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Original Contribution

A Multistate Model for Analyzing Transitions Between Body Mass Index Categories During Childhood

The Generation XXI Birth Cohort Study

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Prevalences of overweight and obesity in young children have risen dramatically in the last several decades in most developed countries. Childhood overweight and obesity are known to have immediate and long-term health consequences and are now recognized as important public health concerns. We used a Markov 4-state model with states defined by 4 body mass index (BMI; weight (kg)/height (m)^2) categories (underweight (<-2 standard deviations (SDs) of BMI z score), normal weight ($-2 \leq \text{SD} \leq 1$), overweight ($1 < \text{SD} \leq 2$), and obese (>2 SDs of BMI z score)) to study the rates of transition to higher or lower BMI categories among children aged 4–10 years. We also used this model to study the relationships between explanatory variables and their transition rates. The participants consisted of 4,887 children from the Generation XXI Birth Cohort Study (Porto, Portugal; 2005–2017) who underwent anthropometric evaluation at age 4 years and in at least 1 of the subsequent follow-up waves (ages 7 and 10 years). Children who were normal weight were more likely to move to higher BMI categories than to lower categories, whereas overweight children had similar rates of transition to the 2 adjacent categories. We evaluated the associations of maternal age and education, type of delivery, sex, and birth weight with childhood overweight and obesity, but we observed statistically significant results only for sex and maternal education with regard to the progressive transitions.

body mass index; body mass transitions; childhood obesity; Generation XXI; interval censoring; multistate models

Abbreviations: BMI, body mass index; CI, confidence interval; OR, odds ratio; SD, standard deviation.

Childhood overweight and obesity are of major public health concern and have severe health, social, and economic impacts; they even have the potential to reverse the increase in longevity that has been observed around the world (1, 2). Prevalence may be plateauing in some settings, but in a recent study using data from 128.9 million children, the worldwide prevalences of overweight and obesity in 2016 were still high: 19.2% and 17.5%, respectively, in boys and 7.8% and 5.6%, respectively, in girls (3). In Portugal, the prevalences of overweight and obesity in 2016 were even higher: 33.2% and 31.9%, respectively, in boys and 10.8% and 10.3%, respectively, in girls (3).

The interest in studying overweight and obesity from a life-course perspective, starting as early as possible, comes from the evidence of the early development and high tracking of overweight and obesity across the life course (4, 5). According to this evidence, a great number of children are, even before birth, on a pathway associated with increased risk of overweight or obesity (1). Thus, in order to better define and target public health strategies towards the prevention of overweight/obesity, it is very important to understand its early-life determinants.

Several early-life determinants of childhood overweight/obesity have been identified (6, 7). Some of them, such as age, sex, race, and genetics, cannot be changed, while others are modifiable. For example, birth by cesarean delivery and socioeconomic status have been associated with the development of overweight and obesity across the life course (8–12).

Traditionally, the relationships of these and other variables with overweight and obesity have been studied using simple statistical tests such as Student's t test or analysis of variance. In some longitudinal studies, the influence of these risk factors has been evaluated using the Cox proportional hazards model or its extensions to deal with time-dependent covariates. However, the use of methods such as multistate models to analyze determinants of overweight and obesity could be very interesting, as they are particularly useful for describing the complexities of a disease process involving several states (13–17). They can be used when interest lies in estimating the instantaneous rate of transition between various states, estimating the probability of transition from one state to another within a specific time period, or estimating the average period of a single stay in a given state (mean sojourn time); but they can also be used to examine the association of covariates with transition intensities. Although methods for multistate analysis have been well studied, epidemiologists and clinicians have not taken advantage of these developments, as often user-friendly software is not available (13, 16, 18). Moreover, multistate models must be updated for the constraint of interval censoring, since in most sampling schemes the exact times of state-to-state transitions are not exactly observed but are only known to have occurred during the interval between assessments.

In this study, we aimed to estimate the instantaneous rate of transition among various body mass index (BMI) categories (underweight, normal weight, overweight, and obese) in children between the ages of 4 and 10 years. We also aimed to evaluate the associations of vectors of explanatory variables—maternal age and education at delivery, type of delivery, sex, and birth weight—with the transition intensities, taking into account the fact that the transition times were interval-censored.

