Association between cesarean section and human capital in adulthood: 1982 and 1993 Pelotas birth cohorts, Rio Grande do Sul State, Brazil

Associação entre cesariana e capital humano na idade adulta: as coortes de nascimentos de Pelotas, 1982 e 1993, Rio Grande do Sul, Brasil

Asociación entre cesárea y capital humano en la etapa adulta: cohortes de nacimiento de 1982 y 1993 en Pelotas, Río Grande do Sul, Brasil

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Abstract

This study aims to assess the association between mode of delivery and human capital among young adults enrolled in the 1982 and 1993 Pelotas birth cohorts, Rio Grande do Sul State, Brasil. In 1982 and 1993, the maternity hospitals of the municipality were daily visited, the births identified, and those live births, whose family lived in the urban area of Pelotas, were examined and their mothers interviewed. Information on mode of delivery, vaginal or cesarean, was provided by the mother in the perinatal study. Performance in intelligence tests achieved schooling and income were evaluated in the 30 years visit at the 1982 cohort. At the 1993 cohort, schooling and income were assessed at the 22 years visit, whereas IQ was evaluated at 18 years. Tobacco smoking in adulthood and type of school was used as negative outcomes to strength causal inference. Initially, cesarean section was positively associated with human capital at adulthood, with the exception of income in the 1993 cohort. After controlling for confounders, the magnitude of the associations was strongly reduced, and the regression coefficients were close to the null value. The negative outcome analysis showed that, after controlling for confounding variables, the mode of delivery was not associated with tobacco smoking and type of school. Suggesting that the variables included in the regression model to control for confounding, provided an adequate adjustment and it is unlikely that the results are due to residual confounding by socioeconomic status. On the other hand, considering the short- and long-term risks and the epidemic of cesarean sections, measures should be implemented to reduce its prevalence.

Cesarean Section; Parturition; Intelligence; Educational Status; Income

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Introduction

The prevalence of cesarean sections has increased worldwide, reaching epidemic proportions in some countries and has been named by the World Health Organization (WHO) as a "surgical epidemic" [1]. The highest prevalence has been observed in Latin America and Caribe (40.5%), North America (32.3%), and Oceania (31.1%) [2,3]. In Brazil, the proportion of cesarean section has increased from 15% in 1970 [4] to 55.9% in 2018 (Brazilian Health Informatics Department – DATASUS. http://tabnet. datasus.gov.br/cgi/tabcgi.exe?sinasc/cnv/nvuf.def, accessed on 24/Apr/2020) and is the second highest worldwide, just behind Dominican Republic (56.4%) [2].

Cesarean section following proper medical indication is associated with lower maternal and fetal morbidity and mortality, but without indication, it has short- and long-term negative consequences [1,5,6]. Short-term risks include a higher risk of preterm birth, respiratory morbidity in the newborn, and delayed initiation of breastfeeding [6,7,8,9]. In the long-term, cesarean section is associated with an increased risk of obesity [10,11] and allergic diseases [12] in adolescence or adulthood. Furthermore, it has also been reported that cesarean section would be negatively associated with performance in intelligence tests [13] and school performance [14]. Therefore, cesarean section could have long-term consequences on human capital, that is, resources, skills, and knowledge that improve the individual's capacity in the labor market [15,16].

Regarding the biological plausibility for a putative effect of cesarean section on human capital, gut microbiota is a possible mechanism. A diminished diversity in the microbiota has been observed among cesarean-born children [17,18], as a consequence of the lack of exposure to vaginal microbiota at delivery, the dysbiosis of gut microbiota may affect the immune system, changing the levels of pro-inflammatory cytokines [19] associated with central nervous system function [20]. Also, some changes in tryptophan metabolism, a serotonin precursor, may occur, affecting the memory, humor and response to stressful events [21,22].

Notably, negative associations (especially in analyses not accounting for socioeconomic variables) between cesarean section and human capital are unlikely due to residual confounding, because the prevalence of cesarean section is higher among women with high socioeconomic status [23]. On the other hand, residual confounding could bias a negative association in the direction of the null, or even turn a weak negative or null association into a positive association – i.e., higher human capital among cesarean-born individuals. In the latter scenario, unadjusted associations could be naively interpreted as supportive of a beneficial effect of cesarean section on human capital.

Considering the lack of evidence on the association between cesarean section and human capital and the possibility of strong confounding, analyses accounting for potential socioeconomic (and other) confounders are necessary in order to improve our understanding on the causal relationship between cesarean section and human capital. This study aimed to assess the association between mode of delivery and human capital among young adults enrolled in the 1982 and 1993 Pelotas birth cohorts using two strategies to address residual confounding.

Methods

Study setting, design and participants

This study is based on data from two birth cohorts conducted in Pelotas, a Southern Brazilian city. In 2010, the Gini index was 0.560 (DATASUS. http://tabnet.datasus.gov.br/cgi/ibge/censo/cnv/ginibr. def, accessed on 20/Nov/2020), gross domestic product (GDP) is estimated to be BRL 17,353.15 per capita, and its human development index (HDI-M) is 0.739 (Brazilian Institute of Geography and Statistics. https://ww2.ibge.gov.br/home/estatistica/populacao/censo2010, accessed on 20/Nov/2020).

