Original Article

Analysis of Factors Affecting the Body Mass Index in a National Sample of Iranian Children and Adolescents: Bootstrapping Regression

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Abstract

Background: This study aims to evaluate the effect of some factors, including birth weight, sex, age, waist circumference, family history of obesity, as well as some lifestyle factors as frequency of breakfast days and physical activity, on the body mass index among a nationally representative sample of Iranian children and adolescents by using bootstrapping regression. **Materials and Methods:** This study was conducted as the third survey of a school-based surveillance system (CASPIAN-III study). Total participants were 5570 school students, aged 10-18 years, selected by multistage random cluster sampling from urban and rural areas of 27 provinces of Iran. Multiple linear regressions was used to evaluate the effect of various factors on obesity, but in our data the assumptions of this model violated, and possible solutions were not appropriate, therefore the bootstrapping regression based on the observations and errors resampling approaches was used as an alternative. **Results:** The tests of significance showed that the effects of sex, age, waist circumference, family history obesity and frequency of breakfast days were clearly significant ($P < 0.001$). The effect of vigorous level of physical activity was significant in comparison to mild physical activity ($P = 0.01$). In comparison to low birth weight, medium and high birth weight had significant effect on obesity. **Conclusions:** Bootstrap method is preferable in linear regression because of some theoretical properties like having any distributional assumptions on the residuals and hence allows for inference even if the errors do not follow normal distribution or constant error variance.

Keywords: *Adolescents, body mass index, bootstrap, children, linear regression*

Introduction

Overweight of children and adults is a major public health epidemic worldwide, and childhood obesity is an emerging health problem in low and middle-income nations.[1,2] It is a chronic disease, and plays a main role in the ''insulin resistance'' or ''metabolic'' syndrome, which includes hyperinsulinemia, hypertension, hyperlipidemia, type 2 diabetes mellitus, and an increased risk of atherosclerotic cardiovascular disease.[3] It is associated with the risk of liver disease, sleep apnea, cancer (i.e., colorectal cancer), depression, osteoarthritis, and other medical problems that affect mortality and morbidity.[4] High BMI in children may have outcomes, such as elevated lipid concentrations and blood pressure.[5] Overweight in children and adolescents represents one of the difficult diseases to treat,[6] and prevention of childhood obesity is the main concern for public health, in many industrialized countries and some transition societies.[7] There are currently many efforts for preventing childhood obesity.[8] Nutrition and physical activity (PA) are the main research focus on prevention of over weight.[9] In the past few decades, in developed nations, physical activity levels among adults and children have declined steadily.[10,11] Data from three national surveys among Iranian adults have shown that more than 80% of the Iranian population are physically inactive.[12] And the some local studies performed in Iranian young people have shown a similar pattern.[13] The overweight is the effect of an interplay between genetic and environmental factors.[14] The parental obesity is also one of the main risk factors for pediatric obesity, and many at-risk children will live in families with obese parents. The parental behavior changes as the obesity prevention program

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may have benefits beyond prevention of pediatric obesity, because a change in the eating habits may result in a reduction in parental over weight.[15] Based on World Health Organization (WHO) estimates, by the year 2020, non-communicable diseases (NCD) will account for approximately three quarters of all deaths in the developing world.[16] In this regard, a potential emerging public health issue in developing countries may be the increasing incidence of childhood overweight, which in the near future is likely to create an enormous socio economic and public health burden for poorer societies, due to the new cases of metabolic syndrome among children.[17] In recent years, in addition to problems and disease in adults, the epidemiological transition has made Iranian young people prone to chronic health problem in later life.[18,19] Most writers use linear or logistic regression to model effects on body mass index (BMI) measures in their literature, but this common approach rely on major modeling assumptions severely, so that the reliability of the statistical analysis depends on the validity and establishment of these assumptions. There are various useful approaches for recognizing and treating violations of the regression assumptions, residual diagnostics and transformation of the response variable have improved the usefulness of these common techniques. However, using these approaches may not provide major modeling assumptions.[20,21]

