The cognitive development from childhood to adolescence of low birth weight children born after medical assisted reproduction – a UK longitudinal cohort study

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Background: Prior research on the consequences of medical assisted reproduction (MAR) documents an increased risk of poor birth outcomes such as low birth weight (LBW), raising concerns for their longer-term cognitive development. However, parents who undergo MAR to conceive have, on average, advantaged socioeconomic backgrounds, which could compensate for the negative effects of being born LBW. Previous studies have not analyzed whether the negative effects of LBW are attenuated amongst MAR conceived children.

Methods: We draw on the UK Millennium Cohort Study (waves 1-6), which contains a sub-sample of (n=396) MAR conceived children at age 3. The dependent variable measures cognitive ability at around ages 3, 5, 7, 11 and 14. We examine the cognitive development of four groups of children: MAR conceived low birth weight (MAR-LBW); MAR conceived non-low birth weight (MAR-NLBW); naturally conceived low birth weight (NC-LBW); NC children non-low birth weight (NC-NLBW). We estimate two sets of linear regression models: baseline models to examine the unadjusted association between cognitive development and low birth weight by mode of conception; models adjusted by socio-demographic family characteristics.

Results: In the baseline models, MAR-LBW children do not show any difference in cognitive ability relative to NC-NLBW. If any, they show higher cognitive ability scores at age 5 (β = 0.21, 95% CI: 0.009, 0.418). Moreover, MAR-LBW conceived children show higher cognitive scores than NC-LBW children until age 7. When we account for family characteristics differences are largely attenuated.

Conclusions: Despite the high incidence of LBW among MAR children, they do not seem to experience any stunting in their cognitive development compared to naturally conceived children. This finding is likely explained by the fact that, on average, MAR children are born in socioeconomically advantaged families.

Keywords: Medical assisted reproduction, Low birth weight, Cognitive development

Introduction

Medical assisted reproduction (MAR) conceptions have increased sharply in the last decades. The increased success rate of techniques such as in-vitro fertilization (IVF), intracytoplasmic sperm injection (ICSI), ovulation induction and artificial insemination, combined with demographic trends in fertility postponement in many high-income countries (1), have led to more than 6 million children born through the use of MAR (2). The rapid increase in MAR conceptions and births over time has driven research about its consequences for children's cognitive development and well-being.

There is a large body of literature showing that MAR children are at higher risk of experiencing adverse birth outcomes as compared to naturally conceived (NC) counterparts (3-5), being four times more likely of being born low birth weight (LBW) and three times more likely of being born premature (6). This difference in birth outcomes is only partially explained by the higher share of multiple birth among MAR conceived children (7), as singleton births have also been shown to experience elevated risks of adverse birth outcomes (6). This evidence raises concerns regarding the longer-term cognitive development of MAR children, since birth outcomes are key predictors of children's cognitive development, health, and socio-economic status (8-12).

Generally, despite the higher risk of poor outcomes among MAR children, studies show that they perform better or similarly to naturally conceived children in terms of cognitive development (13-16). However, prior research has yet to investigate the extent to which the cognitive advantage among MAR conceived children is consistent across the birthweight distribution. We hypothesize that this could occur because parents who undergo MAR to conceive are, on average, from advantaged socioeconomic backgrounds (17), which could compensate for the negative effects of being born LBW (18). The proportion of MAR conceived children is increasing rapidly and cognitive ability in childhood is a key predictor of later life outcomes (10, 11, 19). Thus, it is essential to gain a better understanding of how MAR conceived children develop as they grow older and whether the fact that a high proportion are born LBW constitutes a concern and an impediment to their longer-term development.

This study has two aims. First, we compare cognitive development across early infancy and mid-adolescence in four groups of children: (1) low birth weight (LBW) MAR conceived children, (2) LBW NC children, (3) MAR, and (4) NC children born non-low birth weight (NLBW). Although our focus is particularly to compare MAR LBW children to NC children (both LBW and NLBW), we also include MAR NC as we aim to provide a comprehensive perspective on children's cognitive development based on their mode of conception and birth weight status. Second, we investigate whether family characteristics play a role in explaining these differences. We draw on the UK Millennium Cohort Study (sweeps 1-6), which includes a sub-sample of MAR and naturally conceived children and detailed information on both their cognitive development (measured at ages 3, 5, 7, 11 and 14) and family socio-demographic characteristics.

Methods

Sample description
We use data from the Millennium Cohort Study (MCS), which is a longitudinal cohort study following a sample of about 19,000 children born between 2000 and 2002 in England, Wales, Scotland and Northern Ireland. The first interview was conducted when the children were

approximately 9 months old. Follow up interviews were conducted in 2003, 2005, 2007, 2012, and 2015 when the cohort members were around 3,5,7, 11 and 14 years old. The sample of the MCS is randomly selected at the electoral ward level, and it is stratified to ensure representation of disadvantaged groups. Given the complex sample design, in the analyses we use weights to account for the overrepresentation of participants from ethnically diverse and disadvantaged areas. In the analyses we use data from all the available sweeps (1-6).