In 1982 and 1993, the maternity hospitals of Pelotas were daily visited. The births identified and the live births whose families lived in the urban area of the municipality were examined, and their mothers interviewed, totaling 5,914 newborns in 1982 [24] and 5,249 in 1993 [25]. The proportion of home births in these years and the nonresponse rate at recruitment in the two cohorts were lower than 1%.

The cohort members have been followed for several times, from June 2012 to February 2013, the researchers tried to follow the whole 1982 cohort [26]. Whereas for the 1993 cohort, the 18-year follow-up was conducted from September 2011 to March 2012 [27], and the 22-year follow-up from October 2015 and July 2016 [28]. The cohort members were searched and invited to visit the research clinic. Further details on the study methodology have been published elsewhere [24,25,26,27,28].

In this analysis, those subjects with complete data on mode of delivery and at least one of the outcomes (performance in intelligence tests (IQ), achieved schooling and income) were included.

Exposure

In the perinatal study, mothers were asked about the mode of delivery (vaginal or cesarean).

Outcome

The following indicators of human capital were measured:
a) IQ: intelligence scores were evaluated using the third version of the *Wechsler Adult Intelligence Scale* (WAIS-III) [28,30,31] (including arithmetic, digit symbol, similarities, and picture completion subtests). The tests were administered in the 30 and 18-years follow-up visits in the 1982 and 1993 cohorts, respectively, by trained psychologists who were unaware of the information on the participant mode of delivery.
b) Achieved schooling: information on the complete years of formal education was gathered in the 30 and 22-years follow-up visits in the 1982 and 1993 cohorts, respectively.
c) Income: the individual monthly income (Brazilian Reais) of participants at 30 and 22 years of age was assessed in the 1982 and 1993 cohorts, respectively. They were considered as income from work or any other source.

Covariates

The following covariates (measured in the perinatal study) were considered as possible confounders; maternal skin color; maternal age in complete years; maternal schooling (complete years of formal education), monthly family income (in minimum wages); parity (number of previous deliveries); maternal smoking during pregnancy (yes, no); sex and maternal pre-pregnancy body mass index (information on maternal weight at the beginning of the pregnancy was retrieved from the antenatal card, or self-reported if the information was not available, whereas height was measured at the hospital admission by the hospital staff).

Paternal schooling (complete years of formal education) was collected in the two years visit of the 1982 cohort, whereas for the 1993 cohort this information was gathered in the perinatal study.

Statistical analysis

Data analysis was conducted using Stata version 16.0 (https://www.stata.com). Analysis of variance and chi-square test were respectively used to compare the differences of means and proportions according to the mode of delivery. Crude and adjusted linear regression analyses were performed to assess the association between mode of delivery and human capital (IQ, schooling level, and income). Adjusted analyses were controlled for the above listed confounders. Furthermore, a negative outcome control approach was used to strength the causal inference on the association between mode of delivery and human capital [32,33]. In the analysis of the negative outcome control, multiple linear regression was also used to control the confounders.

Negative outcome control

According to the directed acyclic graph (DAG) [34] (Figure 1), tobacco smoking in adulthood and type of school attended by the cohort member (public or private) were used as negative outcomes. Assuming that mode of delivery is not causally associated with these outcomes and that the same factors that confound the association of mode of delivery with human capital would also bias the association with the negative outcomes, lack of association of mode of delivery with the negative outcomes would be indicative of lack of residual confounding [32,33].
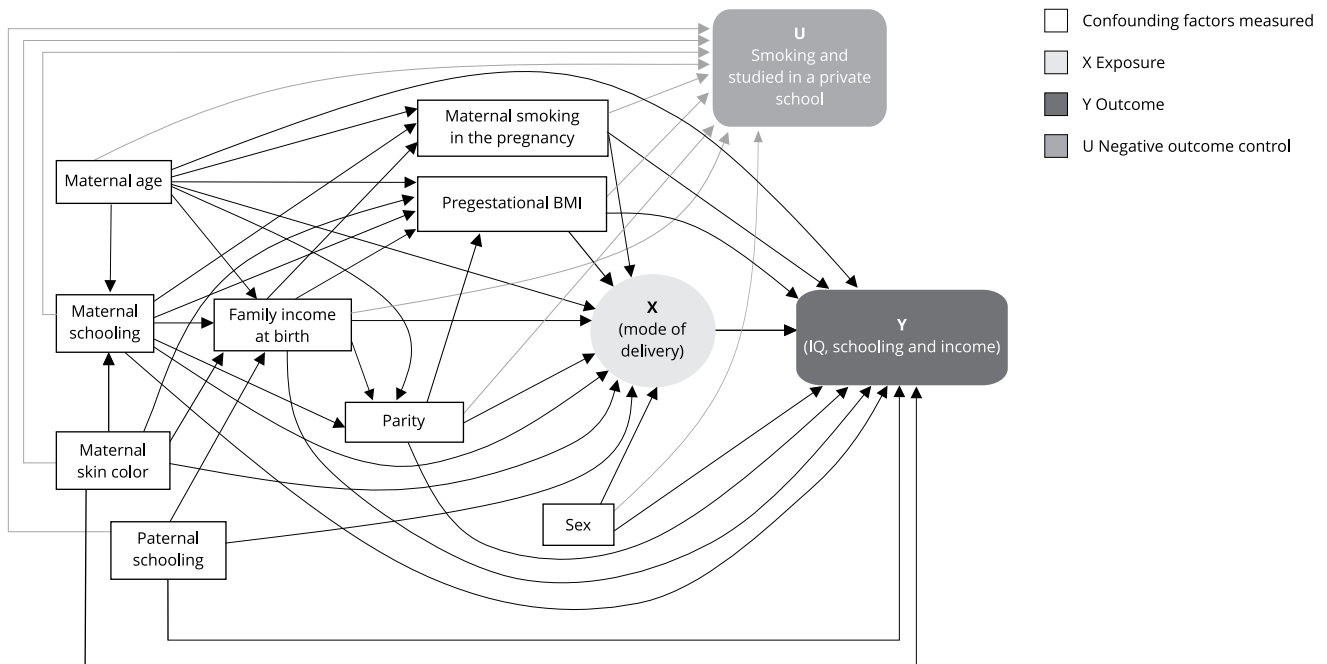
Although the assumption of shared confounders may not apply to all possible confounders of the association of mode of delivery with human capital, it is likely to apply to socioeconomic confounders, which are strong predictors of type of school and smoking behavior. Moreover, socioeconomic factors are likely to be the strongest confounders, considering the strong associations of socioeconomic position at birth with mode of delivery and human capital [23]. The assumption of no causal effect on the negative outcomes is particularly likely for type of school, which is strongly determined by social factors [35]. This is somewhat less plausible for smoking, which also has a strong social component, but also biological (e.g., genetic) determinants [36,37]. However, there is no established mechanism providing biological plausibility for a causal effect of mode of delivery on smoking behavior. Moreover, including this variable allowed performing the negative outcome control analysis in both cohorts.

