UCD GEARY INSTITUTE DISCUSSION PAPER SERIES

The causal effect of breastfeeding on children's cognitive development: A quasi-experimental design

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ABSTRACT

Objective: To estimate the causal effect of breastfeeding on children's cognitive skills as measured at ages 3, 5, 7 and 11.

Design: An instrumental variable (IV) strategy which provides a correction method for dealing with selection bias. Standard linear regression models are compared to two-stage least squares models to test for the presence of endogeneity. The consistency of the results across multiple sources is also tested using data from two prospective longitudinal studies collected 40-years apart.

Setting: The 1958 National Child Development Study (NCDS) and the 2000 UK Millennium Cohort Study (MCS).

Participants: Data on 11,792 (age 3) and 9117 (age 5) children in MCS and 4923 (age 7 and 11) children in NCDS.

Main outcome measures: Cognitive ability is measured by the Bracken School Readiness Assessment (age 3); Foundation Stage Profile (age 5); and tests of general ability including mathematics, comprehension, verbal and non-verbal skills (ages 7 and 11).

Results: The duration of breastfeeding has a small, but significant, effect on children's cognitive skills in the linear regression models at ages 3, 5, 7 and 11, but no effect in the IV models. However, in all cases, the hypothesis that breastfeeding is endogenous is rejected, indicating that the results of the linear regressions are valid.

Conclusion: The relationship between breastfeeding and cognitive ability is not driven by selection bias once a rich set of confounders are included. IV methods can therefore be used to test for the presence of selection bias and are a useful alternative for identifying causal relationships when randomised control trials are not feasible. Showing that the size of the effect is similar for two cohorts born over 40 years apart, and using different measures of ability, are further indications that the relationship between breastfeeding and cognitive ability is not a statistical artefact.

Introduction

The incidence and duration of breastfeeding has long been associated with improvements in children's neurodevelopment[1,2], with breastfed children typically displaying higher scores on cognitive tests than children who were never breastfed. Meta-analyses have identified the size of this effect to be between 2-5 IQ points.[3,4] Explanations underlying the relationship include biochemical, genetic and behavioural theories.[5] Yet much of this evidence is based on observational data and recent studies have questioned the causal nature of this relationship,[6] arguing that the association may be driven by selection bias due to confounding factors that may influence both breastfeeding practices and other parental investments in the child's development.[7] The problem is commonly referred to as endogeneity. The primary method of addressing this issue in the medical and psychological literature is to include a host of potentially confounding factors. Several studies demonstrate that the link is significantly reduced when one controls for relevant factors such as maternal intelligence and the quality of the home environment.[8] Studies which directly address the selection issue using either experimental or quasi-experimental methods typically identify small significant effects. For example, a large-scale cluster-randomised breastfeeding intervention in Belarus finds that breastfeeding increases IQ by six points.[9] Quasi-experimental methods such as sibling-difference estimation can also minimise selection bias by controlling for unobserved family characteristics that affect both siblings. Two recent studies applying this method, while controlling for maternal IQ, find diverging results.[10,11]

This study uses an alternative approach to estimate the effect of breastfeeding on cognitive ability, which has occasionally been applied in epidemiology but is commonly used in econometrics, called Instrumental Variable estimation (IV).[12] IV requires the use of one or more exogenous variables (instruments) which are correlated with the potentially endogenous variable (breastfeeding in this case), but which are not correlated with the outcome of interest (cognitive ability). The instruments are used to remove the endogenous variation of the variable in question. The instruments mimic the random assignment of treatment status (i.e. whether breastfed or not) and hence IV is a quasi-experimental design. An important advantage of this approach is that one can test for the presence of endogeneity/selection bias by comparing the IV estimates with the conventional least squares estimates.[13] This method has important advantages over many of the existing studies which attempt to deal with endogeneity by including a large number of potential confounders. This approach, which deals with "selection on observables", is only valid if one includes all relevant confounders.

IV addresses "selection on unobservables", therefore even if the source of the endogeneity is unknown, it is still possible to derive consistent estimates of the parameters of interests. It shares this with estimates from randomized controlled trials. While sibling difference models can eliminate any bias due to confounding under the assumption that these are common to each sibling, it cannot be assumed to eliminate endogeneity bias.

This study using an IV strategy to identify the causal effect of breastfeeding on children's cognitive skills as measured at ages 3, 5, 7 and 11. We estimate standard linear regression models as typically used in the literature and two-stage least squares models which control for selection bias. A comparison of the models allows us to test for the presence of endogeneity. To test for the consistency of the results across multiple sources, we use data from two prospective longitudinal studies collected forty-years apart.

Method

Data

The Millennium Cohort Study (MCS) is a longitudinal study of 18,819 children who were born in the UK between 2000-2002. The sample was clustered geographically by electoral wards and was constructed to over-represent areas of disadvantage, communities with high concentrations of ethnic minorities (England only), and the three smaller countries of the UK. The sample was identified through Child Benefit records provided by the Department of Social Security. The overall response rate was 72%.[14] Details of the MCS are published elsewhere.[15] This study utilises the first three waves of the survey conducted at nine months, three and five years old. A number of studies have used the MCS data to examine ethnic[16] and social class[17] differences in breastfeeding practices, the impact of breastfeeding on gross and fine motor skills,[18] and the impact of maternal employment on breastfeeding initiation[19] and duration[20].