The analytical sample includes all the singleton and twins with valid information on the variables of interest at each sweep in which the outcome is measured (2-6). We drop the triplets (n=30). These inclusion criteria leads us to exclude 6.58% (N = 966) of cases at age 3; 2% (N = 289) of cases at age 5; 3.46% (N = 455) at age 7; 2.39% (N= 302) at age 11; 8.2% (N = 913) at age 14. The final analytical samples consist of: N = 13,716 observation at age 3; N = 14,175 at age 5; N = 12,714 observations at age 7; 12,336 at age 11; N = 10,220 at age 14. We do not find any systematic association between our key independent variables (MAR conceived and LBW) and the risk of not being included in the sample (see web table W1). We find limited evidence that the analytical sample is positively selected, as having a non-white or non-university educated mother only slightly increases the chance of not being included at each sweep.

Variables
The outcome variable is children's cognitive ability assessed with the British Ability Scales (BAS II). At age 3 and 5, children are assessed with the *naming vocabulary* scale; at age 7 with a *word reading* test; at age 11 with a *verbal similarity* test; and at age 14 with a *word activity* score. Cognitive ability is standardized (to a mean of 0 and a standard deviation of 1) and age-adjusted within each sweep (since there is variation in cohort members' age within each sweep).

We have two key independent variables: (1) mode of conception (MAR or Natural), and (2) whether the child was born LBW. First, we define a child as conceived with MAR if the mother underwent one of the following treatments to conceive: IVF, ICSI, intrauterine insemination, or ovulation induction. The sample of MAR children consists of N = 396 children at age 3, and it reduces, because of attrition, to N = 296 at 14 years old. Despite the reduction of cases, the share of LBW children remains consistent across waves for both NC and MAR children (Web Table W2). Second, following common practice in the literature, we define LBW as birthweight less than 2,500 grams (20). From this, we define four groups of children: (1) low birth weight (LBW) MAR conceived children, (2) LBW NC children, (3) MAR, and (4) NC children born non-low birth weight (NLBW).

We adjust the analyses for a series of child and family-level confounders. As child characteristics we adjust for sex, birth order (first born or higher), and twin births. As family characteristics, we adjust for maternal age at birth (continuous) (21, 22). We also include a binary indicator for maternal education (less than university and university degree); marital status at birth (cohabiting/married and single); whether the mother accessed antenatal care before the 12th week of gestation; whether the mother is from an ethnic minority (white and non-white); and whether the mother smoked during pregnancy (23, 24).

Statistical models

We estimate two sets of linear regression models at each sweep, which were collected at around age 3, 5, 7, 11 and 14 years old. First, we estimate baseline models predicting cognitive ability at each age for each of the four groups mentioned above, including only controls for sex and twin birth. Second, we estimate models adjusting for maternal education, birth order, maternal age, maternal marital status, timing of the first prenatal visit, maternal minority group, and whether the mother smoked during pregnancy.

Results

Descriptive results

Table 1 shows the descriptive statistics of the analytical sample at age 3 by their mode of conception. In our analytical sample 2.9% of the children are MAR conceived. The prevalence of LBW varies considerably by the mode of conception: more than one-fifth of MAR conceived children are LBW, whereas they are about 6% among natural conceptions.

There are also differences in children's characteristics between conception types. Among MAR conceived children, 66% are first born, as compared to 41% among NC children. Most notably, 24% of MAR conceived are born in a multiple birth, while the corresponding figure is only 2% of natural conception.

Family attributes also differ by mode of conception. Mothers who underwent MAR are on average almost 4 years older than mothers who conceived naturally. They are also more likely to be married or cohabit (98%) compared to NC mothers (85%). MAR mothers are also more likely to have a university degree compared to NC mother, 45% and 33%, respectively. MAR mothers are also more likely of being white than NC mothers, a difference of about 5 percentage points. Differences remain also for smoking behaviors and access to antenatal care: MAR mothers are less likely to smoke during pregnancy and access antenatal care earlier respect to mothers of NC children.

Table 1. Child and family characteristic by mode of conception

	NC	MAR
	%	%
Birth Outcomes		
LBW (%)	6.6	21.9
Child characteristics		
First Born (%)	41.5	66.1
Twin (%)	2.1	23.2
Family Characteristics		
Maternal Age at birth (mean/SE)	29.5 (0.34)	33.1 (0.34)
Mother is married or cohabiting at birth (%)	85.9	97.8
Mother of white ethnic origin (%)	89.8	94.5
Mother has a university degree (%)	33.1	45.5
Mother smoked during pregnancy (%)	21.8	9.3
Mother used antenatal care before 12th week (%)	42.5	55.6
N	13,358 (97.1)	396 (2.9)

Note: Descriptive statistics refer to the analytical sample at age 3.