Ethical considerations

The Ethical Review Board of the Faculty of Medicine of the Federal University of Pelotas (UFPel) approved the study, and all participants signed a informed consent form. Project registered by proto-

Figure 1

Directed acyclic graph (DAG) – mode of delivery, human capital and negative control outcomes.

BMI: body mass index; IQ: intelligence quotient.

col of number 16/12 in the 1982 cohort, and in the 1993 cohort the most recent protocol approved is number 1,250,366.

Results

In 2012 and 2013, 3,701 (mean age 30.2 years) participants of the 1982 cohort were interviewed, which added to the 325 deaths identified among the study participants, represented a follow-up rate of 68.1%. For the 1993 cohort, in the 2011 and 2012 visit, 4,106 subjects (mean age 18.5 years) were interviewed, added to those 164 who died, representing 81.3% of the original cohort. In the 2015 and 2016 visit, 3,810 subjects (mean age 22.6 years) were evaluated, and the follow-up rate was 76.3%, after adding the 193 known to have died.

Information on mode of delivery and at least one of the measures of human capital was available for 3,671 subjects in the 1982 cohort, whereas for the 1993 cohort, 4,050 subjects were included in the analysis on the association of mode of delivery with IQ at 18 years, and for schooling level and income at 22 years at least 3,805 individuals were included. Table 1 shows that those subjects included in the analyses were more likely to belong to the families from intermediate socioeconomic categories and

Table 1

Proportion of participants included in the mode of delivery analysis according to baseline characteristics in the 1982 and 1993 Pelotas birth cohorts, Rio Grande do Sul State, Brazil.

	1982 cohort (N = 5,914)		1993 cohort (N = 5,249)	
	Original sample	Included in the analysis	Original sample	Included in the analysis
	n *	n (%)	n *	n (%)
Maternal age (years)				
< 20	845	550 (60.3)	879	751 (82.1)
20-29	3,256	2,106 (61.2)	2,706	2,327 (83.1)
> 30	1,487	1,014 (65.0)	1,470	1,289 (84.1)
Maternal schooling (years)				
≤ 4	1,816	1,182 (60.3)	1,389	1,174 (80.0)
5-8	2,317	1,580 (64.4)	2,341	2,064 (85.2)
9-11	626	399 (61.0)	904	781 (84.6)
≥ 12	823	505 (60.2)	415	342 (80.1)
Family income (MW)				
≤ 1	1167	723 (56.1)	908	782 (80.9)
1.1-3.0	2,642	1,804 (64.7)	2,062	1,787 (83.2)
3.1-6.0	1,056	716 (65.6)	1,177	1,044 (86.7)
6.1-10.0	370	219 (57.3)	425	353 (81.5)
> 10.0	328	192 (57.3)	379	322 (83.6)
Pregestational BMI				
Normal (< 25kg/m²)	3,689	2,412 (62.2)	3,818	3,271 (82.6)
Overweight (≥ 25kg/m²)	1,045	724 (66.1)	1,096	983 (86.3)
Maternal smoking in the pregnancy				
No	3,625	2,385 (62.6)	3,381	2,917 (83.4)
Yes	1,964	1,286 (61.2)	1,675	1,451 (82.8)
Type of delivery				
Vaginal	4,045	2,657 (62.1)	3,506	3,018 (82.8)
Cesarean section	1,544	1,014 (62.1)	1,550	1,350 (84.3)

BMI: body mass index; MW: minimum wage.