The second data source is the National Child Development Study (NCDS) which is a longitudinal study of all persons living in Great Britain who were born between the 3rd and 9th of March 1958. The 1958 perinatal mortality survey comprised of 17,500 babies who were followed in 6 subsequent waves at ages 7, 11, 16, 23, 33, 42 and 46. Details of the study can be found elsewhere.[21] This analysis uses data from the first two waves which comprised of interviews with children, parents, schools and reports from a medical examiner.

Measures

Cognitive Scores

Cognitive development at age 3 in the MCS is measured using the Bracken Basic Concept Scale-Revised (BBCS-R) School Readiness Assessment. Six of the eleven sub-tests of the BBCS-R were used to assess the children's knowledge of colours, letter identification, numbers/counting, sizes, comparisons and shape recognition.[22] The assessment is conducted in the home by a trained interviewer. The Bracken scale has been validated and correlates well with other standard measures of cognitive ability, such as the PPVT-R (r=0.74 to 0.88). It has also been used to predict future academic achievement.[23] The normed standardised composite score is used which represents the percentage of children in the sample who ranked at or below the child's score. The BBCS-R is available for 13,651 children. Cognitive development at age 5 is measured using three of the six domains from the Foundation Stage Profile (FSP) which is administered at school. The first principle component of the communication, language and literacy domain, the mathematical development domain, and the knowledge and understanding of the world domain is used. The remaining non-cognitive measures of the FSP, including the child's social and emotional development, physical development and creative development, are not included. The FSP is available for 11,708 children and there is a high intercorrelation between the three domains ranging from r=0.726 (p<0.001) to r=0.851 (p<0.001). There is also a high correlation between the age 3 and 5 scores (r=0.446 p<0.000).

Cognitive development in the NCDS is measured using tests of general ability administered at school at ages 7 and 11.[24,25,26] The age 7 measure is based on the first principal component from the mathematical, verbal and drawing sub-domains. The intercorrelations between these three domains range from r=0.308 (p<0.001) to r=0.50 (p<0.001). The age 11 measure is based on the first principal component from the mathematics, comprehension, verbal and non-verbal sub-domains. The intercorrelations range from r=0.629 (p<0.001) to r=0.975 (p<0.001). The age 7 cognitive scores are available for 14497 children and age 11 scores for 14,127 children. The correlation between the early and later scores is (r=0.723 p<0.001).

For comparison purposes all four cognitive measures are standardised to have a mean of 100 and a standard deviation of 15.

Breastfeeding

MCS: Duration of exclusive breastfeeding is defined as the number of weeks the child was exclusively fed breastmilk from birth, excluding other forms of supplementary formula or solids. Duration of non-exclusive breastfeeding is defined as the number of weeks the child was fed breast milk. While this data were collected retrospectively at nine months postpartum, the reliability and validity of breastfeeding recall has been demonstrated in other studies.[27] In the age 3 and age 5 estimation samples 67.9% (n=8004) and 69.8% (n=6362) initiated breastfeeding respectively and the mean duration of breastfeeding for those who do initiate was 8.9 (SD=7.4) and 8 (SD=7.4) weeks of exclusive breastfeeding respectively, and 17.2 (SD=15.5) weeks of non-exclusive breastfeeding for the age 3 and 5 samples.

NCDS: Duration of exclusive breastfeeding is not available in the NCDS data. Therefore a binary variable indicating whether the child was breastfed for at least a month is used. In the sample, 46% (SD=0.50) of children were breastfed.

Confounders

The advantage of the cohort data is that it provides a wealth of information on child and family characteristics. The *MSC* confounders include gender (base category is male), age in months, ethnicity (base category is white), birth weight in kilograms, number of days of gestation, and the child's rank by age among his/her natural siblings (birth order). Maternal characteristics include age at the time of the child's birth, marital status at the time of birth (base category is single), maternal education, measured based on the highest academic qualification attained, maternal stress as measured by the Malaise Inventory questionnaire[28] at nine months, and an indicator of whether the mother smoked during pregnancy. Family characteristics include a measure of the quality of the home environment as measured by the Home Observation for Measurement of the Environment (HOME)[29] and a measure of parental investment based on the first two factors from a principle component analysis including items related to the how often someone in the home teaches the child to learn the alphabet, count, sing, draw, play sport, and how often someone reads to the child and takes them to the library. A limitation of this data is that maternal/paternal intelligence is not available, therefore a number of factors associated with parental intelligence including mother's and father's height[30] and a binary indicator of whether the mother experiences literacy difficulties, is controlled for.

While such a rich set of factors are not available for the NCDS data, the following factors are included: gender (base category is male), birth weight in kilograms, number of

weeks of gestation, birth order; maternal and paternal age at birth, maternal and paternal education as measured by the school-leaving age, maternal and paternal height, a measure of the number of amenities in the home such as use of bathroom, indoor lavatory, hot water supply, and a measure of parental time inputs based on the frequency with which either the mother and father takes the child for outings or reads to them.

