Late Adiposity Rebound and the Probability of Developing and Reversing Childhood Obesity

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Objective To evaluate the associations between late adiposity rebound (at or after 7.0 years of age) and the probability of developing and reversing obesity during elementary school years.

Study design Using nationally representative cohorts from Early Childhood Longitudinal Studies, Kindergarten Class of 1998-1999 and 2010-2011, weighted extended Cox hazard models were used to assess the probability of developing and reversing obesity (cut-offs for extended models were 6 and 12 months after kindergarten entry, respectively). Measurements used in the study were collected 6 times between kindergarten and fifth grade (Early Childhood Longitudinal Studies, Kindergarten Class of 1998-1999) and 8 times between kindergarten through fourth grade (Early Childhood Longitudinal Studies, Kindergarten Class of 2010-2011).

Results Among children with obesity at kindergarten entry, within 6 months, the risk of developing obesity was 73% and 76% lower for boys with late adiposity rebound than their classmates without late adiposity rebound (hazard ratio 0.27 and 0.24). Six months after entering kindergarten, similar association was observed for both boys and girls. Among children without obesity at kindergarten entry, within 12 months, the probability of reversing obesity was 52% and 54% higher for boys with late adiposity rebound than their peers without late adiposity rebound (hazard ratio 1.52 and 1.54). Twelve months after entering kindergarten, the probability of reversing obesity among both sexes with late adiposity rebound was 6-8 times that among children without late adiposity rebound.

Conclusions Late adiposity rebound was significantly associated with a decreased risk of developing obesity and an increased probability of reversing obesity among kindergarteners. *(J Pediatr 2020;216:128-35)*.

Recent studies propose that a pathway to obesity is established early in life before children enter kindergarten[1-3]; children who are experiencing obesity at the age of 3-5 years are already at an increased risk of becoming adults with obesity.[4] Rapid weight gain during the first 5 years of life is also associated with becoming an adult with overweight or obesity.[5]

This early establishment of pathway to obesity may be partially explained by the timing of adiposity rebound.[6] After an increase in body mass index (BMI) during the first year of life, the BMI of a child decreases until it reaches its lowest point.[7] Adiposity rebound is the second rise of BMI after the lowest BMI, typically occurring around the time children enter kindergarten (age of 5-6 years).[7,8] The timing of adiposity rebound is thought to be associated with the development of adiposity[9-12]; children with early timing of adiposity rebound are at an increased risk of obesity and other health problems such as type 2 diabetes, coronary heart disease, polycystic ovary disease, and metabolic syndrome later in life.[6,13-16]

Although many studies demonstrate the association between early adiposity rebound and obesity, few studies examine if late adiposity rebound is also associated with the development of obesity.[6,7,12,17]

Using 2 nationally representative cohorts of kindergarteners in 1998-1999 (Early Childhood Longitudinal Studies, Kindergarten Class of 1998-1999 [ECLS-K]) and 2010-2011 (Early Childhood Longitudinal Studies, Kindergarten Class of 2010-2011 [ECLS-K:2011]), the primary aim of this study is to evaluate the relationship between late adiposity rebound and the risk of developing childhood obesity among those without obesity at baseline. The secondary goal is to show the relationship between late adiposity rebound and the probability of reversing obesity among those with obesity at baseline.

BMI	Body mass index
CL	Confidence Limits
ECLS-K	Early Childhood Longitudinal Studies, Kindergarten Class of 1998-1999
ECLS-K:2011	Early Childhood Longitudinal Studies, Kindergarten Class of 2010-2011
HR	Hazard ratio
NCES	National Center for Education Statistics
SES	Socioeconomic status

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Methods

ECLS-K and ECLS-K:2011 were 2 longitudinal studies of 21 260 and 18 174 children respectively enrolled in public and private kindergarten in 1998-1999 and 2010-2011.[18,19] Both samples were nationally representative cohorts of children from kindergarten through eighth grade (ECLS-K) and kindergarten through fifth grade (ECLS-K:2011, data are only available until fourth grade). Children were selected using a complex, multistage probability sampling; and written informed consent was obtained from parents. For the ECLS-K cohort, measurements were collected twice a year in the fall and spring for kindergarten (mean ages, 5.7 years and 6.2 years) and first grade (mean ages, 6.7 years and 7.1 years - for the fall of first grade, data were collected from a representative subsample of one-third of the children), and once a year in the spring for third (mean age, 9.2 years), fifth (mean age, 11.2 years), and eighth grade (mean age, 14.1 years). For the ECLS-K:2011 cohort, measurements were collected twice a year in the fall and spring for kindergarten (mean ages, 5.6 years and 6.1 years), first (mean ages, 6.6 years and 7.1 years), and second grade (mean ages, 7.6 years and 8.1 years), and once a year in the spring for third (mean age, 9.1 years) and fourth grade (mean age, 10.1 years). To compare the 2 cohorts and focus on the changes in weight status during elementary school years, data points until fifth grade were used in the ECLS-K cohort.

Trained assessors obtained the weight (in pounds, using a digital scale) and height (in inches, using a portable measuring board) of children. BMI was calculated and converted to age- and sex-specific z scores and BMI percentiles using the 2000 Centers for Disease Control and Prevention growth charts.[20] Using the Centers for Disease Control and Prevention's standard thresholds, obesity was defined as BMI percentiles above 95th percentile.

