

RESEARCH ARTICLE

Elective and nonelective cesarean section and obesity among young adult male offspring: A Swedish population-based cohort study

Viktor H. Ahlqvist¹, Margareta Persson², Cecilia Magnusson^{1,3}, Daniel Berglind^{1,3*}

1 Department of Global Public Health Sciences, Karolinska Institutet, Stockholm, Sweden, **2** Department of Nursing, Umeå University, Umeå, Sweden, **3** Centre for Epidemiology and Community Medicine, Region Stockholm, Stockholm, Sweden

* daniel.berglind@ki.se



Abstract

Background

Previous studies have suggested that cesarean section (CS) is associated with offspring overweight and obesity. However, few studies have been able to differentiate between elective and nonelective CS, which may differ in their maternal risk profile and biological pathway. Therefore, we aimed to examine the association between differentiated forms of delivery with CS and risk of obesity in young adulthood.

Methods and findings

Using Swedish population registers, a cohort of 97,291 males born between 1982 and 1987 were followed from birth until conscription (median 18 years of age) if they conscripted before 2006. At conscription, weight and height were measured and transformed to World Health Organization categories of body mass index (BMI). Maternal and infant data were obtained from the Medical Birth Register. Associations were evaluated using multinomial and linear regressions. Furthermore, a series of sensitivity analyses were conducted, including fixed-effects regressions to account for confounders shared between full brothers. The mothers of the conscripts were on average 28.5 (standard deviation 4.9) years old at delivery and had a prepregnancy BMI of 21.9 (standard deviation 3.0), and 41.5% of the conscripts had at least one parent with university-level education.

Out of the 97,291 conscripts we observed, 4.9% were obese (BMI \geq 30) at conscription. The prevalence of obesity varied slightly between vaginal delivery, elective CS, and nonelective CS (4.9%, 5.5%, and 5.6%, respectively), whereas BMI seemed to be consistent across modes of delivery. We found no evidence of an association between nonelective or elective CS and young adulthood obesity (relative risk ratio 0.96, confidence interval 95% 0.83–1.10, $p = 0.532$ and relative risk ratio 1.02, confidence interval 95% 0.88–1.18, $p = 0.826$, respectively) as compared with vaginal delivery after accounting for prepregnancy maternal BMI, maternal diabetes at delivery, maternal hypertension at delivery, maternal smoking, parity, parental education, maternal age at delivery, gestational age, birth weight standardized according to gestational age, and preeclampsia. We found no evidence of an

OPEN ACCESS

Citation: Ahlqvist VH, Persson M, Magnusson C, Berglind D (2019) Elective and nonelective cesarean section and obesity among young adult male offspring: A Swedish population-based cohort study. *PLoS Med* 16(12): e1002996. <https://doi.org/10.1371/journal.pmed.1002996>

Academic Editor: Ali S. Khashan, University College Cork, IRELAND

Received: September 2, 2019

Accepted: November 5, 2019

Published: December 6, 2019

Peer Review History: PLOS recognizes the benefits of transparency in the peer review process; therefore, we enable the publication of all of the content of peer review and author responses alongside final, published articles. The editorial history of this article is available here: <https://doi.org/10.1371/journal.pmed.1002996>

Copyright: © 2019 Ahlqvist et al. This is an open access article distributed under the terms of the [Creative Commons Attribution License](https://creativecommons.org/licenses/by/4.0/), which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Data Availability Statement: Swedish secrecy law prohibits us from making register data publicly available. The data supporting our findings were used under license and ethical approval for the

current study. Readers interested in obtaining microdata or replicating our study may seek similar approvals and inquire through Statistics Sweden. For further advice see: <https://www.scb.se/en/services/guidance-for-researchers-and-universities/>.

Funding: This work was supported by the Stockholm County Council [ALF 20180266 to DB]. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Competing interests: The authors have declared that no competing interests exist.

Abbreviations: BMI, body mass index; CI, confidence interval; CS, cesarean section; IQR, interquartile range; MBR, Medical Birth Register; OR, odds ratio; RRR, relative risk ratio; WHO, World Health Organization.

association between any form of CS and overweight (BMI \geq 25) as compared with vaginal delivery. Sibling analysis and several sensitivity analyses did not alter our findings. The main limitations of our study were that not all conscripts had available measures of anthropometry and/or important confounders (42% retained) and that our cohort only included a male population.

Conclusions

We found no evidence of an association between elective or nonelective CS and young adulthood obesity in young male conscripts when accounting for maternal and prenatal factors. This suggests that there is no clinically relevant association between CS and the development of obesity. Further large-scale studies are warranted to examine the association between differentiated forms of CS and obesity in young adult offspring.

Trial registration

Registered as observational study at ClinicalTrials.gov Identifier: [NCT03918044](https://clinicaltrials.gov/ct2/show/study/NCT03918044).

Author summary

Why was this study done?

- The global prevalence of cesarean deliveries is increasing, and clarification of any harmful consequences for offspring health is warranted.
- There is evidence of an association between delivery by cesarean section and obesity, but it may be driven by unmeasured confounding.
- It has been suggested that elective but not nonelective cesarean section is associated with offspring obesity, but the knowledge base to support this notion is scant.

What did the researchers do and find?

- A register-based total-population cohort of 97,291 Swedish males was followed up for levels of overweight and obesity in early adulthood using objective measures of weight and height at military conscription. Sibling comparison was used to address bias from familial factors.
- Delivery by cesarean section, regardless of whether elective or nonelective, was not associated with overweight or obesity among Swedish men in young adulthood.

What do these findings mean?

- Mode of delivery may not be an important factor in the origins of overweight and obesity.

- Cesarean section may not serve a role in the obesity epidemic and, as such, should not be a target for intervention when attempting to reduce the burden of obesity.
- Future research should include female offspring when examining the role of cesarean section in obesity to critically evaluate any sex-specific role of cesarean section in obesity.

Introduction

Globally [1], and in Sweden [2], there has been an unprecedented increase in the prevalence of cesarean deliveries since the early 1990s. Between 1990 and 2014 the world prevalence of cesarean section (CS) increased by 285% (6.7% versus 19.1% of all births) [1], albeit with large regional disparities. The indications for CS are many, and CS is often warranted to avoid fetal and/or maternal morbidity and mortality [3]. However, indications for CS are to some degree subjective [4], and changes in maternal risk profiles do not explain the increased prevalence of CS [5,6]. Maternal preference and/or fear of childbirth has been described to be a contributing factor to the increase in CS rates [7–9]. Notably, the World Health Organization (WHO) states that, on a population level, rates of CS higher than 10%–15% are not associated with additional reductions in maternal, neonatal, and infant mortality rates [3].

The large increases of CS have sparked an interest in its long-term effects on offspring health [3]. Indeed, CS has been associated with various negative outcomes—e.g., asthma [10,11], allergic rhinitis [11], and food allergies [12], as well as overweight and obesity [10,13–16]. Proposed mechanisms explaining the observed association between CS and subsequent morbidity in the offspring include, but are not limited to, hormonal surge [17], lack of stress exposure [17], DNA methylation [18–20], and microflora transmission (hygiene hypothesis) [20,21].