Tables 1 and 2 report the descriptive statistics for the dependent variables and the confounding factors, by breastfeeding status. The association of each is shown as an odds ratio.

Missing Data

Due to the relatively high frequency of missing data for father's height and the HOME score in the MSC study, two binary variable indicating the missing values in each variable are included in the analysis. For those datasets casewise deletion is used which results in final estimation sample sizes of 11,792 (age 3) and 9117 (age 5) in MSC and 5770 (age 7 and 11) children in NCDS. Alternative multiple imputation methods to account for missing data were experimented with which did not substantially change the findings.

Statistical methods

Both ordinary least square regression (OLS) and instrumental variable regression (IV) are used as the outcomes of interest (measures of cognitive ability) are continuous. IV is used to deal with the possible endogeneity of the incidence and duration of breastfeeding or *selection on unobservables*. This approach has been used increasingly in epidemiology to estimate causal effects in the absence of a randomized assignment of the treatment[31,32,33,34]. This requires identifying one or more variables which predict breastfeeding but which do not directly affect the outcome of interest. Intuitively, one might think of the instrumental variables as mimicking the exogenous assignment of individuals to different levels of treatment. A few studies have used IV to deal with the endogeneity of breastfeeding in relation to child health outcomes with a variety of instrumental variables, however none to date have studied cognitive outcomes[35,36,37].

Instrumental Variable: Caesarean sections

The instrumental variables used here are two binary variables indicating whether the baby was born either by elective or by emergency caesarean section. There is considerable evidence that delivery by caesarean section reduces the probability of the initiation of

breastfeeding.[38,39,40,41], and can shorten the duration of breastfeeding for mothers who do initiate[42,43]. An often cited explanation for this is that caesarean sections may lead to a delay in the initiation of early skin-to-skin contact (SSC)[44] which may occur for both practical and medical purposes. Early SSC promotes the release of oxytocin through sensory stimulation causing the breast temperature to rise, providing warmth for the baby and therefore aiding successful breastfeeding.[45] In addition, newborns have heightened odour cues directly following delivery when placed in SSC which helps them locate the nipple and begin suckling within one hour post-delivery.[46] Caesarean sections can act as a barrier to early SSC, with one study citing that early SSC is initiated for 11% of women who had a caesarean section, compared to 81% of women who had a normal delivery.[47] This delay in SSC is associated with a decrease in the incidence of breastfeeding. A meta-review of 30 experimental and quasi-experimental studies finds that early SSC is associated with higher rates of breastfeeding initiation and duration[48], therefore identifying a potential channel through which caesarean section can affect breastfeeding. Other explanations for the negative association between caesarean sections are breastfeeding include abdominal soreness and perceived lack of breast milk.[49,50]

In order for an instrumental variable to be valid, it must be correlated with the variable of interest i.e. breastfeeding, but uncorrelated with the dependent variable i.e. cognitive ability. There is no evidence that c-sections affect a child's cognitive ability. A study of 27,000 infants, found no correlation between mode of delivery and children's Stanford-Binet IQ scores at age 4[51], while a smaller study found that caesarian delivery was not a significant predicator of first grade math or verbal scores[52]. There is also evidence that caesarean section has no impact on intelligence in adulthood[53] and that relationship is maintained once one controls for breastfeeding[54,55].

In the MCS estimation sample 9.55% (SD=0.29) women had an elective caesarean section and 12.5% (SD=0.33) had an emergency caesarean section. The corresponding figures in the NCDS sample are 1.3% (SD=0.11) for both groups. The IV models were estimated using elective and emergency caesarean section separately and combined, however the results were not significantly different, therefore both are included in the presented results.

Statistical Model

The model can be written as:

$$\text{Cognitive Ability} = \beta_1 \text{Breastfeeding} + \beta_2 X + \varepsilon \quad (1)$$
$$\text{Breastfeeding} = \gamma_1 \text{C-Section} + \gamma_2 X + \eta \quad (2)$$

The parameter of interest is β_1. X is a vector of controls (including a constant) with β_2 the corresponding vector of parameters. If one ignores the endogeneity of breastfeeding then equation (1) can be estimated directly by ordinary least squares. If breastfeeding is endogenous (which would imply it is correlated with ε) the parameters of (1), if estimated by OLS, will be biased and inconsistent. If not, the system can be estimated simultaneously. IV is also known as Two Stage Least Squares. The first stage (2) is estimated and the predicted values for breastfeeding are calculated. In the second stage these are used to replace the actual values for breastfeeding in (1) which is then estimated as normal. For convenience, (2) is written with one instrumental variable but in practice we will use two. Given suitable instrumental variables, IV provides consistent estimates of the parameters. The IV estimates will be less efficient in general because of the additional uncertainty introduced by estimating (2). For this reason IV should not be used unless it is necessary. It is possible to test for this using the Durbin-Wu-Hausman test[56]. Essentially this tests whether OLS estimates of (1) are mis-specified due to endogeneity by comparing them with the corresponding IV estimates. If one can reject mis-specification then it is appropriate to use the more efficient OLS estimates i.e. one is concluding that, in this case, breastfeeding is not endogenous. If one cannot reject mis-specification, then one should select the IV estimates.

