OBESITY/PREGNANCY

Caesarean section and obesity in young adult offspring: Update of a systematic review with meta-analysis

Berenike Quecke[1] | Yannick Graf[1] | Adina-Mihaela Epure[1] |
Valérie Santschi[2] | Arnaud Chiolero[1,3,4] | Cristian Carmeli[1] |
Stéphane Cullati[1,5]

[1]Population Health Laboratory (#PopHealthLab), University of Fribourg, Fribourg, Switzerland

[2]La Source, School of Nursing Sciences, HES-SO University of Applied Sciences and Arts Western Switzerland, Lausanne, Switzerland

[3]Institute of Primary Health Care (BIHAM), University of Bern, Bern, Switzerland

[4]School of Population and Global Health, McGill University, Montreal, Canada

[5]Department of Readaptation and Geriatrics, University of Geneva, Geneva, Switzerland

Correspondence
Stéphane Cullati, Population Health Laboratory (#PopHealthLab), University of Fribourg, Route des Arsenaux 41, CH - 1700 Fribourg, Switzerland.
Email: stephane.cullati@unifr.ch

Summary

As compared with vaginal delivery (VD), caesarean section (CS) birth could be associated with increased risk of obesity in young adult offspring. We aimed to evaluate this association by updating data from a systematic review with meta-analysis of observational studies. From 3774 records identified in PubMed and Embase, we retained six studies and added five studies from the last systematic review, for a total of 11 studies. Crude estimates of the association were retrieved from nine cohort studies ($n = 143{,}869$), and maximally adjusted estimates were retrieved from eight cohort studies. Young adults born by CS had higher risk of obesity (body mass index [BMI] ≥ 30 kg/m^2) than young adults born by VD, corresponding to a crude pooled risk ratio (RR) of 1.30 [95% confidence interval (CI) 1.13 to 1.50] and a maximally adjusted pooled RR of 1.22 [95% CI 1.02 to 1.46]. In a sensitivity analysis pooling, five studies that included maternal prepregnancy BMI, a major potential confounding factor, in the set of controlled covariates, the RR was 1.08 [95% CI 0.92 to 1.27]. We concluded that the association between CS and obesity in young adulthood was mostly explained by confounding from maternal prepregnancy BMI.

KEYWORDS
caesarean section, meta-analysis, obesity, offspring, young adulthood

1 | INTRODUCTION

The prevalence of caesarean section (CS) births and obesity are growing in high-income countries.[1,2] The mode of delivery at birth might affect health and the risk of disease in adult life,[3] including obesity. The hypothetical mechanisms that might underpin the association remain disputed. Indeed, several studies have shown that

the risk of obesity in adulthood was higher in offspring delivered by CS than other deliveries,[4–6] whereas others have not shown such an association.[7–9] An alteration in the gut microbiome of the newborn has been suggested as a potential mechanism for the association,[10] but puberty[11] as well as adequate nutrition in childhood and adolescence could play a role in the association.[12] In 2014, a systematic review by Darmasseelane et al. confirmed the association between CS and adulthood overweight and obesity in offspring. However, in this review, estimates were not adjusted for possible confounders, particularly maternal prepregnancy body mass index (BMI). Another

systematic review by Sutharsan et al.[13] identified a moderate association but concluded that most of the associations reported could be attributed to publication bias favoring positive results or to residual confounding. Recently, a Swedish national register study found no evidence of an association between CS and obesity in young adult male conscripts.[8]

Here, we updated the systematic review of Sutharsan et al.[13] to determine the association between CS delivery and obesity in young adult offspring.

2 | METHODS

We updated the data from a systematic review of studies reporting adult measures of obesity by mode of delivery (vaginal delivery [VD]; CS, elective or not) following PRISMA guidelines for reporting systematic reviews and meta-analyses.[14]

2.1 | Definition of outcomes and exposures

Our outcome of interest was obesity in humans aged 18 or above. We considered any obesity measures, expressed on a metric scale (e.g., kg/m^2) or a standardized scale (e.g., z-score), that were determined anthropometrically. Obesity was classified according to the World Health Organization standard,[15] namely, ≥ 30 kg/m^2. Our exposure of interest was CS. We included studies comparing CS, elective or nonelective, versus VD, natural or operative.