* Those subjects who were known to have died were excluded.

have mothers who were overweight at the beginning of the pregnancy. However, the magnitude of these differences was small, being less than 8.3 percentage points.

Table 2 shows that from 1982 to 1993, among those included in these analyses, most mothers were aged 20-29 years, had from five to eight years of schooling, and about two of every three families had an income lower than three minimum wages. In the same period, the prevalence of cesarean section slightly increased from 27.6% to 30.9%. Concerning human capital, mean IQ were 98.0 and 96.5 points at 30 and 18 years, respectively.

In both cohorts, socioeconomic condition (family income at birth, maternal and paternal schooling) and maternal age were positively associated with human capital at adulthood and cesarean section (Table 3 and 4). Only in the 1993 cohort, maternal age was not associated with income of the individual in adult life (Table 4). Prevalence of cesarean section was higher among those subjects whose mother was overweight at the beginning of the pregnancy, whereas, in the 1982 cohort, IQ and income at adulthood were lower among offspring of overweight mothers. For both cohorts, we observed that cesarean section was higher among non-smoking mothers and human capital was higher among offspring of mothers who did not smoke during pregnancy (Table 3 and 4).

In the unadjusted analysis, cesarean section was positively associated with human capital at adulthood, except for individual income in the 1993 cohort at 22 years. After covariate adjustment, the point estimates were strongly attenuated and the statistical evidence for an association became substantially lower than conventional significance levels (p > 0.3 for all adjusted associations) (Table 5). Moreover, the 95% confidence intervals (95%CI) were narrow and only included coefficients of small magnitude.

Table 2

Distribution of the studied population according to the mode of delivery and human capital in the 1982 and 1993 Pelotas birth cohorts, Rio Grande do Sul State, Brazil.

Characteristic measured at birth	1982 cohort (N = 3,671)		1993 cohort (N = 4,368)	
	n	%	n	%
Maternal age (years)				
< 20	550	15.0	751	17.2
20-29	2,106	57.4	2,327	53.3
> 30	1,014	27.6	1,289	29.5
Maternal schooling (years)				
≤ 4	1,182	32.2	1,174	26.9
5-8	1,580	43.1	2,064	47.4
9-11	399	10.9	781	17.9
≥ 12	505	13.8	342	7.8
Family income (MW)				
≤ 1	723	19.8	782	18.2
1.1-3.0	1,804	49.4	1,787	41.7
3.1-6.0	716	19.6	1,044	24.4
6.1-10.0	219	6.0	353	8.2
> 10	192	5.2	322	7.5
Mode of delivery				
Vaginal childbirth	2,657	72.4	3,018	69.1
Cesarean section	1,014	27.6	1,350	30.9
Characteristic measured at adulthood				
IQ (points)	98.0 (12.6) *		96.5 (12.7) *	
Schooling (years)	11.3 (4.2) *		9.7 (2.5) *	
Monthly income (Brazilian Reais)	1,000 (530-1,891) **		960 (300-1,400)	

IQ: intelligence quotient; MW: minimum wage.

* Mean (standard deviation);

** Median (interquartile range).

Table 3

Mode of delivery, IQ, income, and schooling at adulthood according to the confounding variables in the 1982 Pelotas birth cohort, Rio Grande do Sul State, Brazil.