The association between CS and offspring overweight and obesity has recently received further attention [10,15,22–25]. Notably, the unprecedented increase in CS has occurred at the same time as the obesity epidemic [26], which may suggest a connection between the two trends. However, as previous studies have noted [22,23,25], the association between CS and obesity may be mainly driven by unmeasured confounding. Yuan and colleagues [15] conducted a careful investigation aiming to control for such confounding, but they still observed an association between CS and offspring obesity. Yuan and colleagues [15] did not, however, differentiate between elective and nonelective CS. To the best of our knowledge, only a few studies have investigated effects of elective and nonelective CS separately [23–25]. This is unfortunate because the indications for and the obstetric risks of CS may depend on the type of CS, which could make the confounding structure differ importantly between the types of CS. Notably, one of the likely candidates for unmeasured confounding is confounding by indication, which could inflate the risk for obesity in the nonelective CS group [23], given that nonelective CS may be more likely to be conducted on the basis of fetal indication and obstetric complications [27,28]. Additionally, elective and nonelective CS may differ in fetal stress exposure [29] and microflora transmission [30], which could have implications for associations to subsequent obesity. Furthermore, given the rise in CS [1], there could be different implications for public health in the presence of different risks of development of obesity depending on the type of CS delivery. Despite few studies differentiating between elective and nonelective CS, at 12 months [24] but not at 3 and 5 years of age [23], there have been reported

elevated risks of obesity in elective CS. However, large-scale longitudinal studies are warranted, and there is a necessity to examine whether this indicated association persists into young adulthood.

Objective

Here, we aim to examine the association between differentiated forms of delivery with CS and risk of obesity in young adulthood in a large, total-population sample of male conscripts based on objectively measured anthropometry. We evaluate the role of confounding by indication by separately studying elective and nonelective CS, carefully controlling for confounding factors including prepregnancy maternal body mass index (BMI), and by sibling comparisons, hence adjusting for shared familial factors.

Methods

Study design

A male total population-based cohort was constructed using the following Swedish population-based registries: (1) the Swedish Military Service Conscription Registry [31], (2) the Swedish Medical Birth Register (MBR) [32], (3) the Multi-Generation Register [33], and (4) the population and housing censuses from 1970 and 1990 [33]. Registers were linked via a personal identification number, a unique ID code assigned to each Swedish resident at birth. Furthermore, all full brothers and parents were identified and matched using a unique family identification number through the Multi-Generation Register. The study was approved by the Regional Ethical Review Board, Stockholm (Dnr: 2016/1445-31/1). The study protocol and statistical analysis plan were registered on April 17, 2019, at clinicaltrials.gov (NCT03918044) to increase transparency and reduce the risk for post hoc analysis.

Study population

Using the MBR, which contains validated birth data on approximately 99% of the Swedish population [32], all male singletons born between 1982 and 1987 available in the MBR were sampled ($n = 300,344$) (Fig 1). The first exclusion criterion was not having available information on the mode of delivery ($n = 16,970$). The sampled singletons were then matched to their conscription data if they conscripted before 2006 using the Swedish Military Service Conscription Registry ($n = 229,632$). During the study period, conscription was mandatory by law in Sweden for all male citizens up to the age of 47 [34]. The study period was selected because of the changes in conscription procedures occurring after the set period. During the study period, males could only be exempt from conscriptions (requiring state approval) if they suffered from chronic disease or severe handicap [35]. Except for in sensitivity analyses, we excluded those with extreme values of weight (≤ 40 or ≥ 150 kg), height (≤ 150 or ≥ 210 cm), and/or BMI (≤ 15 or ≥ 60 kg/m²) at conscription ($n = 105$) in accordance with previous studies [36]. All analyses were conducted as complete-case analyses because we a priori hypothesized any missing data to be missing completely at random and potentially missing not at random in a few cases; therefore, we excluded all individuals with missing height and/or weight at conscription ($n = 76,410$) and/or those with missing information on other characteristics of interest (e.g., maternal BMI and maternal smoking) ($n = 55,826$) (S1 Table). In total, 97,291 male conscripts with a median age of 18 years at follow-up (i.e., conscription) remained eligible for analysis and were included in the final analytical sample. In addition, we identified 9,676 matchable full brothers.

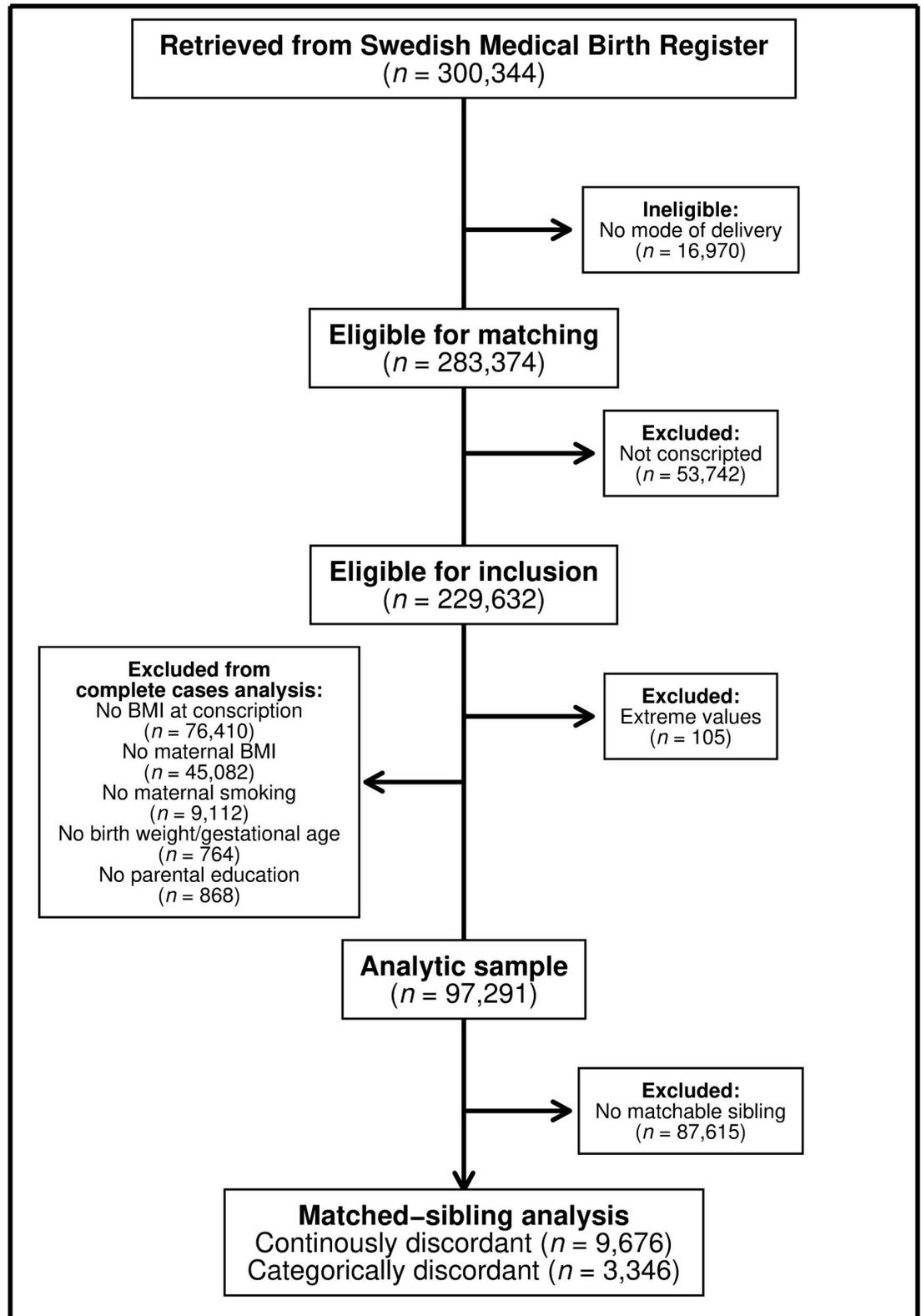


Fig 1. Flowchart of the derivation of the analytical sample. BMI, body mass index.