METHODS

Study population

The participants in this study were part of the Generation XXI birth cohort (19). This cohort of children was assembled after delivery between April 2005 and August 2006, during the hospital stay, at the 5 public clinics providing obstetrical and neonatal care in the metropolitan area of Porto, Portugal. Follow-up evaluations of the cohort were carried at 4 years of age (between April 2009 and July 2011), at 7 years of age (between April 2012 and March 2014), and at 10 years of age (between July 2015 and July 2017). Of the 8,647 initial cohort members, 7,459 (86%), 6,889 (80%), and 6,392 (74%) were assessed at the 4-, 7-, and 10-year follow-up evaluations, respectively. Only singletons without congenital abnormalities who underwent anthropometric evaluation at age 4 years ($n = 5{,}497$) and in at least 1 of the subsequent follow-up waves (i.e., anthropometric evaluation at age 7 years and/or age 10 years) were considered. The final sample for this study comprised 4,887 children.

Information on family and personal history of disease, sociodemographic characteristics, maternal prepregnancy anthropometric parameters, and intrauterine exposures was collected during a face-to-face interview with the mother conducted during the hospital stay by trained interviewers. These interviews took place 24–72 hours after delivery. Data on delivery and newborn characteristics were abstracted from clinical records by the same interviewers. The variable "maternal education" corresponded to the total number of years of education attained by the mother. Birth weight, abstracted from the clinical records, was categorized into 3 groups: <2,500 g, 2,500–4,000 g, and >4,000 g.

At 4, 7, and 10 years of age, trained researchers performed anthropometric measurements on the child, according to standard procedures. Height was measured using a stadiometer to the nearest 0.1 cm, and weight was measured with a digital scale to the nearest 0.1 kg, while the child stood barefooted in underwear. BMI was calculated as weight (kg)/height (m)^2 and then converted into standard deviation (SD) scores (BMI z scores), adjusted for specific age and sex categories using the World Health Organization growth reference values (20). The common BMI categories were defined according to the cutoff points proposed by the World Health Organization as <-2 SDs of the BMI z score for underweight, $-2 \leq \mathrm{SD} \leq 1$ for normal weight, $1 < \mathrm{SD} \leq 2$ for overweight, and >2 SDs of the BMI z score for obesity (20).

Overview of the multistate models

A multistate model is a model for a time-continuous stochastic process $\{X(t)\colon t \in T\}$ which at any time occupies one of a few possible states. In biomedical applications, the states may be based on health conditions, disease stages, or a nonfatal complication in the course of an illness. In this study we implemented a multistate model that described how a child moves between a series of BMI states. Graphically, these models are usually illustrated using diagrams with boxes representing the BMI states and with arrows presenting possible transition between the states. In this study, we considered the 4-state model depicted in Figure 1, and we assumed that subjects could be in any given state at time $t = 0$. This model involved 4 states which were built using predefined BMI categories. The 6 possible transitions are identified by the arrows: 1) from "underweight" to "normal weight," 2) from "normal weight" to "underweight," 3) from "normal weight" to "overweight," 4) from "overweight" to "normal weight," 5) from "overweight" to "obese," and 6) from "obese" to "overweight."

We emphasize that the multistate model should reflect the underlying progression of BMI categories rather than the observed progression. For instance, although a participant could be in the normal weight category at one assessment and then in the obese category at the next, this does not imply that the transitions occurred instantaneously. For example, a direct transition between the "underweight" state and the "overweight" state was not allowed, since we assumed that a child classified as "underweight" must pass (sometime in the interim) through the intermediate "normal weight" state before becoming "overweight."

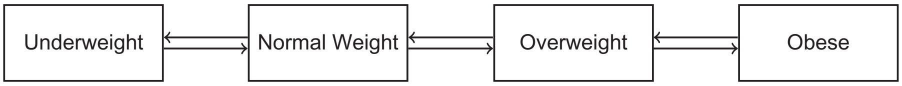

Figure 1. Model of progression between body mass index (weight (kg)/height (m)^2) categories. Children advance between adjacent stages of body mass index and optionally recover to an adjacent state.

When participants are followed continuously and the exact times of transition are known or are only subject to right-censoring, a wide range of multistate modeling and estimation strategies are available (21). However, in our cohort, as in most, it is not possible to observe participants continuously throughout the life span, because participants are in fact observed only at periodic visits during the follow-up evaluations. In this case, the exact times of state-to-state transitions are interval-censored. The transition is only known to have occurred within a bounded time interval, that is, between follow-up assessments.