A range of other tests can be utilised when applying IV. To use IV one needs at least as many instruments as there are endogenous variables, otherwise the model is "under-identified". Even if one has more instruments available than are required, the practise is to use them since it will allow one to better predict the endogenous variable. In such cases the model is "over-identified" and it is possible to test whether the over-identifying restrictions are satisfied using the Sargan/Hansen J test – this is also known as an "instrument validity test".[57] A failure of this test means that at least one of the instruments is invalid and hence those estimates would not be consistent. It should also be noted that the desirable feature of IV, providing consistent estimates, is a large sample property and the estimator is still biased in finite samples. Furthermore the advantage of using IV depends on there being a strong correlation between the instruments and the endogenous variable. If the correlation is low

then the estimated coefficients in IV can be badly biased towards OLS even if one has a very large sample[58] while the estimated standard errors will also be biased[59]. A common test for the presence of weak instruments is the F test for the joint significance of the instruments in the first stage equation. As a rule of thumb a value greater than 10 is considered satisfactory[60]. Applications of IV in health sciences have not, in general, utilised these tests so it is very difficult to evaluate the reliability of such IV estimates.

Results

Tables 3 and 4 reports the effect of breastfeeding on children's cognitive ability at age 3 and age 5 respectively in the MSC. Tables 5 and 6 reports the effect of breastfeeding on children's cognitive ability at age 7 and age 11 respectively in the NCDS. For each table, the linear regression model is reported in the first column and the two-stage least squares model is reported in the second two columns. The linear regression, which does not control for the potential endogeneity, show that breastfeeding is significantly associated with cognitive ability at ages 3, 5, 7 and 11, when adjusted for all confounders simultaneously. For the MCS, the fully adjusted effect is that each week of exclusive breastfeeding is associated with an increase in cognitive ability by 0.07 (SE=0.02 $p<0.001$) at age 3 and 0.04 (SE=0.02 $p<0.05$) at age 5. This translates into four weeks of breastfeeding being associated with an increase in ability of 1.9% and 1% of a standard deviation respectively. For the NCDS, being breastfed is associated with an increase in ability by 1.37 (SE=0.39 $p<0.001$) at age 7 and 1.61 (SE=0.37 $p<0.001$) at age 11. Therefore breastfed for more than one month is associated with an increase in ability of 9.1% and 10.7% of a standard deviation respectively. The majority of the confounders are statistically significant, with gender, birth order, mother's age, parental education and social class, and parental investment consistently making significant contributions across both datasets and time periods.

The first stage results from the two-stage least squares model are reported in the second columns of each table. The instrumental variables – emergency and elective c-section – are negatively associated with the duration of breastfeeding in the MCS models (β=-0.92, SE=0.19 $p<0.001$ and β=-0.90 SE=0.22 $p<0.001$ respectively in age 3 model; β=-1.21, SE=0.21 $p<0.001$ and β=-1.31 SE=0.25 $p<0.001$ respectively in age 5 model) and the incidence of breastfeeding in the NCDS models (β=-24, SE=0.05 $p<0.001$ and β=-0.13 SE=0.06 $p<0.028$ respectively in age 7 and age 11 models). The second stage models

reported in column 3 show that breastfeeding is no longer significantly associated with children's cognitive ability in the age 3 ($\beta=0.28$, SE=0.32 p<0.392, 5 ($\beta=0.46$, SE=0.28 p<0.098), 7 ($\beta=-0.62$, SE=6.24 p<0.920) and 11 ($\beta=-3.41$, SE=5.83 p<0.558) models.

The over-identification tests reported at the end of the tables show that, in all cases, one cannot reject the hypotheses that the instruments are valid. The reported test for weak instruments is greater than 10 in all models suggesting that the instruments are not weak. The non-significance of the Durbin-Wu-Hausman (DWH) tests for the age 3 (DWH=0.436 p=0.509), 5 (DWH=2.554 p=0.110), 7 (DWH=0.130 p=0.718) and 11 (DWH=0.731 p=0.393) models imply that there is no evidence that the OLS models are mis-specified (for any reason) and hence the results of the OLS models should be used as they are more efficient than the IV estimates.

Discussion

This paper adds to the long established debate on the causal nature of the relationship between breastfeeding and cognitive ability. The ordinary least squares results show that breastfeeding has a small, but statistically significant effect, on children's cognitive ability at age 3, 5, 7 and 11, with four weeks of breastfeeding increasing cognitive scores by about 1-2% of a standard deviation, and being breastfed for one month of more increasing cognitive scores by about 10% of a standard deviation. The IV results, on the other hand, suggest that there is no association between breastfeeding and children's cognitive scores. The instruments used, emergency and elective caesarean sections, reduce the incidence of breastfeeding, and are shown to be valid. However the statistical test for endogeneity shows that the relationship between breastfeeding and cognitive ability is not endogenous and hence the OLS results, which are both more efficient and consistent, should be used. Caution is therefore advised in interpreting the results of any IV model without the accompanying endogeneity tests. The IV estimates should only be used when the relationship between two variables is endogenous, however it is only possible to test for the presence of endogeneity test ex post, therefore conducting the IV analysis, and identifying suitable instruments, was necessary. Overall the analysis suggests that the relationship between breastfeeding and cognitive ability is not driven by selection bias and that relying on standard linear regressions is appropriate once a suitably rich set of confounders are included.