Regression analyses

Table 2 shows the standardized regression coefficients by mode of conception (MAR or NC) and weight status at birth (LBW or NLBW). The reference category are naturally conceived children born non low birth weight (NC NLBW). The full model results are presented in Web Tables W3 and W4. Figure 1 reports the predicted cognitive scores for the four groups.

Panel A reports coefficients estimated in the baseline models, which include controls for the cohort members' sex and multiple birth (Figure 1, left panel). At each age, MAR conceived children (both LBW and NLBW) show higher or equal cognitive ability scores with respect to NC children. NC children born LBW consistently show the lowest cognitive ability scores, whilst MAR NLBW children show the highest predicted scores. MAR LBW children generally show equal or slightly higher cognitive scores with respect to NC NLBW conceived children. At age 3, there are no differences between MAR LBW and NC NLBW children ($\beta = 0.021$, 95% CI: -0.198, 0.241). In contrast, at age 5, MAR LBW children show higher cognitive ability scores ($\beta = 0.21$, 95% CI: 0.009, 0.418). Starting at age 7, the differences become smaller in magnitude and MAR LBW do not show notable differences in cognitive ability as compared to NC NLBW children (age 7: $\beta = 0.163$, 95% CI: -0.148, 0.474; age 11: $\beta = 0.003$, 95% CI: -0.318, 0.325; age 14: $\beta = 0.156$, 95% CI: -0.205, 0.517). When NC LBW children are used as the reference category (results not shown), MAR LBW display higher cognitive ability scores up to age 7 (at age 3: $\beta = 0.293$, 95% CI: 0.690, 0.517; at age 5: $\beta = 0.430$, CI: 0.218, 0.641; at age 7: $\beta = 0.381$, 95% CI: 0.069, 0.693); after this age, the advantage is attenuated.

Panel B reports coefficients for the adjusted models, in which we include controls for family characteristics (Figure 1, right panel). In contrast to the models presented in panel A, we do not find any difference between NC and MAR conceived children as coefficients are largely attenuated and differences become close to zero. The only group of children showing a persistent negative cognitive performance are NC LBW children, who continue to show the lowest predicted cognitive ability at all ages.

Sensitivity analyses

We performed three sensitivity analyses. First, given that some MAR techniques are more invasive and more strongly associated with adverse birth outcomes than others (6, 25), we restricted our definition of MAR by considering only children conceived with IVF and ICSI and replicated the analyses. Results are identical. Second, we restricted the analyses to only children present in all waves of the survey to account for attrition in our analytical sample. Also in this case, our results are unchanged. Third, research has recently questioned the use of LBW as an indicator of birth outcomes and developmental potential (26, 27). We replicated analyses using an indicator of small for gestational age and results are consistent. Results are presented in Web Tables W5-7.

Table 2. Linear Models regressing cognitive ability (standardized) on mode of conception and birth weight status

	Age 3 BAS naming vocabulary	Age 5 BAS naming vocabulary	Age 7 BAS word reading	Age 11 BAS verbal similarity	Age 14 BAS word activity
Panel A: Baseline Models[a]					
NC NLBW	Reference	Reference	Reference	Reference	Reference
NC LBW	-0.272	-0.216	-0.218	-0.121	-0.105
	(-0.348, -0.196)	(-0.306, -0.127)	(-0.303, -0.133)	(-0.210, -0.032)	(-0.208. -0.001)
MAR NLBW	0.181	0.324	0.345	0.228	0.226
	(0.052, 0.311)	(0.211, 0.437)	(0.232, 0.457)	(0.093, 0.358)	(0.068, 0.384)
MAR LBW	0.021	0.213	0.163	0.003	0.156
	(-0.198, 0.241)	(0.009, 0.418)	(-0.148, 0.474)	(-0.318, 0.325)	(-0.205, 0.517)
Panel B: Adjusted Models[b]					
NC NLBW	Reference	Reference	Reference	Reference	Reference
NC LBW	-0.200	-0.118	-0.182	-0.093	-0.062
	(-0.267, -0.132)	(-0.196, -0.040)	(-0.266, -0.097)	(-0.179, -0.008)	(-0.161, 0.051)
MAR NLBW	-0.067	0.046	0.115	0.002	-0.028
	(-0.192, -0.058)	(-0.060, 0.153)	(0.004, 0.226)	(-0.130, 0.126)	(-0.180, 0.123)
MAR LBW	-0.198	0.017	-0.074	-0.162	-0.023
	(-0.401, 0.005)	(-0.159, 0.193)	(-0,369, 0.220)	(-0.472, 0.148)	(-0.386, 0.339)
N	13,716	14,175	12,714	12,336	10,220

Note: [a] Baseline models include: sex, multiple birth. [b] Adjusted models include: sex, multiple birth, maternal education, whether the child is first born, maternal age at the time of birth, maternal marital status at the time of birth, timing of the first prenatal visit, ethnic origin, whether the mother smoked during pregnancy. NC NLBW: naturally conceived born non-low birth weight. NC LBW: naturally conceived born low birth weight. MAR NLBW: conceived with medical assisted reproduction and born non-low birth weight. MAR LBW: conceived with medical assisted reproduction and born low birth weight.