	N	Cesarean section	IQ (points)	Schooling (years)	Income (BRL)
		% (95%CI)	Mean (95%CI)	Mean (95%CI)	Mean (95%CI)
Maternal skin color		p = 0.002 *	p < 0.001 *	p = 0.024 *	p = 0.019
White	3,012	28.7 (26.7; 30.2)	99.2 (98.8; 99.7)	11.6 (11.5; 11.7)	1,616 (1,553; 1,679)
Black	658	21.5 (19.1; 24.1)	92.1 (91.1; 93.0)	9.9 (9.6; 10.2)	978 (842.5; 1,111)
Maternal age (years)		p < 0.001 *	p < 0.001 *	p < 0.001 *	p = 0.006 *
< 20	550	22.2 (19.7; 25.1)	94.6 (93.5; 95.6)	10.2 (9.9; 10.6)	1,192 (1,045; 1,341)
20-29	2,106	25.4 (23.9; 26.8)	98.5 (98.0; 99.1)	11.4 (11.2; 11.6)	1,573 (1,497; 1,649)
> 30	1,014	36.7 (33.3; 38.1)	98.7 (98.0; 99.5)	11.7 (11.5; 12.0)	1,522 (1,413; 1,631)
Maternal schooling (years)		p < 0.001 *	p < 0.001 **	p < 0.001 **	p < 0.001 **
≤ 4	1,182	19.8 (18.1; 21.7)	92.2 (91.6; 92.9)	9.2 (9.0; 9.4)	997 (901.1; 1,092)
5-8	1,580	26.1 (24.4; 27.9)	97.5 (97.0; 98.1)	11.1 (11.0; 11.3)	1,355 (1,273; 1,438)
9-11	399	33.6 (30.1; 37.4)	103.2 (102.1; 104.3)	13.2 (12.8; 13.5)	1,871 (1,707; 2,035)
≥ 12	505	45.4 (42.0; 48.8)	108.6 (107.6; 109.6)	15.3 (15.0; 15.7)	2,852 (2,706; 2,998)
Paternal schooling (years)		p < 0.001 *	p < 0.001 **	p < 0.001 **	p < 0.001 **
≤ 4	884	19.7 (17.6; 21.9)	92.5 (91.8; 93.3)	9.2 (9.0; 9.5)	1,067 (954.0; 1,180)
5-8	1,435	26.8 (24.9; 28.8)	97.5 (96.9; 98.1)	11.2 (11.0; 11.4)	1,329 (1,240; 1,418)
9-11	406	35.5 (31.7; 39.5)	103.4 (102.2; 104.5)	13.2 (11.8; 13.5)	1,913 (1,746; 2,080)
≥ 12	426	42.3 (38.7; 45.9)	108.2 (107.1; 109.3)	15.1 (14.8; 15.5)	2,815 (2,651; 2,978)
Family income at birth (MW)		p < 0.001 *	p < 0.001 **	p < 0.001 **	p < 0.001 **
≤ 1	723	17.0 (15.0; 19.1)	91.5 (90.7; 92.4)	8.9 (8.6; 9.1)	940 (817.6; 1,061)
1.1-3	1,804	25.1 (23.5; 26.7)	96.6 (96.0; 97.1)	10.7 (10.6; 10.9)	1,255 (1,178; 1,332)
3.1-6	716	36.3 (33.5; 39.2)	102 (101.2; 102.9)	13.1 (12.8; 13.4)	1,894 (1,772; 2,017)
6.1-10	219	41.4 (36.5; 46.4)	106.7 (105.2; 108.3)	14.5 (14.0; 15.0)	2,586 (2,364; 2,807)
> 10	192	46.6 (41.3; 51.9)	110.4 (108.8; 112.1)	15.8 (15.3; 16.3)	3,219 (2,983; 3,456)
Parity		p < 0.001 *	p < 0.001 *	p < 0.001 *	p < 0.001 *
Primiparous	1,472	30.3 (28.5; 32.2)	100.1 (99.5; 100.8)	12.1 (11.9; 12.3)	1,650 (1,559; 1,740)
Multiparous	2,198	25.8 (24.4; 27.3)	96.5 (96.0; 97.1)	10.8 (10.6; 11.0)	1,403 (1,329; 1,477)
Pregestational BMI		p < 0.001 *	p = 0.034 *	p = 0.444 *	p = 0.002
Normal (< 25kg/m²)	2,412	26.5 (25.2; 28.0)	98.9 (98.4; 99.4)	11.6 (11.5; 11.8)	1,623 (1,550; 1,695)
Overweight (≥ 25kg/m²)	724	35.1 (32.4; 38.0)	97.8 (96.9; 98.7)	11.5 (11.2; 11.8)	1,382 (1,249; 1,514)
Maternal smoking in the pregnancy		p < 0.001 *	p < 0.001 *	p < 0.001 *	p = 0.001 *
No	2,385	29.4 (28.0; 30.9)	99.1 (98.6; 99.6)	11.7 (11.5; 11.8)	1,572 (1,501; 1,643)
Yes	1,286	24.3 (22.5; 26.1)	95.9 (95.2; 96.6)	10.7 (10.5; 10.9)	1,371 (1,274; 1,468)
Sex		p = 0.528 *	p = 0.011 *	p < 0.001 *	p < 0.001 *
Male	1,772	27.8 (26.3; 29.4)	98.5 (97.9; 99.1)	10.9 (10.7; 11.1)	1,933 (1,853; 2,013)
Female	1,899	27.3 (25.7; 29.0)	97.5 (96.9; 98.0)	11.7 (11.5; 11.9)	1,099 (1,022; 1,177)

95%CI: 95% confidence interval; BMI: body mass index; IQ: intelligence quotient; MW: minimum wage.

* Test of heterogeneity;

** Linear trend test.

Table 6 shows that the prevalence of smoking in adulthood was lower among the cesarean section-born, and the magnitude of the associations decreased after covariate adjustment. For type of school, the proportion of subjects who studied in a private school was higher among those who were born by cesarean section, and after covariate adjustment the prevalence ratio was close to the null.

Table 4

Mode of delivery, IQ, income, and schooling at adulthood according to the confounding variables in the 1993 Pelotas birth cohort, Rio Grande do Sul State, Brazil.