Under this constraint, the available data for each participant consisted of the dates of the follow-up assessments and the BMI state that was occupied at each follow-up assessment. This sampling scheme poses a variety of estimation challenges because it lacks information on exact transition time and because the number and timing of assessments may vary across participants. Thus, standard multistate methods can no longer be used, and the techniques adapted to accommodate such a sampling scheme must be applied (13).

Specifically, in this study, a time-homogeneous Markov multistate model that described how a child moved between 4 states based on BMI category was implemented. For each child, besides the state occupied at those times, a vector of covariates including maternal age and education at delivery, type of delivery, sex, and birth weight was recorded. Markov models provide sufficient flexibility and reasonable analytical tractability to fit such data. These models have become easier to fit, particularly if an assumption of time homogeneity is made. Recent advances in developed software also allow accommodation for misclassification of the observed states. All analyses were conducted using the “msm” library, available in R (R Foundation for Statistical Computing, Vienna, Austria) (21, 22).

RESULTS

Table 1 presents participants’ characteristics according to BMI state at the 4-year follow-up evaluation. Mean values for maternal age and education are given for each BMI state. Because of the skewness of data for the maternal education variable, quartile medians and interquartile ranges are provided in a table footnote. The mean maternal age at the child’s birth ranged from 26.4 years to almost 30.0 years of age. The mean total duration of maternal education ranged from 10 years to 11 years. Underweight children had younger mothers and mothers with less education and were more likely to be male than normal-weight, overweight, or obese children. The mothers of the normal-weight children had more years of education, were more likely to have a vaginal delivery, and had more sons.

Table 2 presents the associations between BMI categories and potential determinants of childhood overweight and obesity at the 4-year follow-up evaluation. The reference category for the results was “normal weight.” Compared with the reference category, maternal age was inversely associated with underweight (odds ratio (OR) = 0.91, 95% confidence interval (CI): 0.82, 0.99)

Table 1. Characteristics of Participants According to Body Mass Index Category at the 4-Year Follow-up Evaluation, Generation XXXI Birth Cohort Study, Porto, Portugal, 2005–2017

Variable	BMI[a] Category[b]							
	Underweight (*n* = 20)		Normal Weight (*n* = 3,308)		Overweight (*n* = 1,056)		Obese (*n* = 503)	
	No.	%	No.	%	No.	%	No.	%
Maternal age at delivery, years[c]	26.4 (5.6)		29.8 (5.2)		29.8 (5.3)		29.2 (5.6)	
Maternal education at delivery, years[c,d]	9.7 (4.6)		11.3 (4.3)		10.9 (4.2)		9.9 (3.9)	
Child’s sex								
Female	9	45.0	1,589	48.0	545	51.6	273	54.3
Male	11	55.0	1,719	52.0	511	48.4	230	45.7
Type of delivery								
Vaginal	18	90.0	2,088	63.1	639	60.5	306	60.8
Cesarean	2	10.0	1,220	36.9	417	39.5	197	39.2
Birth weight, g								
<2,500	5	25.0	257	7.8	49	4.6	23	4.6
2,500–4,000	15	75.0	2,957	89.4	950	90.0	451	89.7
>4,000	0	0	94	2.8	57	5.4	29	5.7

Abbreviations: BMI, body mass index; IQR, interquartile range; SD, standard deviation.

[a] Weight (kg)/height (m)^2.

[b] BMI categories were defined according to the cutoff points proposed by the World Health Organization as <−2 SDs of the BMI *z* score for underweight, −2 ≤ SD ≤ 1 for normal weight, 1 < SD ≤ 2 for overweight, and >2 SDs of the BMI *z* score for obesity (20).

[c] Values are expressed as mean (standard deviation).

[d] Median values for maternal education: underweight—9.0 years (IQR, 6.0–12.0); normal weight—12.0 years (IQR, 8.0–16.0); overweight—11.0 years (IQR, 8.0–15.0); obese—9.0 years (IQR, 6.0–12.0).