Figure 1. Predicted scores in cognitive development and 95% confidence intervals of MAR and naturally conceived children by their weight status at birth at different age points
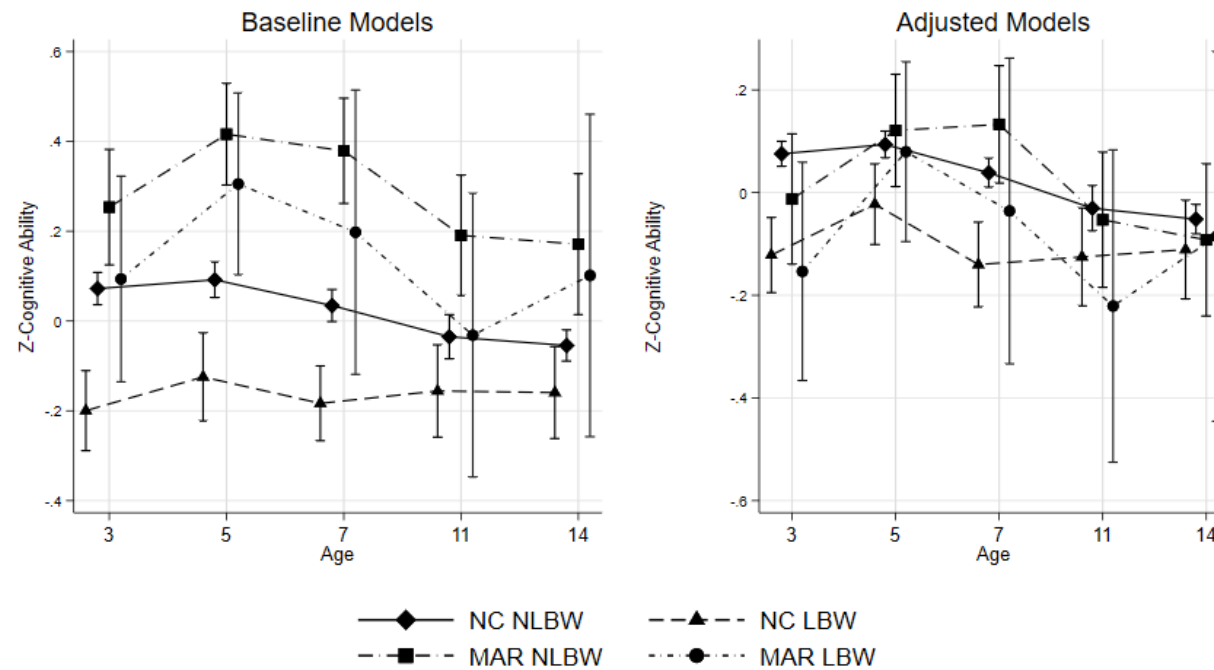
Note: Baseline models include: sex, multiple birth. Adjusted models include: sex, multiple birth, maternal education, birth order, maternal age, maternal marital status, timing of the first prenatal visit, ethnic origin, whether the mother smoked during pregnancy. NC NLBW: naturally conceived born non-low birth weight. NC LBW: naturally conceived born low birth weight. MAR NLBW: conceived with medical assisted reproduction and born non-low birth weight. MAR LBW: conceived with medical assisted reproduction and born low birth weight.

Discussion

Medically assisted conceptions and births have increased considerably in the last decades. Previous research has shown that MAR conceived children are at higher risk of being born with poor birth outcomes, raising concern on their future well-being, including their cognitive development. One potentially important aspect that has been overlooked by the existing literature is whether the MAR advantage is consistent across the birthweight distribution, as MAR children come, on average, from socioeconomically advantaged backgrounds (17), which may compensate for the negative consequences of being born LBW (18). We used a representative UK longitudinal cohort study to investigate the cognitive development of MAR children who were born LBW compared to naturally conceived (low birth weight and non-low birth weight) children from infancy to mid-adolescence, before and after the adjustment for parental characteristics.

