Cesarean Delivery, Overweight throughout Childhood, and Blood Pressure in Adolescence

Linda P. M. Pluymen, MSc[1], Henriëtte A. Smit, PhD[1], Alet H. Wijga, PhD[2], Ulrike Gehring, PhD[3], Johan C. De Jongste, MD, PhD[4], and Lenie Van Rossem, PhD[1]

Objectives To investigate whether children delivered by cesarean had a higher risk of being overweight from early until late childhood and whether they had a higher blood pressure in adolescence compared with children delivered vaginally.

Study design We used data from a Dutch birth cohort study with prenatal inclusion in 1996 and 1997. Mode of delivery (cesarean or vaginal delivery) was ascertained at 3 months after birth by questionnaire. During clinical examinations, height and weight (at age 4, 8, 12, and 16 years) and blood pressure (at age 12 and 16 years) were measured. We used mixed model analysis to estimate associations of cesarean delivery with overweight and blood pressure z scores in 2641 children who participated in at least 1 of the 4 examinations.

Results Children born by cesarean delivery (n = 236, 8.9%) had a 1.52 (95% CI 1.18, 1.96) higher odds of being overweight throughout childhood than children delivered vaginally. Children born by cesarean delivery had no higher systolic blood pressure z-score (0.11 SD, 95% CI –0.04, 0.26), nor a different diastolic blood pressure z-score (–0.00 SD, 95% CI –0.10, 0.09) in adolescence than children delivered vaginally.

Conclusions Compared with children delivered vaginally, children delivered by cesarean had a 52% higher risk of being overweight throughout childhood, but this was not accompanied by a higher blood pressure in adolescence. *(J Pediatr 2016;179:111-7).*

A cesarean delivery is meant to be performed when the health of the child or the mother is at risk. At present, 20%-30% percent of children in most developed countries are born through cesarean delivery.[1] This is worrisome because at such rates, a cesarean delivery does not result in lower maternal or neonatal mortality.[2] Adverse maternal outcomes associated with cesarean delivery[3] will then outweigh the benefits of this procedure. Evidence for health risks in the offspring is also accumulating. Compared with children delivered vaginally, children born by cesarean delivery are at increased risk of autoimmune diseases such as asthma,[4,5] allergies,[4] and type 1 diabetes.[6]

Children born by cesarean delivery also may have a higher risk of being overweight, but the evidence is conflicting.[7-9] Furthermore, few studies have investigated whether the association between cesarean delivery and overweight persists from early until late childhood. This is important because overweight especially in late childhood tracks into adulthood,[10] where it may lead to increased risk of cardiovascular diseases. Although one study observed a higher risk of being overweight when born by cesarean delivery throughout entire childhood,[11] 2 studies only observed a higher risk of being overweight in early childhood but not at older ages.[12,13]

If cesarean delivery is associated with being overweight, it may also be associated with other cardiovascular risk factors in childhood. In a population-based birth cohort, we investigated whether children delivered by cesarean had a higher risk of being overweight throughout childhood, and whether they had a higher blood pressure in adolescence, than children delivered vaginally.

Methods

This study was nested in the Dutch Prevention and Incidence of Asthma and Mite Allergy (PIAMA) study, an ongoing prospective birth cohort study with prenatal inclusion and current follow-up until age 16 years. Pregnant women from the Northern, Western, and central part of The Netherlands were recruited by means of antenatal clinics between 1996 and 1997, which resulted in a baseline population of

BMI	Body mass index
DBP	Diastolic blood pressure
PIAMA	Prevention and Incidence of Asthma and Mite Allergy
SBP	Systolic blood pressure

From the [1]Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht, The Netherlands; [2]Center for Nutrition, Prevention, and Health Services, National Institute for Public Health and the Environment, Bilthoven, The Netherlands; [3]Division of Environmental Epidemiology, Institute for Risk Assessment Sciences,Utrecht University, Utrecht, The Netherlands; and [4]Department of Pediatrics, Erasmus University Medical Center, Sophia Children's Hospital, Rotterdam, The Netherlands

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3963 newborns. Details on the study design are described elsewhere.[14,15] For the aims of the present study, we excluded 67 children with missing data on the method of delivery and 1255 children without data from a clinical examination. The study population, thus, consisted of 2641 children (66.6% of baseline population).The study protocol was approved by the medical ethical committees of the participating institutes, and all parents, and at the age of 16 years also all children, gave written informed consent.

Questionnaires were sent to the parents during pregnancy, 3 months after delivery, annually from the child's age of 1 to 8 years and at 11 and 14 years of age. For the present study, data on exposure and confounders were obtained from questionnaires until the child's age of 1 year. Between 94% and 99% of parents completed these questionnaires. Data on the outcomes of this study were obtained from clinical examinations for which children were invited at 4, 8, 12, and 16 years of age (**Figure 1**; available at www.jpeds.com). Because of funding restrictions, children invited to attend the examination at 4 and 16 years of age,[15] were restricted to research centers located in the central and Northern region.