	n	Cesarean section % (95%CI)	IQ (points) Mean (95%CI)	Schooling (years) Mean (95%CI)	Income (BRL) Mean (95%CI)
Maternal skin color		p = 0.001 *	p < 0.001 *	p < 0.001 *	p < 0.001 **
White	3,357	32.0 (30.6; 33.5)	98.1 (97.7; 98.5)	10.0 (9.9; 10.1)	1,043 (1,006; 1,081)
Black	810	25.0 (22.3; 27.8)	90.6 (89.7; 91.5)	8.8 (8.6; 8.9)	781.7 (707.9; 855.6)
Other	199	27.8 (22.4; 33.9)	92.8 (91.0; 94.6)	9.2 (8.8; 9.5)	906 (753.1; 1,058)
Maternal age (years)		p < 0.001 *	p < 0.001 **	p < 0.001 *	p = 0.092 *
< 20	751	25.1 (22.4; 28.1)	93.8 (92.8; 94.7)	9.2 (9.0; 9.4)	1,051 (973.3; 1,129)
20-29	2,327	28.2 (26.6; 30.0)	96.4 (95.8; 96.9)	9.8 (9.6; 9.9)	955 (910.2; 1,000)
> 30	1,289	38.0 (35.7; 40.4)	98.2 (97.5; 98.9)	10.1 (10.0; 10.2)	1,002 (940.5; 1,063)
Maternal schooling (years)		p < 0.001 *	p < 0.001 **	p < 0.001 **	p < 0.001 **
≤ 4	1,174	22.4 (20.4; 24.6)	90.4 (89.7; 91.1)	8.4 (8.3; 8.6)	862 (800.0; 923.6)
5-8	2,064	27.4 (25.6; 29.2)	95.8 (95.2; 96.3)	9.7 (9.6; 9.8)	1,009 (961.5; 1,056)
9-11	781	38.1 (35.1; 41.3)	102.3 (101.5; 103.2)	10.9 (10.8; 11.1)	1,050 (971.4; 1,128)
≥ 12	342	59.7 (55.0; 64.3)	108.7 (107.4; 110.0)	11.7 (11.5; 12.0)	1,185 (1,056; 1,313)
Paternal schooling (years)		p < 0.001 *	p < 0.001 **	p < 0.001 **	p = 0.001 **
≤ 4	1,022	22.5 (20.2; 24.9)	91.8 (91.1; 92.5)	8.7 (8.5; 8.8)	885 (817.9; 952.8)
5-8	2,002	28.5 (26.7; 30.4)	95.7 (95.2; 96.2)	9.7 (9.6; 9.8)	1,004 (955.8; 1,051)
9-11	749	41.1 (38.0; 44.4)	102.1 (101.2; 103.0)	11.0 (10.9; 11.2)	1,090 (1,008; 1,172)
≥ 12	294	52.3 (47.0; 57.4)	109.5 (108.1; 110.9)	11.6 (11.3; 11.8)	1,060 (919.0; 1,200)
Family income at birth (MW)		p < 0.001 *	p < 0.001 **	p < 0.001 **	p < 0.001 **
≤ 1	782	23.6 (21.0; 26.4)	90.3 (89.5; 91.2)	8.4 (8.2; 8.6)	846 (768.6; 923.9)
1.1-3.0	1,787	24.7 (22.9; 26.5)	95.1 (94.6; 95.7)	9.5 (9.3; 9.6)	994 (943.6; 1,044)
3.1-6.0	1,044	33.4 (30.8; 36.1)	98.5 (97.7; 99.2)	10.4 (10.2; 10.5)	1,003 (936.3; 1,071)
6.1-10.0	353	45.3 (40.6; 50.0)	103.2 (101.9; 104.5)	11.0 (10.7; 11.2)	1,107 (989.2; 1,224)
> 10	322	55.6 (50.6; 60.5)	106.3 (104.9; 107.6)	11.5 (11.2; 11.7)	1,157 (1,024; 1,289)
Parity		p = 0.001 *	p < 0.001 *	p < 0.001 *	p = 0.007 *
Primiparous	1,537	34.0 (31.8; 36.1)	98.4 (97.7; 99.0)	10.3 (10.2; 10.4)	1,047 (991.4; 1,102)
Multiparous	2,831	28.7 (27.1; 30.2)	95.4 (94.9; 95.9)	9.5 (9.4; 9.6)	952.2 (911.5; 992.9)
Pregestational BMI		p < 0.001 *	p = 0.889	p = 0.963 *	p = 0.455 *
Normal (< 25 Kg/m²)	3,271	28.9 (27.5; 30.3)	96.7 (96.2; 97.1)	9.8 (9.7; 9.9)	982.3 (944.2; 1,020)
Overweight (≥ 25 Kg/m²)	983	37.1 (34.3; 39.9)	96.6 (95.8; 97.4)	9.8 (9.6; 10.0)	1,012 (942.8; 1,082)
Maternal smoking in the pregnancy		p < 0.001 *	p < 0.001 *	p < 0.001 *	p = 0.018 *
No	2,917	33.3 (31.7; 34.8)	97.7 (97.3; 98.2)	10.1 (10.0;10.1)	1,013 (973.2; 1,053)
Yes	1,451	25.1 (23.1; 27.1)	93.9 (93.2; 94.5)	9.2 (9.0; 9.3)	929.2 (872.0; 986.4)
Sex		p = 0.979 *	p = 0.076 *	p < 0.001 *	p < 0.001 *
Male	2,118	30.4 (28.7; 32.2)	96.1 (95.5; 96.7)	9.3 (9.2; 9.5)	1,304 (1,259; 1,348)
Female	2,250	30.6 (28.9; 32.4)	96.8 (96.3; 97.3)	10.1 (10.0; 10.2)	676.9 (633.5; 720.4)

95%CI: 95% confidence interval; BMI: body mass index; IQ: intelligence quotient; MW: minimum wage.

