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Title: BORN SMALL FOR GESTATIONAL AGE AND POOR SCHOOL PERFORMANCE; HOW SMALL IS TOO SMALL?

Running head: SGA and poor school performance

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ABSTRACT

Aim: To assess the relationship between severity of small for gestational age (SGA) and risk of poor school performance, and to investigate whether adult stature modifies this risk.

Methods: 1,088,980 term Swedish children born 1973-1988 were categorized into severe SGA (<-3 standard deviations (SD) of expected birth weight), moderate SGA (-2.01 to -3 SD), mild SGA (-1.01 to -2 SD) and appropriate for gestational age (-1 to 0.99 SD). Risk of poor school performance at time of graduating from compulsory school (grades <10th percentile) was calculated using unconditional logistic regression models and adjusted for socioeconomic factors. In a sub-analysis, we stratified boys by adult stature, and adjusted for maternal but not paternal height.

Results: All SGA groups were significantly associated with increased risk of poor school performance, with adjusted odds ratios (aOR) and 95% confidence intervals (CI) ranging from 1.85 (1.65-2.07) for severe SGA to 1.25 (1.22-1.28) for mild SGA. In the sub-analysis, all birth weight groups were associated with increased risk of poor school performance among boys with short staturecompared with non-short stature.

Conclusion: Mild SGA is associated with significantly increased risk of poor school performance, and the risk increases with severity of SGA. Further, this risk diminishes after adequate catch-up growth.

INTRODUCTION

Small for gestational age (SGA) is a statistic term describing size at birth in relation to gestational age (GA). Some SGA foetuses are constitutionally small without underlying pathology, i.e. due to genetic factors [1]. Others are not able to reach their growth potential, due to placental dysfunction, impaired placentation, maternal malnutrition or smoking [1-3]. This pathologic decrease in foetal growth rate is called intrauterine growth restriction (IUGR) [4].

Independent of the underlying cause, the risk of metabolic and cardiovascular morbidity later in life increases for children born SGA [5-7]. Accumulating evidence supports an association between being born SGA and cognitive as well as neurodevelopmental impairment [8-12]. Further, micro and macro structural brain changes in preterm as well as near term SGA foetuses have been demonstrated [13-16].

Several thresholds are used to define SGA, from 2.3rd percentile (<-2 standard deviations (SD)) of expected birth weight for GA, to < 5th, <10th or <15th percentile of the population. In Europe, SGA is defined as <-2 SD of expected birth weight for GA. Thus, children considered appropriate for gestational age (AGA) in Europe might be considered SGA in other parts of the world. There is a suggested linear trend between severity of SGA and increasing risk of impaired cognitive development, which highlights the difficulty in using a single threshold for SGA [17]. Little is known about how severity of SGA affects school performance and academic achievements. Children born mild SGA (defined as birth weight for GA between the 2.3rd and 10th percentile) are not considered SGA in Europe and therefore, no special attention is payed to their growth and cognitive development. Thus, children born mild SGA, who might be at increased risk of poor school performance do not receive early interventions that could promote cognitive development. To our knowledge, there is no previous population-based study investigating how different thresholds of low birth weight for GA affect school performance as by school grades.

Even though the vast majority of children born SGA have linear catch-up growth and reach normal final height, children born SGA have increased risk of short adult stature, compared with children born

AGA [18, 19]. The risk of impaired cognitive development decreases with satisfactory catch-up growth after being born SGA, but it does not disappear [9, 20]. Independent of birth weight, short adult stature is associated with lower intellectual capacity and cognitive difficulties [21, 22]. However, we are not aware of any previous population-based study that investigates the relationship between short adult stature and poor school performance stratified by birth weight for GA.

The aim of the present study was to evaluate the different thresholds for SGA in relation to the subsequent risk of poor school performance when graduating from compulsory school, in order to assess whether the pattern of risk increase is consistent with the European definition of SGA. Furthermore, we wanted to assess if adult stature modifies the association between birth weight and poor school performance.

METHODS

Data sources

This population-based register study used information from the Swedish Medical Birth Register, the National School Register, the Swedish Conscript Register and the Education Register.

The Swedish Medical Birth Register (MBR) was founded in 1973. It is based on mandatory registration of all pregnancies, and contains information on maternal demographics, pregnancy complications and the delivery. It also includes information on infant characteristics and neonatal complications.