2.2 | Literature search

PubMed and EMBASE were searched for any studies published since April 1, 2014, namely, the end date of searches of the most recent systematic review.[13] Details about the search strategies are given in the Supporting Information.

2.3 | Study selection, data extraction, and study quality assessment

Titles and abstracts of identified studies were independently screened by two reviewers (YG and BQ). Studies were included if they were (1) observational studies, cross-sectional or longitudinal; (2) written in English, French, German or Italian; (3) published from April 1, 2014 to February 25, 2020; and (4) participants had at least one measurement of their weight status at age 18 years or older. In addition, articles had to meet the following criteria: (1) the study determined obesity in humans anthropometrically, (2) the measurements were expressed on the metric scale (e.g., kg/m^2) or a standardized scale (e.g., z-score), and (3) studies reported the association between CS and offspring obesity. We did not consider studies for which (1) the full text was not available and authors were not contactable ($n = 1$), (2) the full article

was not yet published ($n = 3$), (3) BMI was not studied as an outcome ($n = 3$), (4) CS was not studied as an exposure ($n = 1$), (5) the population age fell below the age limit ($n = 2$), and (6) the format did not correspond to a research article ($n = 1$). All searches were limited to human studies. We had no limitation concerning the country or sex of participants. Data were extracted by use of a prepiloted data collection form (YG and BQ). Study authors were contacted when essential data were not available in the published studies ($n = 2$). The methodological quality of each study was assessed by using the tool of Sutharsan et al.,[13] comprising 10 criteria related to bias in observational studies (Figure S1).[16] Each study was assessed by one reviewer (YG or BQ), and each quality assessment was reviewed by a second senior author (CC or SC).

2.4 | Statistical analysis

Studies reporting associations in terms of odds ratios or risk ratios (RRs) were used for meta-analysis. Odds ratios were converted to RRs and 95% confidence intervals (CIs) were estimated. For each study, we considered both crude estimates, whereby the mode of delivery was the only covariate in the linear regression models, and maximally adjusted estimates, whereby maternal and child factors reported in Table 1 were included as additional covariates. We pooled estimates from each cohort study by using the Hartung–Knapp inverse-variance random-effects meta-analytic mode.[17,18] This method provides reliable coverage accuracy of confidence intervals in meta-analysis of a few studies. The interstudy variance was estimated by using the DerSimonian–Laird method implemented in the meta R package.[19] The potential heterogeneity across studies was assessed by the I^2 statistic.

3 | RESULTS

The flow of the study selection is presented in Figure S2. Our searches retrieved 3774 records (934 PubMed; 2840 EMBASE) published after April 1, 2014. After eliminating duplicates, 3433 records were screened for inclusion based on titles and abstracts and 17 records based on full texts. Six studies were eventually retained. They were complemented with five eligible studies published before April 1, 2014, and retrieved from the review of Sutharsan et al.,[13] which resulted in 11 studies included in the present systematic review. Of these, two studies were excluded (BMI assessed with a continuous metric) and nine studies were included in meta-analyses of crude estimates (Figure S3) and eight studies in meta-analyses of maximally adjusted estimates (Figure 1). Characteristics, including quality scores, are shown in Table 1. The 11 studies represented six countries and two studies were limited to male participants.[8,20] Crude RRs from all studies were >1 (Figure S3).