The mode of delivery, cesarean or vaginal, was reported by the parents in the questionnaire at the child's age of 3 months. Exposure was defined as "born by cesarean," with vaginal delivery as the reference category.

Outcomes

At ages 4, 8, and 12 years, trained research staff measured weight and height at the hospital or at the child's home using portable measuring equipment. At age 16 years, weight and height were measured at the hospital only, using a calibrated weighing scale (Seca 813; Seca, Birmingham, United Kingdom) and stadiometer (Seca 222; Seca). Weight was measured to the nearest 0.1 kg, and standing height (cm) was measured to nearest decimal. Both anthropometric variables were measured while the children were wearing underwear only. Weight in kg was divided by height squared in m^2 to calculate body mass index (BMI). Overweight (including obesity) was defined based on international age- and sex-specific cut-off points for BMI.[16]

At values of BMI equal or above the cut-off points, the outcome was defined as being overweight, and below the cut-off point as not being overweight. Furthermore, because of a low number of obese children in our study population (n = 44, 61, 16, and 13 at age 4, 8, 12, and 16 years, respectively), we did not investigate associations in obese children separately. To supplement the analysis with BMI as a categorical variable, we also used a continuous dependent variable (ie, using age- and sex-specific BMI SDS according to reference data from the 1997 Dutch Growth Study).[17] The BMI SDS, thus, represent the deviation in BMI from the mean BMI of the general population of children of the same age and sex.

Systolic (SBP) and diastolic blood pressure (DBP) were measured during the clinical examinations at age 12 and 16 years. After subjects were calm and in a seated position for 10 minutes, 2 blood pressure measurements, with an interval of 5 minutes, were performed on the nondominant upper arm using an automatic oscillometric device, the M6 Monitor (OMRON Healthcare Europe B.V., Hoofddorp, The Netherlands). The proportion of children with left arm blood pressure measurements at age 12 years was 84.8% and did not differ between children delivered vaginally and by cesarean (84.9% and 83.5% respectively, *P* value of .50). The proportion of children with left arm blood pressure measurements at age 16 years was 87.3%, and was also not statistically significantly different between children delivered vaginally and by cesarean (87.5% and 82.6% respectively, *P* value of .32). The cuff was adjusted to the subjects arm circumference (large cuff when circumference ≥22 cm) and was placed directly on the skin. In case 2 consecutive measurements differed by more than 5 mm Hg, another measurement was taken. Subjects were instructed not to move their arm or talk during the measurements. Blood pressure measurements were averaged and then standardized by age-, sex-, and height-specific blood pressure z scores, according to the Fourth Report on the Diagnosis, Evaluation and Treatment of High Blood Pressure in Children and Adolescents.[18]

Collection and Definitions of Covariates

The child's sex, birth weight, gestational age, maternal age, maternal smoking during pregnancy, maternal prepregnancy BMI, maternal gestational weight gain, gestational diabetes, and maternal educational level were considered as a priori confounders. Child's sex, birth weight in grams, gestational age in weeks, place of delivery (at home or at the hospital), and maternal age at delivery in years were reported in the questionnaire for 3-month-olds. Prematurity was defined as a gestational age below 37 weeks. Maternal smoking during pregnancy was assessed in the pregnancy questionnaire and was defined as smoking during at least the first 4 weeks of pregnancy. Maternal prepregnancy BMI (kg/m^2) was calculated from prepregnancy weight in kg and height in cm as reported in the questionnaire for 1-year-olds and then dichotomized into no overweight (BMI <25 kg/m^2) and overweight (BMI ≥ 25 kg/m^2). Gestational weight gain in kg was also administered at 1 year of age and dichotomized into excessive and no excessive maternal weight gain. Excessive weight gain was defined as a weight gain greater than the upper range of the Institute of Medicine 2009 guidelines,[19] which is dependent on prepregnancy weight status. Maternal educational level was assessed at the child's age of 1 year and was used as a measure for socioeconomic status. Educational level was categorized into low (no education, primary school, lower secondary education), intermediate (intermediate vocational education, higher secondary education, pre-university education), and high education (higher professional education and university).