<https://doi.org/10.1371/journal.pmed.1002996.g001>

Exposure—Mode of delivery

Using the Swedish MBR, we obtained information on recorded mode of delivery (vaginal or cesarean delivery), which was supplemented with information on indication for cesarean delivery (elective or nonelective), which yielded our primary trichotomized exposure coded as (1) vaginal delivery, (2) delivery by elective CS, and (3) delivery by nonelective CS. In accordance with the reporting standard in the MBR, we define elective CS as prelabor CS and nonelective CS as CS after the onset of labor. There was no alteration in the reporting procedure of elective or nonelective CS in the MBR during the period of study. Additionally, to facilitate comparison with previous studies, we report the dichotomized exposure: (1) vaginal delivery and (2) delivery by any form of CS. Finally, in a post hoc sensitivity analysis, the exposures (1) vaginal delivery, (2) instrumental vaginal delivery (forceps or vacuum extraction), (3) delivery by elective CS, and (4) delivery by nonelective CS were used to diminish the assumption of homogeneity in vaginal deliveries.

Outcome—Young adulthood BMI

The primary outcome was obesity defined according to categories of BMI (kg/m^2) categorized using WHO's [37] standards: underweight (BMI < 18.5), normal weight (BMI 18.5–24.9), overweight (BMI 25–29.9), and obese (BMI \geq 30). Although our aim is to examine obesity, we quantify associations between CS and all categories of BMI as compared with normal weight BMI. Weight in kilograms and height in centimetres were measured at conscription using a standardized scale and a stadiometer [36] under supervision of a nurse or physician [38]. To facilitate comparisons with previous studies, we also examined the odds of obesity (BMI \geq 30) using all other BMI categories as reference outcome (BMI < 30). Finally, we estimated the association between our primary exposure (vaginal/elective CS/nonelective CS) and BMI at conscription as a continuous variable.

Confounders

We considered a series of confounders that have been previously associated with cesarean delivery and metabolic or adiposity-related factors in offspring. From the MBR data on pre-pregnancy maternal BMI [39,40] (continuous), maternal diabetes at delivery [41,42] (yes/no), maternal hypertension at delivery [43] (yes/no), self-reported maternal smoking [44,45] at the commencement of pregnancy (nonsmoker, 1–9 cig/day, \geq 10 cig/day), parity [46,47] (treated as categorical), birth weight in grams [48,49] standardized according to week of gestational age using the total population as reference (continuous), preeclampsia [50,51] (ICD-8: 63703–63710 and ICD-9 642E-642G) (yes/no), gestational age [49,52] (continuous), and maternal age at delivery [53,54] (continuous) were collected. Using the population and housing censuses, we identified the highest level of paternal and maternal education [55,56] (categorical) to serve as a proxy for household socioeconomic status.

Statistical analyses

We descriptively present the distribution of the outcomes and confounders over the total analytic cohort and over the primary exposures (vaginal, elective CS, and nonelective CS) using appropriate measures of central tendency and dispersion. For our main analysis, we employed multinomial logistic regression to estimate crude and confounder-adjusted relative risk ratios (RRRs) with 95% confidence intervals (CIs). All standard errors were estimated using the robust (sandwich) method to account for the correlation between brothers [57]. All statistical analyses were performed using Stata 15.1 (Stata Corp, College Station, TX, United States).

Sensitivity analyses

We descriptively present the available characteristics of the individuals not participating in conscription and those excluded due to missing data and compare these to the conscripted and analytic sample, respectively, using χ^2 test (categorical), t test (continuous), and Wilcoxon rank-sum test (continuous skewed). In the sensitivity analysis, we introduced several multinomial logistic models. First, a model in which we introduced a cubic transformation of maternal age and maternal BMI, in addition to the untransformed factor, to relax the assumption of linearity was used. Second, a model in which we adjusted for gestational weight gain [58] in a subset of individuals with available measures of maternal BMI at delivery ($n = 96,050$) standardized by categories of BMI and gestational week according to Swedish reference values [59] was used. Third, using information on previous cesarean deliveries recorded after 1973, we adjusted for whether a mother had ever had a CS before (binary). Previous cesarean delivery may impact the association between a subsequent cesarean delivery and obesity [15]. Fourth, we included those with available data previously excluded for extreme values at conscription ($n = 62$) to ascertain that our exclusion did not alter our primary findings. In our final multinomial model, we examined the association between any form of cesarean delivery and BMI categories. For our secondary outcomes, we employed logistic regression to examine the association between our primary exposure and obesity and linear regression, treating BMI as a continuous outcome. Furthermore, we employed multinomial logistic regression with fixed effects (conditional) [60] and fixed-effects linear regression [22] in a subset of 3,346 and 9,676 discordant full brothers, respectively, to account for unmeasured familial confounding (genetic and environmental) [61]. The fixed-effects regressions were adjusted for the same factors as our main analysis, excluding highest parental education, which did not vary between full brothers. In the post hoc analysis, we examine the influence of CS on ordered BMI categories, employing a generalized ordered logit model that was relaxed of proportionality assumptions [62], and we further relaxed linearity of all continuous factors (maternal prepregnancy BMI, maternal age, birth weight standardized according to gestational age, and gestational age) using restricted cubic splines with five knots at Harrell's recommended positions [63]: 5th, 27.5th, 50th, 72.5th, and 95th percentiles. Because previous validity reports [32] have noted that there may be some misclassification of the type of CS in the MBR and that this misclassification is primarily present in preterm deliveries that were misclassified as elective while being nonelective, we repeated our main analysis excluding those born preterm (<37 full weeks of gestation) and repeated our main analysis restricted to those born at term (≥ 37 and <42 weeks of gestation). Finally, as gestational age may act as a collider under certain causal pathways, we repeated our main analysis, excluding adjustment for gestational age.

Compliance with ethical standards

The study was approved by the Regional Ethical Review Board, Stockholm (Dnr: 2016/1445-31/1). The requirement to obtain informed consent was waived by the Regional Ethical Review Board, Stockholm (Dnr: 2016/1445-31/1). All research was performed in accordance with relevant guidelines/regulations.

Results

Descriptive statistics

In our cohort of 97,291 conscripts, we observed that 4.9% were obese at conscription (Table 1). The prevalence of obesity among those born by vaginal delivery was 4.9% (CI 95% 4.7–5.0), which was not statistically significantly different from those born by elective CS

Table 1. Sample characteristics of the full analytical cohort by mode of delivery.