There are two main findings. First, the baseline model results show that, despite the higher incidence of adverse birth outcomes such as LBW among MAR conceived (four-fold in our sample), there is no evidence that they experience a stunted cognitive development. Rather, MAR LBW children show the same or slightly better (at age 5) cognitive ability as NC NLBW children. Moreover, we find that MAR LBW children show higher cognitive scores than NC LBW children up to age 7, after which the advantage diminishes. There may be two potential explanations for this pattern. On the one hand, MAR LBW children's parents – who, on average, come from advantaged socio-economic background - may provide advantages with their parental investments: higher socioeconomic resources (which could translate, for example, into better childcare, better access to neonatal and postnatal care), and committed parenting due to the difficulty of conceiving thorough MAR and the desire to become parents (28). At early ages, differences in parental socio-economic background and/or parental investments may explain the cognitive advantages observed among MAR LBW relative to NC LBW children. However, this advantage may diminish over childhood when schooling more equally influences cognitive development across groups. On the other hand, it may be possible that the initial disadvantage of being born LBW in NC LBW children fades away over time, as prior studies document that the negative effect of LBW become smaller as children grow older (18, 29, 30) because, for example, neonatal and obstetric technologies have largely improved for the general population, ameliorating the consequences of being born LBW (30). Finally, differently from a previous study on the overall cognitive development of MAR children using the same data (15), we find that MAR NLBW show consistently higher cognitive ability respect to all other groups.

The second main finding is that differences in cognitive ability are likely explained by confounding parental characteristics. When we adjust for family characteristics, we find that most differences between group become small. Parents who underwent MAR treatments to conceive are in fact more educated, older, accessed antenatal care earlier, and smoked less during pregnancy. This suggests that parents from higher socio-economic backgrounds are better able to compensate for a possible initial disadvantage of being born LBW (31, 32). This finding is in line with research showing how poor fetal health and birth outcomes are associated with cognitive impairments later in life only among families with a lower socio-economic background (31, 33). There may be two mechanisms through which MAR parents compensate for the negative consequences of being born LBW. First, as we mentioned above, there may be some parenting-specific features (i.e. commitment, effort, financial resources) compensating for LBW. Second, the determinants of being born LBW are likely to differ between MAR conceived and NC children. For example, in the MAR conceived group, LBW determinants may be related to the experience of sub-fertility (4) instead of other causes such

as smoking in pregnancy, a more common cause in the group who conceives naturally. Moreover, the proportion of first born – which is associated with increased risk of LBW (34) - in the MAR conceived group is higher than in the NC group. Ultimately, differences in the determinants of LBW could translate in differences in the developmental risk associated with being born with poorer birth outcomes.

This study is not free of limitations. First, the sample size of MAR children is small, and this may affect the precision of our estimates. In particular, due to attrition, in the later sweeps the confidence intervals become wider making it more difficult to interpret differences between the groups. In order to attenuate this issue we considered as MAR all the children who were conceived through different types of MAR techniques, although the consequences of these techniques may differ (25). We repeated the analyses focusing only on a sub-sample of children conceived through IVF and ICSI (the more invasive techniques), and results were consistent. Second, our study focuses on the UK context, where the costs of MAR treatments are not subsidized resulting in MAR families being particularly selected and advantaged. Results should be generalized to other contexts with caution, especially to contexts where the subsidization is more generous (35). This study has nonetheless also considerable strengths. First, we investigate the consequences of MAR across a large number of children's development stages, providing evidence both on early childhood and mid adolescence, which are often understudied (13). Second, the richness of the data allows us to control for a large set of confounders which enable us to further understand the mechanisms underlying the results.

In this study, we show that MAR conceived children born LBW do not show any hampered cognitive development from infancy to mid adolescence. Most importantly, this group seem to have a stronger cognitive performance of NC LBW and similar or stronger than NC NLBW children. The role of family resources may play a crucial role in explaining this finding. Overall, the findings provide a reassuring picture: despite the increased risk of being born with poorer birth outcomes, MAR conceived children - regardless of their birth weight status - perform as well or better than NC children. Future research should further investigate which are the family characteristics and parental investments specific to the MAR families that may be able to ameliorate the consequences of being born with poor birth outcomes.

Acknowledgment

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Appendix - WEB TABLES

Table W1. Linear probability models regressing being excluded from the analytical sample on the variables used in the analyses