Crude estimates revealed a higher risk of obesity for young adults born by CS than VD (pooled RR 1.30 [95% CI 1.13 to 1.50, I^2 49%]) (Figure S3) and maximally adjusted estimates (RR 1.22 [95% CI 1.02

TABLE 1 Characteristics of longitudinal studies included in the meta-analysis

First author, year	Sample, birth year, country	Sample size	Mean age or age range at outcome	Obesity measure	BMI range	Measure of association
Goldani, 2011[4]	Population based, 1978–1979, Brazil	2057 M = 992 F = 1065	23–25 years	BMI	BMI ≥ 30 kg/m²	PR_{ob}
Rooney, 2011[21]	Population based, 1988, USA	453	18–20 years	BMI	BMI ≥ 30 kg/m²	RR_{ob}
Barros, 2012[9]	Population based, 1982, Brazil	4288 n.a. n.a.	23 years	BMI	BMI ≥ 30 kg/m²	$PR_{ob\ all}$ $PR_{ob\ M}$ $PR_{ob\ F}$
Mamun, 2013[7]	Population based, 1981–1983, Australia	2382	21 years	BMI	BMI ≥ 30 kg/m²	OR_{ob}
Svensson, 2013[20]	Conscription record (all males), 1977–1983, Denmark	21,051	≈18 years	BMI	BMI ≥ 30 kg/m²	PR_{ob}
Yuan, 2016[22]	Population based, ≈1982–1995, USA	14,763	19–28 years	BMI	BMI ≥ 30 kg/m²	RR_{ob} (model 1) RR_{ob} (model 2)
Hansen, 2018[5]	Population based, 1988–1989, Denmark	695 M = 320 F = 375	20 years	BMI	BMI ≥ 25 kg/m²	$OR_{ow\ and\ ob}$ (model 2)
Sogunle, 2019[6]	Population based, 1990, South Africa	889 M = 444 F = 454	21–24 years	BMI	BMI ≥ 30 kg/m²	$IRR_{ob\ all}$ $IRR_{ob\ M}$ $IRR_{ob\ F}$
Ahlqvist, 2019[8]	Conscription record, 1982–1987, Sweden	Total = 97,291 (all male) eCS = 4147 n-eCS = 4120	18 years	BMI	BMI ≥ 30 kg/m²	$RRR_{eCS,\ ob}$ $RRR_{n-eCS,\ ob}$

Abbreviations: BMI, body mass index; CS, caesarean section; eCS, elective CS; n-eCS, nonelective CS; F, female; IRR, incidence rate ratio; M, male; n.a, not available; ob, obesity; OR, odds ratio; ow, overweight; PR, prevalence risk; RR, relative risk; RRR, relative risk reduction. Quality score[13] range from 0 (lowest quality) to 1 (highest quality).

TABLE 1 (Continued)

First author, year	Crude estimates	Maximally adjusted estimates	Adjusted for maternal prepregnancy BMI	Analysis adjusted for	Quality score (max. = 1)
Goldani, 2011[4]	1.46 (1.15, 1.85)	1.58 (1.23, 2.02)	No	Maternal factors: education and smoking Child factors: birth weight, sex, physical activity, smoking, education and income	0.52
Rooney, 2011[21]	n.a.	n.a.	No	None	0.37
	2.78 (1.30, 5.94)	Adolescent and adulthood models were not adjusted.			
Barros, 2012[9]	1.10 (0.89, 1.37)	1.10 (0.87, 1.41)	Yes	Maternal factors: age, prepregnancy, weight and height, skin color, smoking and education Family factors: family income, type of payment for delivery Child factors: birth order and birth weight, education, physical activity, smoking and alcohol consumption	0.82
	1.13 (0.82, 1.55)	0.94 (0.60, 1.31)	Yes	ditto	
	1.08 (0.81, 1.46)	1.33 (0.94, 1.89)	Yes	ditto	
Mamun, 2013[7]	1.3 (0.9, 1.8)	0.94 (0.63, 1.41)	Yes	Maternal factors: age, prepregnancy BMI, smoking, education, gestational weight gain, hypertensive disorder Family factors: parental ethnicity Child factors: gestation, birth weight, breast feeding,	0.86
Svensson, 2013[20]	1.41 (1.22, 1.63)	1.35 (1.14, 1.59)	No	Maternal factors: age, gestational hypertensive disorder, diabetes, marital status, maternal hospitalization for infection Child factor: birth weight, gestational age. Parity	0.74
Yuan, 2016[22]	1.23 (1.11, 1.37)	1.10 (0.98, 1.24)	Yes	Maternal factors: age, height, prepregnancy BMI, pre pregnancy smoking, gestational diabetes, preeclampsia, pregnancy-induced hypertension, previous caesarean delivery Child factors: ethnicity, region, year of birth, gestational age, birth weight, sex, birth order	0.83
	ditto	1.08 (0.96, 1.21)		Ditto, but modeling prepregnancy BMI as a continuous variable.	
Hansen, 2018[5]	2.02 (1.07, 3.82)	2.17 (1.10, 4.27)	Yes	Maternal factors: prepregnancy BMI, age, education, smoking in pregnancy, parity, pre-eclampsia, gestational diabetes Child factors: birth weight, gestational age	0.77
	n.a.	n.a.			