As it is not generally considered ethical to randomise children into breastfeeding and infant feeding, most research in this area is based on observational data that cannot distinguish correlation from causality. The observed association between breastfeeding and children's IQ may be driven by unobservable characteristics of the family such as self-efficacy, conscientiousness, etc. that may result in families to both breastfeeding and providing a cognitively stimulating environment for their child. Therefore any observed relationship between breastfeeding and cognitive scores may be a result of such residual confounding. The instrumental variable method used here provides a non-experimental method for identifying causality and testing for such confounding, when experimentation is not possible. A significant strength of the study is that it demonstrates the relationship between breastfeeding and cognitive ability is stable, both across time and at different children's ages. While the breastfeeding measures used in the two datasets are not equivalent, re-estimating the MCS results using a binary indicator for being breastfeed for more than one month identifies an effect of 9.3% ($\beta=1.40$, SE=0.26 p<0.001) and 7.0% ($\beta=1.05$, SE=0.30 p<0.001) of a standard deviation at ages 3 and 5 respectively, which is equivalent to the NCDS results of 9-10%. Showing that the size of the effect is similar for two cohorts born over 40 years apart is a further indication that the relationship between breastfeeding and cognitive ability is not a statistical artefact. In addition, the effects are also similar across ages, with slightly stronger effects at the earlier ages. A further strength of the study is that the result are replicated using multiple measures of cognitive ability.

A weakness of the study is the absence of a measure of maternal intelligence in both datasets. While a number of factors, such as education, literacy difficulties and height, which are shown to be correlated with intelligence, are controlled for it, is still possible that the results of the OLS models are biased upwards. While some studies find that the relationship between breastfeeding and IQ operates through maternal intelligence[61,62], other studies find that this is not the case, and that including parental IQ reduces the size of the effect, yet it still has a statistically significant impact on child cognitive ability[63,64,65]. In addition, the IV method used here deals with unobserved confounders such that the absence of any particular variable, such as maternal intelligence, should not lead to inconsistent estimates. Another limitation of the study is the relatively high proportion of missing data across both datasets which substantially reduces the estimation sample sizes. There is some evidence the dropout rate within the NCDS is higher for males, those with low educational attainment and less stable employment patterns and those living in disadvantaged circumstances[66] and thus it is possible that our results may be subject to attrition bias. Yet, re-estimating the analysis using

multiple imputation methods yields similar results suggesting that this is not the case. The study also relies on retrospective data collected when the child was 9 months (MCS) and 7 years (NDCS), therefore it is possible the measures of breastfeeding are subject to recall bias, particularly in the NCDS data.

The results are consistent with previous findings from experimental[67] and quasi-experimental[68] studies that control for maternal intelligence, which find that breastfeeding has a small but significant effect on children's cognitive ability. This is in line with other studies using sibling difference models to identify a casual effect between breastfeeding and later educational achievement[69]. The method of IV deals with *selection on unobservables* where one or more covariates is correlated with the disturbance term. This can be caused either by omitted variables or simultaneity. Much of the literature on breastfeeding has addressed this problem by seeking to include rich set of confounders or by using sibling differences methods. These methods only address *selection on observables*. The IV method discussed here is not subject to these constraints. That said, IV is not a panacea and careful testing is required for its appropriate use.

While the purpose of this study if not to identify the likely explanations for the observed relationship between breastfeeding and cognitive ability, other studies have suggested a number of potential mechanisms. For example, the act of breastfeeding itself may affect maternal behaviour[70] both directly and indirectly. Infant sucking releases prolactin and oxytocin in the mother, which are thought to contribute to mothering behaviour which enhances the mother-child interaction, thus promoting neurodevelopment[71]. In addition, there is epigenetic evidence of the positive effects of licking and grooming by mother rats of their pups on neurocognitive development[72], which suggest that the physical act of breastfeeding might lead to permanent physiological changes. Specifically, there is further evidence that the association between breastfeeding and IQ is moderated by genetic variation in FADS2 which controls dietary fatty acid pathways; an effect which was replicated in two birth cohort studies and controlled for maternal cognitive ability[73]. An experimental study finds that breast milk mediates IQ through its impact on brain growth and white matter growth in particular[74]. In addition, several components of breast milk, such as long chain polyunsaturated fatty acids (LCPUFA),[75] growth factors,[76] and cholesterol choline, and fat soluble vitamins[77], can have a direct effect on neurodevelopment and subsequently IQ[78]. However definite research identifying the precise causal mechanisms of these relationship is lacking and a review found that formula milk supplemented with LCPUFA had no positive effects on the physical, visual, or cognitive development of term children[79]. This is supported

by recent findings that the relationship between breastfeeding and IQ is mediated by maternal confounding factors rather than LCPUFA[80]. The literature on the mechanisms linking breastfeeding to IQ is therefore controversial and further research identifying the causal mechanisms is required.