	Age 3	Age 5	Age 7	Age 11	Age 14
Mar conceived	-0.00259	-0.00782	9.94e-05	-0.0101	2.56e-05
	(-0.0252 - 0.0200)	(-0.0182 - 0.00257)	(-0.0149 - 0.0151)	(-0.0269 - 0.00663)	(-0.0437 - 0.0437)
Born LBW	0.0236	0.00868	0.00645	0.0110	-0.0190
	(0.00117 - 0.0460)	(-0.00262 - 0.0200)	(-0.00533 - 0.0182)	(-0.00378 - 0.0259)	(-0.0463 - 0.00839)
Female	-0.0186	-0.00846	-0.0104	-0.0161	-0.0196
	(-0.0280 - -0.00918)	(-0.0134 - -0.00350)	(-0.0158 - -0.00503)	(-0.0234 - -0.00875)	(-0.0340 - -0.00514)
Twin	-0.0128	0.0195	0.00167	0.0133	0.0444
	(-0.0435 - 0.0179)	(-0.00895 - 0.0479)	(-0.0199 - 0.0233)	(-0.0154 - 0.0419)	(-0.0155 - 0.104)
First Born	Reference	Reference	Reference	Reference	Reference
Second born	0.00462	0.00503	-0.000373	-0.000429	-0.00658
	(-0.00498 - 0.0142)	(-0.00076 - 0.0108)	(-0.00689 - 0.00615)	(-0.00826 - 0.0074)	(-0.0255 - 0.0124)
Third born +	0.0137	0.00507	0.00657	0.00327	-0.00235
	(-7.47e-05 - 0.0276)	(-0.00186 - 0.0120)	(-0.00249 - 0.0156)	(-0.00816 - 0.0147)	(-0.0275 - 0.0228)
Married/cohabiting	0.000322	-0.00807	-0.0112	-0.0137	-0.00545
	(-0.0161 - 0.0167)	(-0.0164 - 0.000228)	(-0.0223 - -0.000159)	(-0.0271 - -0.000397)	(-0.0300 - 0.0191)
University degree	0.0255	0.00365	0.00793	0.00821	0.0227
	(0.0160 - 0.0349)	(-0.00124 - 0.00855)	(0.00157 - 0.0143)	(-4.85e-05 - 0.0165)	(0.00800 - 0.0373)
Maternal age	-0.000579	-0.000172	-6.84e-05	7.09e-05	-0.00102
	(-0.00155 - 0.000394)	(-0.000773 - 0.000429)	(-0.000731 - 0.000594)	(-0.000676 - 0.000818)	(-0.00272 - 0.000679)
Care <12th week	0.00795	0.000699	0.000169	0.00808	0.00746
	(-0.000228 - 0.0161)	(-0.00386 - 0.00526)	(-0.00562 - 0.00596)	(0.00112 - 0.0150)	(-0.00873 - 0.0236)
Smoked in pregnancy	-0.00439	0.00238	0.00532	0.00397	0.0227
	(-0.0161 - 0.00727)	(-0.00466 - 0.00942)	(-0.00321 - 0.0138)	(-0.00665 - 0.0146)	(0.000530 - 0.0448)
White	-0.111	-0.0206	-0.00851	-0.0112	-0.00865
	(-0.139 - -0.0835)	(-0.0308 - -0.0104)	(-0.0203 - 0.00326)	(-0.0231 - 0.000647)	(-0.0351 - 0.0178)
Constant	0.154	0.0431	0.0382	0.0394	0.118
	(0.115 - 0.193)	(0.0229 - 0.0633)	(0.0173 - 0.0590)	(0.0140 - 0.0649)	(0.0606 - 0.176)
Observations	14,658	14,438	13,144	12,616	11,112
R-squared	0.032	0.007	0.005	0.007	0.007

Table W2. Distribution of LBW by mode of conception across waves. Row Percentages.

	Age 3		Age 5		Age 7		Age 11		Age 14	
	NLBW	LBW	NLBW	LBW	NLBW	LBW	NLBW	LBW	NLBW	LBW
	%		%		%		%		%	
NC	93.4	6.6	93.1	6.9	93	7	92.8	7.2	92.3	7.7
MAR	78.1	21.9	77.1	22.9	78.2	21.8	75.1	24.9	77	23

Table W3. Linear Models regressing cognitive ability (standardized) on mode of conception and birth weight status (full baseline models)

	Age 3	Age 5	Age 7	Age 11	Age 14
	BAS	BAS	BAS	BAS	BAS
	naming vocabulary	naming vocabulary	word reading	verbal similarity	word activity
NC NLBW	Reference	Reference	Reference	Reference	Reference
NC LBW	-0.272	-0.216	-0.218	-0.121	-0.105
	(-0.348 - -0.196)	(-0.306 - -0.127)	(-0.303 - -0.133)	(-0.209 - -0.0318)	(-0.208 - -0.00146)
MAR NLBW	0.181	0.324	0.345	0.226	0.226
	(0.0518 - 0.311)	(0.211 - 0.437)	(0.232 - 0.457)	(0.0934 - 0.358)	(0.0676 - 0.384)
MAR LBW	0.0215	0.213	0.163	0.00350	0.156
	(-0.198 - 0.241)	(0.00875 - 0.418)	(-0.148 - 0.474)	(-0.318 - 0.325)	(-0.205 - 0.517)
Female	0.238	0.0591	0.162	-0.0754	0.0187
	(0.201 - 0.275)	(0.0179 - 0.100)	(0.124 - 0.201)	(-0.117 - -0.0339)	(-0.0304 - 0.0678)
Multiple birth (1=twin)	-0.0968	-0.0624	-0.138	0.0411	0.121
	(-0.243 - 0.0495)	(-0.202 - 0.0776)	(-0.303 - 0.0279)	(-0.122 - 0.204)	(-0.0901 - 0.331)
Constant	-0.0437	0.0644	-0.0420	0.000497	-0.0666
	(-0.0817 - -0.00578)	(0.0229 - 0.106)	(-0.0854 - 0.00146)	(-0.0546 - 0.0556)	(-0.109 - -0.0243)
Observations	13,716	14,175	12,714	12,336	10,220
R-squared	0.021	0.007	0.013	0.004	0.002