Table 2. Odds Ratios for the Association Between Baseline Characteristics and Body Mass Index Category at 4 Years of Age (Multinomial Logistic Regression Model), Generation XXI Birth Cohort Study, Porto, Portugal, 2005–2017

Group	BMI[a] Category[b]					
	Underweight		Overweight		Obese	
	OR	95% CI	OR	95% CI	OR	95% CI
Maternal age at delivery, years	0.91[c]	0.82, 0.99	1.00	0.98, 1.01	0.99	0.96, 1.00
Maternal education at delivery, years	0.94	0.82, 1.06	0.98[c]	0.96, 0.99	0.93[c]	0.90, 0.95
Child's sex						
Female	1.00	Referent	1.00	Referent	1.00	Referent
Male	1.24	0.35, 2.13	0.86[c]	0.71, 0.99	0.77[c]	0.58, 0.96
Type of delivery						
Vaginal	1.00	Referent	1.00	Referent	1.00	Referent
Cesarean	0.20[c]	0.12, 0.25	1.12	0.97, 1.26	1.15	0.98, 1.21
Birth weight, g						
<2,500	4.16[c]	3.12, 5.19	0.58[c]	0.25, 0.91	0.56[c]	0.12, 0.99
2,500–4,000	1.00	Referent	1.00	Referent	1.00	Referent
>4,000	0.003[c]	0.001, 0.005	1.90[c]	1.55, 2.23	2.06[c]	2.05, 2.07

Abbreviations: BMI, body mass index; CI, confidence interval; OR, odds ratio.

[a] Weight (kg)/height (m)^2.

[b] For definitions of BMI categories, see Table 1. The reference category was normal weight.

[c] $P < 0.05$.

and maternal education was inversely associated with overweight and obesity (for each 1-year increase, OR = 0.98 (95% CI: 0.96, 0.99) for overweight and OR = 0.93 (95% CI: 0.90, 0.95) for obesity). Male children at age 4 years were less likely to be overweight or obese than females (OR = 0.86 (95% CI: 0.71, 0.99) for overweight and OR = 0.77 (95% CI: 0.58, 0.96) for obesity). Compared with the normal-weight category, children born by cesarean delivery were less prone to be underweight (OR = 0.20, 95% CI: 0.12, 0.25). For birth weight, the reference group was 2,500–4,000 g. Compared with the normal-weight state, children in the category <2,500 g were more likely to be underweight, whereas those in category >4,000 g were less likely to be underweight. Reverse results were obtained for overweight and obesity in comparison with normal weight.

A natural way to model the rates of transition between well-defined BMI states is to use a multistate model. Multistate data can be summarized by counting, for each state s, the number of times an observation from the state r was followed by the state s. The displayed results in Table 3 are simply frequencies of pairs of consecutively observed states and do not reflect the underlying progression of performance status. As we can observe, the obese BMI state was followed by a less severe BMI state (normal weight or overweight) on 240 occasions, although for the overweight BMI state, that happened on 456 occasions. One child moved from the underweight state to the obese state.

The primary results of the multistate analysis are displayed in Table 4. The maximum likelihood estimate and corresponding 95% confidence interval for each possible instantaneous transition are presented. Since direct transitions between nonadjacent states were not permitted (it was assumed that a child transitioning to a nonadjacent state must have passed through an adjacent state in between, rather than jumping straight to a nonadjacent state), the instantaneous transition rates were equal to zero in those cases.

Table 4 shows the estimated intensities representing the instantaneous hazard (risk) of progression between the BMI states. Results shown in this table reveal that children in the overweight state were as likely to transit to the normal-weight state as to the obese state (0.0101 vs. 0.0099). A transition from normal weight to overweight was more than 15 times more likely (0.0061) than a transition from normal weight to underweight

Table 3. Distribution of Children (Number) According to Consecutively Observed Body Mass Index States Between the Ages of 4 and 10 Years, Generation XXI Birth Cohort Study, Porto, Portugal, 2005–2017

BMI[a] Category[b] at Current Assessment[c]	BMI Category at Next Assessment			
	Underweight	Normal Weight	Overweight	Obese
Underweight	13	16	0	1
Normal weight	50	4,902	852	125
Overweight	0	456	1,057	435
Obese	0	19	221	868

Abbreviation: BMI, body mass index.

[a] Weight (kg)/height (m)^2.

[b] For definitions of BMI categories, see Table 1. The reference category was normal weight.

[c] Counts were taken over all individuals in the 3 follow-up periods; participants may be represented more than once.

