade 3 thinness; normal

weight; overweight; obesity and severe obesity in low and normal BW groups. As for the potential confounding variables associated in the multinomial logistic regression, we took a broad range of predictors into consideration, from prenatal to postnatal.

However, there were several limitations in our study. First, the cross-sectional nature precluded us from making cause-and-effect inferences and observing continuous age-effects and long-term effects. Because aetiology of thinness and obesity could not be drawn, cohort studies are still needed to track growth trajectory of low BW children. Second, the information, including height and weight, was collected by questionnaires because of the large sample size, and there was underlying bias of self-reported data. Also, misunderstandings of the questions on neonatal outcome is another underlying risk. In addition, the BW records might have been wrongly recalled by the parents or guardians, thus the degree and direction of potential bias in the results were unknown. Our results suggest a need for carefully designed longitudinal studies with precise physical examination and indicators to document thinness and obesity among children with low BW.

CONCLUSIONS

In summary, low BW was positively associated with an increased risk of thinness and severe obesity but not associated with obesity. We call for special attention for children with abnormal BW for healthier physical development during growth, and their mothers by creating a favourable environment with recommendation on physical activity and nutrition and limitation of their alcohol and tobacco consumption to lower the risk of low BW. We hope the pattern of thinness and obesity in different BW groups may provide valuable insights to direct healthcare policies for improving outcomes and quality in later life.

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Contributors ZJ, YY, FJ, HH and XJ helped perform the study. XJ and SL designed the research; CC drafted the manuscript and performed statistical analyses; SL and HH contributed to the interpretation of results and critically reviewed the manuscript; SL had primary responsibility for final content. All authors read and approved the final manuscript and declared no conflict of interest. We are grateful to all parents and teachers of the children for their assistance and cooperation in this study.

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Competing interests None declared.

Patient consent for publication Not required.

Ethics approval This study was conducted according to the guidelines in the World Medical Association (2000) Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects (http://www.wma.net/en/30publications/10policies/b3/) and the Guidelines for the Ethical Conduct of Medical Research Involving Children, revised in 2000 by the Royal College of Paediatrics and Child Health: Ethics Advisory Committee (Arch Dis Child 2000, 82, 177–182). All procedures involving human subjects were approved by the institutional review boards of the Shanghai Municipal Commission of Health and Family Planning. Verbal informed consent was obtained from all participants, witnessed and formally recorded. Parents were given notification and information about the survey at the beginning of the questionnaire; it is difficult to get written consent in this large-scale population-based cross-sectional study in China.

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement All data relevant to the study are included in the article.

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