Other Covariates

Besides a priori confounders, we considered confounding by paternal and child factors. We found no statistically significant or meaningful differences between children delivered vaginally and by cesarean with regard to paternal educational level at birth, and paternal smoking status (smoking in the house and number of cigarettes smoked per day) at the child's age

of 3 months and 1 year, measures of child dietary intake and physical activity level or sedentary behavior at 12 years of age (**Table I**; available at www.jpeds.com). Because nonstatistically significant differences also may cause confounding, we performed sensitivity analyses including the paternal and child lifestyle factors after the main analyses. Furthermore, we considered duration of breastfeeding, antibiotic use, and infections as factors that may lie on the causal pathway between cesarean delivery and overweight or blood pressure. Duration of breastfeeding was ascertained in the questionnaires for 3-month-olds and 1-year-olds. When the infant was 3 months old, the parents were asked how long the child was breastfed and whether the mother was still breastfeeding. If the mother was still breastfeeding, we used data from the questionnaire of 1-year-olds to assess total breastfeeding duration. Total breastfeeding duration was categorized as "no breastfeeding," "0-16 weeks of breastfeeding," and "breastfeeding for more than 16 weeks." Antibiotic use was reported in the 2 year old questionnaire by asking: "how often did your child receive treatment with antibiotics in the past 12 months?" Answering options were "never," "once," "twice," and "3 time or more."

Statistical Analyses

Statistical analyses were performed with SAS software v 9.2 (SAS Institute, Cary, North Carolina). Generalized linear mixed models with a random intercept were used to assess the association of cesarean delivery with overweight throughout childhood (PROC GLIMMIX) and to assess the association of cesarean delivery with SBP and DBP z score in adolescence (PROC MIXED). In these models, cesarean delivery was included as the independent variable with vaginal delivery as the reference category. We adjusted for potential confounders in a multivariable model. Because the prevalence of gestational diabetes in our study population was very low (<3%) based on information from 30% of the study population, we did not adjust for gestational diabetes in the analysis. In additional models, we separately controlled for duration of breastfeeding, for antibiotic use at 2 years of age, and for doctor-diagnosed asthma and respiratory infections at 2 years of age. In the analyses where SBP and DBP z score were the outcome variables, we also added the child's BMI at age 12 years. To examine whether the size of the associations remained constant throughout childhood, we added an interaction term between cesarean delivery and age at the clinical examination to the adjusted model. We used an alpha level of 0.20 to test for interactions.[20]

We performed 4 sensitivity analyses. First, we investigated whether the association of cesarean delivery with overweight changed meaningfully after including paternal education and smoking, and child lifestyle factors. Second, we investigated whether the association of cesarean delivery with overweight is dependent on BMI status by excluding obese children from the analyses. Third, because mothers of children in our study population less often smoked during pregnancy and more often had a high educational level than mothers of children who did not participate, we investigated whether these covariates modified the effect of cesarean delivery on overweight and blood pressure by adding an interaction term with method of delivery to the model. Fourth, because only children from the central and Northern region were invited to the examination at 16 years of age, we investigated whether the association of cesarean delivery with overweight and blood pressure was different in children from these regions compared with children from the Western region, who were not invited to the examination at 16 years of age.

To investigate potential heterogeneity of the reference group, we performed stratified analysis for 2 categories of the reference group of children delivered vaginally: those who were delivered vaginally at home and those who were delivered vaginally at the outpatient clinic of the hospital. In The Netherlands, women can choose the place of delivery and are encouraged to deliver at home when they have no medical indication. In 1997 when most of the children in this cohort were born, the prevalence of home delivery in The Netherlands was 35%.[21] Maternal characteristics of these 2 subgroups may differ, and it has previously been observed in the PIAMA study that hospital delivery, compared with home delivery, was positively associated with overweight at 8 years of age.[22] The strength of the association between cesarean delivery and overweight throughout childhood might, thus, depend on the place of delivery in the reference category.

Measures of associations are expressed as ORs for the association of cesarean delivery with overweight, and as a mean difference in blood pressure z score (SBP and DBP) between children delivered vaginally and by cesarean, accompanied by 95% CIs.

Approach to Missing Data

Of the 2641 children with data on overweight in this study, 304 children (11.5%) participated in all 4 clinical examinations, 668 children (25.3%) participated in 3 examinations, 836 children (31.6%) participated in 2 examinations, and 833 children (31.5%) participated in 1 clinical examination. Of the 1578 children with data on blood pressure, 676 children (42.8%) participated in both examinations. As a test of robustness, we also investigated the associations in these subgroups of children. We did not impute missing values. Although multiple imputation is preferred when missing values are not missing completely at random, it has been shown that imputing missing outcome data is not necessary when performing a longitudinal data analysis.[23,24] The methods we used can handle missing values under the assumption that missing values are missing at random (ie, that missing values are related to previously observed data). We observed a positive association between the propensity to contribute data at 16 years of age and being born at home, being breastfed for longer, mothers not smoking during pregnancy, mothers having a higher educational level, and mothers not being overweight before pregnancy ($P \leq .05$). Missing overweight values were not related to the mode of delivery (mean number of data points = 2.17 for children delivered vaginally and by cesarean, $P = .98$), and there was no association between the propensity to contribute data at the last time point and the mode of delivery (29.3% of those delivered by cesarean had data on overweight at 16 years of age vs 30.2% of those delivered vaginally, $P = .74$).