Table W4. Linear Models regressing cognitive ability (standardized) on mode of conception and birth weight status (full adjusted models)

	Age 3 naming vocabulary	Age 5 naming vocabulary	Age 7 word reading	Age 11 verbal similarity	Age 14 word activity
NC NLBW	Reference	Reference	Reference	Reference	Reference
MAR NLBW	-0.200 (-0.267 - -0.132)	-0.118 (-0.196 - -0.040)	-0.182 (-0.266 - -0.097)	-0.093 (-0.179 - -0.008)	-0.062 (-0.161 - 0.038)
MAR LBW	-0.067 (-0.192 - 0.057)	0.046 (-0.060 - 0.153)	0.115 (0.004 - 0.226)	-0.002 (-0.130 - 0.126)	-0.028 (-0.180 - 0.123)
Female	-0.198 (-0.401 - 0.006)	0.017 (-0.159 - 0.193)	-0.037 (-0.328 - 0.253)	-0.162 (-0.472 - 0.148)	-0.023 (-0.386 - 0.340)
Multiple birth (1= twin)	0.248 (0.214 - 0.282)	0.065 (0.028 - 0.102)	0.159 (0.124 - 0.194)	-0.075 (-0.115 - -0.035)	0.015 (-0.031 - 0.061)
First Born	-0.156 (-0.281 - -0.030)	-0.148 (-0.279 - -0.017)	-0.190 (-0.341 - -0.038)	-0.011 (-0.170 - 0.149)	0.064 (-0.131 - 0.259)
Married / cohabiting	0.330 (0.287 - 0.374)	0.295 (0.259 - 0.331)	0.238 (0.189 - 0.287)	0.225 (0.178 - 0.271)	0.184 (0.129 - 0.239)
University degree	0.168 (0.115 - 0.220)	0.111 (0.054 - 0.167)	0.197 (0.134 - 0.259)	0.101 (0.027 - 0.174)	0.169 (0.092 - 0.245)
Maternal age	-0.288 (-0.332 - -0.243)	-0.405 (-0.449 - -0.361)	-0.339 (-0.383 - -0.295)	-0.336 (-0.387 - -0.284)	-0.422 (-0.479 - -0.365)
Care <12th week	0.019 (0.016 - 0.023)	0.022 (0.019 - 0.026)	0.019 (0.015 - 0.024)	0.020 (0.016 - 0.024)	0.020 (0.016 - 0.025)
Smoked in pregnancy	-0.016 (-0.050 - 0.018)	-0.027 (-0.060 - 0.005)	-0.003 (-0.041 - 0.035)	-0.036 (-0.076 - 0.004)	0.008 (-0.036 - 0.052)
White	-0.084 (-0.125 - -0.044)	-0.050 (-0.095 - -0.006)	-0.210 (-0.263 - -0.157)	-0.077 (-0.138 - -0.016)	-0.048 (-0.104 - 0.007)
Constant	0.886 (0.785 - 0.987)	0.811 (0.713 - 0.909)	-0.122 (-0.205 - -0.039)	0.085 (-0.053 - 0.222)	0.108 (0.046 - 0.170)
	-1.479 (-1.629 - -1.329)	-1.242 (-1.400 - -1.083)	-0.483 (-0.650 - -0.317)	-0.546 (-0.766 - -0.326)	-0.634 (-0.825 - -0.442)
Observations	13,716	14,175	12,714	12,336	10,220
R-squared	0.179	0.179	0.108	0.074	0.092

Table W5. Linear Models regressing cognitive ability (standardized) on mode of conception (ICSI/IVF only) and birth weight status

	Age 3	Age 5	Age 7	Age 11	Age 14
	BAS	BAS	BAS	BAS	BAS
	naming vocabulary	naming vocabulary	word reading	verbal similarity	word activity
NC NLBW	Reference	Reference	Reference	Reference	Reference
NC LBW	-0.260	-0.205	-0.217	-0.119	-0.0951
	(-0.336 - -0.184)	(-0.293 - -0.116)	(-0.301 - -0.134)	(-0.206 - -0.0319)	(-0.198 - 0.00806)
MAR (ICSI/IVF) NLBW	0.321	0.353	0.400	0.0918	0.0598
	(0.111 - 0.532)	(0.146 - 0.560)	(0.199 - 0.601)	(-0.189 - 0.373)	(-0.187 - 0.306)
MAR (ICSI/IVF) LBW	-0.0691	0.167	0.150	-0.176	-0.0610
	(-0.297 - 0.159)	(-0.0813 - 0.416)	(-0.277 - 0.578)	(-0.647 - 0.296)	(-0.471 - 0.349)
Female	0.238	0.0597	0.163	-0.0741	0.0194
	(0.201 - 0.275)	(0.0186 - 0.101)	(0.124 - 0.201)	(-0.116 - -0.032)	(-0.0291 - 0.067)
Multiple birth (1=twin)	-0.0831	-0.0302	-0.105	0.0722	0.141
	(-0.230 - 0.0637)	(-0.170 - 0.109)	(-0.272 - 0.0612)	(-0.089 - 0.233)	(-0.0659 - 0.348)
Constant	-0.0414	0.0679	-0.0386	0.00401	-0.0641
	(-0.079 - -0.003)	(0.0267 - 0.109)	(-0.0821 - 0.00497)	(-0.051 - 0.059)	(-0.107 - -0.0217)
Observations	13,713	14,174	12,715	12,336	10,220
R-squared	0.021	0.005	0.012	0.003	0.001