TABLE 1 (Continued)

First author, year	Crude estimates	Maximally adjusted estimates	Adjusted for maternal prepregnancy BMI	Analysis adjusted for	Quality score (max. = 1)
Sogunle, 2019[6]	1.75 (1.05, 2.92)	1.64 (1.01, 2.68)	No	Maternal factors: education, parity Child factors: birth weight, sex,	0.54
	3.79 (1.07, 13.38)	4.01 (1.14, 14.09)		ditto	
	1.49 (0.87, 2.54)	1.44 (0.85, 2.44)		ditto	
Ahlqvist, 2019[8]	1.14 (1.00, 1.13)	1.02 (0.88, 1.18)	Yes	Maternal factors: pre-pregnancy maternal BMI, diabetes at delivery, hypertension at delivery, smoking, age, preeclampsia Child factors: parity, birth weight standardized according to gestational age, gestational age Family factors: parental education	0.89
	1.18 (1.02, 1.35)	0.96 (0.83, 1.10)	Yes	ditto	

Abbreviations: BMI, body mass index; CS, caesarean section; eCS, elective CS; n-eCS, nonelective CS; F, female; IRR, incidence rate ratio; M, male; n.a., not available; ob, obesity; OR, odds ratio; ow, overweight; PR, prevalence risk; RR, relative risk; RRR, relative risk reduction. Quality score[13] range from 0 (lowest quality) to 1 (highest quality).

to 1.46, I^2 63%]) (Figure 1). In analyses restrained to the five studies with adjustment for maternal prepregnancy BMI, the RR was 1.08 (95% CI 0.92 to 1.27, I^2 23%) (Figure 1). The low heterogeneity in the two subgroups indicates that the heterogeneity in all eight studies could be explained in part by the difference in the adjustment for potential confounders. Restraining the analyses to studies published before and after the Sutharsan et al. review[13] (Figure S4) and to studies adjusting for predelivery diabetes (Figure S5) did not change the results. After removing the three studies with the lowest quality score,[4,6,21] the absolute size of the association was smaller: the crude RR was 1.24 (95% CI 1.09 to 1.41) and the adjusted RR 1.14 (95% CI 0.95 to 1.37). The funnel plot shows a symmetric pattern, indicating a low probability of publication bias (Figure S6).

4 | DISCUSSION

4.1 | Main findings

In this systematic review and meta-analysis, we pooled results from nine studies involving 143,869 participants to determine the association between CS delivery and obesity in young adult offspring. CS increased the pooled crude risk of obesity in adult offspring by 30% as compared with young adults born by VD. Maximal adjustment reduced the risk to 22%, which opens the argument for a substantive role of potential confounding factors. Adjustment methods varied across studies, causing high between-study heterogeneity. Sensitivity analysis excluding three studies with the lowest quality score revealed that CS was no longer associated with offspring obesity in the adjusted analysis (RR 1.14 [95% CI 0.95 to 1.37]). This finding suggested that the above risk of 22% may be overestimated. It is highly probable that the association of CS with the risk of obesity observed in the current meta-analysis may be driven by confounding in studies unadjusted for maternal prepregnancy BMI (the risk reduced from 1.43 in unadjusted analyses to 1.08 in adjusted analyses) as well as by other residual confounding factors.

