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# Smoking overrules many other risk factors for small for gestational age birth in less educated mothers

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ABSTRACT

*Background:* Although there is convincing evidence for the association between small for gestational age (SGA) and socioeconomic status (SES), it is not known to what extent explanatory factors contribute to this association.
*Aim:* To examine to what extent risk factors could explain educational inequalities in SGA.
*Study design:* In this study fully completed data were available for 3793 pregnant women of Dutch origin from a population-based cohort (ABCD study). Path-analysis was conducted to examine the role of explanatory factors in the relation of maternal education to SGA.
*Results:* Low-educated pregnant women had a higher risk of SGA offspring compared to the high-educated women (OR 1.98, 95% CI 1.35–2.89). In path-analysis, maternal cigarette smoking and maternal height explained this association. Maternal age, hypertension, chronic disease, late entry into antenatal care, neighborhood income, underweight, environmental cigarette smoking, drug abuse, alcohol use, caffeine intake, fish intake, folic acid intake, anxiety, and depressive symptoms did not play a role in the association between maternal education and SGA birth.
*Conclusion:* Among a large array of potential factors, the elevated risk of SGA birth among low-educated women appeared largely attributable to maternal smoking and to a lesser extent to maternal height. To reduce educational inequalities more effort is required to include low-educated women especially in prenatal intervention programs such as smoking cessation programs instead of effort into reducing other SGA-risk factors, though these factors might still be relevant at the individual level.



## 1. Introduction

Small for gestational age birth (SGA) is strongly related to perinatal mortality and morbidity [1,2]. SGA infants, usually defined as birth weight below the 10th population centile on the basis of gestational age, are for instance more likely to have necrotizing enterocolitis, respiratory distress syndrome [3], hypoglycemia [4], and adverse neurologic outcome [5]. Moreover, SGA born adults may have an increased risk of type 2 diabetes mellitus and ischemic heart disease [6]. Therefore, reducing the incidence of SGA is of paramount importance.

SGA results from complex interactions between factors of the mother, fetus, and environment [7]. Many risk factors, including cigarette smoking [8], short stature [9], caffeine intake [10], and maternal psychosocial stress [11], have been identified. Furthermore, SGA has been associated with socioeconomic status (SES) [12,13]. Some researchers reported that social deprivation was independently associated with SGA [14], but the majority of researchers suggested that after adjustment for known mediating factors, socioeconomic status may not be a relevant independent contributor to birthsize [15]. Although much research has focused on socioeconomic differences in SGA, little research has evaluated the underlying pathways. Some studies highlighted a single factor, such as maternal smoking, and late entry into antenatal care [7] as explanatory factors in the relation between SES and SGA. From a public health point of view it is of interest to assess and compare the effects of different explanatory factors on the relation of SES to SGA. Furthermore, it is not known whether any residual socioeconomic disparities remain after adjustment for strongly suspected mediators [15]. In the present study we applied maternal education as an indicator of SES, as it was described as the best predictor of socioeconomic differences in birth outcomes [13].

The aim of the present paper is therefore (i) to assess the association between SGA and maternal education and (ii) to examine to

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what extent risk factors could explain educational inequalities in SGA. This study was conducted in a large population based cohort and involved ethnic Dutch participants only to avoid bias by ethnic background [15].

## 2. Methods

The present study is part of the ABCD study, a population-based birth cohort study. Details of this study were described previously [16]. In brief, between January 2003 and March 2004 all pregnant women in Amsterdam, The Netherlands, were invited to participate during their first antenatal visit with their obstetric caregiver. In total 12 373 women were informed about the study and 8266 women returned the pregnancy questionnaire (median gestational age 12.95; IQR 2.43 weeks; response rate 67%) and enrolled in the study. For the present study, twin pregnancies (n = 135) were excluded, because birth weight differs between singleton and multiple births. In addition, participants with missing data on education (n = 69) were excluded. Those with a Dutch ethnicity, defined if both mother and grandmother were born in the Netherlands, were selected for the present study, leaving 3919 participants in our study population. Furthermore, still births (n = 31), births below 24 weeks of gestation (n = 2), and termination of pregnancy (n = 9) were excluded, as well as participants with missing data on birth weight (n = 44) and gestational age (n = 6). Moreover, 44 cases were excluded because of at least one missing covariable. Finally, there were 3783 participants with fully completed data. The institutional review boards of the participating hospitals approved the study. All mothers gave written informed consent. The ABCD study complies with the principles laid down in the Declaration of Helsinki.