Known predictors of childhood obesity including sex, race/ethnicity (non-Hispanic white; non-Hispanic black; Hispanic; non-Hispanic Asian; other), and socioeconomic status (SES: as a categorical variable, the bottom 25%; middle 50%; top 25%) were considered in multivariable models. The SES variable was created by the National Center for Education Statistics (NCES) using both parents' education levels, occupational prestige scores, and household income. Further description of the method was published elsewhere.[18,19]

To effectively utilize the longitudinal data with missing follow-up points and to address different lengths of follow-up and the possibility of developing and reversing obesity after the follow-up period (censored data), survival analyses were used to answer both research questions. The term "probability" was used interchangeably with "risk," especially for positive outcomes such as reversing obesity.[21]

Based on the weight status at kindergarten entry, children were grouped into 2 categories: "With obesity" and "without obesity." The subgroup of children with obesity was used to estimate the risk of developing obesity during elementary school years; the subgroup of children without obesity was used to estimate the probability of reversing obesity during the same period. Because the average age of adiposity rebound is known to be 5-6 years,[12] age of 7.0 years was used as the cut-off for "late adiposity rebound." The student was categorized as having "late adiposity rebound" when the lowest raw BMI of the student was recorded at or after the age of 7.0 years. For both subsets of children with and without obesity at baseline, the adiposity rebound and sex variables did not meet the proportional hazards assumption. Therefore, extended Cox hazard models were stratified by sex to calculate the probability of developing and reversing obesity. Based on the graphical results of Kaplan-Meier curves, single heaviside functions with a cut-off point of 6 and 12 months after kindergarten entry were used. In other words, the hazard ratio (HR) differed significantly between the time frames before and after each cut-off point. For missing data, comparisons of the continuous and categorical variables were performed using the Student's t-test and χ^2 test, respectively.

To account for the complex sampling design, variances were estimated using Taylor series linearization. The NCES constructed main sampling weights that adjusted for different nonresponse patterns (which could lead to bias in the estimates).[22] Therefore, NCES survey weights and adjustments were included in the models to account for nonresponse unless noted otherwise. For the missing data analysis, survey weights were not used because including survey weights eliminated children with missing data from the analysis. All tests of hypotheses were 2-sided and conducted at a 0.05 level of significance. All statistical analyses were performed using SAS v 9.4 (SAS Institute, Cary, North Carolina) and R v 3.5.2 (R Foundation for Statistical Computing, Vienna, Austria).

Totals of 3888 out of 21 409 students in the ECLS-K cohort and 4379 out of 18 174 students in the ECLS-K:2011 cohort were missing either baseline weight information (n = 2393 and 2515), all subsequent weight measurements (n = 770 and 470), or other covariates such as race/ethnicity and SES (n = 725 and 1394); these children were excluded from the analyses (**Table I**; available at www.jpeds.com). Between included and excluded children at baseline, there were no differences in the percentages of male and children experiencing obesity. However, excluded children were more likely to be black, Hispanic, or Asian and have low SES than included children in both cohorts.

Results

Children with late adiposity rebound were less likely to be experiencing obesity than their peers without late adiposity rebound at kindergarten entry (ECLS-K 8.0 % vs 12.1%; ECLS-K:2011 9.2% vs 15.7%) (**Table II**). From 1998-1999 to 2010-2011, the overall prevalence of obesity had increased from 11.5% to 14.3%. Although the prevalence of obesity increased in both children with and without late adiposity rebound, the degree of increase was greater

Table II. Demographics of children at kindergarten entry

Demographics	Full		Without late adiposity		With late adiposity	
	Unweighted	% or mean (SE)	Unweighted	% or mean (SE)	Unweighted	% or mean (SE)
ECLS-K (1998-1999)	**n = 17 521**		**n = 14 855**		**n = 2666**	
Male, %	8923	51.2 (0.39)	7435	50.3 (0.41)	1488	56.4 (1.23)
Age in mo, mean	68.4	68.5 (0.07)	68.1	68.1 (0.08)	70.4	70.4 (0.11)
Race/ethnicity, %						
Non-Hispanic white	9846	58.0 (1.55)	8215	57.0 (1.55)	1631	63.7 (1.89)
Non-Hispanic black	2561	15.6 (1.17)	2258	16.1 (1.25)	303	12.4 (1.05)
Hispanic	3092	18.9 (1.05)	2682	19.4 (1.06)	410	16.4 (1.28)
Asian	1022	2.7 (0.18)	848	2.7 (0.19)	174	2.9 (0.29)
Other	1000	4.8 (0.96)	852	4.8 (0.91)	148	4.6 (1.31)
Obesity, %	2003	11.5 (0.29)	1794	12.1 (0.32)	209	8.0 (0.55)
BMI percentile, mean	63.3	63.6 (0.46)	64.5	64.6 (0.50)	59.2	59.7 (0.64)
SES, %						
High (top 25%)	4468	23.7 (0.84)	3696	23.1 (0.84)	772	27.5 (1.44)
Middle (50%)	8787	50.5 (0.76)	7469	50.5 (0.74)	1318	50.4 (1.50)
Low (bottom 25%)	4266	25.7 (0.92)	3690	26.4 (0.93)	576	22.1 (1.27)
ECLS-K:2011 (2010-2011)	**n = 13 795**		**n = 10 960**		**n = 2935**	
Male, %	7086	51.7 (0.45)	5475	50.5 (0.50)	1611	55.9 (1.08)
Age in mo, mean	67.5	67.5 (0.11)	67.2	67.2 (0.10)	68.6	67.6 (0.19)
Race/ethnicity, %						
Non-Hispanic white	6936	53.0 (1.97)	5397	52.4 (1.99)	1539	55.3 (2.24)
Non-Hispanic black	1744	12.9 (1.44)	1462	13.6 (1.53)	282	10.2 (1.37)
Hispanic	3268	24.2 (1.49)	2604	24.5 (1.60)	664	23.5 (1.47)
Asian	1000	4.3 (0.71)	743	4.1 (0.60)	257	5.0 (1.20)
Other	847	5.6 (0.58)	654	5.5 (0.53)	193	6.0 (0.93)
Obesity, %	1955	14.3 (0.48)	1692	15.7 (0.57)	263	9.2 (0.68)
BMI percentile, mean	61.1	61.5 (0.43)	61.4	61.7 (0.47)	59.7	60.3 (0.74)
SES, %						
High (top 25%)	3504	24.4 (0.99)	2637	23.5 (0.99)	867	27.9 (1.50)
Middle (50%)	6931	50.5 (0.82)	5547	51.4 (0.81)	1384	47.2 (1.36)
Low (bottom 25%)	3360	25.1 (1.18)	2676	25.2 (1.18)	684	24.9 (1.51)