Table 1 MCS: Association of dependent variable and potential confounders by breastfeeding status

	Not breastfed		Breastfed >1 month		Odds ratio (95% CIs)	P value
	Mean (SD) or %	N	Mean (SD) or %	N		
Cognitive ability age 3	97.69 (14.58)	7103	103.12 (14.82)	5968	1.03 (1.02 to 1.03)	<0.001
Cognitive ability age 5	98.43 (15.56)	6039	102.24 (13.87)	5163	1.02 (1.01 to 1.02)	<0.001
Age 3 (in months)	37.81 (2.61)	7975	37.60 (2.45)	6686	0.97 (0.96 to 0.98)	<0.000
Age 5 (in months)	63.53 (3.03)	7863	63.49 (3.00)	6583	0.99 (0.98 to 1.00)	0.358
Birth Order	1.97 (1.14)	10316	1.92 (1.08)	7925	0.96 (0.94 to 0.99)	<0.005
Birth Weight (kilos)	3.33 (0.58)	10310	3.39 (0.58)	7912	1.21 (1.15 to 1.27)	<0.001
Days of gestation	276.80 (13.95)	10215	277.73 (13.79)	7846	1.00 (1.00 to 1.01)	<0.001
Mother's age at child's birth	26.96 (5.96)	10311	30.01 (5.48)	7921	1.10 (1.09 to 1.10)	<0.001
Mother's depression score	1.82 (1.88)	10010	1.55 (1.67)	7609	0.92 (0.90 to 0.94)	<0.001
Mother's height	163.22 (6.95)	10145	163.88 (7.06)	7820	1.01 (1.01 to 1.02)	<0.001
Father's height	177.43 (7.53)	6850	178.15 (7.43)	6281	1.01 (1.01 to 1.02)	<0.001
HOME score	12.17 (1.64)	6528	12.65 (1.27)	5426	1.26 (1.22 to 1.29)	<0.001
Parental investment 1	0.008 (0.99)	7903	0.005 (0.99)	6644	1.01 (0.98 to 1.05)	0.428
Parental investment 2	0.17 (0.97)	7906	0.23 (0.98)	6644	1.53 (1.47 to 1.58)	<0.001
Emergency c-section	12%	10315	13%	7925	1.05 (0.96 to 1.15)	0.271
Elective c-section	10%	10315	9%	7925	0.88 (0.80 to 0.98)	<0.05
Female	48%	10316	49%	7925	1.04 (0.98 to 1.10)	0.189
Ethnicity						
Mixed	2%	219	4%	324	2.22 (1.86 to 2.64)	<0.001
Indian	2%	170	4%	287	2.53 (2.09 to 3.07)	<0.001
Pakistani/Bangladeshi	6%	645	8%	612	1.42 (1.27 to 1.60)	<0.001
Black	2%	168	6%	484	4.32 (3.61 to 5.16)	<0.001
Chinese or other ethnicity	1%	77	2%	189	3.68 (2.82 to 4.81)	<0.001
Mother single at birth	13%	10282	6%	7907	0.42 (0.38 to 0.47)	<0.001
Ever smoked when pregnant	40%	10255	19%	7899	0.35 (0.32 to 0.37)	<0.001
Mother's education						
O level/GCSE grades A-C	40%	3851	31%	2243	1.97 (1.81 to 2.15)	<0.001
A/ AS/ S Levels	8%	777	13%	915	3.98 (3.54 to 4.48)	<0.001
Diplomas in Higher Educ.	7%	668	12%	854	4.32 (3.83 to 4.89)	<0.001
First Degree	6%	581	23%	1668	9.71 (8.64 to 10.91)	<0.001
Higher Degree	1%	133	7%	476	12.10 (9.87 to 14.84)	<0.001
Mother's literacy difficulties	12%	10297	8%	7913	0.68 (0.61 to 0.75)	<0.001

Table 2 NCDS: Association of dependent variable and potential confounders by breastfeeding status