Sample characteristics	Total (N = 97,291)	Vaginal delivery (N = 89,024)	Elective cesarean section (N = 4,147)	Nonelective cesarean section (N = 4,120)
Offspring characteristics				
Age at conscription (years), median (IQR)	18 (18, 18)	18.0 (18, 18)	18 (18, 18)	18 (18, 18)
BMI category at conscription, No. (%)				
Underweight	5,945 (6.1)	5,491 (6.2)	224 (5.4)	230 (5.6)
Normal weight	71,511 (73.5)	65,479 (73.6)	3,044 (73.4)	2,988 (72.5)
Overweight	15,041 (15.5)	13,720 (15.4)	650 (15.7)	671 (16.3)
Obese	4,794 (4.9)	4,334 (4.9)	229 (5.5)	231 (5.6)
BMI (kg/m ²) at conscription, mean (SD)	22.8 (3.7)	22.8 (3.6)	23.0 (3.8)	23.1 (3.8)
Birth weight (g), mean (SD)	3,615.9 (518.3)	3,633.1 (499.4)	3,444.0 (554.7)	3,416.8 (754.1)
Weeks of gestation, mean (SD)	39.5 (1.6)	39.6 (1.5)	38.2 (1.3)	39.0 (2.6)
Maternal characteristics				
Maternal age at birth (years), mean (SD)	28.5 (4.9)	28.4 (4.9)	30.6 (5.3)	28.7 (5.2)
Maternal prepregnancy BMI, mean (SD)	21.9 (3.0)	21.9 (3.0)	22.3 (3.4)	22.4 (3.2)
Maternal BMI category, No. (%)				
Underweight	7,450 (7.7)	6,847 (7.7)	313 (7.5)	290 (7.0)
Normal weight	77,080 (79.2)	70,875 (79.6)	3,139 (75.7)	3,066 (74.4)
Overweight	10,933 (11.2)	9,727 (10.9)	562 (13.6)	644 (15.6)
Obese	1,828 (1.9)	1,575 (1.8)	133 (3.2)	120 (2.9)
Parity, median (IQR)	2.0 (1.0, 2.0)	2.0 (1.0, 2.0)	2.0 (1.0, 3.0)	1.0 (1.0, 2.0)
Maternal diabetes mellitus, No. (%)	463 (0.5)	354 (0.4)	77 (1.9)	32 (0.8)
Maternal hypertension, No. (%)	204 (0.2)	164 (0.2)	16 (0.4)	24 (0.6)
Preeclampsia, No. (%)	1,515 (1.6)	1,162 (1.3)	103 (2.5)	250 (6.1)
Maternal smoking at the commencement of pregnancy, No. (%)				
Not smoking	70,814 (72.8)	64,915 (72.9)	3,068 (74.0)	2,831 (68.7)
1–9 cig/day	16,677 (17.1)	15,163 (17.0)	683 (16.5)	831 (20.2)
≥10 cig/day	9,800 (10.1)	8,946 (10.0)	396 (9.5)	458 (11.1)
Socioeconomic factor				
Highest parental education, No. (%)				
Primary education	8,416 (8.7)	7,635 (8.6)	398 (9.6)	383 (9.3)
Secondary education	48,509 (49.9)	44,538 (50.0)	1,938 (46.7)	2,033 (49.3)
University education	40,366 (41.5)	36,851 (41.4)	1,811 (43.7)	1,704 (41.4)

Abbreviations: BMI, body mass index; cig, cigarette; IQR, interquartile range; No., number; SD, standard deviation

<https://doi.org/10.1371/journal.pmed.1002996.t001>

(5.5%, CI 95% 4.8–6.2, $p = 0.057$). The prevalence of obesity among those born by nonelective CS was 5.6% (CI 95% 4.9–6.3), which was statistically significantly higher as compared with those born by vaginal delivery ($p = 0.032$). The mean BMI was lower among those born by vaginal delivery (22.8, CI 95% 22.8–22.8) as compared with those born by elective CS (23.0, CI 95% 22.9–23.1, $p = 0.010$) or nonelective CS (23.1, CI 95% 22.9–23.2, $p < 0.001$). Although statistically different (all $p < 0.05$), most covariates did not vary substantially with mode of delivery. However, those with vaginal delivery had higher birth weight, lower maternal BMI, and lower occurrence of maternal prepregnancy obesity. The elective CS group had higher occurrence of university-level parental education and of maternal diabetes mellitus. The nonelective CS group had a higher occurrence of preeclampsia and maternal smoking at the commencement of pregnancy.

Table 2. Cesarean section deliveries and their associations to obesity, overweight, and underweight in offspring.

Mode of delivery	Crude								
	Underweight versus normal weight			Overweight versus normal weight			Obese versus normal weight		
	RRR	95% CI	<i>p</i>	RRR	95% CI	<i>p</i>	RRR	95% CI	<i>p</i>
Vaginal	1	-	-	1	-	-	1	-	-
Elective cesarean section	0.88	0.76–1.01	0.064	1.02	0.93–1.11	0.669	1.14	0.99–1.30	0.069
Nonelective cesarean section	0.92	0.80–1.05	0.220	1.07	0.98–1.17	0.113	1.17	1.02–1.34	0.027
	Adjusted ^a								
	Underweight versus normal weight			Overweight versus normal weight			Obese versus normal weight		
	RRR	95% CI	<i>p</i>	RRR	95% CI	<i>p</i>	RRR	95% CI	<i>p</i>
Vaginal	1	-	-	1	-	-	1	-	-
Elective cesarean section	0.88	0.76–1.01	0.079	0.99	0.90–1.08	0.818	1.02	0.88–1.18	0.826
Nonelective cesarean section	0.94	0.81–1.08	0.359	0.99	0.90–1.08	0.764	0.96	0.83–1.10	0.532

Empty cells (-) indicate reference group.

^aAdjusted for prepregnancy maternal BMI, maternal diabetes at delivery, maternal hypertension at delivery, maternal smoking, parity, parental education, maternal age at delivery, birth weight standardized according to gestational age, preeclampsia, and gestational age.

Abbreviations: BMI, body mass index; CI, confidence interval; RRR, relative risk ratio

<https://doi.org/10.1371/journal.pmed.1002996.t002>

Mode of delivery and offspring obesity

In our primary analysis (Table 2), there was no statistically significant association between elective CS and obesity (RRR 1.14, CI 95% 0.99–1.30, *p* = 0.069), whereas a similar association between nonelective CS and obesity differed from unity (RRR 1.17, CI 95% 1.02–1.34, *p* = 0.027) as compared with vaginal delivery. We observed no association between elective or nonelective CS and obesity (RRR 1.02, CI 95% 0.88–1.18, *p* = 0.826 and RRR 0.96, CI 95% 0.83–1.10, *p* = 0.532, respectively) as compared with vaginal delivery when accounting for prepregnancy maternal BMI, maternal diabetes at delivery, maternal hypertension at delivery, maternal smoking, parity, parental education, maternal age at delivery, gestational age, birth weight standardized according to gestational age, and preeclampsia. Neither elective nor nonelective CS were associated with overweight at conscription as compared with vaginal delivery.

Sensitivity analysis

Characteristics in individuals who were and were not conscripted did not differ materially overall, although differences were statistically significant in our large sample (all *p* < 0.05, S1 Table). Similarly, although every characteristic except mean BMI and maternal preeclampsia were statistically different (*p* < 0.05), there was no major discrepancy between those with incomplete records and those retained in the analytical cohort. However, we noted that parental university education was more common among the conscripted as compared with the not conscripted (38.4% versus 29.7%, *p* < 0.05) and more common among the retained analytical cohort as compared with those with incomplete records (41.5% versus 36.1%, *p* < 0.05).

The stratification of vaginal deliveries into vaginal instrumental deliveries and vaginal deliveries did not alter our main findings; there was no meaningful change in any estimate as compared with our main analysis (S2 Table).

Our further sensitivity analyses (S3 Table), in which we (1) relax linearity assumptions of confounders, (2) account for standardized gestational weight gain, (3) account for a history of cesarean delivery, and (4) include those previously excluded at conscription, did not differ to any meaningful extent from our main analysis. In our last multinomial model (S4 Table),

when treating all CSs as one group, we did not observe any association between CS and obesity after accounting for confounders (RRR 0.98, CI 95% 0.89–1.09, $p = 0.775$) as compared with vaginal delivery. When treating obesity as a binary outcome (S5 Table), there was no association between elective or nonelective CS and obesity in our fully adjusted model (RRR 1.02, CI 95% 0.88–1.18, $p = 0.772$ and RRR 0.96, CI 95% 0.84–1.11, $p = 0.603$, respectively) as compared with vaginal delivery. There was no association between elective (mean difference: 0.05, CI 95% –0.06 to 0.16, $p = 0.338$) or nonelective CS (mean difference: 0.02, CI 95% –0.09 to 0.14, $p = 0.675$) and continuous BMI when accounting for proposed confounders as compared with vaginal delivery (S6 Table). When employing multinomial fixed-effects regression, in a subset of discordant siblings, we observed a statistically significant association ($p = 0.04$) between nonelective CS and overweight (RRR 1.99, CI 95% 1.05–3.77) as compared with vaginal delivery (S7 Table). No other fixed-effects regression (linear or multinomial logistic) differed meaningfully from our main analysis (S7 Table and S8 Table).