The National School Register (NSR) has collected records of the final grades from the municipal nine-year compulsory school since 1988. Private compulsory schools, which during the study period comprised less than 5% of the students, were included in 1993.

The Swedish Conscript Register contains information on Swedish citizens conscripted for military service. Conscription was mandatory for males without severe handicaps or chronic diseases until 2006. The majority were conscripted between the ages of 18-25, when data from a health examination, including height and weight, were registered.

The Education Register provides data on the highest educational level for all Swedish residents.

All people living in Sweden are allocated a 10-digit personal identification number that is used in all official registers and makes linkage between registers possible.

Study population

The MBR provided information on 1,570,964 children, born in Sweden between 1973 and 1988, with known GA. In order to remove the possible negative impact of GA on cognitive development, all children considered preterm (GA <37 completed gestational weeks) or post term (GA ≥42 completed gestational weeks) were excluded. Further, children with malformations, chromosome aberrations and children born in a multiple pregnancy were excluded. Socioeconomic conditions were considered important for the outcome and hence, children whose mothers were born outside the Nordic countries and children born by mothers aged <18 years were excluded. Children with birth weight <-5 SD were considered misclassified, and thereby excluded. The final cohort consisted of 564,071 boys and 524,909 girls, in total 1,088,980 children (Figure 1).

Exposures

The studied exposure was defined as birth weight for GA and sex, based on the Swedish reference curve [23]. Last menstrual period was the Swedish standard for estimation of GA, until the late 1980's. Birth weight for GA was classified as SGA, AGA and large for gestational age (LGA). SGA was divided into mild SGA (-1.01 to -2 SD of expected birth weight for GA), moderate SGA (-2.01 to -3 SD), and severe SGA (<-3 SD). AGA was defined as -1 to 0.99 SD of expected birth weight for GA. LGA was classified into mild LGA (1 to 1.99 SD of expected birth weight for GA), moderate LGA (2 to 2.99 SD) and severe LGA (≥3 SD).

Outcome

The outcome was poor school performance, defined as final grades below the 10^{th} percentile of the study population's final grades at time of graduating from compulsory school. Data on final grades were obtained from the NSR, where final grades were registered in 95.5% of the children born 1973-

1981 and in 95.1% of the children born 1982-1988. During the first nine years of the study period (children born 1973-1981), school performance was measured with a norm-referenced grading system. The grades in an age group followed a Gaussian distribution curve. For each school subject, the student was given a grade on a five-point scale with one as the lowest and five as the highest grade. A grade point average was calculated for each student and used for comparison. Throughout the study period, the grading system changed to goal-oriented criterion-referenced grades. The students received grades in 16 different school subjects, where pass, pass with distinction and pass with special distinction generated 10, 15 and 20 points, respectively. A summary score of the 16 grades, with a maximum of 320 points was used for comparison (children born 1982-1988) [24]. In order to be able to compare the grades between the two systems, we defined poor school performance as final grades below the 10^{th} percentile for both grading systems.

Covariates

Potential socioeconomic confounders were maternal age and maternal and paternal educational level. Maternal age was categorised into 18-25 years, 25-29.9 years and ≥30 years. Educational level was categorised according to the Swedish educational system, where compulsory school corresponds to 9 years in school, upper secondary school 10-12 years and university level >12 years in school. Data on highest maternal and paternal educational levels were collected in 2009. Further, for children born 1982 or later, we had data on maternal smoking habits and BMI. Smoking information (non-smoker, 1-10 cigarettes daily and >10 cigarettes daily) was collected in early pregnancy and in pregnancy week 32. BMI was classified into low weight (BMI <18.5), normal weight (BMI 18.5-24), obesity class 1 (BMI 25-29) and obesity class 2-3 (BMI ≥30). Potential confounding birth characteristics were sex and Apgar score at 5 min (Table 1).

Short adult stature was defined as a height <-2 SD of the mean height for men at conscription, which corresponded to ≤167 cm. Short maternal height (collected from MBR) was likewise defined as maternal height <-2 SD of mean maternal height in the study population, which corresponded to ≤154 cm.