Table V. Baseline characteristics of mothers and children in the total study population and by mode of delivery

Variables*	Total study sample n = 2641		Cesarean delivery n = 236		Vaginal delivery n = 2405	
Boys	50.8	(1 342)	54.7	(129)	50.4	(1 213)
Gestational age <37 wk	4.8	(127)	10.2	(24)	4.5	(107)†
Birth weight <2500 g	3.6	(96)	13.1	(31)	2.7	(65)†
Birth weight >4000 g	3.6	(95)	6.8	(16)	3.3	(79)†
Maternal age, y, mean (SD)	30.7	(3.8)	30.7	(3.8)	30.7	(3.8)
Maternal smoking	15.9	(418)	19.6	(46)	15.6	(372)
Maternal overweight	20.4	(495)	30.7	(66)	19.4	(429)†
Excessive gestational weight gain	30.8	(733)	42.7	(91)	29.6	(642)†
Any breastfeeding	84.0	(2 203)	82.6	(195)	84.2	(2 008)
>16 wk breastfeeding	36.8	(964)	30.1	(71)	37.4	(893)
Maternal education						
Low	20.4	(535)	24.2	(56)	20.0	(479)
Intermediate	42.0	(1 102)	39.8	(92)	42.2	(1 010)
High	37.6	(988)	35.9	(83)	37.8	(905)
Antibiotic use at age 1-2 y						
Never	59.7	(1 541)	60.7	(139)	59.6	(1402)
≥ ×3x	6.9	(179)	8.3	(19)	6.8	(160)
Asthma diagnosis at age 1-2 y	4.6	(120)	4.8	(11)	4.6	(109)
Respiratory infection diagnosis at age 1-2 y	11.1	(283)	8.4	(19)	11.4	(264)

*Values are percentages (n) unless stated otherwise.
†Differs significantly ($P < .05$) from children delivered by cesarean.

Results

Children who participated in our study (n = 2641) were breastfeed longer, less often had mothers who smoked during pregnancy, and more often had highly educated mothers than children who originally participated in the PIAMA study but did not have data on being overweight (n = 1322) (**Table II**; available at www.jpeds.com). Similar differences were observed when comparing children with blood pressure measurements (n = 1578) with children without blood pressure measurements (n = 2385) (**Table III**; available at www.jpeds.com). There were small differences in baseline characteristics between children from the Northern and central region and children from the Western region (**Table IV**; available at www.jpeds.com).

Children born by cesarean delivery (8.9%) were more often delivered before 37 weeks of gestation, were almost 5 times more likely to have a low birth weight, and were 2 times more likely to have a high birth weight compared with children delivered vaginally (**Table V**). Mothers of children born by cesarean delivery were more often overweight before pregnancy and more often had excessive weight gain during pregnancy compared with mothers of children delivered vaginally.

Of the children delivered vaginally, 49.2% (1183/2405) were delivered at home. Baseline characteristics of children delivered at home vs hospital are shown in **Table VI** (available at www.jpeds.com).

Association of Cesarean Delivery with Overweight throughout Childhood

At ages 4, 8, 12, and 16 years, the prevalence of overweight was higher in children delivered by cesarean than in children delivered vaginally (**Table VII**). Children delivered by cesarean also had a higher BMI SDS throughout childhood than children delivered vaginally (**Figure 2**; available at www.jpeds.com). After adjustment for confounders, children delivered by cesarean had a 1.52 (95% CI 1.18, 1.96) higher odds of being overweight throughout childhood than children delivered

Table VII. Percentage of overweight children and mean SBP and DBP by age at measurement and mode of delivery*

Cardiovascular risk factors	Age, y	N	Cesarean delivery n = 236		N	Vaginal delivery n = 2405		Mean difference (SD)
Overweight, %	4	120	26.7	(32)	1119	18.6	(208)	-
(n)	8	195	22.6	(44)	1996	13.6	(272)	-
	12	128	19.5	(25)	1370	11.6	(159)	-
	16	69	10.1	(7)	728	9.2	(67)	-
SBP in mm Hg,	12	122	116.4	(10.5)	1339	115.0	(9.4)	1.4 (9.5)
mean (SD)	16	68	118.7	(10.8)	723	116.0	(9.8)	2.7 (9.9)
SBP z score,	12	122	0.81	(0.96)	1339	0.67	(0.89)	0.14 (0.90)
mean (SD)	16	68	0.27	(0.98)	723	0.12	(0.87)	0.15 (0.88)
DBP in mm Hg,	12	122	67.1	(7.2)	1339	66.7	(6.5)	0.4 (6.5)
mean (SD)	16	68	66.5	(6.9)	723	66.3	(6.8)	0.2 (6.7)
DBP z score,	12	122	0.35	(0.64)	1339	0.31	(0.58)	0.04 (0.59)
mean (SD)	16	68	–0.03	(0.62)	723	–0.03	(0.60)	0.00 (0.60)

*Values are % (N) for overweight and mean (SD) for SBP and DBP.