	Not breastfed		Breastfed >1 month		Odds ratio (95% CIs)	P value
	Mean (SD) or %	N	Mean (SD) or %	N		
Cognitive ability age 7	98.92 (15.14)	7753	101.86 (14.35)	5926	1.01 (1.01- 1.01)	<0.001
Cognitive ability age 11	98.79 (14.80)	6988	102.51 (14.62)	5470	1.02 (1.01-1.02)	<0.001
Birth Order	2.25 (1.48)	1467	2.11 (1.36)	4440	0.93 (0.91-0.96)	<0.001
Birth Weight (kilos)	3.31 (0.54)	7665	3.38 (0.49)	5894	1.30 (1.22-1.39)	<0.001
Days of gestation	280.29 (13.1)	7065	281.84 (11.1)	5528	1.01 (1.01-1.01)	<0.001
Mother's age at child's birth	27.62 (5.78)	7933	27.42 (5.52)	6078	0.99 (0.99-1.00)	0.042
Father's age at child's birth	30.69 (6.40)	7608	30.50 (6.29)	5963	0.99 (0.99-1.00)	0.087
Mother's age left education	14.81(1.68)	5310	15.30(2.26)	4237	1.13(1.11-1.16)	<0.001
Father's age left education	14.83(1.34)	5493	15.25(1.81)	4357	1.19(1.16-1.22)	<0.001
Mother's height	161.70 (6.53)	6720	162.43 (6.44)	5306	1.02 (1.01-1.02)	<0.001
Father's height	174.05 (7.55)	6542	175.05 (7.32)	5206	1.02 (1.01-1.02)	<0.001
Household amenities	2.60 (0.89)	8121	2.67 (0.81)	6245	1.10 (1.06-1.14)	<0.001
Mother's parental investment	3.11 (0.96)	8090	3.23 (0.90)	6242	1.15 (1.11-1.19)	<0.001
Father's parental investment	2.68 (1.16)	7781	2.78 (1.11)	6059	1.08 (1.05-1.11)	<0.001
Emergency c-section	2%	7941	1%	6081	0.71 (0.51-0.99)	0.041
Elective c-section	1%	7941	1%	6081	0.70 (0.52-0.94)	0.018
Female	48%	4055	49%	6925	1.03 (0.97-1.11)	0.272
Ever smoked when pregnant	37%	7834	27%	6027	0.65 (0.61-0.70)	<0.001
Parental social class II	16%	1058	14%	713	0.83 (0.75-0.92)	<0.001
Parental social class III	46%	3014	44%	2271	0.91 (0.86-0.99)	0.029
Parental social class IV	5%	377	7%	365	1.25 (1.07-1.45)	0.004
Parental social class V	14%	907	17%	912	1.34 (1.21-1.48)	<0.001
Parental social class VI	2%	112	4%	196	2.27 (1.79-2.87)	<0.001
Parental social class VII	1%	65	1%	36	0.70 (0.47-1.05)	0.089

Table 3 MCS: Duration of Exclusive breastfeeding & Cognitive Ability at age 3 (n=11792)

	OLS		Two-Stage Least Squares			
	Cognitive Score		Wks Breastfed		Cognitive Score	
	B(SE)	P	B(SE)	P	B(SE)	P
Duration Exclusive Breastfed	0.07 (0.02)	<0.001			0.28 (0.32)	0.392
Female	2.91 (0.24)	<0.001	0.15 (0.12)	0.219	2.88 (0.24)	<0.001
Age (in months)	0.36 (0.05)	<0.001	-0.03 (0.02)	0.200	0.37 (0.05)	<0.001
Ethnicity						
Mixed	0.03 (0.75)	0.969	2.53 (0.43)	<0.001	-0.50 (1.13)	0.658
Indian	-1.95 (0.87)	0.025	1.58 (0.52)	0.002	-2.29 (1.13)	0.042
Pakistani/Bangladeshi	-7.97 (0.68)	<0.001	1.74 (0.42)	<0.001	-8.33 (0.91)	<0.001
Black	-3.77 (0.87)	<0.001	1.92 (0.51)	<0.001	-4.16 (1.21)	0.001
Chinese or other ethnicity	-2.38 (1.44)	0.098	-0.61 (0.81)	0.454	-2.25 (1.90)	0.238
Birth Order	-2.53 (0.13)	<0.001	0.09 (0.07)	0.230	-2.56 (0.14)	<0.001
Birth Weight (kilos)	0.31 0.27)	0.239	-0.24 (0.14)	0.074	0.38 (0.29)	0.192
Days of gestation	0.04 (0.01)	<0.001	0.02 (0.01)	<0.001	0.03 (0.01)	0.015
Mother's age at child's birth	0.31 (0.02)	<0.001	0.16 (0.01)	<0.001	0.28 (0.05)	<0.001
Mother single at birth	-2.08 (0.50)	<0.001	0.02 (0.22)	0.940	-2.09 (0.50)	0.000
Ever smoked when pregnant	-0.50 (0.28)	0.081	-1.07 (0.14)	<0.001	-0.27 (0.45)	0.547
Mother's depression score	-0.14 (0.07)	0.039	-0.14 (0.03)	<0.001	-0.11 (0.09)	0.203
Mother's education						
O level/GCSE grades A-C	2.61 (0.32)	<0.001	0.82 (0.15)	<0.001	2.44 (0.42)	<0.001
A/ AS/ S Levels	4.42 (0.46)	<0.001	2.11 (0.24)	<0.001	3.98 (0.82)	<0.001
Diplomas in Higher Education	4.93 (0.47)	<0.001	2.25 (0.25)	<0.001	4.46 (0.86)	<0.001
First Degree	7.06 (0.45)	<0.001	4.22 (0.24)	<0.001	6.18 (1.44)	<0.001
Higher Degree	7.45 (0.68)	<0.001	4.84 (0.41)	<0.001	6.44 (1.70)	<0.001
Mother's literacy difficulties	-0.62 (0.42)	0.138	0.04 (0.21)	0.837	-0.63 (0.43)	0.138
Mother's height	0.02 (0.02)	0.331	0.01 (0.01)	0.502	0.01 (0.02)	0.417
Father's height	0.06 (0.02)	0.001	0.03 (0.01)	0.001	0.06 (0.02)	0.008
HOME score	1.02 (0.10)	<0.001	0.19 (0.05)	<0.001	0.98 (0.11)	<0.001
Parental investment 1	2.10 (0.12)	<0.001	0.07 (0.07)	0.300	2.09 (0.13)	<0.001
Parental investment 2	1.84 (0.14)	<0.001	0.73 (0.07)	<0.001	1.69 (0.28)	<0.001
Emergency c-section			-0.92(0.19)	<0.001		
Elective c-section			-0.90(0.22)	<0.001		

Weak-identification test (Staiger-Stock)	18.11 (0.000)
Over-identification test (Sargan-Hansen J)	0.168 (0.682)
Endogeneity test (Durbin-Wu-Hausman)	0.436 (0.509)

Notes: Reference groups are male, white, married/cohabitating, mother did not smoke during pregnancy, GCSE grades d-g, mother has no literacy difficulties.