among children without late adiposity rebound (12.1% to 15.7% vs 8.0% to 9.2%). Except for the subgroup of children without obesity in the ECLS-K:2011 cohort, the mean BMI percentile did not differ between children with and without late adiposity rebound (**Table III**; available at www.jpeds.com).

In both cohorts, children with late adiposity rebound were more likely to be white and less likely to be black or Hispanic than their classmates without late adiposity rebound (**Table II**). They were also more likely to have high SES than children without late adiposity rebound.

The prevalence of obesity each year in each subgroup of children is shown in **Tables IV** and **V** (available at www.jpeds.com).

In the ECLS-K cohort, among 15 518 kindergarteners without obesity, 1835 (12.1%, 95% confidence limits [CL] 11.4%-12.9%) developed obesity at some point before or during fifth grade. Six months after entering kindergarten, the risk of developing obesity was 0.29 and 0.22 times lower for boys and girls with late adiposity rebound than their peers who did not have late adiposity rebound, respectively (**Figure, A** and **Table VI**).

In the ECLS-K:2011 cohort, among 11 840 kindergarteners without obesity, 1375 (11.6%, 95% CL 10.7%-12.5%) developed obesity at some point before or during fourth grade. As with the previous cohort, 6 months after entering kindergarten, the risk of developing obesity was 0.22 and 0.17 times lower for boys and girls with late adiposity rebound than their peers who did not have late adiposity rebound, respectively (**Figure, B** and **Table VI**).

For girls, the risk of developing obesity was not associated with late adiposity rebound within 6 months after entering kindergarten. For both cohorts, Hispanic ethnicity was associated with a higher risk of developing obesity for both sexes (HR 1.38 and 1.50 for boys and HR 1.83 and 1.28 for girls); black race was also associated with a higher corresponding risk among girls (HR 1.83 for ECLS-K and HR 1.52 for ECLS-K:2011). For both sexes, children from the top 25% of SES had a significantly lower risk of developing obesity than children from the middle 50% of SES.

In the ECLS-K cohort, among 2003 kindergarteners with obesity, 670 (33.8%, 95% CL 31.4%-36.2%) reversed obesity at some point before or during fifth grade. Twelve months after entering kindergarten, the probability of reversing obesity was 8.46 and 8.00 times higher for boys and girls with late adiposity rebound than their peers who did not have late adiposity rebound, respectively (**Figure, C** and **Table VII**). Among those who had reversed obesity, the risk of reverting back to obesity was significantly lower for those with late adiposity rebound (**Table VIII**; available at www.jpeds.com).