As regards, In recent years, in addition to problems in adults, the epidemiological transition has made Iranian young people prone to chronic health problem, and increasing incidence of childhood overweight in the near future is likely to create an enormous socioeconomic and public health burden.[17,18] Therefore, it seems more research on the effects of various factors on obesity in Iranian children and adolescents is necessary. In present study, we assessed the effect of some factors including birth weight, sex, age, waist circumference, family history of obesity, as well as some lifestyle factors as frequency of breakfast days and physical activity on the BMI among children and adolescents aged from 10 to 18 years of the CASPIAN-III study. In our study the assumptions of the linear regression model violated, and possible solutions like lognormal or Box Cox power transformations of the response variable (BMI) were not appropriate. When inferences are based on certain parametric assumptions, which may seem tentative, or parametric inference is impossible, the bootstrap method is often used as an alternative, because this method does not need these assumptions.[22] Therefore, our study aims to evaluate the effect of some factors on the BMI among a nationally-representative sample of Iranian children and adolescents by using bootstrap resampling technique in multiple regression analysis and shows that the conclusions drawn about the BMI of children and adolescent are reliable without assumptions about the distribution of the linear regression model.

Material and Methods

Study population and data source

This school-based nationwide health survey was conducted in Iran as the national survey of school student high risk behaviors (2009–2010). It was conducted as the third study of the school-based surveillance system entitled Childhood and Adolescence Surveillance and Prevention of Adult.

Non communicable disease (CASPIAN-III) Study. It was performed with corporation of the Ministry of Health and Medical Education; Ministry of Education and Training, Child Health Promotion Research Center, Isfahan University of Medical Sciences; and Endocrinology and Metabolism Research Institute of Tehran University of Medical Sciences. The survey was performed among 5570 students aged 10–18 years, who were selected by multistage random cluster sampling from urban and rural areas of 27 provinces of Iran. Eligible schools for our study were stratified according to information bank of Ministry of Education, and then, they were selected randomly. In selected schools, students were also selected randomly.[23] Study protocols were reviewed and approved by ethical committees and other relevant national regulatory organizations. After complete explanation of the study objectives and protocols for the students and their parents, a written informed consent was obtained from the parents and oral assent from students. The study was approved by institutional review boards at national and provincial level.[24]

Procedure and measurements

We prepared the questionnaires in Farsi based on the WHO Global School Health Survey, and added some more questions to the questionnaires of parents. Questions were about family dietary habits like days of breakfast consumption in the week, students' past history like birth weight (w <2500 gr, 2500 < w <4000 gr, w >4000 gr) and familial history of chronic diseases, for example family, history of obesity. The validity of their content was affirmed based on observations of an experts' panel and item analysis. Reliability measures (0.87) were assessed based on a pilot study. Under the supervision of expert health care professionals, the students filled out the self-administered questionnaire at school. A team of trained health care professionals and physicians recorded information in a checklist and conducted the examinations under standard protocol by using calibrated instruments, and measured weight, height, waist circumference and blood pressure under standard protocols by using calibrated instruments. Weight was recorded in light clothing to the nearest 0.1 kg on a SECA digital weighing scale (SECA, Germany) and height was measured without shoes to the nearest 0.1 cm, BMI was calculated as the weight (kg) divided by the height squared $(m)^2$. We used the WHO growth curves to define BMI categories. Waist

circumference (WC) was measured by a non-elastic tape to the nearest 0.2 cm at the end of expiration at the midpoint between the top of iliac crest and the lowest rib in standing position.[25] Blood pressure was measured three times and the average was considered as the actual value. A venous blood sample was collected after a 12 h fast to assess serum levels of total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and fasting blood glucose (FBG).[24] The questions concerning the sociodemographic characteristics, the child's birth weight, and family dietary habits were included in the "parents' questionnaire." To evaluate the pattern of physical activity, three indicators were used including (i) Hours of physical education at school; (ii) screen time physical activity: Hours of watching television and working Computer (email, search, chat,…) and (iii) hours spent on sport club training. The questionnaires were filled out confidentially under the supervision of trained nurses.[25]