* Test of heterogeneity;

** Linear trend test.

Table 5

IQ, schooling level, and income at adulthood according to mode of delivery in the 1982 and 1993 Pelotas birth cohorts, Rio Grande do Sul State, Brazil.

| | Mode of delivery | | p-value |
	Vaginal	Cesarean section	
1982 cohort			
IQ (points)			
Mean (95%CI)	96.9 (96.4; 97.4)	100.8 (100.0; 101.5)	
β crude (95%CI)	Ref. (0)	3.9 (3.0; 4.8)	< 0.001
β adjusted (95%CI)	Ref. (0)	0.4 (-0.4; 1.2)	0.314
Schooling (years)			
Mean (95%CI)	10.9 (10.8; 11)	12.3 (12.0; 12.5)	
β crude (95%CI)	Ref. (0)	1.4 (1.1; 1.7)	0.001
β adjusted (95%CI)	Ref. (0)	0.08 (-0.2; 0.3)	0.557
Income (BRL)			
Mean (95%CI)	1,401 (1,334; 1,469)	1,765 (1,656; 1,874)	
β crude (95%CI)	Ref. (0)	363.4 (235.4; 491.4)	0.001
β adjusted (95%CI)	Ref. (0)	31.8 (-88.0; 151.6)	0.603
1993 cohort			
IQ (points)			
Mean (95%CI)	95.4 (95.0; 95.9)	98.7 (98.0; 99.4)	
β crude (95%CI)	Ref. (0)	3.3 (2.4; 4.1)	0.001
β adjusted (95%CI)	Ref. (0)	-0.2 (-1.0; 0.6)	0.643
Schooling (years)			
Mean (95%CI)	9.5 (9.4; 9.6)	10.2 (10.1; 10.4)	
β crude (95%CI)	Ref. (0)	0.70 (0.53; 0.86)	0.001
β adjusted (95%CI)	Ref. (0)	-0.008 (-0.2; 0.1)	0.916
Income (BRL)			
Mean (95%CI)	970.7 (931.5; 1,010)	1,020 (960.3; 1,080)	
β crude (95%CI)	Ref. (0)	49.4 (-22.1; 121.0)	0.176
β adjusted (95%CI)	Ref. (0)	31.6 (-41.5; 104.7)	0.396

β: linear regress; 95%CI: 95% confidence interval; 95%CI: 95% confidence interval; Ref.: reference.

Note: adjusted for: skin color, maternal age, maternal schooling, paternal schooling, family income at birth, parity, maternal smoking in the pregnancy, pregestational body mass index and sex.

Discussion

In these two cohorts that have been prospectively followed since birth in Pelotas, cesarean section is positively associated with human capital at adulthood. However, after covariate adjustment, the associations vanished and the regression coefficients were close to the null.

Few studies have evaluated the long-term consequences of cesarean section on human capital [13,14,38,39,40,41,42,43], and to our knowledge the consequences of cesarean section on human capital in adulthood have not been previously evaluated. Some of these studies suggested that children born from cesarean sections have lower scores on cognitive tests in the areas of reading, writing, grammar, mathematics, vocabulary, and problem solving [13], and an increased chance of poor school performance among adolescents [14]. Although the studies found statistically significant associations, the effect was small and probably not causally related, because most of these studies failed to adjust for confounding variables. Moreover, some studies have adjusted the estimates for possible mediators, which may have underestimated the magnitude of the associations [34] or introduced a collider bias [44].

Table 6

Negative outcome control analysis in the 1982 and 1993 Pelotas birth cohorts, Rio Grande do Sul State, Brazil.

| | Type of delivery | | p-value |
	Vaginal	Cesarean section	
1982 cohort			
Smoking at 30 years			
PR crude (95%CI)	Ref. (1)	0.83 (0.73; 0.96)	0.010
PR adjusted (95%CI)	Ref. (1)	0.94 (0.82; 1.08)	0.387
Studied in a private school			
PR crude (95%CI)	Ref. (1)	1.16 (1.03; 1.30)	0.014
PR adjusted (95%CI)	Ref. (1)	1.01 (0.90; 1.13)	0.900
1993 cohort			
Smoking at 22 years			
PR crude (95%CI)	Ref. (1)	0.90 (0.81; 1.01)	0.086
PR adjusted (95%CI)	Ref. (1)	1.08 (0.95; 1.22)	0.222

95%CI: 95% confidence interval; PR: prevalence ratio; Ref.: reference.
Note: adjusted for: skin color, maternal age, maternal schooling, paternal schooling, family income at birth, parity, maternal smoking in the pregnancy, pregestational body mass index and sex.

The observed absence of an association could be due to the lack of an effect of mode of delivery on human capital or to residual confounding. In order to assess the likelihood of residual confounding bias in our analyses, we used the negative outcome control approach [32,33]. Similarly to what was observed for human capital, the association with the negative outcomes disappeared after covariate adjustment, this suggests that the variables included in the regression model provided an adequate confounding adjustment [32,33]. Because in our setting the prevalence of cesarean section is positively associated with socioeconomic status [23], which is also strongly related to human capital [45]. Socioeconomic confounding would tend to underestimate the association in the case of a strong negative effect of cesarean section on human capital or, in the case of a weak negative or no true causal effect, lead to a positive association [32,33]. Indeed, in our study, the positive associations of mode of delivery, with either human capital or the negative outcome control variables, disappeared after covariate adjustment. These findings reinforce the hypothesis that mode of delivery has no relevant long-term consequence on human capital in the studied population.