Statistics

Risk of poor school performance was calculated using unconditional logistic regression. We estimated odds ratios (OR) and corresponding 95% confidence intervals (CI). Children born AGA (-1 to 0.99 SD) were used as reference category. We used direct acyclic graphs (DAGs) to identify potential confounders. The minimal sufficient set of confounders was maternal and paternal educational level. As maternal and paternal educational level are regarded important factors for the child's academic achievements [25], they were included in the multivariable models. We excluded study subjects with missing information on parental educational level in the adjusted models.

The effect of smoking on the foetus is often regarded mainly as growth retarding and smoking is an important risk factor for SGA birth. Smoking can therefore be seen as a mediator of SGA birth rather than a confounder of poor school performance. Even though smoking has been associated with poor school performance [26, 27], it is not clear if the observed association is due to smoking per se, or rather as a result of other factors related to a less advantageous home environment and low socioeconomic status [28]. Therefore, we did not consider smoking to be a confounder in the present study.

Further, to estimate the effect of adult stature on school performance across different birth weights for GA, we made a sub-analysis in boys born 1982-1988 with known final height. Short adult stature was defined as height <-2 SD at conscription. The study population was divided into six groups; 1) moderate or severe SGA with non-short adult stature, 2) moderate or severe SGA with short adult stature, 3) mild SGA with non-short adult stature, 4) mild SGA with short adult stature, 5) AGA with non-short adult stature and 6) AGA with short adult stature. As there were too few individuals with known adult stature for separate analyses, we combined moderate and severe SGA into one group. We conducted multivariate unconditional logistic regression to estimate the risk of poor school performance. In Model 1, we adjusted for the same confounders as above (maternal and paternal educational level). In Model 2, we adjusted for the same confounders as in Model 1, but also for maternal height in order to adjust for the genetic contribution to short adult stature. Of the 111,759

boys with known adult stature, we had complete data on potential confounders for 107,977 individuals, which constituted our final sample size for Model 2 analysis. We considered boys born AGA with non-short adult stature as the reference category.

IBM SPSS Statistics 2.3 was used in all statistical calculations.

This study was approved by the Ethics Committee of the Medical Faculty of Uppsala University (no. 2014/103).

RESULTS

Poor school performance was associated with young maternal age, low parental educational level, maternal smoking and obesity. Boys had worse poor school performance than girls. Among those born 1982-1988 (goal-achieved grades), 12.0% of the boys and 8.0% of the girls had poor school performance. The corresponding rates among those born 1973-1981, (relative grades), were 14.7% for boys and 7.1% for girls. Further, poor school performance was more common among children born with low, compared with normal Apgar score at 5 min. Table 1 summarizes the characteristics of the study population.

Table 2a presents the associations between standardized birth weight by gestational age and sex and poor school performance at time of graduating from compulsory school among children born 1982-1988. Compared with being born AGA, being born severe (<-3 SD), moderate (-2.01 to -3 SD) as well as mild SGA (-1.01 to -2 SD) was associated with a significantly increased risk of poor school performance. Further, the associations showed a dose response pattern with adjusted ORs (aOR); 95% CIs 1.63 (1.38-1.93); 1.45 (1.35-1.56) and 1.27 (1.23-1.30) for severe SGA, moderate SGA and mild SGA, respectively.

Table 2b similarly shows the associations between standardized birth weight by gestational age and sex and poor school performance at time of graduating from compulsory school among children born 1973-1981. Risks of poor school performance were significantly increased across the SGA groups, and followed the same pattern as for the children born 1982-1988, but the associations were slightly

stronger (aORs; 95% CI 1.85 (1.65-2.07) for severe SGA; 1.50 (1.43-1.58) for moderate SGA; 1.25 (1.22-1.28) for mild SGA, respectively).

Table 3 shows the results for boys born 1982-1988. Compared with boys born AGA with non-short adult stature, being born moderate or severe SGA with non-short stature was associated with moderately increased risk of poor school performance (aOR; 95% CI 1.40 (1.16-1.70)). Moderate or severe SGA with short adult stature (16 subjects), had no statistically significant association with poor school performance. Further, mild SGA with non-short adult stature was associated with a slightly, but statistically significantly increased risk of poor school performance. Mild SGA with short adult stature was associated with the highest risk of poor school performance (aOR; 95% CI 1.62 (1.21-2.17). Being born AGA with short adult stature had similar risk estimates as moderate or severe SGA with non-short adult stature.