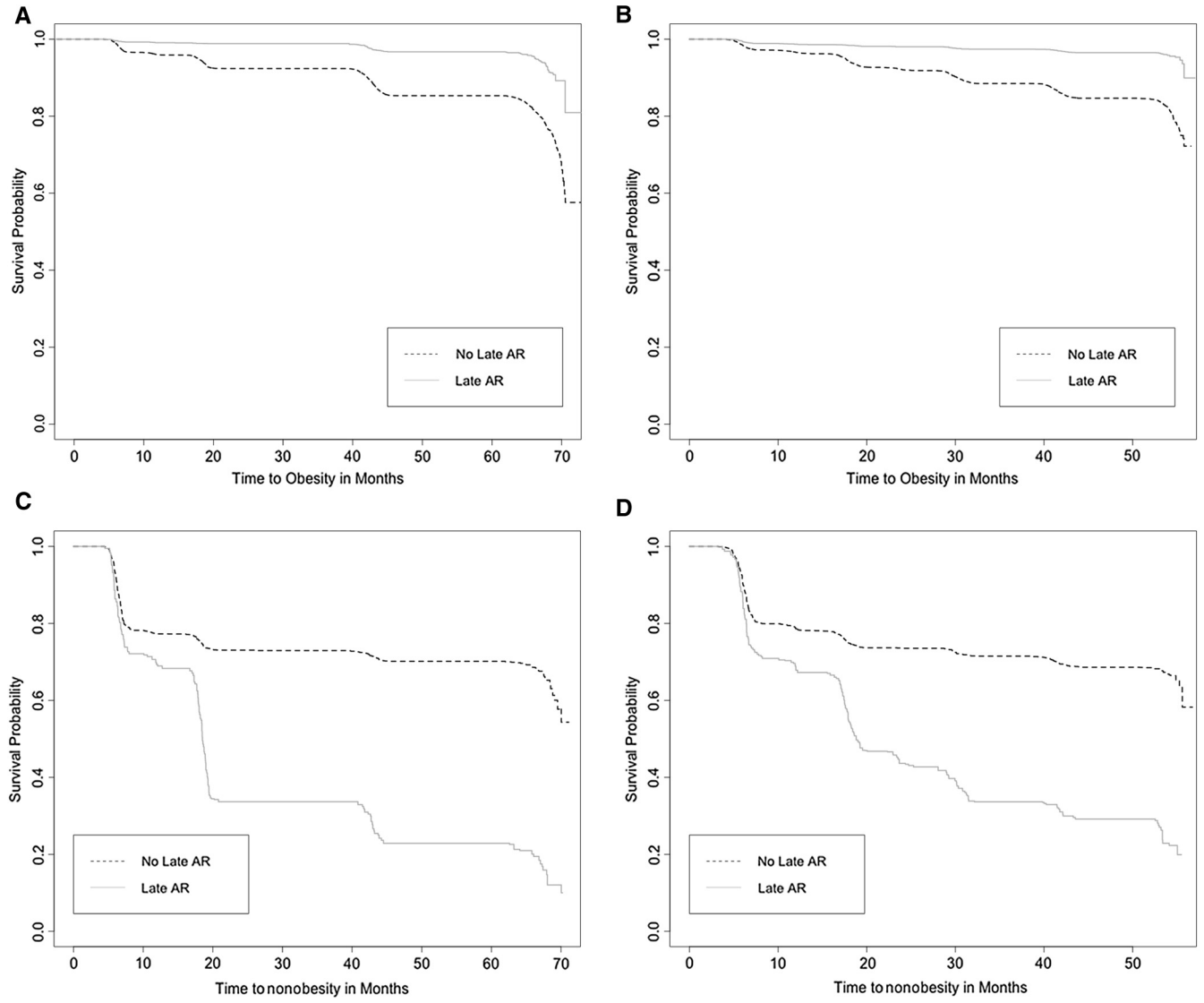

Figure. The probability of developing and reversing obesity. **A,** The risk of developing obesity among children without obesity at kindergarten entry (ECLS-K). **B,** The risk of developing obesity among children without obesity at kindergarten entry (ECLS-K:2011). **C,** The probability of reversing obesity among children with obesity at kindergarten entry (ECLS-K). **D,** The probability of reversing obesity among children with obesity at kindergarten entry (ECLS-K:2011). *AR*, adiposity rebound.

In the ECLS-K:2011 cohort, among 1955 kindergarteners with obesity, 697 (35.9%, 95% CL 33.4%-38.4%) reversed obesity at some point before or during fourth grade. As with the previous cohort, 12 months after entering kindergarten, the probability of reversing obesity was 6.22 and 5.56 times higher for boys and girls with late adiposity rebound than their peers who did not have late adiposity rebound, respectively (**Figure, D** and **Table VII**). Again, late adiposity rebound was significantly associated with the risk of reverting back to obesity among these children (**Table VIII**).

The probability of reversing obesity within the first 12 months after entering kindergarten was associated with late adiposity rebound only among boys (HR 1.52 for ECLS-K and HR 1.54 for ECLS-K:2011). For boys, Hispanic ethnicity was associated with a lower probability of reversing obesity.

For sensitivity analyses, different cut-off points for the age of "late adiposity rebound" were used. When the cut-off age for "late adiposity rebound" was 6.0 years and 6.5 years, 54.8%-56.4% and 29.6%-33.4% of children were categorized as having late adiposity rebound, respectively. In these analyses, children with late adiposity rebound still had a significantly lower risk of developing obesity than their peers without late adiposity rebound. Also, children with late adiposity rebound had a significantly higher probability of reversing obesity than their peers without late adiposity rebound. Furthermore, the associations between late adiposity rebound and the probability of developing and reversing obesity were stronger within the first 6 and 12 months after entering kindergarten, respectively (data not shown, available upon request).

Table VI. Estimated HRs for "time to obesity" among kindergarteners without obesity at baseline