There was no difference between our main analyses and when excluding those born preterm, restricting to those born at term, not adjusting gestational age (S9 Table), or treating BMI categories as an ordered outcome (S10 Table).

Discussion

Main findings

In this longitudinal cohort of 97,291 male conscripts, we found that there was no association between elective or nonelective CS and young adulthood obesity when accounting for possible confounding factors and conducting several predefined sensitivity analyses as compared with vaginal delivery. To the best of our knowledge, we have presented the largest and most comprehensive differentiation between elective and nonelective CS so far.

Comparison with previous research

In contrast with previous research [10,13,15,16], we did not observe any association between CS and young adulthood obesity. This could be explained by previous studies' limited ability to adjust for maternal prepregnancy BMI [16], small sample sizes [10,13,15,16], and/or inability to differentiate between elective/prelabor and nonelective/acute CS [10,16]. To the best of our knowledge, the largest previous study on CS and offspring overweight/obesity that differentiated between types of CS was conducted on children (5 years old), with only 145 exposed cases, and described a significant association between CS on maternal request and overweight/obesity (odds ratio [OR] 1.18, CI 95% 1.00–1.41) [64]. In contrast, a meta-analysis [13] suggested that there was no association between prelabor CS and obesity in adulthood. However, this analysis was limited to very few participants (prelabor CS = 252 and vaginal delivery = 17,506).

Although a majority of previous studies have had limitations, studies with less uncertainty have suggested that there may be an attenuation with age in the association between CS and obesity [15,23]. The attenuation by age could potentially explain our findings. However, childhood obesity not persisting into young adulthood or adulthood may be of less relevance for clinical manifestation of obesity-related consequences [65–67].

Contrary to our findings, a recent study [24] on very young children (12 months old) suggested a strong association between elective CS and overweight (OR 2.01, CI 95% 1.13–3.58) but no such association for emergency CS (OR 1.08, CI 95% 0.66–1.76). The authors hypothesize that this may be a function of lack of fetal stress exposure induced by the onset of labor, which may be absent in elective CS, and that emergency CS may be exposed to maternal microbiota to a greater extent than elective CS. However, adjusting for intrapartum antibiotics

did not alter their findings, suggesting that microbiota exposure did not explain the low risk in the emergency CS [24]. Contrary to the suggestion that CS supports the hygiene hypothesis, there have been suggestions that CS is a risk factor for childhood obesity that is independent of second- and third-trimester antibiotic use [68], although antibiotic use may also independently influence childhood obesity [68].

In addition to the aforementioned discrepancies between our study and previous studies, it should be noted that our cohort was born between 1982 and 1987, which could have implications for the comparability to more recent birth cohorts [24]. However, several studies conducted on younger children with more recent birth years have suggested null associations similar to those we observed in our cohort [22,23,25].

In our cohort, only accounting for maternal prepregnancy BMI attenuated the association between elective or nonelective CS and obesity by 15% and 16%, respectively (RRR 1.14 versus 0.99 and 1.17 versus 1.01) (S11 Table). Indeed, this was the strongest confounder in the association between either form of CS and obesity in our study. As obesity has a high heritability [69] and/or could be a function of fetal programming [70], it is plausible that taking maternal prepregnancy BMI into account captures both genetic predispositions transferred from mother to offspring and the fetal exposure to an obesogenic state in the mother. Using our fixed-effects linear regression, which accounts for familial confounding shared between brothers (e.g., obesogenic familial environment and obesity-related genetic traits), we did not observe any association between any form of CS and offspring obesity. Notably, we observed an association between nonelective CS and overweight in our multinomial discordant sibling sample. However, this may be explained by the small number of exposed cases and the possibility of residual confounding. Hence, we suspect there to be an association between nonelective CS and overweight as a function of confounding by medical indication for CS [23]. Indeed, if there is a causal effect of CS on overweight/obesity, an association should be present in elective CS as well [23].

Despite unnecessary CS being subject to some criticism [71], it is of interest to further study unnecessary CS and its possible association to offspring morbidity [72]. Although Swedish registers enable us to differentiate between elective and nonelective CS, they do not enable us to perform detailed classifications of CS using such classifications as the Robson classification [73], which may provide further insight into the potential role of CS in offspring health.

Strengths and limitations

The strengths of our study lie in our longitudinal design, large sample size, ability to control for a series of possible confounders, and ability to differentiate between elective and nonelective CS. Furthermore, the usage of MBR and the Swedish Military Service Conscription Registry enabled us to retrieve objective and standardized measures of exposure (birth mode) and outcome (BMI), limiting measurement error and information bias.

Despite the strengths of our study, there are several limitations that should be acknowledged. First, although conscription was mandatory by law under the period of study, there may be selection bias present in our cohort because those offspring with severe health conditions are not eligible for conscription [35]. Despite the potential for selection bias, we did not observe major differences, albeit most factors are statistically significantly different ($p < 0.05$), between our analytic sample and the excluded populations, with the exception of highest parental education (S1 Table). However, caution is warranted when generalizing and interpreting our findings. Second, there are still potential unmeasured confounders that we failed to account for. Third, we were limited to any record of previous CS in the MBR after 1973, which may fail to capture some previous CSs and fail to fully account for the motives to

perform an elective CS. Fourth, the usage of registers limited us to a formal diagnosis of maternal conditions, which may only capture the most severe cases of maternal health. Furthermore, there may be some misclassification of nonelective CS among preterm deliveries [32]. However, our analysis excluding preterm deliveries and restricting to at-term deliveries was consistent with our main analysis, suggesting that this misclassification of nonelective CS does not influence our conclusion. Despite this, a certain proportion of misclassification is expected and could inflate the risk estimate of an offspring developing obesity in the elective CS group, if an offspring of a nonelective CS is at higher risk of developing obesity as compared with those with a true elective CS, given medical indications. Fifth, despite the ability to control for unmeasured confounding, sibling analysis has several limitations, such as increased bias from nonshared confounders and increased attenuation from measurement error, as compared with conventional analysis [57]. However, our collection of CS by medical records and standardized measurement of BMI reduces the impact of measurement error. Furthermore, by accounting for observed nonshared confounders, we limit any additional confounding to nonshared unobserved confounders. Despite this, caution is warranted when directly interpreting the estimates from sibling analysis. Finally, our cohort consisted of a male population, which limits the generalizability to females. However, studies including female populations have suggested no difference between males and females in the association between CS and obesity [14,15,23,25,64]. The generalizability of our study may be limited to countries with rates of CS similar to those in Sweden during the study period.

Conclusions

We observed no association between elective or nonelective CS and young adulthood obesity in young male conscripts when accounting for maternal and prenatal factors. Furthermore, we note that most of the crude association between CS and obesity could be explained by maternal prepregnancy BMI. This suggests that there is no clinically relevant association between CS and the development of obesity. Further large-scale studies are warranted to examine the association between differentiated forms of CS and obesity in young adult offspring.

Supporting information

S1 Table. Descriptive characteristics of the total population, eligible population, and the step-by-step excluded population.

(DOCX)

S2 Table. Relative risk ratios associated with instrumental vaginal delivery, elective cesarean section, and nonelective cesarean section as compared with vaginal delivery of underweight, overweight, and obesity relative to normal weight.

(DOCX)

S3 Table. Sensitivity analysis on associations between elective and nonelective cesarean section as compared with vaginal delivery of underweight, overweight, and obesity relative to normal weight.

(DOCX)

S4 Table. Association between pooled cesarean section and underweight, overweight, and obesity as compared with normal weight.