4.2 | Comparison with other studies

This is the fourth meta-analysis assessing the association of CS with obesity in young adulthood. An overview of these meta-analyses is given in Table S2. The meta-analysis of Li et al.[22] included nine studies, of which only three showed estimates for young adulthood.[4,9,21] Therefore, the authors did not conduct a formal subgroup analysis for young adulthood. They found 50% higher odds in adults born by CS, with high between-study heterogeneity (95% CI 1.02 to 2.20; I^2 74%). The adjusted pooled OR was significantly high, as was the between-study heterogeneity (odds ratio 1.50; 95% CI 1.02 to 2.20; I^2 74%). Darmasseelane et al.[23] included 11 studies with a combined population of ≈35,000 participants and also considered only the effect of CS on adults. Their findings revealed 22% increased odds of obesity in adults born by CS (95% CI 1.05 to 1.42; $p = 0.01$; I^2 22%), and the

Study	Risk ratio	95% CI	Weight
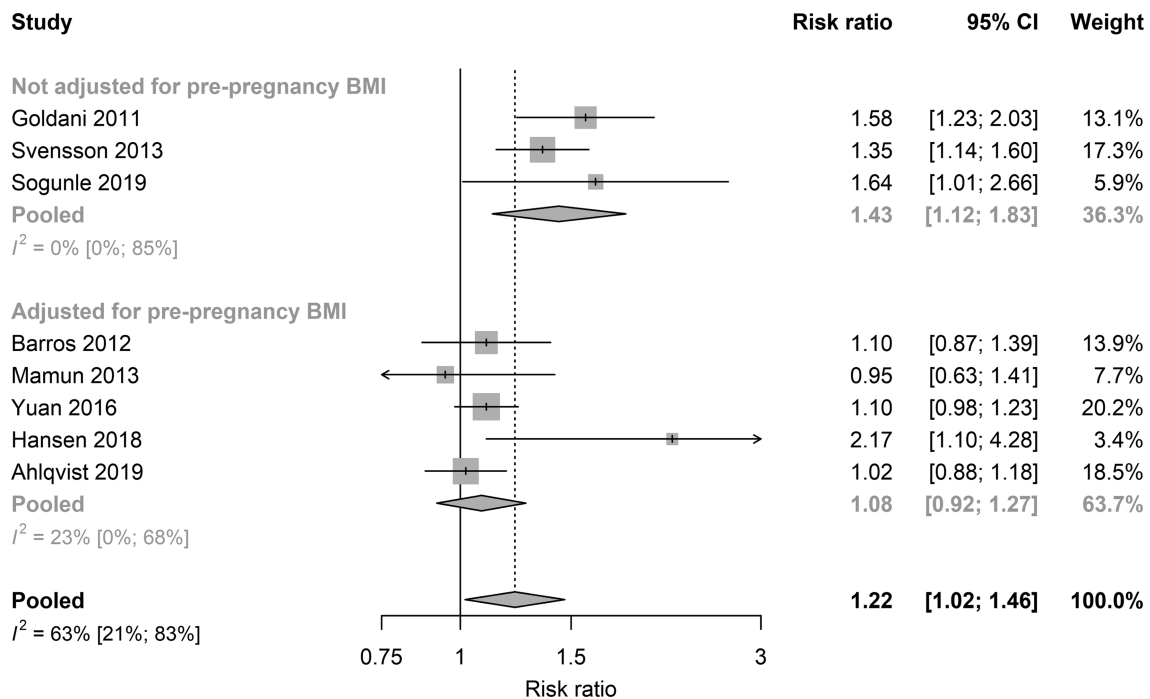
FIGURE 1 Forest plot of maximally adjusted risk ratios with subgroups defined by adjustment for prepregnancy BMI. Pooled estimates are represented by a diamond. The size of the grey square for each study is related to the amount of variance that a study contributes to the meta-analysis (column "weight")