Statistical analysis

The bootstrap is actually a variant of simulation, with the major difference that repeated samples are drawn with replacement from the data set at hand, it is a general procedure to statistical inference based on creation a sampling distribution for a statistic by resampling, it is able to provide accurate answers in cases where other methods are simply not available, or where the usual approximations and parametric assumptions are invalid.[26] In general, we would like to get the estimate of the corresponding population parameter $\hat{\theta} = t(\hat{F})$ and some scales for its accuracy. In this case, the bootstrap method can be used. Suppose that we draw a simple random sample of size n, $S = \{x_1, \ldots, x_n\}$ from a population of size N, that N is very large than n. Then we draw a bootstrap sample of size n, with replacement, from among the original data points of the sample S. And the bootstrap algorithm creates by generating a large number of independent bootstrap samples $S_1^*, S_2^*, \ldots, S_B^*$; each of size n. Next, we calculate the statistic $\hat{\theta}$ for each of the bootstrap samples, that is $\hat{\theta}_b^* = t(S_b^*)$, b = 1,…, B. Then the distribution of $\hat{\theta}$ around the original estimate $\hat{\theta}$ is similar to the sampling distribution of $\hat{\theta}_b^*$ the estimator $\hat{\theta}$ around the population parameter θ. So that, the mean of the bootstrapped statistics estimates the expectation of the bootstrapped statistics: $\hat{\theta}^* = \frac{1}{B}\sum_{b=1}^{B}\hat{\theta}_b^*$ And $\widehat{Bias}^* = \frac{1}{B}\sum_{b=1}^{B}\hat{\theta}_b^* - \hat{\theta}$ is an estimate of the bias of $\hat{\theta}$, hat is $\hat{\theta}$ - θ. Also, the estimated bootstrap variance of $\hat{\theta}^*$; $\widehat{Var}^*(\hat{\theta}^*) = \frac{1}{B-1}\sum_{b=1}^{B}[\hat{\theta}_b^* - \frac{1}{B}\sum_{b=1}^{B}\hat{\theta}_b^*]^2$ estimates the sampling variance of $\hat{\theta}^*$.[27] There are various ways to constructing bootstrap confidence intervals: Bootstrap percentile interval, bootstrap BCa interval. The *BCa* confidence interval is a modification of the percentiles used in the percentile confidence interval based on the computation of two coefficients called "bias correction" and "acceleration."[28] There are two fundamentally different approaches in applying the bootstrap to linear regression problems: Observations and residual resampling. Bootstrapping observations are more suitable for the case of random regressors and Bootstrapping residuals are more appropriate for the case of deterministic regressors. But resampling case is safer to use in general: It will also work if the assumptions necessary to use residual resampling do hold.[21]

In this paper, with using the Kolmogorov-Smirnov test, probability–probability plot and the scatter plot of residuals versus predicted values, we realized that parametric assumptions of the linear regression model have been violated; also, possible solutions like transformations of the response variable (BMI) were not appropriate. Therefore, bootstrap resampling methods based on the observations and errors resampling were considered to evaluate the effect of various factors on obesity, and we showed that the conclusions drawn about the BMI of children and adolescent are reliable without theoretical properties and distributional assumptions on the residuals of linear regression model. Statistical analysis soft-wares (SPSS version 18.0 and R-3.1.0 for Windows) were used for data entry and analysis. In all the analyses, a two-tailed *P* value less than 0.05 ($P < 0.05$) was considered statistically significant.

Results

This study included 5570 school students (49.8% girls and 50.2% boys). Participants had a mean (SD) age of 14.7 (2.4) years without significant difference among girls and boys. Overall, nearly 70% of the population lived in urban areas and about 94% of students studied in public schools. The mean numbers of household members and children in each family were 5.21 and 3.58 persons, respectively. Descriptive characteristics of the study participant are shown in Table 1.