(DOCX)

S5 Table. Association between mode of delivery and obesity status (BMI \geq 30). BMI, body mass index.

(DOCX)

S6 Table. Linear association between mode of delivery and continuous body mass index.

(DOCX)

S7 Table. Relative risk ratios associated with elective cesarean section and nonelective cesarean section as compared with vaginal delivery of underweight, overweight, and obesity relative to normal weight in a subset of discordant full brothers.

(DOCX)

S8 Table. Fixed-effects linear association between mode of delivery and continuous body mass index in a subset of full brothers.

(DOCX)

S9 Table. Association between mode of delivery and underweight, overweight, and obesity as compared with normal weight, excluding those born before 37 weeks of gestation (pre-term), restricting to those born between 37 weeks and 41 weeks and 6 days of gestation (at term), and not adjusting for gestational age.

(DOCX)

S10 Table. Crude and adjusted association between mode of delivery and underweight, overweight, and obesity as compared with normal weight using generalized ordered logit estimation.

(DOCX)

S11 Table. Association between mode of delivery and underweight, overweight, and obesity as compared with normal weight, only adjusting for maternal prepregnancy body mass index.

(DOCX)

Author Contributions

Conceptualization: Viktor H. Ahlqvist, Cecilia Magnusson, Daniel Berglind.

Formal analysis: Viktor H. Ahlqvist.

Methodology: Viktor H. Ahlqvist, Margareta Persson.

Supervision: Cecilia Magnusson, Daniel Berglind.

Writing – original draft: Viktor H. Ahlqvist.

Writing – review & editing: Margareta Persson, Cecilia Magnusson, Daniel Berglind.

References

1. Betran AP, Ye J, Moller AB, Zhang J, Gulmezoglu AM, Torloni MR. The Increasing Trend in Caesarean Section Rates: Global, Regional and National Estimates: 1990–2014. PLoS ONE. 2016; 11(2): e0148343. <https://doi.org/10.1371/journal.pone.0148343> PMID: 26849801
2. The National Board of Health and Welfare (Socialstyrelsen). Statistikdatabas för graviditeter, förlossningar och nyfödda. [Statistics on Pregnancies, Deliveries and Newborn Infants]. Stockholm: The National Board of Health and Welfare (Socialstyrelsen); 2019. Swedish.
3. Betran AP, Torloni MR, Zhang JJ, Gulmezoglu AM; WHO Working Group on Caesarean Section. WHO Statement on Caesarean Section Rates. BJOG. 2016; 123(5):667–70. <https://doi.org/10.1111/1471-0528.13526> PMID: 26681211

4. Barber EL, Lundsberg LS, Belanger K, Pettker CM, Funai EF, Illuzzi JL. Indications contributing to the increasing cesarean delivery rate. *Obstet Gynecol.* 2011; 118(1):29–38. <https://doi.org/10.1097/AOG.0b013e31821e5f65> PMID: 21646928
5. Declercq E, Menacker F, Maccorman M. Maternal risk profiles and the primary cesarean rate in the United States, 1991–2002. *Am J Public Health.* 2006; 96(5):867–72. <https://doi.org/10.2105/AJPH.2004.052381> PMID: 16571712
6. Mylonas I, Friese K. Indications for and Risks of Elective Cesarean Section. *Dtsch Arztebl Int.* 2015; 112(29–30):489–95. <https://doi.org/10.3238/arztebl.2015.0489> PMID: 26249251
7. Nieminen K, Stephansson O, Ryding EL. Women's fear of childbirth and preference for cesarean section—a cross-sectional study at various stages of pregnancy in Sweden. *Acta Obstet Gynecol Scand.* 2009; 88(7):807–13. <https://doi.org/10.1080/00016340902998436> PMID: 19488882
8. Ryding EL, Wijma B, Wijma K, Rydhstrom H. Fear of childbirth during pregnancy may increase the risk of emergency cesarean section. *Acta Obstet Gynecol Scand.* 1998; 77(5):542–7. PMID: 9654177
9. Florica M, Stephansson O, Nordstrom L. Indications associated with increased cesarean section rates in a Swedish hospital. *Int J Gynaecol Obstet.* 2006; 92(2):181–5. <https://doi.org/10.1016/j.ijgo.2005.10.016> PMID: 16364324
10. Keag OE, Norman JE, Stock SJ. Long-term risks and benefits associated with cesarean delivery for mother, baby, and subsequent pregnancies: Systematic review and meta-analysis. *PLoS Med.* 2018; 15(1):e1002494. <https://doi.org/10.1371/journal.pmed.1002494> PMID: 29360829
11. Bager P, Wohlfahrt J, Westergaard T. Cesarean delivery and risk of atopy and allergic disease: meta-analyses. *Clin Exp Allergy.* 2008; 38(4):634–42. <https://doi.org/10.1111/j.1365-2222.2008.02939.x> PMID: 18266879
12. Koplin J, Allen K, Gurrin L, Osborne N, Tang ML, Dharmage S. Is cesarean delivery associated with sensitization to food allergens and IgE-mediated food allergy: a systematic review. *Pediatr Allergy Immunol.* 2008; 19(8):682–7. <https://doi.org/10.1111/j.1399-3038.2008.00731.x> PMID: 19076564
13. Darmasseelane K, Hyde MJ, Santhakumaran S, Gale C, Modi N. Mode of delivery and offspring body mass index, overweight and obesity in adult life: a systematic review and meta-analysis. *PLoS ONE.* 2014; 9(2):e87896. <https://doi.org/10.1371/journal.pone.0087896> PMID: 24586295
14. Li HT, Zhou YB, Liu JM. The impact of cesarean section on offspring overweight and obesity: a systematic review and meta-analysis. *Int J Obes (Lond).* 2013; 37(7):893–9.
15. Yuan C, Gaskins AJ, Blaine AI, Zhang C, Gillman MW, Missmer SA, et al. Association Between Cesarean Birth and Risk of Obesity in Offspring in Childhood, Adolescence, and Early Adulthood. *JAMA Pediatr.* 2016; 170(11):e162385. <https://doi.org/10.1001/jamapediatrics.2016.2385> PMID: 27599167
16. Kuhle S, Tong OS, Woolcott CG. Association between cesarean section and childhood obesity: a systematic review and meta-analysis. *Obes Rev.* 2015; 16(4):295–303. <https://doi.org/10.1111/obr.12267> PMID: 25752886
17. Hyde MJ, Mostyn A, Modi N, Kemp PR. The health implications of birth by Cesarean section. *Biol Rev Camb Philos Soc.* 2012; 87(1):229–43. <https://doi.org/10.1111/j.1469-185X.2011.00195.x> PMID: 21815988
18. Schlinzig T, Johansson S, Gunnar A, Ekstrom TJ, Norman M. Epigenetic modulation at birth—altered DNA-methylation in white blood cells after Cesarean section. *Acta Paediatr.* 2009; 98(7):1096–9. <https://doi.org/10.1111/j.1651-2227.2009.01371.x> PMID: 19638013
19. Almgren M, Schlinzig T, Gomez-Cabrero D, Gunnar A, Sundin M, Johansson S, et al. Cesarean delivery and hematopoietic stem cell epigenetics in the newborn infant: implications for future health? *Am J Obstet Gynecol.* 2014; 211(5):502.e1–8.
20. Dahlen HG, Downe S, Kennedy HP, Foureur M. Is society being reshaped on a microbiological and epigenetic level by the way women give birth? *Midwifery.* 2014; 30(12):1149–51. <https://doi.org/10.1016/j.midw.2014.07.007> PMID: 25128348
21. Neu J, Rushing J. Cesarean versus vaginal delivery: long-term infant outcomes and the hygiene hypothesis. *Clin Perinatol.* 2011; 38(2):321–31. <https://doi.org/10.1016/j.clp.2011.03.008> PMID: 21645799
22. Rifas-Shiman SL, Gillman MW, Hawkins SS, Oken E, Taveras EM, Kleinman KP. Association of Cesarean Delivery With Body Mass Index z Score at Age 5 Years. *JAMA Pediatr.* 2018; 172(8):777–9. <https://doi.org/10.1001/jamapediatrics.2018.0674> PMID: 29889944
23. Masukume G, O'Neill SM, Baker PN, Kenny LC, Morton SMB, Khashan AS. The Impact of Cesarean Section on the Risk of Childhood Overweight and Obesity: New Evidence from a Contemporary Cohort Study. *Sci Rep.* 2018; 8(1):15113. <https://doi.org/10.1038/s41598-018-33482-z> PMID: 30310162