DISCUSSION

Statement of principal findings

We found that being born term SGA was associated with increased risk of poor school performance at time of graduating from compulsory school. The risk increased with increasing severity of SGA, with a statistically significant risk increase even for mild SGA (birth weight for GA of -1.01 to -2 SD). The observed risk might be an underestimation as children with high probability of poor school performance are more likely to not complete compulsory school, and hence are not included in our analysis. Our results imply that the European definition of SGA fails to capture a large number of children with increased risk of poor school performance. Further, we observed a positive relationship between short adult stature and poor school performance, indicating that the risk of poor school performance after SGA-birth diminishes if the child catches up adequately in height.

Strengths and limitations

The major strength of the study was the large size of the cohort, with more than 1,000,000 children with data on birth weight, GA, socioeconomic status of the family and final grades from compulsory

school. The large, relatively homogenous cohort permitted analysis of subgroups of SGA. The smallest subgroup, including children born with birth weight by GA ≤-3 SD, comprised more than 1000 individuals. Further, our sub-analysis of adult stature comprised almost 140,000 boys. The size of the cohort makes results from the stratification of SGA-levels and school grades more robust than in studies of smaller cohort size. Further, the population-based study design implies that the result of this study can be generalized to other populations in similar settings.

The recording of GA and birth weight in the Swedish Medical Birth Register (MBR) during the study period has been considered valid and has a low error rate [29]. The data were recorded prospectively in MBR as well as in the National School Register (NSR) and in the Conscript Register, which minimizes the risk of recall bias. Medical professionals recorded data on adult stature, at conscription as well as maternal height in early pregnancy. However, a major limitation with our study is the lack of information on paternal height, allowing us only partially to adjust for the genetic contribution to short adult stature.

In cases of severely affected cognitive development, there is a marked risk that the child did not graduate from compulsory school, and is thereby not included in our study. This is also true for data on adult stature, as individuals with impaired cognitive development were less likely to conscript for military service. Indeed, the proportion of boys with poor school performance was markedly higher among those with missing data on adult stature (18.8%), compared with those with data available (6.5% for non-short stature, 10.5% for short stature). This was particularly notable among boys with moderate or severe SGA with short adult stature, where only 16 out of 24 subjects with poor school performance had complete data and could be included in the analysis. Hence, there is a risk that we underestimate the risk for poor school performance in children born SGA.

Another limitation is the change in grading system that took place during our study period. The relative grades used during the first nine years, used a mean grade for comparison and were normally distributed. The later, goal-achieved grades, used a grade score, and showed a distribution skewed towards greater values. This makes direct comparisons between the two study periods difficult.

However, we used the 10th percentile within each grading system as the threshold for defining poor school performance, and we observed similar results for both grading systems. This can be regarded as a strength of the study, as it shows reproducibility in two different grading systems.

Comparison to earlier studies

Earlier studies on term children born SGA and cognitive development are diverse in terms of both the definition of SGA, varying from 2.3rd to 15th percentile, and definitions of cognitive disability [30]. In a review from 2010, de Bie showed a subtle, but statistically significant decrease in intelligence level and cognitive disabilities in children born SGA, even though different definitions of SGA make comparisons more difficult [10]. Other studies, with smaller cohorts, have shown results similar to ours, with a small, but statistically increased risk of poor school performance and lower intelligence levels for children born SGA, but without looking into different levels of SGA within the same population [11, 31-33]. We are only aware of one previous study that used multiple thresholds reflecting different severity classes of SGA when studying learning difficulties. O'Keeffe et al. measured three aspects of learning difficulties; first by a questionnaire where the mother assessed the child's school performance, and second by a reading test and an IQ test. Their results are in line with ours, indicating that severe SGA is more strongly associated with learning difficulties than mild SGA [17]. To our knowledge, our study is the first study that investigates the risk of poor school performance measured as grades and stratified for birth weight by GA.

Multiple previous studies have investigated the association between being born SGA and subsequent intelligence quotient (IQ) score, both in childhood and in adulthood. Concordant with our results, some studies observed a significant difference in IQ between individuals born SGA and AGA, and this association was more prominent among SGA children with insufficient catch up growth [9, 11, 34]. However, not all studies observed an association between being born SGA and lower IQ [35, 36]. Our results suggest that among children born SGA, catch-up growth plays an equally important role for subsequent school performance, and this is true for all birth weights, including AGA as well as mild, moderate and severe SGA. To our knowledge, this has not been shown previously.