mean BMI difference was 0.44 kg/m^2 (95% CI 0.17 to 0.72; $p = 0.002$; I^2 39%). The low heterogeneity may be explained by the authors not using adjusted data but only applied a sensitivity analysis. Sutharsan et al.[13] examined the effect on both childhood and young adulthood. Yet only five studies took the latter into account ($n = 30,231$). Sutharsan et al.[13] used the same quality assessment instrument as we did and adjusted for confounders. The authors found a 28% increase in the effect on obesity (95% CI 1.02 to 1.56).

4.3 | Strengths and limitations

The strength of our systematic review lies primarily in a large population size with participants from four continents. We included five studies[4,7,9,20,21] included in the previous meta-analysis from Sutharsan et al.[13] in our update of meta-analysis for better comparability. Furthermore, we used quality assessment of each study. Because we investigated a strictly adult population, the timing of outcome assessment and duration of follow-up were adequate for the outcome to occur.

Confidence was limited by a high between-study heterogeneity, which could be due in part to differences in the set of factors adjusted for. The four studies with the highest quality score,[7–9,24] which is particularly determined by the adjustment for confounders, revealed the lowest adjusted estimates. Thus, a lack of adjustment could explain in part the higher effect sizes of the other studies. Even in maximally adjusted models, we could not exclude residual confounding explaining a part of the observed association. Four studies did not

adjust for maternal prepregnancy BMI, probably the most significant confounding factor, which is associated with increased risk of CS and also increased BMI in offspring.[25,26] There is also evidence for such mechanisms regarding other maternal risk factors such as low socio-economic status[27,28] and maternal smoking during pregnancy,[29,30] which were not part of the adjustment of all included studies. Gestational diabetes could also be a confounding factor,[31,32] but our subgroup analysis (Figure S5) showed similar results between studies adjusting for predelivery diabetes and those that did not; thus predelivery diabetes may not be a major confounder of the association between CS and offspring obesity. Potential measurement errors were related to two limitations: first, self-reported BMI from included studies[5,24] and, second, whether data about the exposure was collected soon after birth[4–9,20,21] or retrospectively recalled.[24] Because of not fitting effect sizes, we had to exclude two studies from the meta-analysis.[33,34] In addition, we did not explore the different types of exposure (elective and nonelective CS), and our search was limited to studies published in English, German, French, or Italian. Finally, we included in the meta-analysis only nine and eight studies for the crude and adjusted estimates, respectively, but representing a total of 143,416 participants for the adjusted estimates (Table S2).

4.4 | Conclusions and public health implications

This systematic review and meta-analysis updates evidence on the association between CS and obesity in young adulthood. Our findings did not support an association between CS and obesity in young adult

offspring. With a substantial decrease in the RR upon adjustment for prepregnancy BMI, we identified the latter as a major confounder and probably responsible for the association seen in previous studies and meta-analyses.

AUTHOR CONTRIBUTIONS

All authors designed the study. BQ and YG performed the literature search, screening and data extraction, under the supervision of CC and SC. CC developed the statistical model and analyzed the data. All authors reviewed the study findings. BQ and YG drafted the manuscript with contributions by CC and SC. All co-authors revised the first draft of the manuscript. All authors approved the final version of the manuscript before submission.

CONFLICT OF INTEREST

We declare no conflicts of interest.

DATA SHARING

Access to data requires contacting the last author.