### 2.1. Main variables

The years of education after primary school were obtained by questionnaire. Maternal education was categorized [13] as low (less than 6 years), mid (6 to 10 years), and high (more than 10 years). Newborns were categorized as SGA if their birth weight was below the 10th percentile for gestational age on the basis of gender and parity specific standards from the Perinatal Registration of the Netherlands (PRN) [17].

### 2.2. Covariables

Possible covariables that might explain the association between maternal education and SGA were selected according to the literature [15,18] and were obtained from the pregnancy questionnaire. Covariables were as follows: maternal height (cm; continuous), neighborhood income (continuous), chronic health problem (no/yes), pregnancy-induced hypertension (yes/no), pre-existing hypertension (yes/no), maternal age (continuous), maternal cigarette smoking (no/yes: yes when at least one cigarette per day), environmental smoking (no/yes: yes when at least one cigarette per day), anxiety (State-Trait Anxiety Inventory [STAI]), non-medical drug abuse (no/yes), underweight (body mass index kg/m$^2$ < 18.5: yes/no), depressive symptoms (Center for Epidemiologic Studies Depression scale [CES-D]), late entry into antenatal care (<18 weeks, ≥18 weeks), alcohol consumption (no/yes), folic acid supplementation (yes/no), fatty fish intake (<10 g, 10–20 g, >20 g), caffeine intake (<100 g, 100–200 g, 200–300 g, >300 g). A chronic health problem was categorized as yes if the mother reported a chronic disease that is associated with SGA, like asthma (n = 57), thyroid disease or thyroid medicine use (n = 24), and leiomyoma (n = 2). Chronic health problems like renal disease and severe maternal heart condition were not reported. Maternal overweight and maternal diabetes were not included because these variables were inversely associated with SGA.

Neighborhood income data (not based on the questionnaire) were registered by Statistics Netherlands, based on mean income per individual in a neighborhood (sum of income divided by the number of residents in a neighborhood) in euro's divided by 1000. The CES-D is designed to determine depressive symptoms in the week previous to the acquisition of the questionnaire. The CES-D is a 20-item scale (each item is scored on a four-point scale) which was found to have good validity and reliability [19]. Depressive symptoms were categorized as low (reference: 20–29), mid (30–41) or high (42–80). Anxiety was assessed using the Dutch version of the STAI [20], which has 20 items with each having 4-points scale. Anxiety was categorized as low (reference: 20–34), mid (35–48), or high (49–80). Pre-existing hypertension and pregnancy-induced hypertension were defined combining self-reported data from the questionnaire and data from the PRN, as described previously [21].

### 2.3. Statistical analysis

Differences in general characteristics among educational levels were tested with ANOVA analysis for continuous normally distributed variables and a Chi-square test for categorical variables. To explore the associations of covariates with SGA, logistic regression analyses were performed. Path analysis mediation models were used to identify potential determinants of SGA that may explain the relation of SGA to SES. Each path model consists of the following regression equations: a regression equation that describes the relationship between SGA and SES (adjusted for all the mediators), and the regression equations describing the relationship between each mediator and SES. Using path analysis, the regression equations were estimated simultaneously accounting for the correlation between explanatory factors [22]. Only factors that were associated with both maternal education and SGA ($p < 0.1$) were considered as possible explanatory factors in the relation of maternal education to SGA and were included in further analyses. The objective of the analyses was to evaluate the extent to which determinants of SGA mediated the former association. Associations between maternal education and the mediating risk factors were modeled with the maximum likelihood algorithm implemented in M-PLUS using weighted least squared parameter estimates and a probit link [23]. Categorical variables were treated as continuous latent response variables. The indirect effects of the mediating risk factors were determined by calculating the product of the coefficients along a path. For the binary outcome (SGA birth), we used the standardized coefficients [22]. The proportion of the relationship between SGA and SES mediated by each of the mediators was determined by dividing each of the corresponding indirect effects by the absolute total effect [24]. A proportion mediated more than 5% was considered as clinically relevant, hence factors with smaller proportion mediated were not considered as mediators. The assumptions required to test mediation hypotheses were met, although we cannot assert that associations were not confounded [25]. Maternal education was included as categorical variable with high-education as reference group. SPSS 15.0, SPSS Inc., Chicago, USA was used for the univariate analyses and M-PLUS (Muthen and Muthen) was used for the path analysis mediation models. A p-value < 0.05 was considered as significant.

## 3. Results

General characteristics of the study population are described in Table 1. Low-educated women more often were multiparous, were younger, had a shorter height, lived in a lower-income neighborhood area, and were more likely to have a late entry into antenatal care. They generally scored worse on lifestyle and lifestyle-related characteristics (e.g. more smoking and more anxiety), except for alcohol consumption (less in low-educated women).