Table 4. Matrix of Estimated Transition Intensities for a Multistate Model of Transition Between Body Mass Index Categories Between Ages 4 and 10 Years, Generation XXI Birth Cohort Study, Porto, Portugal, 2005–2017

BMI[a] Category[b]	BMI Category							
	Underweight		Normal Weight		Overweight		Obese	
	MLE[c]	95% CI	MLE	95% CI	MLE	95% CI	MLE	95% CI
Underweight	−0.0256	−0.0419, −0.0157	0.0256	0.0157, 0.0419	0[d]		0[d]	
Normal weight	0.0004	0.0003, 0.0005	−0.0065	−0.0070, −0.0060	0.0061	0.0058, 0.0066	0[d]	
Overweight	0[d]		0.0101	0.0092, 0.0111	−0.0200	−0.0214, −0.0187	0.0099	0.0090, 0.0108
Obese	0[d]		0[d]		0.0083	0.0073, 0.0095	−0.0083	−0.0096, −0.0073

Abbreviations: BMI, body mass index; CI, confidence interval; MLE, maximum likelihood estimate.

[a] Weight (kg)/height (m)^2.

[b] For definitions of BMI categories, see Table 1. The reference category was normal weight.

[c] Maximum likelihood estimate of the transition intensities.

[d] Zero was defined in the model for the nonadjacent states. The underlying model specified that a child transitioning to a nonadjacent state must have passed through an adjacent state in between, rather than jumping straight to a nonadjacent state.

(0.0004). The most likely transition intensity was from underweight to normal weight (0.0256).

The estimated 12-month and 24-month transition probability matrices are given in Table 5. The estimated probability of a normal-weight child being underweight or obese 12 months later was approximately 0.4% (0.36% for underweight and 0.38% for obesity). The probability of being overweight after that period was approximately 6.3%. Considering the period of 24 months, children in the normal-weight state had a 0.6% probability of being underweight, an 11.0% probability of being overweight, and a 1.4% probability of being obese after that period. For a child in the overweight state, the estimated probability of transitioning to the normal-weight state after 12 months was slightly higher than the probability of transitioning to the obese state: 10.4% vs. 10.1% (18.0% vs. 17.3% after 24 months). A child currently in the obese state had a 0.5% probability of transitioning to the normal-weight state after 12 months. After 24 months, the chance increased to 1.9%.

Table 6 presents hazard ratios from the discrete-time event history models. Statistically significant results were found only for sex and maternal education. In addition, these statistical findings were significant only for the progressive transitions—that is, a transition to normal weight among children who were underweight, a transition to overweight status among those who were normal weight, and a transition to obese status among those who were overweight. As can be seen in Table 6, results show that these risk factors changed across transitions. While females were more likely to experience transitions to normal

Table 5. Estimated 12-Month and 24-Month Probabilities of Transitioning Between Body Mass Index Categories Between Ages 4 and 10 Years, Generation XXI Birth Cohort Study, Porto, Portugal, 2005–2017

Month and BMI[a] Category[b]	Current BMI Category							
	Underweight		Normal Weight		Overweight		Obese	
	MLE[c]	95% CI	MLE	95% CI	MLE	95% CI	MLE	95% CI
12 months								
Underweight	0.7359	0.6129, 0.8240	0.2545	0.1697, 0.3737	0.0093	0.0060, 0.0139	0.0004	0.0002, 0.0005
Normal weight	0.0036	0.0026, 0.0049	0.9290	0.9244, 0.9329	0.0635	0.0598, 0.0676	0.0038	0.0034, 0.0043
Overweight	0.0002	0.0001, 0.0003	0.1043	0.0951, 0.1136	0.7947	0.7828, 0.8063	0.1008	0.0928, 0.1106
Obese	0[d]		0.0053	0.0045, 0.0062	0.0848	0.0747, 0.0961	0.9099	0.8980, 0.9206
24 months								
Underweight	0.5424	0.3718, 0.6877	0.4246	0.2908, 0.5810	0.0304	0.0201, 0.0435	0.0025	0.0016, 0.0038
Normal weight	0.0061	0.0044, 0.0080	0.8706	0.8629, 0.8778	0.1098	0.1030, 0.1163	0.0135	0.0122, 0.0149
Overweight	0.0007	0.0006, 0.0009	0.1803	0.1667, 0.1952	0.6467	0.6276, 0.6638	0.1723	0.1600, 0.1851
Obese	0[d]		0.0186	0.0159, 0.0216	0.1449	0.1280, 0.1625	0.8364	0.8169, 0.8552

Abbreviations: BMI, body mass index; CI, confidence interval; MLE, maximum likelihood estimate.