ORCID

Berenike Quecke https://orcid.org/0000-0002-5013-8126
Yannick Graf https://orcid.org/0000-0003-0570-5133
Adina-Mihaela Epure https://orcid.org/0000-0002-8104-0244
Valérie Santschi https://orcid.org/0000-0002-4452-8857
Arnaud Chiolero https://orcid.org/0000-0002-5544-8510
Cristian Carmeli https://orcid.org/0000-0002-1463-4587
Stéphane Cullati https://orcid.org/0000-0002-3881-446X

REFERENCES

1. Vogel JP, Betrán AP, Vindevoghel N, 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-e270. https://doi.org/10.1016/S2214-109X(15)70094-X

2. Jaacks LM, Vandevijvere S, Pan A, et al. The obesity transition: stages of the global epidemic. *Lancet Diabetes Endocrinol*. 2019;7(3): 231-240. https://doi.org/10.1016/S2213-8587(19)30026-9

3. Hyde MJ, Mostyn A, Modi N, Kemp PR. The health implications of birth by Caesarean section. *Biol Rev*. 2012;87(1):229-243. https://doi.org/10.1111/j.1469-185X.2011.00195.x

4. Goldani HA, Bettiol H, Barbieri MA, et al. Cesarean delivery is associated with an increased risk of obesity in adulthood in a Brazilian birth cohort study. *Am J Clin Nutr*. 2011;93(6):1344-1347. https://doi.org/10.3945/ajcn.110.010033

5. Hansen S, Halldorsson TI, Olsen SF, et al. Birth by cesarean section in relation to adult offspring overweight and biomarkers of cardiometabolic risk. *Int J Obes (Lond)*. 2018;42(1):15-19. https://doi.org/10.1038/ijo.2017.175

6. Sogunle E, Masukume G, Nelson G. The association between caesarean section delivery and later life obesity in 21–24 year olds in an Urban South African birth cohort. *PLoS One*. 2019;14(11):e0221379. https://doi.org/10.1371/journal.pone.0221379

7. Mamun AA, Sutharsan R, O'Callaghan M, et al. Cesarean delivery and the long-term risk of offspring obesity. *Obstetrics Gynecol*. 2013; 122(6):1176-1183. https://doi.org/10.1097/AOG.0000000000000016

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

9. Barros FC, Matijasevich A, Hallal PC, et al. Cesarean section and risk of obesity in childhood, adolescence, and early adulthood: evidence from 3 Brazilian birth cohorts. *Am J Clin Nutr*. 2012;95(2):465-470. https://doi.org/10.3945/ajcn.111.026401

10. Endo A, Tang MLK, Salminen S. 1.8 Gut microbiota in infants. *World Rev Nutr Diet*. 2015;113:87-91. https://doi.org/10.1159/000360322

11. Siervogel RM, Demerath EW, Schubert C, et al. Puberty and body composition. *HRP*. 2003;60(Suppl. 1):36-45. https://doi.org/10.1159/000071224

12. Ishaq SL, Rapp M, Byerly R, et al. Framing the discussion of microorganisms as a facet of social equity in human health. *PLoS Biol*. 2019; 17(11):e3000536. https://doi.org/10.1371/journal.pbio.3000536

13. Sutharsan R, Mannan M, Doi SA, Mamun AA. Caesarean delivery and the risk of offspring overweight and obesity over the life course: a systematic review and bias-adjusted meta-analysis. *Clinical Obesity*. 2015;5(6):293-301. https://doi.org/10.1111/cob.12114

14. Moher D, Liberati A, Tetzlaff J, Altman DG, Group TP. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med*. 2009;6(7):e1000097. https://doi.org/10.1371/journal.pmed.1000097

15. Puska P, Nishida C, Porter D. Obesity and overweight, 2021. Published online 2003. Accessed February 19. https://www.who.int/dietphysicalactivity/media/en/gsfs_obesity.pdf

16. Shamliyan T, Kane RL, Dickinson S. A systematic review of tools used to assess the quality of observational studies that examine incidence or prevalence and risk factors for diseases. *J Clin Epidemiol*. 2010; 63(10):1061-1070. https://doi.org/10.1016/j.jclinepi.2010.04.014

17. Guolo A, Varin C. Random-effects meta-analysis: the number of studies matters. *Stat Methods Med Res*. 2017;26(3):1500-1518. https://doi.org/10.1177/0962280215583568

18. Hartung J, Knapp G. On tests of the overall treatment effect in meta-analysis with normally distributed responses. *Stat Med*. 2001;20(12): 1771-1782. https://doi.org/10.1002/sim.791

19. Schwarzer G, Carpenter JR, Rücker G. *Meta-Analysis with R*. Springer International Publishing; 2015 10.1007/978-3-319-21416-0.