Table VIII. Association of cesarean delivery with overweight throughout childhood (OR) and SBP and DBP z score in adolescence (mean difference in z score)

Cesarean vs vaginal delivery	Overweight OR (95% CI)		SBP z score β (95% CI)		DBP z score β (95% CI)	
Crude model*	1.69‡	(1.35, 2.13)	0.15‡	(0.00, 0.30)	0.03	(−0.06, 0.12)
Adjusted model*,†	1.52‡	(1.18, 1.96)	0.11	(−0.04, 0.26)	−0.00	(−0.09, 0.10)

*In children with ≥ 1 measurements of weight and height and blood pressure. respectively.
†Estimates are adjusted for sex, birth weight, gestational age, maternal age at delivery, maternal smoking during pregnancy, maternal prepregnancy BMI, gestational weight gain. and maternal educational level.
‡Significant at $P < .05$.

vaginally (**Table VIII**). Neither additional adjustment for duration of breastfeeding, for antibiotic use at age 2 years, nor for doctor's diagnosed asthma and respiratory infections at age 2 years altered the OR (OR 1.50, 95% CI 1.16, 1.94, OR 1.60, 95% CI 1.14, 2.26, and OR 1.64, 95% CI 1.16, 2.31). The OR varied between 1.37 and 1.73 depending on the age at which overweight was determined, but was not statistically significantly different between ages ($P = .79$ for interaction of age and mode of delivery). Lastly, the OR for the association of cesarean delivery with overweight was of similar magnitude in children with 1, 2, or 3 measurements (range OR 1.39-1.76) (**Table IX**; available at www.jpeds.com) and was lower in children with 4 measurements (OR 1.28, 95% CI 0.63, 2.60).

Sensitivity Analyses

The OR of cesarean delivery with overweight did not change meaningfully after adjustment for paternal and child lifestyle factors (OR 1.50, 95% CI 1.06, 2.13), nor after exclusion of obese children (OR 1.50, 95% CI 1.06, 2.13). The OR did not differ according to maternal smoking status during pregnancy ($P = .89$ for interaction) or maternal educational level ($P = .11$ for interaction). In spite of the differences in baseline characteristics between regions, the association of cesarean delivery with overweight was similar in children from the Northern/central region (OR 1.54, 95% CI 1.03, 2.30) and in children from the Western region (OR 1.49, 95% CI 0.76, 2.93).

Association of Cesarean Delivery with Blood Pressure in Adolescence

In adolescence, mean SBP z score and mean DBP z score were higher in children delivered by cesarean than children delivered vaginally (**Table VII**). After adjustment for confounders, children delivered by cesarean had a slightly higher SBP z-score, which was not statistically significant (mean difference in z score 0.11 SD, 95% CI −0.04, 0.26) and had similar DBP z score (mean difference in z score −0.00 SD, 95% CI −0.09, 0.10) compared with children delivered vaginally (**Table VIII**). Additional adjustment for breastfeeding duration or for BMI at 12 years of age did not change the results (data not shown). The mean difference in SBP and DBP z score between children delivered vaginally and by cesarean was similar at age 12 and 16 years (P for interaction of age and mode of delivery: 0.25 for SBP and 0.22 for DBP). In children with blood pressure measurements at both time points, children delivered by cesarean neither had a different SBP z score (−0.07 SD, 95% CI −0.28, 0.14), nor a different DBP z score (−0.08 SD, 95% CI −0.22, 0.06) than children delivered vaginally (**Table X**; available at www.jpeds.com).

Associations Stratified According to the Place of Delivery of Children Delivered Vaginally

Children delivered by cesarean had a 1.46 (95% CI 1.05, 2.03) higher odds of being overweight throughout childhood than children delivered vaginally in the outpatient clinic of the hospital and a 1.63 (95% CI 1.15, 2.32) higher odds of being overweight than children delivered vaginally at home (data not shown). No statistically significant differences in SBP z-score and DBP z score were observed between children delivered by cesarean and the 2 subgroups of children delivered vaginally.

Discussion

Children who were delivered by cesarean had a 1.52 times higher risk of being overweight throughout childhood, but had no different systolic or diastolic blood pressure in adolescence than children who were delivered vaginally. In some countries with a high cesarean delivery rate, cesarean delivery is strongly related to higher income and higher level of education (eg, if cesarean delivery can be performed on maternal request, if women consider this good quality care, or if they fear the physiological consequences of vaginal delivery).[25] In The Netherlands, however, cesarean delivery is not directly related to SES, especially because standard policy at the time of the birth of the study population was to pursue vaginal delivery and to only perform a cesarean delivery under strict medical indications (such as abnormal position of the baby, previous cesarean delivery, or dystocia).[26] A strength of our study is the prenatal inclusion and data collection that enabled us to adjust for important confounders, such as maternal overweight before pregnancy and gestational weight gain. We could also investigate the potential confounding by paternal factors and measures of child dietary intake, physical activity level, and sedentary behavior at age 12 years.