Perspectives

Short adult stature is more common among children born SGA. Approximately 10% of children born SGA do not catch up in height during childhood. In our study, 10.0% of children born moderate or severe SGA had short adult stature, compared with 5.2% of children born mild SGA, and 1.9% of AGA children. In similarity with our results, short adult stature has previously been associated with lower intelligence performance [21, 37]. Some, but not all of those children, have a growth hormone (GH) deficiency [38, 39]. It has been shown that GH therapy increases the catch-up growth and thereby reduces the risk for short adult stature [40-42]. Further, there is some evidence that children born SGA who receive GH therapy have an improved cognitive development compared with their counterparts not receiving GH therapy [33]. In Sweden, children born SGA are considered for GH therapy if their height at age 4 years is below -2.5 standard deviation scores (SDS) of the population, and below -1 SDS of their own target height, as determined by their parents' height. Although our results show that children born mild SGA (-1.01 to -2 SD) with insufficient catch-up growth have an increased risk of poor school performance, it is still unclear if GH therapy could counteract this effect. The potential effect of GH therapy on cognitive development in children born SGA with inadequate catch-up growth needs further investigation.

In Europe, children with a birth weight for GA between -1 and -2 SD are not considered SGA and their growth is therefore not more carefully monitored during childhood and adolescence. Further, children born mild SGA with short adult stature had a similar risk of poor school performance as moderate to severe SGA children with non-short adult stature. Our results suggest that with the present European definition of SGA, children with increased risk of inadequate catch-up growth and poor school performance are lost to more extensive follow-up during childhood.

Early positive parenting improves cognitive as well as psychomotor functions in children born SGA [43]. Parental support might therefore help cognitive development in children born mild SGA. Further, support and encouragement of breast-feeding is an additional approach to promote cognitive

development of these children [44]. More research is needed to identify additional approaches that support and improve cognitive development in children born mild SGA.

In conclusion, the results of our study indicate that not only children born moderate to severe, but also mild SGA (-1.01 to -2 SD) have an increased risk of performing poorly in compulsory school. Further, children born mild SGA with short adult stature, reflecting inadequate catch-up growth, are at the greatest risk. We therefore suggest that the growth of children born mild SGA should be closely monitored, as early interventions can improve their cognitive development.

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DISCLOSURE

The authors have no conflicts of interest to declare.

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Table 1. Characteristics of the study population, n= 1,088,980.

	Poor school performance					
	Born 1982-1988			Born 1973-1981		
	Total	Cases	Rate (%)	Total	Cases	Rate (%)
Birth weight for gestational age (SD)[1]						
<-3	1021	171	16.7	1612	383	25.7
-3 to -2.01	7224	1068	14.8	12,696	2048	16.1
-2 to -1.01	47,681	6106	12.8	73,737	9840	13.3
-1 to 0.99	345,641	33,970	9.8	422,715	44,668	10.6
1 to 1.99	79,595	6989	8.8	83,884	8281	9.9
2 to 2.99	12,831	1344	9.5	13,121	1664	11.3
≥3	1388	163	10.5	1496	229	13.3
Maternal age						
18-25	131,694	19,980	15.2	205,224	30,662	14.9
25-29.9	185,970	16,460	8.9	236,021	21,327	9.0
≥30	179,224	13,370	7.5	170,292	15,124	8.9
Maternal educational level (years)[2]						
≤9	71,717	14,670	20.5	120,679	22,858	18.9
10-12	252,624	28,690	11.4	257,808	29,718	11.5
>12	167,837	5678	3.4	155,350	5623	3.6
Missing	4710	766	16.3	6696	1223	18.3
Paternal educational level (years)[2]						
≤9 years	109,338	17,200	15.7	155,971	25,964	16.6
10-12 years	232,859	25,390	10.9	227,447	24,946	11.0
>12 years	138,654	4264	3.1	135,918	4369	3.2
Missing	16,037	2949	18.4	21,197	4143	19.5
Daily smoking in early pregnancy						
Yes	128,402	22,380	17.4			
No	310,163	21,460	6.9			
Missing	58,323	5959	10.2			
Maternal BMI in early pregnancy						
<18.5	27,235	3170	11.6			
18.5-24	278,544	25,230	9.1			
25-29	41,590	5485	13.2			
≥30	7682	1347	17.5			
Missing	141,837	14,580	10.3			
Sex						
Boy	252,736	30,360	12.0	311,335	45,813	14.7
Girl	224,707	19,450	8.0	300,202	21,300	7.1
Apgar at 5 min						
1-3	661	80	12.1	827	118	14.3
4-6	2288	272	11.9	3245	420	12.9
7-10	475,435	47,640	10.0	477,195	52,192	10.9
Missing	18,253	1788	9.8	65,311	14,383	22.0

[1] Standardized birth weight measured in standard deviations (SD) in relation to gestational week and sex, according to the Swedish reference standards for birth weight [23].