[a] Weight (kg)/height (m)^2.

[b] For definitions of BMI categories, see Table 1. The reference category was normal weight.

[c] Maximum likelihood estimate of the transition intensities.

[d] $P < 0.00001$.

weight among those who were underweight (hazard ratio = 1/0.15 = 6.67), the hazard ratios of 1.16 (95% CI: 1.00, 1.35) and 1.34 (95% CI: 1.08, 1.65) show that males were more likely to experience a transition to overweight among those who were normal weight and a transition to obesity among those who were overweight, respectively. A similar pattern was observed when analyzing the covariable maternal education. For example, considering the transition to normal-weight status among children who were underweight, the hazard ratio of 1.23 (95% CI: 1.01, 1.51) revealed a 23% increase in the "hazard" of becoming normal weight per year of maternal education; opposite associations were observed for the remaining progressive transitions, with hazard ratios of 0.98 (normal weight to overweight) and 0.96 (overweight to obese) per year of maternal education, respectively.

DISCUSSION

Over the last several decades, the prevalence of overweight and obesity among children has risen sharply (3). Although this fact is well known and well documented, to the best of our knowledge, little is known about the rates of transition between BMI categories in childhood and the determinants of these transitions.

Three major findings emerged from our analyses. First, in the cross-sectional analysis at age 4 years, some determinants were associated with the different BMI categories. Maternal age was inversely associated with underweight, and maternal education was inversely associated with overweight and obesity. It is known from previous studies that one of the main determinants of overweight and obesity is socioeconomic position, and maternal education is one of the most consistent indicators of socioeconomic position (8, 9, 11, 23). Females were more likely to be overweight and obese, which is not a consistent finding of previous studies, since some studies have found a higher prevalence of overweight and obesity in females and others a higher prevalence in males, and in still others no association was found (7, 9, 23). Being born by cesarean delivery was associated with lower odds of being underweight and, although the finding was not statistically significant, with higher odds of being overweight and obese. These results are in accordance with previous literature showing an association between birth by cesarean delivery and overweight and obesity across the life course (10, 12). A low birth weight was associated with higher odds of being underweight and lower odds of being overweight or obese. On the opposite end of the spectrum, a high birth weight was associated with lower odds of being underweight and higher odds of being overweight and obese. This is in accordance with the tracking phenomenon, which states that a child born with a high or low weight will have a high or low weight throughout life (24, 25). Several studies have also demonstrated that a high birth weight is associated with overweight and obesity later in life (23, 26, 27).

Second, using the longitudinal approach, which was one of the strengths of our analysis, the most likely transitions observed were transitions from underweight to normal weight and from normal weight to overweight. The estimated probability of a normal-weight child becoming overweight or obese after 24 months was approximately double the probability after 12 months (12.3% for overweight and 6.7% for obesity, respectively). The same pattern occurred when considering a child observed in the overweight state. In this case, the probability of being in the obese state after 24 months was 17.2%, while the probability after 12 months was 10.1%. These results seem to be in accordance with studies showing an increase in the prevalence of overweight and obesity with age (7).

Third, our results identified determinants affecting different transitions. In the present study, a higher level of maternal education was associated with a higher probability of an underweight child's becoming normal weight and with lower probabilities of a normal-weight child's becoming overweight and an overweight child's becoming obese. Thus, a higher level of maternal education seems to protect children from unhealthy weight transitions (i.e., protecting them from transitioning from lower weight status to overweight or obesity, as well as promoting a transition from underweight to normal weight). Males had a lower probability of transitioning from underweight to normal weight and higher probabilities of transitioning from normal weight to overweight and from overweight to obesity. The association between type of delivery and transition intensity was not statistically significant; however, our findings showed a trend in the association with type of delivery across BMI states, suggesting that children born by cesarean delivery may be more likely to transition to higher levels of BMI.

We chose the World Health Organization growth reference values (20) for calculation of the BMI z scores in this study because 1) they are the most commonly used values in European populations, 2) longitudinal data were used to establish them, and 3) they are currently the reference values for children in Portugal.