A limitation of our study is missing outcome data at different waves of follow-up, especially at ages 4 and 16 years when we invited samples of children to attend the examinations, and at ages 12 and 16 years with participation rates of 47% and 37%, respectively. We do not expect that missing data has led to biased results: first, the selection of children invited to the

examination at 4 years of age was unrelated to mode of delivery and confounders.[15] Also, stratified analysis showed that the association of cesarean delivery with being overweight did not differ between geographic regions of birth in spite of differences in baseline characteristics between the regions. Second, besides missing data at different waves of follow-up, there was a proportion of children who did not participate in either 1 of the 4 clinical examinations and who were, thus, excluded from our study. Sensitivity analysis showed that the effect of cesarean delivery on overweight was not different according to smoking status or maternal educational level. Thus, the selection of more healthy participants in our study population is unlikely to have led to biased results. This is in line with a meta-analysis that found no difference in the association of cesarean delivery with overweight between studies conducted in high-income vs middle-income countries.[7] Third, we observed that missing values for overweight and blood pressure did not depend on the mode of delivery and the longitudinal data analysis methods we used to take account of these missing values in the analyses. Fourth, we observed that the association of cesarean delivery with overweight was similar in children with 1, 2, and 3 measurements of height and weight. In children with all 4 measurements, the association was not statistically significant but this may be due to the small sample of children delivered by cesarean with complete data (n = 24). The discrepancy in overweight between children delivered vaginally and by cesarean became smaller at age 16 years because of a relatively large drop in the percentage of overweight children delivered by cesarean. We also compared BMI SDS between children delivered vaginally and by cesarean and observed that the difference in BMI SDS also substantially decreased at this age. As children get older, other factors that determine whether a child develops overweight become more important. We did not observe differences in measures of dietary intake, physical activity level, or sedentary behavior at 12 years of age between children delivered vaginally and by cesarean. A strength of using longitudinal data analysis is that we could incorporate the data despite the small sample of children delivered by cesarean at age 16 years, as these analyses deal with missing values over time. This may explain why the difference in overweight between children delivered vaginally and by cesarean became smaller with age, and the strength of the association of cesarean delivery with overweight remained similar throughout childhood. Future follow-up may clarify whether the sample of children delivered by cesarean at age 16 years was unrepresentative by chance.

The increased risk of overweight in children delivered by cesarean may be caused by bacteria in the gut. Because infants delivered by cesarean are not exposed to the maternal vaginal flora during delivery, the colonization of bacteria in their gut is different from that of children delivered vaginally.[27] Moreover, the fact that the association of cesarean delivery with overweight did not depend on the reference category (ie, delivered vaginally at home or at the hospital) strengthens the likelihood that it is caused by the cesarean delivery per se and not by the environment of the delivery or by unmeasured maternal factors associated with the place of delivery.

Our finding of an increased risk of overweight that persisted throughout childhood when delivered through cesarean is in line with findings from a previous study that used similar data analysis methods.[11] In 2 studies, children delivered by cesarean had a higher risk of overweight in early childhood but not in late childhood.[12,13] Possibly, differences in data analysis methods may explain this discrepancy in results. Although one study used longitudinal data analysis methods to account for correlations between repeated measurements,[11] the other studies analyzed each age category separately, thus, ignoring these correlations.[12,13]

We expected that the increased prevalence of overweight in children delivered by cesarean also would lead to higher levels of SBP and DBP.[28] A previous study found slightly increased SBP in 23-year-olds who were delivered by cesarean, which was explained by increased BMI.[29] In our study, blood pressure z-scores were not different between children delivered vaginally and by cesarean at the age of 12 and 16 years. This might suggest that the association of cesarean delivery with increased blood pressure does not emerge until early adulthood.

An increased risk of overweight after cesarean delivery that persists into adolescence is worrisome, because overweight in childhood tracks into adulthood.[30] Although only 8.9% of the children in this study were born by cesarean delivery, currently 20%-30% of children in most developed countries are delivered this way.[1] An increase in the cesarean delivery rate worldwide may, thus, be another contributing factor to the prevalence of overweight. ■

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Reprint requests: Linda P. M. Pluymen, MSc, Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, PO Box 85500, 3508 GA Utrecht, The Netherlands. E-mail: l.p.m.pluymen@umcutrecht.nl

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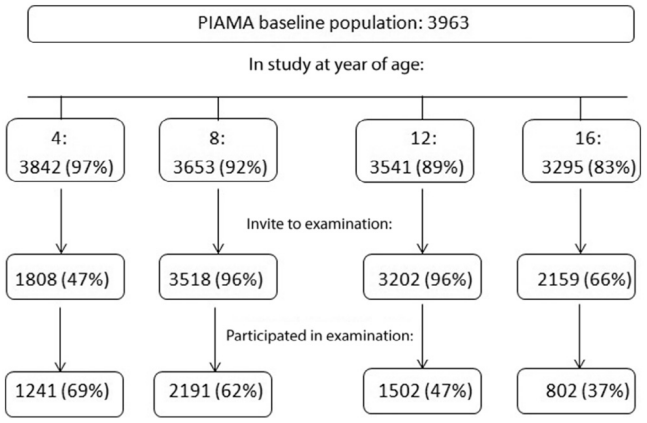

Figure 1. Flow chart of the clinical examinations in the PIAMA study.