[2] Highest educational level registered in the Education Register in year 2009

Table 2a. Associations between standardized birth weight by gestational age and sex and poor school performance at time of graduating from compulsory school among term born children 1982-1988, n= 496,888.

Poor school performance		
Birth weight for gestational age (SD)	**Odds ratio (95% Confidence Interval)**	
	Crude	**Adjusted[1]**
<-3 SD	1.85 (1.57-2.18)*	1.63 (1.38-1.93)*
-3 to -2.01 SD	1.59 (1.49-1.70)*	1.45 (1.36-1.56)*
-2 to -1.01 SD	1.35 (1.31-1.39)*	1.27 (1.23-1.30)*
-1 to 0.99 SD	1.00	1.00
1 to 1.99 SD	0.88 (0.86-0.91)*	0.91 (0.88-0.93)*
2 to 2.99 SD	0.96 (0.91-1.02)	0.98 (0.92-1.03)
≥3 SD	1.08 (0.92-1.27)	1.10 (0.93-1.30)

[1] adjusted for maternal and paternal education

* p <0.01

Table 2b. Associations between standardized birth weight by gestational age and sex and poor school performance at time of graduating from compulsory school among term born children 1973-1981, n= 611,537.

Poor school performance		
Birth weight for gestational age (SD)	**Odds ratio (95% Confidence Interval)**	
	Crude	**Adjusted[1]**
<-3 SD	2.01 (1.80-2.25)*	1.85 (1.65-2.07)*
-3 to -2.01 SD	1.63 (1.55-1.71)*	1.50 (1.43-1.58)*
-2 to -1.01 SD	1.30 (1.27-1.33)*	1.25 (1.22-1.28)*
1 to -0.99 SD	1.00	1.00
1 to 1.99 SD	0.93 (0.90-0.95)*	0.94 (0.92-0.96)*
2 to 2.99 SD	1.07 (1.02-1.13)*	1,08 (1,02-1,14) *
≥3 SD	1,30 (1,13-1,49)*	1,27 (1,1-1,46)*

[1] adjusted for maternal and paternal education

* $p < 0.01$

Table 3. Rates and associations between standardized birth weight by GA and sex and poor school performance at time of graduating from compulsory school among term born boys 1982-1988 , n= 111,759.

Poor school performance							
Birth weight for gestational age (SD)	**Short adult stature[1]**	**Total**	**Cases**	**Rate (%)**	**Odds ratio (95% Confidence Interval)**		
					Crude	**Model 1[2]**	**Model 2[3]**
<-2 SD	no	1877	173	9.2	1.51 (1.29-1.77)**	1.42 (1.21-1.66)**	1.40 (1.16-1.70)**
<-2 SD	yes	210	24	11.4	1.92 (1.26-2.94)**	1.60 (1.04-2.46)*	1.36 (0.81-2.29)
-2 to -1.01 SD	no	11,936	947	7.9	1.28 (1.20-1.38)**	1.21 (1.12-1.30)**	1.20 (1.11-1.30)**
-2 to -1.01 SD	yes	650	68	10.5	1.74 (1.35-2.24)**	1.52 (1.18-1.96)**	1.62 (1.21-2.17)**
-1 to 0.99 SD	no	95,246	6073	6.4	1.00	1.00	1.00
-1 to 0.99 SD	yes	1840	188	10.2	1.70 (1.46-1.98)**	1.52 (1.30-1.78)**	1.37 (1.14-1.66)**

[1] Defined as height less than –2 standard deviations (SD) from the average male height in the study population (mean height =180 cm, -2 SD =167 cm)

[2] Model 1 is adjusted for maternal and paternal education

[2] Model 2 is adjusted as Model 1 and additionally for maternal height

* $p < 0.05$

** $p < 0.01$

Figure 1. Selection of study population