Predictor*	Estimated HR	*P* value	95% CI	Estimated HR	*P* value	95% CI
ECLS-K (1998-1999)	**Male (n = 7808)**			**Female (n = 7710)**		
Adiposity rebound (within 6 mo)†						
Late	0.27	.02	0.14, 0.86	0.49	.13	0.20, 1.23
Not late	1.00	-	-	1.00	-	-
Adiposity rebound (after 6 mo)†						
Late	0.29	<.0001	0.23, 0.38	0.22	<.0001	0.16, 0.31
Not late	1.00	-	-	1.00	-	-
Race/ethnicity						
Non-Hispanic white	1.00	-	-	1.00	-	-
Non-Hispanic black	1.17	.10	0.97, 1.43	1.83	<.0001	1.52, 2.20
Hispanic	1.38	<.001	1.17, 1.63	1.27	.02	1.05, 1.53
Non-Hispanic Asian	1.30	.05	1.00, 1.69	0.77	.15	0.54, 1.10
Other	1.19	.20	0.92, 1.54	1.24	.15	0.93, 1.64
SES						
High (top 25%)	0.68	<.0001	0.58, 0.81	0.68	<.0001	0.57, 0.82
Middle	1.00	-	-	1.00	-	-
Low (bottom 25%)	1.08	.35	0.92, 1.25	1.01	.87	0.86, 1.20
ECLS-K:2011 (2010-2011)	**Male (n = 5995)**			**Female (n = 5845)**		
Adiposity rebound (within 6 mo)†						
Late	0.24	<.001	0.11, 0.52	0.50	.08	0.23, 1.10
Not late	1.00	-	-	1.00	-	-
Adiposity rebound (after 6 mo)†						
Late	0.22	<.0001	0.17, 0.29	0.17	<.0001	0.12, 0.24
Not late	1.00	-	-	1.00	-	-
Race/ethnicity						
Non-Hispanic white	1.00	-	-	1.00	-	-
Non-Hispanic black	1.23	.08	0.98, 1.55	1.52	<.001	1.20, 1.92
Hispanic	1.50	<.0001	1.24, 1.80	1.28	.02	1.05, 1.57
Non-Hispanic Asian	1.29	.10	0.95, 1.74	0.55	<.01	0.36, 0.84
Other	1.30	.20	0.95, 1.78	1.05	.80	0.73, 1.50
SES						
High (top 25%)	0.70	<.001	0.58, 0.85	0.72	<.01	0.58, 0.89
Middle	1.00	-	-	1.00	-	-
Low (bottom 25%)	1.08	.43	0.90, 1.29	1.14	.19	0.94, 1.38

*Reference categories for categorical predictors are not late (adiposity rebound); non-Hispanic white (race/ethnicity); middle 50% (SES).
†Adiposity rebound cut-off point for the single heaviside extended Cox model was 6 months after kindergarten entry, based on the graphical results of Kaplan-Meier curves. In other words, the HR differed significantly between before and after the cut-off point.

For the subgroup of children without obesity in the ECLS-K:2011, additional analysis was performed to adjust for baseline BMI percentile. Although the baseline BMI percentile was associated with the risk of developing obesity, it did not significantly modify the association between late adiposity rebound and the risk of developing obesity (data not shown, available upon request).

Discussion

The age at adiposity rebound varies among population and time.[12] The French study that initially linked early adiposity rebound to obesity determined the mean age of adiposity rebound at 5.5 years of age; a New Zealand study showed the mean age of adiposity rebound at 6.6 and 6.0 years of age for boys and girls, respectively.[7,17] More recent data from the US and other countries suggested that adiposity rebound may occur earlier than the age indicated by previous studies.[8,12,23,24] Although early adiposity rebound has been linked to increasing the risk of obesity and other comorbidities, little is known whether the age at adiposity rebound has a continuous effect on the risk of obesity. In other words, are only those with "early" adiposity rebound at an increased risk of obesity or are those with average adiposity rebound still at an increased risk of obesity compared with those with late adiposity rebound? The current study used a conservative cut-off (age of 7.0 years) to define late adiposity rebound and showed that adiposity rebound did not have to occur as early as previous studies have suggested (before 5 years of age) to have a hazardous impact on future obesity.

Results from this study highlight important implications for obesity intervention programs and policies. First, more obesity interventions should take place among younger children. The mean age of adiposity rebound is around 5-6 years when children enter kindergarten.[7,8] The significant association between adiposity rebound and the risk of developing obesity suggests that the pathway to obesity may be set before children enter kindergarten; interventions in elementary schools may be less effective than interventions for younger children. Cunningham et al proposed a similar hypothesis because one-half of the childhood obesity incidence between kindergarten and eighth grade occurred among children who were experiencing overweight during the preschool years.[25]

Second, if an intervention takes place when the children are around the age of 5-6 years, care must be taken in classifying

Table VII. Estimated HRs for "time to reversing obesity" among kindergarteners experiencing obesity at baseline