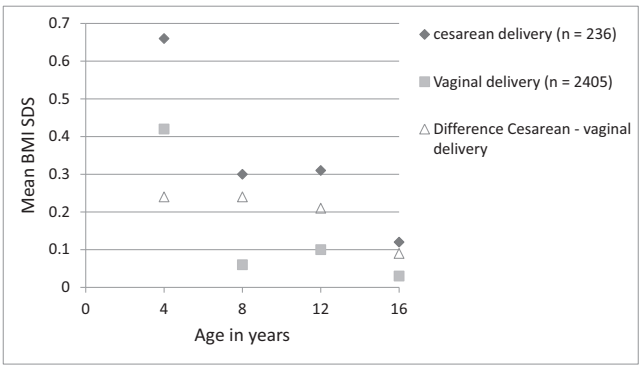

Figure 2. Mean BMI SDS throughout childhood in children delivered vaginally or by cesarean.

Table I. Comparison of paternal and child lifestyle factors between children delivered vaginally and by cesarean

	Cesarean delivery (n = 236)	Vaginal delivery (n = 2405	*P* value
Paternal educational level at child's birth, %			.11
Low	28.8	22.9	
Intermediate	33.6	34.6	
High	37.6	42.5	
Father smoking indoors, %			
At child's age 3 mo	21.3	18.5	.29
At child's age 1 y	22.4	18.6	.16
Father number of cigarettes per d, mean (SD)			
At child's age 3 mo	6.2 (4.2)	6.9 (5.2)	.34
At child's age 1 y	5.9 (5.3)	6.7 (5.4)	.36
Child age 12 y intake number of d per wk, mean (SD)			
Fruit	7.2	6.9	.09
Savory snacks	3.8	3.8	.76
Candy	6.3	6.3	.79
Snacks	2.3	2.4	.62
Soft drinks	3.7	3.7	.90
Energy drink	1.09	1.05	.10
Breakfast	8.9	8.9	.86
Child age 12 y active sports, mean (SD)			
n, d/ wk	4.2	4.2	.95
n, d/wk ≥ 1 h	4.7	4.8	.45
n, d/wk 0.5-1 h	3.1	3.4	.22
Child age 12 y sedentary behavior, mean (SD)			
n, d/wk watching TV	7.6	7.9	.14
n, h/d watching TV	2.5	2.6	.08
n, d/wk on computer, internet, handheld gaming console	6.9	6.6	.13
n, h/d on computer, internet, handheld gaming console	2.3	2.3	.96

Table II. Baseline characteristics for participants vs nonparticipants

Variables*	Participants (n = 2641)	Nonparticipants (n = 1322)	*P* value
Cesarean delivery	8.9 (236)	7.6 (96)	.18
Boys	50.8 (1342)	54.0 (714)	.06
Prematurity	4.8 (127)	5.1 (67))	.85
Birth weight <2500 g	3.6 (96)	4.4 (58)	.21
Birth weight >4000 g	3.6 (95)	3.0 (40)	.31
Maternal smoking	15.9 (418)	21.6 (286)	<.0001
Maternal overweight	20.4 (495)	18.7 (247)	.26
Excessive gestational weight gain	30.8 (733)	29.4 (389)	.28
>16 wk breastfeeding	36.8 (964)	23.5 (311)	<.0001
Maternal education			<.0001
Low	20.4 (535)	30.1 (368)	
Intermediate	42.0 (1102)	40.5 (495)	
High	37.6 (988)	29.4 (359)	

*Values are percentages (n).

Table III. Baseline characteristics for children with and without blood pressure measurements

Variables*	Participants (n = 1578)	Nonparticipants (n = 2385)	*P* value
Cesarean delivery,	8.6 (136)	8.5 (196)	.85
Boys,	48.9 (772)	53.8 (1283)	<.01
Prematurity	4.5 (71)	5.3 (124)	.85
Birth weight <2500 g	3.2 (51)	4.3 (101)	.07
Birth weight >4000 g	3.4 (54)	3.4 (78)	.95
Maternal smoking	14.1 (222)	20.2 (464)	<.0001
Maternal overweight	17.9 (266)	21.4 (415)	.01
Excessive gestational weight gain	27.9 (406)	29.0 (640)	.28
>16 wk breastfeeding	39.8 (627)	27.5 (625)	<.0001
Maternal education			<.0001
Low	17.3 (273)	27.6 (602)	
Intermediate	40.6 (640)	42.2 (920)	
High	42.0 (663)	30.1 (657)	

*Values are percentages (n).