24. Cai M, Loy SL, Tan KH, Godfrey KM, Gluckman PD, Chong YS, et al. Association of Elective and Emergency Cesarean Delivery With Early Childhood Overweight at 12 Months of Age. *JAMA Netw Open*. 2018; 1(7):e185025. <https://doi.org/10.1001/jamanetworkopen.2018.5025> PMID: 30646378
25. Masukume G, McCarthy FP, Baker PN, Kenny LC, Morton SM, Murray DM, et al. Association between caesarean section delivery and obesity in childhood: a longitudinal cohort study in Ireland. *BMJ Open*. 2019; 9(3):e025051. <https://doi.org/10.1136/bmjopen-2018-025051> PMID: 30878984
26. Wang Y, Beydoun MA, Liang L, Caballero B, Kumanyika SK. Will all Americans become overweight or obese? estimating the progression and cost of the US obesity epidemic. *Obesity (Silver Spring)*. 2008; 16(10):2323–30.
27. Källén K, editor. Den ökade andelen kejsarsnittsförlossningar och dess orsaker 1973–2009. [The increasing proportion of cesarean deliveries and their causes 1973–2009]. Stockholm: Svensk Förening för Obstetrik och Gynekologi; 2010. Swedish.
28. Kolas T, Hofoss D, Daltveit AK, Nilsen ST, Henriksen T, Hager R, et al. Indications for cesarean deliveries in Norway. *Am J Obstet Gynecol*. 2003; 188(4):864–70. <https://doi.org/10.1067/mob.2003.217> PMID: 12712077
29. Mears K, McAuliffe F, Grimes H, Morrison JJ. Fetal cortisol in relation to labour, intrapartum events and mode of delivery. *J Obstet Gynaecol*. 2004; 24(2):129–32. <https://doi.org/10.1080/01443610410001645389> PMID: 14766445
30. Azad MB, Konya T, Maughan H, Guttman DS, Field CJ, Chari RS, et al. Gut microbiota of healthy Canadian infants: profiles by mode of delivery and infant diet at 4 months. *CMAJ*. 2013; 185(5):385–94. <https://doi.org/10.1503/cmaj.121189> PMID: 23401405
31. Nordesjö L, Schéle R. Validity of an ergometer cycle test and measures of isometric muscle strength when prediction some aspects of military performance. *Försvarsmedicin (Swedish journal of defence medicine)*. 1974; 10:11–23.
32. National Board of Health Welfare. The Swedish Medical Birth Register—A summary of content and quality. Stockholm, Sweden: National Board of Health and Welfare; 2003 [cited 2019 Oct 1]. Available from: <https://www.socialstyrelsen.se/publikationer/>.
33. Statistics Sweden. Multi-generation register 2016—A description of contents and quality. Örebro: Statistics Sweden; 2017.
34. Värnplikslag. [Conscription Law], 1941:967 (1941).
35. Rasmussen F, Johansson M. The relation of weight, length and ponderal index at birth to body mass index and overweight among 18-year-old males in Sweden. *European Journal of Epidemiology*. 1998; 14(4):373–80. <https://doi.org/10.1023/a:1007411613576> PMID: 9690756
36. Ahlqvist VH, Persson M, Ortega FB, Tynelius P, Magnusson C, Berglind D. Birth weight and grip strength in young Swedish males: a longitudinal matched sibling analysis and across all body mass index ranges. *Sci Rep*. 2019; 9(1):9719. <https://doi.org/10.1038/s41598-019-46200-0> PMID: 31273289
37. World Health Organization. Obesity: preventing and managing the global epidemic. Report of a WHO consultation. Geneva: World Health Organization; 2000 [cited 2019 Oct 1]. Available from: https://www.who.int/nutrition/publications/obesity/WHO_TRS_894/en/.
38. Rasmussen F, Johansson M, Hansen HO. Trends in overweight and obesity among 18-year-old males in Sweden between 1971 and 1995. *Acta Paediatr*. 1999; 88(4):431–7. <https://doi.org/10.1080/08035259950169837> PMID: 10342544
39. Yu Z, Han S, Zhu J, Sun X, Ji C, Guo X. Pre-pregnancy body mass index in relation to infant birth weight and offspring overweight/obesity: a systematic review and meta-analysis. *PLoS ONE*. 2013; 8(4):e61627. <https://doi.org/10.1371/journal.pone.0061627> PMID: 23613888
40. Chu SY, Kim SY, Schmid CH, Dietz PM, Callaghan WM, Lau J, et al. Maternal obesity and risk of cesarean delivery: a meta-analysis. *Obes Rev*. 2007; 8(5):385–94. <https://doi.org/10.1111/j.1467-789X.2007.00397.x> PMID: 17716296
41. Hillier TA, Pedula KL, Schmidt MM, Mullen JA, Charles MA, Pettitt DJ. Childhood obesity and metabolic imprinting: the ongoing effects of maternal hyperglycemia. *Diabetes Care*. 2007; 30(9):2287–92. <https://doi.org/10.2337/dc06-2361> PMID: 17519427
42. Metzger BE, Lowe LP, Dyer AR, Trimble ER, Chaovarindr U, et al.; Hapo Study Cooperative Research Group. Hyperglycemia and adverse pregnancy outcomes. *N Engl J Med*. 2008; 358(19):1991–2002. <https://doi.org/10.1056/NEJMoa0707943> PMID: 18463375
43. Fraser A, Nelson SM, Macdonald-Wallis C, Sattar N, Lawlor DA. Hypertensive disorders of pregnancy and cardiometabolic health in adolescent offspring. *Hypertension*. 2013; 62(3):614–20. <https://doi.org/10.1161/HYPERTENSIONAHA.113.01513> PMID: 23918754
44. Ino T. Maternal smoking during pregnancy and offspring obesity: meta-analysis. *Pediatr Int*. 2010; 52(1):94–9. <https://doi.org/10.1111/j.1442-200X.2009.02883.x> PMID: 19400912