Predictor*	Estimated HR	*P* value	95% CI	Estimated HR	*P* value	95% CI
ECLS-K (1998-1999)	**Male (n = 1115)**			**Female (n = 888)**		
Adiposity rebound (within 12 mo)†						
Late	1.52	.01	1.09, 2.10	1.03	.91	0.64, 1.66
Not Late	1.00	-	-	1.00	-	-
Adiposity rebound (after 12 mo)†						
Late	8.46	<.0001	5.81, 12.31	8.00	<.0001	5.51, 11.63
Not late	1.00	-	-	1.00	-	-
Race/ethnicity						
Non-Hispanic white	1.00	-	-	1.00	-	-
Non-Hispanic black	1.11	.48	0.83, 1.50	0.83	.32	0.57, 1.20
Hispanic	0.54	<.0001	0.41, 0.72	1.44	.01	1.08, 1.92
Non-Hispanic Asian	0.59	.03	0.37, 0.95	1.68	.03	1.05, 2.69
Other	0.56	.03	0.34, 0.94	0.63	.21	0.31, 1.29
SES						
High (top 25%)	1.26	.07	0.98, 1.63	1.20	.34	0.83, 1.72
Middle	1.00	-	-	1.00	-	-
Low (bottom 25%)	1.06	.66	0.82, 1.37	0.70	.02	0.53, 0.94
ECLS-K:2011 (2010-2011)	**Male (n = 1091)**			**Female (n = 864)**		
Adiposity rebound (within 12 mo)†						
Late	1.54	<.01	1.15, 2.08	1.32	.22	0.85, 2.03
Not late	1.00	-	-	1.00	-	-
Adiposity rebound (after 12 mo)†						
Late	6.22	<.0001	4.51, 8.56	5.56	<.0001	3.81, 8.11
Not late	1.00	-	-	1.00	-	-
Race/ethnicity						
Non-Hispanic white	1.00	-	-	1.00	-	-
Non-Hispanic black	1.05	.74	0.78, 1.42	0.64	.02	0.44, 0.94
Hispanic	0.69	<.01	0.53, 0.88	0.92	.55	0.69, 1.22
Non-Hispanic Asian	0.88	.56	0.57, 1.36	0.93	.78	0.56, 1.55
Other	0.83	.36	0.55, 1.24	0.79	.31	0.50, 1.25
SES						
High (top 25%)	1.28	.08	0.97, 1.69	1.31	.08	0.97, 1.76
Middle	1.00	-	-	1.00	-	-
Low (bottom 25%)	0.92	.49	0.72, 1.17	0.74	.04	0.55, 0.99

*Reference categories for categorical predictors are not late (adiposity rebound); non-Hispanic white (race/ethnicity); middle 50% (SES).
†Adiposity rebound cut-off point for the single heaviside extended Cox model was 12 months after kindergarten entry, based on the graphical results of Kaplan-Meier curves. In other words, the HR differed significantly between the time frames before and after the cut-off point.

children who need intervention and interpreting the results of the intervention. Jackson et al reported that BMI z scores were least stable between kindergarten and first grade.[3] The current study shows that many children who were set to develop obesity based on adiposity rebound were not experiencing obesity when they entered kindergarten. Likewise, many children who were set to reverse obesity were experiencing obesity when they entered kindergarten. Misclassifying a child who needs an intervention to a group of children who do not need an intervention and vice versa could decrease the effectiveness of an intervention. Furthermore, including children in the intervention who were set to reverse obesity regardless of the intervention may bias the results and effectiveness of the intervention (and conclude that the intervention was effective when in fact it was not).

One of the strongest determinants of adiposity rebound onset was maternal BMI. Studies have shown that children follow different growth trajectories when their parents have obesity compared with children of parents without obesity.[16,17,26,27] Nevertheless, some modifiable factors may influence the onset of adiposity rebound and, therefore, be useful for obesity interventions. Rolland-Cachera et al found that high protein intake at the age of 2 years was associated with early adiposity rebound.[10] A few other studies supported this finding by showing the association between high protein intake in infancy and later high fatness.[28,29] Ip et al found that in a sample of Latino children in the US, higher caloric intake was associated with early adiposity rebound.[30] Further research is needed but examining nutritional balance for infants and young children may be a starting point for delaying the timing of adiposity rebound.

Although the initial prevalence of obesity increased from 1998-1999 to 2010-2011, the overall patterns of developing and reversing obesity remained similar in the 2 cohorts. The prevalence of childhood obesity in this study was similar to that of the National Health and Nutrition Examination Survey data (10.4% among 2- to 5-year-olds and 15.3% among 6- to 11-year-olds in 1999-2000; 12.1% among 2- to 5-year-olds and 18.0% among 6- to 11-year-olds in 2009-2010),[31,32] As with the National Health and Nutrition Examination Survey data, the prevalence of obesity at kindergarten entry increased from 1998-1999 (11.5%) to 2010-2011 (14.2%).[33]

The study has several limitations. First, the baseline BMI measurement occurred when children were in kindergarten; the exact timing of early adiposity rebound was not recorded for those who experienced it before kindergarten entry. However,

because the cut-off was 7.0 years of age, the exact timing of adiposity rebound for these children did not significantly affect the results. Furthermore, in sensitivity analyses, changing the cut-off did not alter the pattern of association, suggesting that the association between adiposity rebound and obesity is robust to different cut-off values. Second, because child assessments were recorded once or twice a year (or even less frequently in the ECLS-K cohort), accurately estimating when children changed their weight status was not possible. Third, the exclusion of children with missing data may have resulted in an under-estimation of associations among race/ethnicity, SES, and the risk of developing obesity or the probability of reversing obesity; and not all children had measurements for all follow-up periods. However, the missing data analyses showed minimal bias, and the survival analysis method adequately used the data with some missing follow-up points. Fourth, one of the significant predictors of adiposity rebound, maternal BMI, was not available for the study.

Interventions for obesity may be taking place too late to prevent or reverse obesity among those who are already on their path to obesity.[34,35] As with previous studies, this study suggests that interventions, at least for some children, should take place before the child enters kindergarten. Further research on identifying the determinants of early adiposity rebound and the methods to delay the timing of adiposity rebound is warranted. ■

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50 Years Ago in *The Journal of Pediatrics*

Neonatal Septicemia

Gotoff SP, Behrman RE. J Pediatr 1970;76:142-53.