Table W6. Linear Models regressing cognitive ability (standardized) on mode of conception and birth weight status using only observation present in every wave of the survey

	Age 3	Age 5	Age 7	Age 11	Age 14
	BAS	BAS	BAS	BAS	BAS
	naming vocabulary	naming vocabulary	word reading	verbal similarity	word activity
NC NLBW	Reference	Reference	Reference	Reference	Reference
NC LBW	-0.235	-0.199	-0.190	-0.172	-0.105
	(-0.342 - -0.129)	(-0.321 - -0.0777)	(-0.301 - -0.0792)	(-0.287 - -0.0581)	(-0.208 - -0.00146)
MAR NLBW	0.264	0.356	0.362	0.222	0.226
	(0.107 - 0.421)	(0.214 - 0.498)	(0.227 - 0.497)	(0.0852 - 0.359)	(0.0676 - 0.384)
MAR LBW	0.0747	0.208	0.181	0.0413	0.156
	(-0.188 - 0.338)	(-0.0272 - 0.443)	(-0.213 - 0.576)	(-0.225 - 0.308)	(-0.205 - 0.517)
Female	0.220	0.0182	0.145	-0.0998	0.0187
	(0.172 - 0.269)	(-0.0368 - 0.0733)	(0.0949 - 0.195)	(-0.148 - -0.0512)	(-0.0304 - 0.0678)
Multiple birth (1=twin)	-0.151	-0.0532	-0.140	0.0884	0.121
	(-0.312 - 0.00909)	(-0.250 - 0.144)	(-0.343 - 0.0628)	(-0.108 - 0.285)	(-0.0901 - 0.331)
Constant	-0.0844	0.0414	-0.0284	0.0401	-0.0666
	(-0.129 - -0.0402)	(-0.00893 - 0.0917)	(-0.0758 - 0.0190)	(-0.0189 - 0.0990)	(-0.109 - -0.0243)
Observations	8,884	9,573	9,222	9,604	10,220
R-squared	0.019	0.006	0.011	0.006	0.002

Table W7. Linear Models regressing cognitive ability (standardized) on mode of conception and small for gestational age status

	Age 3 BAS naming vocabulary	Age 5 BAS naming vocabulary	Age 7 BAS word reading	Age 11 BAS verbal similarity	Age 14 BAS word activity
NC Non-small for gestational age (NSGA)	Reference	Reference	Reference	Reference	Reference
NC small for gestational age (SGA)	-0.277	-0.307	-0.160	-0.192	-0.150
	(-0.342 - -0.211)	(-0.377 - -0.236)	(-0.226 - -0.0931)	(-0.273 - -0.112)	(-0.224 - -0.0764)
MAR NSGA	0.153	0.284	0.330	0.220	0.214
	(0.0300 - 0.276)	(0.173 - 0.395)	(0.218 - 0.443)	(0.0940 - 0.346)	(0.0566 - 0.370)
MAR SGA	0.0634	0.202	0.220	-0.107	0.127
	(-0.196 - 0.323)	(-0.00136 - 0.405)	(-0.106 - 0.547)	(-0.465 - 0.251)	(-0.210 - 0.464)
Female	0.239	0.0619	0.167	-0.0709	0.0195
	(0.203 - 0.274)	(0.0211 - 0.103)	(0.128 - 0.205)	(-0.113 - -0.0290)	(-0.0294 - 0.0685)
Multiple birth (1=twin)	-0.153	-0.0714	-0.189	0.0337	0.113
	(-0.298 - -0.00723)	(-0.205 - 0.0627)	(-0.348 - -0.0290)	(-0.119 - 0.186)	(-0.0905 - 0.317)
Constant	-0.0287	0.0858	-0.0388	0.0120	-0.0551
	(-0.0660 - 0.00860)	(0.0457 - 0.126)	(-0.0834 - 0.00576)	(-0.0418 - 0.0658)	(-0.0984 - -0.0119)
Observations	13,607	14,041	12,595	12,216	10,125
R-squared	0.023	0.013	0.013	0.007	0.004

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