There were non-constant error variance, and non-normality distribution for residuals (Kolmogorov-Smirnov Z = 6.091, $P < 0.001$), and possible transformations of the response variable did not improve the usefulness of the linear regression model. Thse results are shown in Table 2.

Therefore, the two approaches of bootstrapping regression were used to evaluate the effect of some factors on obesity among children and adolescents, then we compared results of the two approaches. The illustration of the bootstrap (B = 1000 bootstrap samples) regression results based on the observations from the data given is shown in Table 3.

And the illustration of the bootstrap (B = 1000 bootstrap samples) regression results based on the resampling errors from the data given is shown in Table 4.

As shown in Tables 3 and 4, both approaches were similar, and the regression of BMI on covariates was significant as result of variance analysis ($P < 0.05$). There was a little bias in the bootstrap coefficients, and the tests

of significance showed that the effects of sex, age, waist circumference, family history obesity and frequency of breakfast days were clearly significant ($P < 0.001$). To evaluate the effects of the pattern of physical activity and the birth weight, dummy variables were used. The effect of moderate level of physical activity was not significant in comparison to mild level of physical activity ($P = 0.1$), but the effect of vigorous level of physical activity was significant in comparison to mild level of PA ($P = 0.012$), vigorous PA had inverse association with BMI of children and adolescents due to negative regression coefficient, and adolescents with vigorous physical activity were less obese than adolescents with mild physical activity. In comparison to low birth weight, medium and high birth weight had significant effect on obesity, and the adolescents with medium and high birth weight were more obese than adolescents with low birth weight. By performing the resampling scheme many times, a good estimate can be obtained of the distribution of the statistics of interest, in this case slopes and intercept. These distributions can be seen as approximations to the true distributions of the estimators, and therefore statistics of interest such as bias, standard deviation, and confidence intervals can be derived from them in the usual manner. In this article, the distributions of the bootstrap regression coefficients estimations for observations resampling are graphed in Figure 1a-j. The shape of these graphs showed that a histogram of the replicates with an overlaid smooth density estimate and the skewness of the distribution of regression parameter estimate from the bootstrap replicate.

Table 1: Descriptive characteristics of the study participant

Age	14.732.413[1]
Birth weight	
Low birth weight	755 (14.37)[2]
Medium birth weight	3954 (75.25)[2]
High birth weight	545 (10.38)[2]
Body mass index	19.42±4.098[1]
Family history of obesity	
Yes	1623 (39.96)[2]
No	2438 (60.03)[2]
Frequency of breakfast days	4.53±2.472[1]
Physical activity	
Low PA	1695 (33.35)[2]
Moderate PA	1681 (33.05)[2]
Vigorous PA	1709 (33.60)[2]
Sex	
Male	2796 (50.2)[2]
Female	2774 (49.8)[2]
waist circumference	68.72±2.689[1]

1 Indicates: Mean±SD, 2 Indicates: Number (percentage)

Table 2: Kolmogorov–Smirnov (K-S) test result

Kurtosis	Skewness	*P*	Kolmogorov-Smirnov Z
11.43	0.3	<0.001	6.091

Discussion

At the present time, childhood obesity is a main public health problem and its prevalence has been increasing worldwide. Both genetic and lifestyle factors may be causes of this problem.[29] In fact a complex interaction between genetic, environmental and behavioral factors is known to be the underlying cause of early obesity.[30,31] The main objective of the present study was to investigate the effect of some factors, including birth weight, sex, age, waist circumference, family history of obesity, as well as some lifestyle factors, such as frequency of breakfast days and physical activity, on the BMI among a nationally representative sample of Iranian

Table 3: The summary statistics of regression coefficients for bootstrap regression based on the observations (*n*=4046, B=1000)