Table IV. Baseline characteristics according to region

Variables*	Region: Northern and middle (n = 2817)	Region: Western (n = 1146)	*P* value
Cesarean delivery	8.9	7.6	.20
Boys	52.5	50.2	.20
Birth weight >4000 g	3.7	2.6	.09
Birth weight <2500 g	3.7	3.3	.71
Gestational age, mean (SD)	39.9 (1.7)	39.7 (1.7)	.001*
Maternal age, y, mean (SD)	30.5 (3.8)	30.0 (4.2)	.002*
Maternal smoking	17.1	19.4	.10
Maternal overweight	19.0	22.4	.03*
Excessive gestational weight gain	29.2	35.2	.02*
Pregnancy diabetes	2.2	4.8	.06
>16 wk breastfeeding	33.6	30.0	.000*
Maternal education, % high	46.6	38.3	.000*
Born in hospital	51.9	66.3	.000*
Presence of siblings at birth	51.3	49.0	.19

*Values are percentages, unless stated otherwise.

Table VI. Baseline characteristics by mode and place of delivery

Variables*	Cesarean delivery n = 236	Vaginal delivery at home n = 1184	Vaginal delivery at hospital N = 1221
Boys	54.7 (129)	51.8 (613)	49.1 (600)
Birth weight in g, mean (SD)	3453 (789)	3584 (453)	3473 (555)
Born <37 weeks gestation	10.2 (24)	0.8 (9)	7.7 (94)
Maternal age in y, mean (SD)	30.7 (3.8)	30.8 (3.7)	30.5 (3.9)
Maternal smoking	19.6 (46)	15.6 (183)	15.6 (189)
Maternal overweight	30.7 (66)	14.4 (159)	24.5 (270)
Excessive gestational weight gain	42.7 (91)	25.2 (275)	34.1 (367)
>16 wk breastfeeding	30.1 (71)	54.7 (644)	32.7 (395)
Maternal education			
Low	24.2 (56)	19.1 (226)	20.9 (253)
Intermediate	39.8 (92)	41.0 (484)	43.4 (526)
High	35.9 (83)	39.9 (471)	35.8 (434)

*Values are percentages (n) unless stated otherwise.

Table IX. Association of cesarean delivery with overweight throughout childhood by number of repeated measurements

Cesarean vs vaginal delivery	n	Cesarean n	Crude model OR (95% CI) overweight	Adjusted model* OR (95% CI) overweight	Adjusted model† OR (95% CI) overweight
≥1 obs.	2641	236	1.69*,‡ (1.35, 2.13)	1.51*,‡ (1.17, 1.94)	1.52*,‡ (1.18, 1.96)
1 obs.	833	77	1.78*,‡ (1.03, 3.09)	1.69 (0.92, 3.10)	1.76 (0.95, 3.26)
2 obs.	836	66	1.74*,‡ (1.13, 2.68)	1.42 (0.86, 2.32)	1.39 (0.84, 2.29)
3 obs.	668	69	1.91*,‡ (1.34, 2.74)	1.60*,‡ (1.07, 2.38)	1.55*,‡ (1.04, 2.32)
4 obs.	304	24	1.12 (0.59, 2.12)	1.19 (0.60, 2.35)	1.28 (0.63, 2.60)

obs., observations.
*Most parsimonious model: adjusted for maternal prepregnancy overweight, excessive gestational weight gain, and birth weight.
†Final model: most parsimonious model additionally adjusted for sex, gestational age, maternal age, maternal smoking during pregnancy, and maternal educational level.
‡Significant at $P < .05$.

Table X. Association of cesarean delivery with blood pressure in adolescence by number of repeated measurements

			SBP z score age 12-16 y		DBP z score age 12-16 y	
Cesarean vs vaginal delivery	n	Cesarean delivery n	Crude β (95% CI)	Adjusted* β (95% CI)	Crude β (95% CI)	Adjusted* β (95% CI)
≥1 obs.	1578	136	0.15*,† (0.00, 0.30)	0.11 (–0.04, 0.26)	0.03 (–0.06, 0.12)	–0.00 (–0.09, 0.10)
2 obs.	676	54	0.02 (–0.18, 0.22)	–0.07 (–0.28, 0.14)	–0.03 (–0.17, 0.10)	–0.08 (–0.22, 0.06)

*Adjusted for maternal prepregnancy overweight, excessive gestational weight gain, sex, birth weight, gestational age, maternal age, maternal smoking during pregnancy, and maternal educational level.
†Significant at $P < .05$.