Gotoff and Behrman defined neonatal septicemia as generalized bacterial infection documented by positive blood culture in the first 4 weeks of life; it was categorized as early-onset sepsis (EOS) and late-onset sepsis (LOS; after 72 hours). A presumptive diagnosis was based on clinical evidence. Infected amniotic fluid was a major source of neonatal septicemia. The most common organisms causing EOS were *Escherichia coli*, *Streptococcus faecalis*, and *Staphylococcus aureus*; beta hemolytic streptococci were also reported. Organisms isolated in LOS included *Pseudomonas*, *Proteus*, *Klebsiella-Aerobacter,* and *S aureus*. First-line antibiotic therapy for EOS and LOS were ampicillin plus kanamycin and methicillin/oxacillin plus kanamycin, respectively, for 7-10 days. Whole blood as a plasma expander, injection sodium bicarbonate injection, and glucose infusion were being given for shock. Hydrocortisone injection and isoproterenol infusion as vasopressors were indicated in nonresponders. Intravascular coagulation was managed with fresh heparinized whole blood and heparin injection.

Fifty years later, neonatal sepsis remains the third-leading global cause of death under age 5 years. The subdivision into EOS and LOS is now universally accepted. The major causative organisms for EOS in developed countries are group B streptococci and *E coli*. More than 50% of cases of LOS are caused by coagulase-negative staphylococci (CONS), and the remainder are caused by gram-negative organisms. In developing countries, common organisms causing neonatal sepsis include *S aureus*, *E coli*, and *Klebsiella* species. Absolute neutrophil count, C-reactive protein, and procalcitonin are increasingly being used to support the diagnosis. Urine culture, gastric aspirate examination, and body surface cultures are not routinely recommended. Today, first-line antibiotics for EOS are ampicillin/benzyl penicillin plus aminoglycoside (gentamicin) for 7-10 days. For LOS, combinations of third-generation cephalosporins plus aminoglycoside, ampicillin plus gentamicin, or vancomycin/flucloxacillin plus gentamicin/cefotaxime are recommended, based on local resistance patterns and whether hospital-acquired or community-acquired.[1,2] Treatment is given for 7-10 days except for meningitis, which is treated for 21 days. Fresh-frozen plasma is recommended for intravascular coagulation. Newer therapies in the pipeline include immunoglobulins, colony-stimulating factors, anti–tumor necrosis factor, and interleukin antagonists.

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Table I. Demographics of children with and without baseline, all subsequent weight information, and/or covariates

Demographics	Included children		Excluded children		
	No. of children	% or mean (SD)	No. of children	% or mean (SD)	
ECLS-K (1998-1999)	**n = 17 521**		**n = 3888**		***P* value**
Male, %	8923	51.0	2027	52.3	.12
Age in mo, mean	17 521	68.4 (4.3)	1593	68.2 (4.5)	.09
Race/ethnicity, %					<.0001
Non-Hispanic white	9846	56.2	1942	50.6	
Non-Hispanic black	2561	14.6	663	17.3	
Hispanic	3092	17.7	734	19.1	
Asian	1022	5.8	344	9.0	
Other	1000	5.7	154	4.0	
Obesity, %	2003	11.4	169	11.3	.88
SES, %					<.0001
High (top 25%)	4468	25.5	632	16.3	
Middle (50%)	8787	50.2	1258	32.4	
Low (bottom 25%)	4266	24.4	1998	51.4	
ECLS-K:2011 (2010-2011)	**n = 13 795**		**n = 4379**		
Male, %	7086	51.4	2202	50.7	.47
Age in mo, mean	13 795	67.5 (4.4)	1980	67.2 (4.7)	.02
Race/ethnicity, %					<.0001
Non-Hispanic white	6936	50.3	1553	35.8	
Non-Hispanic black	1744	12.6	653	15.1	
Hispanic	3268	23.7	1322	30.5	
Asian	1000	7.3	543	12.5	
Other	847	6.1	264	6.1	
Obesity, %	1955	14.2	262	14.1	.89
SES, %					<.0001
High (top 25%)	3504	25.4	479	21.7	
Middle (50%)	6931	50.2	1096	49.6	
Low (bottom 25%)	3360	24.4	635	28.7	

The results in this table are not survey-adjusted and are of unweighted analysis because including survey weights eliminated children with missing data from the analysis (thereby making the comparison not possible).
The results in this table included information when available and, therefore, do not have equal number of children for all variables.

Table III. The mean BMI percentiles for children with and without late adiposity rebound in each subgroup

Cohort	Mean BMI percentiles					
	Without obesity			With obesity		
Late adiposity rebound	**Yes**	**No**	***P* value**	**Yes**	**No**	***P* value**
ECLS-K (1998-1999)	56.3	56.4	.90	97.9	98.0	.12
ECLS-K:2011 (2010-2011)	55.3	58.3	<.0001	98.1	98.1	.65

Table IV. Changes in weight statuses among children who were not experiencing obesity when they entered kindergarten