Variables	Average of estimates	S.E.	Bias	*P*	5%, 95% percentile CI	5%, 95% BC_a CI
Constant	8.148	1.318	0.110	<0.001*	(5.664, 9.618)	(7.665, 9.132)
Sex	−0.629	0.131	0.031	<0.001*	(−0.869, −0.419)	(−0.798, −0.428)
Age	0.516	0.071	0.022	<0.001*	(0.388, 0.593)	(0.493,0.571)
Waist circumference	0.064	0.035	0.011	<0.001*	(0.029, 0.130)	(0.050, 0.059)
Family history obesity	0.722	0.141	0.034	<0.001*	(0.492, 0.944)	(0.568, 0.923)
Frequency of breakfast days	−0.070	0.024	0.002	0.012*	(−0.108, −0.028)	(−0.111, −0.034)
Mild PA	-	-	-	-	-	-
Moderate PA	−0.230	−0.139	−0.011	0.1	(−0.453, −0.015)	(−0.477 , −0.035)
Vigorous PA	−0.374	0.143	0.012	0.012*	(−0.583, −0.137)	(−0.609, −0.165)
Low birth weight	-	-	-	-	-	-
High birth weight	−0.451	−0.227	−0.024	0.048*	(0.096, 0.804)	(0.154, 0.871)
Medium birth weight	0.385	0.131	0.011	0.006*	(0.167, 0.604)	(0.183, 0.646)

R^2= 0.1973, Residual standard error: 3.674, F-statistic: 110.2, *P*: < 2. 2e-16. **P* value is significant.

Table 4: The summary statistics of regression coefficients for bootstrap regression based on the resampling errors (*n*=4046, B=1000)

Variables	Average of estimates	S.E.	Bias	*P* value	5%, 95% percentile CI	5%, 95% BC_a CI
Constant	8.518	0.422	0.740	<.001*	(7.838, 9.283)	(7.665, 9.132)
Sex	−0.598	0.109	0.000	<.001*	(−0.795,−0.425)	(−0.798, −0.428)
Age	0.538	0.022	0.000	<.001*	(0.497, 0.576)	(0.493,0.571)
Waist circumference	0.053	0.002	0.000	<.001*	(0.049,0.057)	(0.050, 0.059)
Family history obesity	0.761	0.111	0.005	<.001*	(0.582,0.938)	(0.568,0.923)
Frequency of breakfast days	−0.071	0.023	0.001	0.002*	(−0.110, −0.033)	(−0.111, −0.034)
Mild PA	-	-	-	-	-	-
Moderate PA	−0.239	−0.137	−0.002	0.066	(−0.473, −0.029)	(−0.477 , −0.035)
Vigorous PA	−0.381	0.132	−0.005	0.008*	(−0.623, −0.175)	(−0.609,−0.165)
Low birth weight	-	-	-	-	-	-
High birth weight	−0.466	−0.225	−0.009	0.042*	(0.110, 0.840)	(0.154 ,0.871)
Medium birth weight	0.395	0.134	0.001	0.002*	(0.153 , 0.617)	(0.183 , 0.646)

R^2=0.2607, Residual standard error: 3.449, F-statistic: 158.1, *P*: < 2.2e-16. **P* value is significant