20. Svensson E, Hyde M, Modi N, Ehrenstein V. Caesarean section and body mass index among Danish men. *Obesity*. 2013;21(3):429-433. https://doi.org/10.1002/oby.20310

21. Rooney BL, Mathiason MA, Schauberger CW. Predictors of obesity in childhood, adolescence, and adulthood in a birth cohort. *Matern Child Health J*. 2011;15(8):1166-1175. https://doi.org/10.1007/s10995-010-0689-1

22. Li H-T, Zhou Y-B, Liu J-M. The impact of cesarean section on offspring overweight and obesity: a systematic review and meta-analysis. *Int J Obes (Lond)*. 2013;37(7):893-899. https://doi.org/10.1038/ijo.2012.195

23. 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

24. Yuan C, Gaskins AJ, Blaine AI, et al. Cesarean birth and risk of offspring obesity in childhood, adolescence and early adulthood. *JAMA Pediatr*. 2016;170(11):e162385. https://doi.org/10.1001/jamapediatrics.2016.2385

25. Chu SY, Kim SY, Schmid CH, et al. Maternal obesity and risk of cesarean delivery: a meta-analysis. *Obes Rev*. 2007;8(5):385-394. https://doi.org/10.1111/j.1467-789X.2007.00397.x

26. Eshriqui I, Valente AMM, Folchetti LD, de Almeida-Pititto B, Ferreira SRG. Pre-pregnancy BMI is associated with offspring body composition in adulthood before adiposity-related disorders: a retrospective cohort. *Public Health Nutrition* Published online December. 2020;28(6):1-8. https://doi.org/10.1017/S1368980020005285

27. McLaren L. Socioeconomic status and obesity. *Epidemiol Rev*. 2007; 29(1):29-48. https://doi.org/10.1093/epirev/mxm001

28. Miani C, Ludwig A, Breckenkamp J, et al. Socioeconomic and migration status as predictors of emergency caesarean section: a birth cohort study. *BMC Pregnancy Childbirth*. 2020;20(1):32. https://doi.org/10.1186/s12884-020-2725-5

29. 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):812-815. https://doi.org/10.3109/14767058.2013.842551

30. Ino T. Maternal smoking during pregnancy and offspring obesity: meta-analysis. *Pediatr Int*. 2010;52(1):94-99. https://doi.org/10.1111/j.1442-200X.2009.02883.x

31. Gorgal R, Gonçalves E, Barros M, et al. Gestational diabetes mellitus: a risk factor for non-elective cesarean section. *J Obstet Gynaecol Res*. 2012;38(1):154-159. https://doi.org/10.1111/j.1447-0756.2011.01659.x

32. Kawasaki M, Arata N, Miyazaki C, et al. Obesity and abnormal glucose tolerance in offspring of diabetic mothers: a systematic review and meta-analysis. *PLoS One*. 2018;13(1):e0190676. https://doi.org/10.1371/journal.pone.0190676

33. Bernardi JR, Pinheiro TV, Mueller NT, et al. Cesarean delivery and metabolic risk factors in young adults: a Brazilian birth cohort study. *Am J Clin Nutr*. 2015;102(2):295-301. https://doi.org/10.3945/ajcn.114.105205

34. Barros AJD, Santos LP, Wehrmeister F, et al. Caesarean section and adiposity at 6, 18 and 30 years of age: results from three Pelotas (Brazil) birth cohorts. *BMC Public Health*. 2017;17(1):256. https://doi.org/10.1186/s12889-017-4165-3

SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.