45. Lurie S, Ribenzaft S, Boaz M, Golan A, Sadan O. The effect of cigarette smoking during pregnancy on mode of delivery in uncomplicated term singleton pregnancies. *J Matern Fetal Neonatal Med.* 2014; 27(8):812–5. <https://doi.org/10.3109/14767058.2013.842551> PMID: 24020824
46. Reynolds RM, Osmond C, Phillips DI, Godfrey KM. Maternal BMI, parity, and pregnancy weight gain: influences on offspring adiposity in young adulthood. *J Clin Endocrinol Metab.* 2010; 95(12):5365–9. <https://doi.org/10.1210/jc.2010-0697> PMID: 20702520
47. Menacker F, Declercq E, Maccormack MF. Cesarean delivery: background, trends, and epidemiology. *Semin Perinatol.* 2006; 30(5):235–41. <https://doi.org/10.1053/j.semperi.2006.07.002> PMID: 17011392
48. Gillman MW, Rifas-Shiman S, Berkey CS, Field AE, Colditz GA. Maternal gestational diabetes, birth weight, and adolescent obesity. *Pediatrics.* 2003; 111(3):e221–6. <https://doi.org/10.1542/peds.111.3.e221> PMID: 12612275
49. Heffner LJ, Elkin E, Fretts RC. Impact of labor induction, gestational age, and maternal age on cesarean delivery rates. *Obstet Gynecol.* 2003; 102(2):287–93. [https://doi.org/10.1016/s0029-7844\(03\)00531-3](https://doi.org/10.1016/s0029-7844(03)00531-3) PMID: 12907101
50. Davis EF, Lazdam M, Lewandowski AJ, Worton SA, Kelly B, Kenworthy Y, et al. Cardiovascular risk factors in children and young adults born to preeclamptic pregnancies: a systematic review. *Pediatrics.* 2012; 129(6):e1552–61. <https://doi.org/10.1542/peds.2011-3093> PMID: 22614768
51. Penfield CA, Nageotte MP, Wing DA. Disparate Rates of Cesarean Delivery in Term Nulliparous Women with Hypertensive Disorders of Pregnancy. *Am J Perinatol.* 2019; 36(10):887–1001.
52. Raju TNK, Buist AS, Blaisdell CJ, Moxey-Mims M, Saigal S. Adults born preterm: a review of general health and system-specific outcomes. *Acta Paediatr.* 2017; 106(9):1409–37. <https://doi.org/10.1111/apa.13880> PMID: 28419544
53. Myrskylä M, Fenelon A. Maternal age and offspring adult health: evidence from the health and retirement study. *Demography.* 2012; 49(4):1231–57. <https://doi.org/10.1007/s13524-012-0132-x> PMID: 22926440
54. Cleary-Goldman J, Malone FD, Vidaver J, Ball RH, Nyberg DA, Comstock CH, et al. Impact of maternal age on obstetric outcome. *Obstet Gynecol.* 2005; 105(5 Pt 1):983–90. <https://doi.org/10.1097/01.AOG.0000158118.75532.51> PMID: 15863534
55. Lissner L, Johansson SE, Qvist J, Rossner S, Wolk A. Social mapping of the obesity epidemic in Sweden. *Int J Obes Relat Metab Disord.* 2000; 24(6):801–5. <https://doi.org/10.1038/sj.ijo.0801237> PMID: 10878690
56. Witt WP, Wisk LE, Cheng ER, Mandell K, Chatterjee D, Wakeel F, et al. Determinants of cesarean delivery in the US: a lifecourse approach. *Matern Child Health J.* 2015; 19(1):84–93. <https://doi.org/10.1007/s10995-014-1498-8> PMID: 24770955
57. Frisell T, Oberg S, Kuja-Halkola R, Sjölander A. Sibling comparison designs: bias from non-shared confounders and measurement error. *Epidemiology.* 2012; 23(5):713–20. <https://doi.org/10.1097/EDE.0b013e31825fa230> PMID: 22781362
58. Oken E, Rifas-Shiman SL, Field AE, Frazier AL, Gillman MW. Maternal gestational weight gain and offspring weight in adolescence. *Obstet Gynecol.* 2008; 112(5):999–1006. <https://doi.org/10.1097/AOG.0b013e31818a5d50> PMID: 18978098
59. Johansson K, Hutcheon JA, Stephansson O, Chattingius S. Pregnancy weight gain by gestational age and BMI in Sweden: a population-based cohort study. *Am J Clin Nutr.* 2016; 103(5):1278–84. <https://doi.org/10.3945/ajcn.115.110197> PMID: 27009753
60. Pfarr K. femlogit-Implementation of the multinomial logit model with fixed effects. *Stata Journal.* 2014; 14(4):847–62.
61. Curran EA, Dalman C, Kearney PM, Kenny LC, Cryan JF, Dinan TG, et al. Association Between Obstetric Mode of Delivery and Autism Spectrum Disorder: A Population-Based Sibling Design Study. *JAMA Psychiatry.* 2015; 72(9):935–42. <https://doi.org/10.1001/jamapsychiatry.2015.0846> PMID: 26107922
62. Williams R. Generalized Ordered Logit/Partial Proportional Odds Models for Ordinal Dependent Variables. *The Stata Journal.* 2006; 6(1):58–82.
63. Harrell FE. *Regression Modeling Strategies.* New York, NY: Springer; 2001.
64. Li H, Ye R, Pei L, Ren A, Zheng X, Liu J. Cesarean delivery, cesarean delivery on maternal request and childhood overweight: a Chinese birth cohort study of 181 380 children. *Pediatr Obes.* 2014; 9(1):10–6. <https://doi.org/10.1111/j.2047-6310.2013.00151.x> PMID: 23512941
65. Llewellyn A, Simmonds M, Owen CG, Woolacott N. Childhood obesity as a predictor of morbidity in adulthood: a systematic review and meta-analysis. *Obes Rev.* 2016; 17(1):56–67. <https://doi.org/10.1111/obr.12316> PMID: 26440472

66. Bjerregaard LG, Jensen BW, Angquist L, Osler M, Sorensen TIA, Baker JL. Change in Overweight from Childhood to Early Adulthood and Risk of Type 2 Diabetes. *N Engl J Med*. 2018; 378(14):1302–12. <https://doi.org/10.1056/NEJMoa1713231> PMID: 29617589
67. Wrzosek M, Wisniewska K, Sawicka A, Talalaj M, Nowicka G. Early Onset of Obesity and Adult Onset of Obesity as Factors Affecting Patient Characteristics Prior to Bariatric Surgery. *Obes Surg*. 2018; 28(12):3902–9. <https://doi.org/10.1007/s11695-018-3381-y> PMID: 30022421
68. Mueller NT, Whyatt R, Hoepner L, Oberfield S, Dominguez-Bello MG, Widen EM, et al. Prenatal exposure to antibiotics, cesarean section and risk of childhood obesity. *Int J Obes (Lond)*. 2015; 39(4):665–70.
69. Schousboe K, Willemssen G, Kyvik KO, Mortensen J, Boomsma DI, Cornes BK, et al. Sex differences in heritability of BMI: a comparative study of results from twin studies in eight countries. *Twin Res*. 2003; 6(5):409–21. <https://doi.org/10.1375/136905203770326411> PMID: 14624725
70. Drake AJ, Reynolds RM. Impact of maternal obesity on offspring obesity and cardiometabolic disease risk. *Reproduction*. 2010; 140(3):387–98. <https://doi.org/10.1530/REP-10-0077> PMID: 20562299
71. Weaver JJ, Statham H, Richards M. Are there "unnecessary" cesarean sections? Perceptions of women and obstetricians about cesarean sections for nonclinical indications. *Birth*. 2007; 34(1):32–41. <https://doi.org/10.1111/j.1523-536X.2006.00144.x> PMID: 17324176
72. Ye J, Zhang J, Mikolajczyk R, Torloni MR, Gulmezoglu AM, Betran AP. Association between rates of caesarean section and maternal and neonatal mortality in the 21st century: a worldwide population-based ecological study with longitudinal data. *BJOG*. 2016; 123(5):745–53. <https://doi.org/10.1111/1471-0528.13592> PMID: 26331389
73. Vogel JP, Betran AP, Vindevoghel N, Souza JP, Torloni MR, Zhang J, et al. Use of the Robson classification to assess caesarean section trends in 21 countries: a secondary analysis of two WHO multicountry surveys. *Lancet Glob Health*. 2015; 3(5):e260–70. [https://doi.org/10.1016/S2214-109X\(15\)70094-X](https://doi.org/10.1016/S2214-109X(15)70094-X) PMID: 25866355