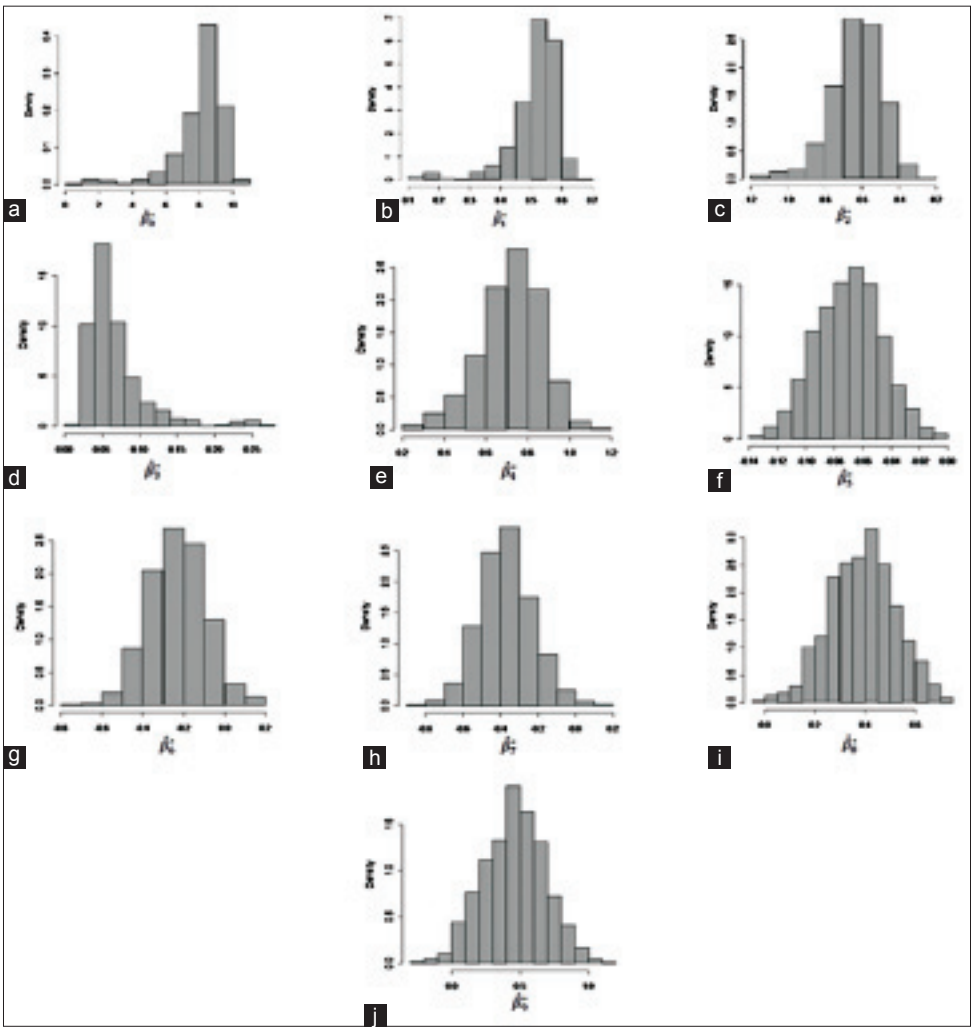

Figure 1: Histograms of observations bootstrap (B=1000, (a), (b), …, (j)) regression parameter estimates

children and adolescents by using bootstrap technique in multiple regression analysis. The results of bootstrapping regression model based on the observations and errors resampling approaches were similar. In results, *BCa* the confidence interval was a modification of the percentiles used in the percentile confidence interval based on the computation of two coefficients called "bias correction" and "acceleration".