	With obesity		Without obesity	
Time period	**No. of children**	**% (95% CL)**	**No. of children**	**% (95% CL)**
ECLS-K (1998-1999)				
Kindergarten fall (mean age, 5.7 y)	0	-	15 518	-
Kindergarten spring (mean age, 6.2 y)	420	2.8 (2.4-3.2)	14 900	97.2 (96.8-97.6)
First grade fall (mean age, 6.7 y)	149	4.2 (3.2-5.3)	3718	95.8 (94.7-96.8)
First grade spring (mean age, 7.1 y)	574	4.8 (4.2-5.4)	11 419	95.2 (94.6-95.8)
Third grade spring (mean age, 9.2 y)	1038	10.1 (9.3-10.9)	9645	90.0 (89.1-90.7)
Fifth grade spring (mean age, 11.2 y)	1093	13.2 (11.9-14.5)	7463	86.8 (85.5-88.1)
ECLS-K:2011 (2010-2011)				
Kindergarten fall (mean age, 5.6 y)	0	-	11 840	-
Kindergarten spring (mean age, 6.1 y)	277	2.3 (2.0-2.7)	11 464	97.7 (97.3-98.0)
First grade fall (mean age, 6.6 y)	120	3.5 (3.1-3.9)	3271	96.5 (96.1-96.9)
First grade spring (mean age, 7.1 y)	443	4.3 (3.6-5.0)	9832	95.7 (95.0-96.4)
Second grade fall (mean age, 7.6 y)	184	5.9 (5.2-6.6)	2899	94.1 (93.4-94.8)
Second grade spring (mean age, 8.1 y)	608	6.5 (5.9-7.2)	8780	93.5 (92.8-94.1)
Third grade spring (mean age, 9.1 y)	781	9.0 (8.2-9.9)	7916	91.0 (90.1-91.8)
Fourth grade spring (mean age, 10.1 y)	813	10.1 (9.2-11.0)	7206	89.9 (89.0-90.8)

Table V. Changes in weight statuses among children who were experiencing obesity when they entered kindergarten

	With obesity		Without obesity	
Time period	**No. of children**	**% (95% CL)**	**No. of children**	**% (95% CL)**
ECLS-K (1998-1999)				
Kindergarten fall (mean age, 5.7 y)	2003	-	0	-
Kindergarten spring (mean age, 6.2 y)	1548	77.8 (75.7-80.0)	422	22.2 (20.0-24.3)
First grade fall (mean age, 6.7 y)	416	83.5 (79.4-87.5)	84	16.5 (12.5-20.6)
First grade spring (mean age, 7.1 y)	1202	76.9 (73.6-80.3)	344	23.1 (19.7-26.4)
Third grade spring (mean age, 9.2 year)	1174	82.4 (79.4-85.3)	241	17.6 (14.7-20.6)
Fifth grade spring (mean age, 11.2 year)	953	81.5 (77.7-85.4)	205	18.5 (14.6-22.3)
ECLS-K:2011 (2010-2011)				
Kindergarten fall (mean age, 5.6 y)	1955	-	0	-
Kindergarten spring (mean age, 6.1 y)	1544	79.2 (76.7-81.7)	396	20.8 (18.3-23.3)
First grade fall (mean age, 6.6 y)	519	82.6 (80.6-84.6)	98	17.4 (15.4-19.4)
First grade spring (mean age, 7.1 y)	1343	79.7 (77.5-81.8)	363	20.3 (18.2-22.5)
Second grade fall (mean age, 7.6 y)	482	83.8 (81.8-85.8)	94	16.2 (14.2-18.2)
Second grade spring (mean age, 8.1 y)	1270	80.0 (77.2-82.9)	303	20.0 (17.1-22.8)
Third grade spring (mean age, 9.1 y)	1159	79.2 (76.6-81.8)	290	20.8 (18.2-23.4)
Fourth grade spring (mean age, 10.1 y)	1078	79.2 (76.9-81.6)	270	20.8 (18.4-23.1)

Table VIII. Estimated HRs for "time to reverting back to obesity" among kindergarteners who reversed obesity

Predictor*	Estimated HR	*P* value	95% CI
ECLS-K (1998-1999)	**n = 670**		
Adiposity rebound			
Late	0.67	<.01	0.51, 0.88
Not late	1.00	-	-
Sex			
Male	1.00	.94	0.80, 1.26
Female	1.00	-	-
Race/ethnicity			
Non-Hispanic white	1.00	-	-
Non-Hispanic black	1.09	.62	0.77, 1.54
Hispanic	1.15	.33	1.87, 1.53
Non-Hispanic Asian	0.89	.67	0.51, 1.54
Other	1.33	.31	0.87, 1.53
SES			
High (top 25%)	0.75	.04	0.56, 0.99
Middle	1.00	-	-
Low (bottom 25%)	1.01	.93	0.77, 1.34
ECLS-K:2011 (2010-2011)	**n = 697**		
Adiposity rebound			
Late	0.49	<.0001	0.38, 0.63
Not late	1.00	-	-
Sex			
Male	1.03	.76	0.84, 1.27
Female	1.00	-	-
Race/ethnicity			
Non-Hispanic white	1.00	-	-
Non-Hispanic black	0.80	.21	0.56, 1.14
Hispanic	1.11	.41	1.86, 1.44
Non-Hispanic Asian	1.06	.81	0.66, 1.70
Other	1.29	.22	0.86, 1.94
SES			
High (top 25%)	0.64	<.01	0.50, 0.87
Middle	1.00	-	-
Low (bottom 25%)	1.09	.48	0.85, 1.40

*Reference categories for categorical predictors are: not late (adiposity rebound); female (sex); non-Hispanic white (race/ethnicity); middle 50% (SES).