This study has some strengths as the prospective design that minimized the likelihood of information bias because the mode of delivery and the outcomes were measured with short recall time. Moreover, a standardized test, employed by trained psychologists was used to assess IQ, which also reduced the likelihood of misclassification. In the same token, confounders were also evaluated with a short recall, decreasing measurement error and, thus, the possibility of residual confounding. Indeed, the negative outcome control analysis suggests that residual confounding is unlikely. Concerning selection bias, the relatively low attrition rate after up to 30 years, and the similar follow-up rate according to several baseline characteristics, including mode of delivery, suggests that it is unlikely that our results are due to these bias. Moreover, sample size was large enough to produce narrow 95%CI, which were only compatible with effects of small magnitude. This indicates that the adjusted analyses were sufficiently powered to detect meaningful effects, thus further corroborating the conclusion of no causal relationship between mode of delivery and human capital. Regarding the limitations, we were not able to specify the mode of delivery, classifying the cesarean section by medical indication and the vaginal delivery by use of intervention.

In this study, we failed to observe any long-term consequence of cesarean section on human capital. On the other hand, considering the short- and long-term risks related to cesarean section that did not follow a medical indication, and its epidemic proportions, public health measures should be implemented to reduce the prevalence of cesarean section. Further studies on this subject should adequately control for confounding factors, especially those related to the socioeconomic level.

Contributors

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Resumo

O estudo buscou avaliar a associação entre modo de parto e capital humano entre adultas jovens nas coortes de nascimentos de Pelotas, Rio Grande do Sul, Brasil, de 1982 e 1993. Em 1982 e 1993, as maternidades de Pelotas foram visitadas diariamente, os nascimentos foram identificados e os nascidos vivos cujas famílias residiam na área urbana foram examinados e suas mães foram entrevistadas. As informações sobre modo de parto (vaginal versus cesáreo) foram coletadas durante a entrevista perinatal. O desempenho em testes de inteligência, nível de escolaridade e renda foram avaliados na visita de 30 anos da coorte de 1982. Para a coorte de 1993, escolaridade e renda foram avaliadas na visita de 22 anos, enquanto o QI foi avaliado aos 18 anos. Tabagismo na vida adulta e tipo de escola foram usados como desfechos negativos para fortalecer a inferência causal. Inicialmente, parto cesáreo mostrou associação positiva com capital humano na vida adulta, com exceção de renda na coorte de 1993. Depois de controlar para fatores de confusão, o tamanho das associações foi reduzido fortemente, e os coeficientes de regressão chegaram perto de valor nulo. A análise de desfechos negativos mostrou que depois de controlar para variáveis de confusão, o modo de parto não esteve associado ao tabagismo ou ao tipo de escola. Os resultados sugerem que as variáveis incluídas no model de regressão para controlar os fatores de confusão resultaram em ajuste adequado, e é improvável que os resultados atuais sejam devidos à confusão por posição socioeconômica. Por outro lado, devido aos riscos no curto e longo prazo e à epidemia de cesarianas, são necessárias medidas para reduzir a prevalência de partos cesáreos.

Cesárea; Parto; Inteligência; Escolaridade; Renda

Resumen

El objetivo de este estudio es evaluar la asociación entre la forma de parto y el capital humano entre adultos jóvenes, que se encontraban en las cohortes de nacimiento de 1982 y 1993, en Pelotas, Río Grande do Sul, Brasil. En 1982 y 1993, se visitaron diariamente los hospitales de maternidad de la ciudad, se identificaron los nacimientos, se examinaron aquellos nacimientos vivos, cuya familia vivía en el área urbana de la ciudad, al igual que se realizaron entrevistas a sus madres. La información sobre la forma de parto (vaginal o cesárea) fue proporcionada por la madre en el estudio perinatal. Se evaluó tanto el rendimiento escolar alcanzado en tests de inteligencia, como los ingresos, transcurridos 30 años de la primera visita en la cohorte de 1982. En la cohorte de 1993, la escolaridad y los ingresos fueron evaluados tras la visita de hacía 22 años, mientras que el CI se evaluó a los 18 años. Fumar tabaco en la etapa adulta y el tipo de financiación de la escuela fueron usados como resultados negativos para la fortaleza de la inferencia causal. Inicialmente, la cesárea estuvo positivamente asociada con el capital humano en la etapa adulta, con la excepción de los ingresos en la cohorte de 1993. Tras controlar los factores de confusión, la magnitud de las asociaciones se vio fuertemente reducida, y los coeficientes de regresión eran cercanos al valor nulo. El análisis de resultado negativo mostró que, tras controlar las variables de confusión, el modo de parto no estuvo asociado con fumar tabaco y el tipo de financiación de la escuela. Sugiriendo que las variables incluidas en el modelo de regresión para el control de los factores de confusión, proporcionaron un ajuste adecuado, y es poco probable que los resultados actuales se deban a factores de confusión residuales por el estatus socioeconómico. Por otro lado, debido a los riesgos a corto y largo plazo y la epidemia de cesáreas, se deben implementar medidas para reducir la prevalencia de las cesáreas.

Cesárea; Parto; Inteligencia; Escolaridad; Renta