Dietary carbohydrates, physical activity, obesity, and the "metabolic syndrome" are predictors of coronary heart disease. Current opinion in lipidology,[32,33] and contrary to others,[19,34] the prevalence of obesity was found significantly higher in boys than in girls. Similarly, the prevalence of being overweight and obese was found to be higher in boys than in girls in Brazilian,[35] Canadian,[36] and Australian[37] adolescents. Unlike these results, in the studies conducted on Egyptian[38] adolescent students, the prevalence of being overweight among girl students was found higher than among boys. Not surprisingly, waist circumference and age were positively associated with BMI. In study about the prevalence of overweight among US children and adolescents, age was positively associated with BMI for boys and girls.[39] Also, another finding in multivariate regression models to examine the association between demographic and lifestyle variables and the BMI of children and adolescents was that BMI is strongly related to age, and age had a strong, positive relation with BMI.[40] In our finding, adolescents with medium and high birth weight were more obese than adolescents with low birth weight. Another study found that birth weight was positively associated with weight, height, and BMI at age 19 years.[41] These findings are consistent with those of studies in populations born at term.[42,43] Childhood obesity increases the risk of obesity in adulthood, but how parental obesity affects the chances of a child's becoming an obese adult is unknown.[29] Present study demonstrated family history had positive association with BMI of children and adolescents. A previous study demonstrated the importance of parental obesity in predicting children's risk of obesity in adulthood, so that in a multilevel model, maternal BMI and family structure (single-parent vs. two parent families) were the only significant predictors of child BMI z scores.[44] our findings are consistent with the results of a previous study conducted with a random sample of 1581 Australian school children aged 7–15 years,[45] which found that having parents, who were overweight increased the risk of children being overweight. The role of physical activity in preventing obesity during adolescence remains unknown.[46] We evaluated changes in activity in relation to changes in BMI, in our finding adolescents with vigorous level of physical activity are less obese than adolescents with mild physical activity, but the effect of moderate level of physical activity is not significant in comparison to mild PA on adolescent BMI. Former analyses of the Growing Up Today Study cohort by regression analysis revealed that, in older children and adolescents, increasing physical activity levels were associated with reduced BMI during the time, all hypothesized factors were in the model simultaneously with several adjustment factors.[47,48] In addition, a last comprehensive survey of prospective observational studies by Must and Tybor detected that increased physical activity and decreased sedentary behavior were protective against relative weight and fatness gains during the childhood and adolescence.[49] Furthermore, Berkey *et al*. showed that increasing sedentary behaviors were related to high BMI in girls.[48] Our result showed that frequency of breakfast days had inverse association with BMI of children and adolescents. Some studies have suggested that skipping breakfast is associated with the overweight/obese status.[50,51] Inverse dependence between breakfast frequency and BMI by results of classic regression models has been recorded in many cross-sectional studies.[52,53] To our knowledge, only three prospective studies assessing a relation between breakfast habits and obesity have been performed in children and adolescents to date.[54,55] In the Growing up Today Study, were collected in 14 000 boys and girls aged 9-14 years. Obesity breakfast skippers had lower BMIs over time when contrasted with obesity breakfast eaters, whereas normal-weight breakfast skippers had higher BMIs over time when contrasted with normal-weight breakfast eaters. But note, when these identical data were analyzed cross-sectionally, results showed that, overall, breakfast skippers were heavier.[56] In the current study, where controlling for the other variables in the model, the effect of each of the risk factors as independent variable on BMI by using bootstrapping regression was similar with documented results of many previous studies by using classic regression methods. The bootstrap method estimate the variation of a statistic from the variation of that statistic between sub-samples, rather than from parametric assumptions and may yield similar results in many situations. This resampling have gained wide acceptance and huge popularity in the field of applied statistics.[26] By performing this resampling scheme many times, a good estimate can be obtained of the distribution of the statistics of interest, in this case slopes and intercept. These sampling distributions can be seen as approximations to the true distributions of the estimators, and therefore statistics of interest can be derived from them in the usual manner.[21] By making B large enough, it is seek to ensure that the bootstrap estimates of the regression parameter is close to the true bootstrap estimates of parameters which based on the all n^n bootstrap samples. It was suggested the bootstrap replications sufficient to be for estimating of variance $50 < B < 100$, $B \approx 1000$ for estimating of standard errors and confidence intervals. Therefore, we used $B = 1000$ for estimating of the statistics of interest. In this article, the bootstrap resampling provided a way of inferences in situation where the standard method might be expected to be inappropriate.[57,58] Disadvantages of this method is bootstrap based on the error procedure assumes the fitted regression model is correct and the errors are identically distributed but is preferable to the bootstrap based on the resampling of observation, for violating the assumption for constant design matrix, and resampling cases is safer to use in general.[57] As a conclusion, here, bootstrap method is preferable in linear regression because of some theoretical properties like having any distributional assumptions on the residuals and hence allows for inference even if the errors do not follow normal distribution or constant error

variance, and realizing the risk factors of obesity and its consequence, obesity prevention model should be addressed as part of the family and school health program.

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Conflicts of interest

There are no conflicts of interest.

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