The strengths of our study included 10 years of cohort data that allowed us to estimate the instantaneous rate transitions, probabilities of transition, and determinants of transition across children's BMI states between the ages 4 and 10 years in the Generation XXI birth cohort. Although there have been several studies regarding the prevalence of childhood overweight/obesity (1–3), data regarding its incidence is scarce, especially at such a young age. Finally, we used a multistate model, a method that has been used to analyze transitions between states in some diseases, but to the best of our knowledge these models have not yet been applied to examine BMI transitions in children (13, 16, 18). Although this method is novel, it is important to emphasize that it takes into account not only the time but also an important issue related to the sampling scheme: censoring. Traditionally, these events are studied using extensions of the Cox proportional hazards model. However, the parameterization of the covariate in these models is often very restrictive, providing constant estimates over the whole study period (28). These models can reveal that different determinants affect different transitions, which would not be possible with other models (e.g., the Cox regression model). They can also show that the determinants affect each transition in a different way. For example, it would be very unlikely that the association of some determinants with transitions to higher BMI categories would be the same as or similar to the association with transitions to lower BMI categories. In fact, opposite associations are often expected, as shown in our multistate modeling analysis for the variables sex and maternal education.

There was interval censoring in the analyses of the outcome time variable. This type of censoring occurs because the exact

Table 6. Hazard Ratios From Discrete-Time Event-History Models of Transitions Between Body Mass Index Categories Between Ages 4 and 10 Years, Generation XXI Birth Cohort Study, Porto, Portugal, 2005–2017

Variable	BMI[a] Status[b] Transition											
	From Underweight to Normal Weight		From Normal Weight to Underweight		From Normal Weight to Overweight		From Overweight to Normal Weight		From Overweight to Obese		From Obese to Overweight	
	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI
Maternal age at delivery, years	1.01	0.88, 1.15	0.97	0.88, 1.06	0.99	0.98, 1.00	1.00	0.98, 1.03	0.98	0.97, 1.01	0.98	0.95, 1.01
Maternal education at delivery, years	1.23[c]	1.01, 1.51	1.14	0.98, 1.32	0.98[c]	0.97, 0.98	1.03	0.99, 1.05	0.96[c]	0.93, 0.98	1.03	0.99, 1.07
Child's sex												
Female	1.00	Referent	1.00	Referent	1.00	Referent	1.00	Referent	1.00	Referent	1.00	Referent
Male	0.15[c]	0.02, 0.80	0.51	0.14, 1.85	1.16	1.00, 1.35	1.02	0.82, 1.26	1.34[c]	1.08, 1.65	0.84	0.62, 1.15
Type of delivery												
Vaginal	1.00	Referent	1.00	Referent	1.00	Referent	1.00	Referent	1.00	Referent	1.00	Referent
Cesarean	1.81	0.45, 3.24	0.93	0.31, 2.77	1.10	0.95, 1.29	0.87	0.70, 1.09	1.01	0.82, 1.26	0.83	0.60, 1.13
Birth weight, g												
<2,500	0.46	0.11, 1.96	2.92	0.91, 3.29	0.88	0.85, 1.18	0.91	0.52, 1.59	0.97	0.62, 1.50	0.50	0.20, 1.24
2,500–4,000	1.00	Referent	1.00	Referent	1.00	Referent	1.00	Referent	1.00	Referent	1.00	Referent
>4,000	1.00	0.01, 3.10	0.87	0.04, 1.70	1.43	0.97, 2.11	1.35	0.86, 2.12	0.92	0.56, 1.51	1.09	0.57, 2.07

Abbreviations: BMI, body mass index; CI, confidence interval; HR, hazard ratio.

[a] Weight (kg)/height (m)^2.

[b] For definitions of BMI categories, see Table 1. The reference category was normal weight.

[c] $P < 0.05$.

transition time is not known; we only know that the transition occurs within some interval of time (time between assessments). In this case, statistical inference is more complicated, because there is little software available for dealing with this constraint and because of the "poor" amount of information that an interval could entail. This limitation, together with the reduced number of children undergoing some of the observed transitions, may lead to lack of statistical power in some cases. This may have limited our findings.

Our findings demonstrated mobility across BMI states during childhood. Transitions towards higher adiposity states were associated with lower levels of maternal education, independently of the child's initial state (i.e., BMI at age 4 years). Thus, these findings highlight the importance of developing prevention and intervention strategies targeting early life, especially socioeconomic factors.

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