Table 4 MCS: Duration of Exclusive breastfeeding & Cognitive Ability at age 5 (n=9117)

	OLS		Two-Stage Least Squares			
	Cognitive Score		Wks Breastfed		Cognitive Score	
	B(SE)	P	B(SE)	P	B(SE)	P
Duration Exclusive Breastfed	0.04 (0.02)	0.034			0.48 (0.28)	0.098
Female	2.45 (0.27)	<0.001	0.31 (0.14)	0.026	2.32 (0.29)	<0.001
Age (in days)	0.95 (0.05)	<0.001	0.01 (0.02)	0.577	0.94 (0.05)	<0.001
Ethnicity						
Mixed	-0.07 (0.82)	0.929	2.03 (0.47)	<0.001	-0.92 (1.05)	0.380
Indian	0.75 (0.99)	0.449	0.97 (0.57)	0.089	0.31 (1.06)	0.772
Pakistani/Bangladeshi	-2.94 (0.74)	0.449	0.76 (0.42)	0.071	-3.26 (0.85)	<0.001
Black	-2.70 (0.95)	0.004	0.95 (0.57)	0.094	-3.07 (1.08)	0.005
Chinese or other ethnicity	-3.45 (1.43)	0.016	0.50 (0.88)	0.573	-3.65 (1.85)	0.049
Birth Order	-1.76 (0.15)	<0.001	0.13 (0.08)	0.127	-1.84 (0.17)	<0.001
Birth Weight (kilos)	1.64 (0.30)	<0.001	-0.06 (0.15)	0.700	1.70 (0.32)	<0.001
Days of gestation	0.00 (0.01)	0.632	0.02 (0.01)	0.005	-0.01 (0.02)	0.727
Mother's age at child's birth	0.18 (0.03)	<0.001	0.15 (0.01)	<0.001	0.12 (0.05)	0.011
Mother single at birth	-1.36 (0.60)	0.022	-0.03 (0.26)	0.902	-1.35 (0.66)	0.040
Ever smoked when pregnant	-0.84 (0.33)	0.010	-0.99 (0.16)	<0.001	-0.43 (0.43)	0.318
Mother's depression score	-0.30 (0.08)	<0.001	-0.19 (0.04)	<0.001	-0.22 (0.10)	0.026
Mother's education						
O level/GCSE grades A-C	3.33 (0.37)	<0.001	0.83 (0.17)	<0.001	2.98 (0.48)	<0.001
A/ AS/ S Levels	5.25 (0.53)	<0.001	2.27 (0.27)	<0.001	4.30 (0.84)	<0.001
Diplomas in Higher Education	4.51 (0.54)	<0.001	2.27 (0.28)	<0.001	3.57 (0.85)	<0.001
First Degree	6.75 (0.51)	<0.001	4.25 (0.27)	<0.001	4.98 (1.30)	<0.001
Higher Degree	7.07 (0.78)	<0.001	4.90 (0.46)	<0.001	5.05 (1.53)	0.001
Mother's literacy difficulties	-1.23 (0.49)	0.012	0.22 (0.24)	0.356	-1.31 (0.55)	0.017
Mother's height	-0.01 (0.02)	0.770	-0.00 (0.01)	0.886	-0.01 (0.02)	0.698
Father's height	0.01 (0.02)	0.743	0.02 (0.01)	0.043	-0.01 (0.02)	0.899
HOME score	0.64 (0.11)	<0.001	0.17 (0.05)	0.001	0.57 (0.13)	<0.001
Parental investment 1	1.08 (0.14)	<0.001	0.09 (0.07)	0.234	1.05 (0.15)	<0.001
Parental investment 2	1.32 (0.16)	<0.001	0.75 (0.08)	<0.001	1.01 (0.27)	<0.001
Emergency c-section			-1.21 (0.21)	<0.001		
Elective c-section			-1.31 (0.25)	<0.001		

Weak-identification test (Staiger-Stock)	26.44 (0.000)
Over-identification test (Sargan-Hansen J)	1.205 (0.272)
Endogeneity test (Durbin-Wu-Hausman)	2.554 (0.110)

Notes: Reference groups are male, white, married/cohabitating, mother did not smoke during pregnancy, GCSE grades d-g, mother has no literacy difficulties. Country indicators for England, Scotland, Wales and Northern Ireland included but not reported.

Table 5 NCDS: Breastfeeding & Cognitive Ability at age 7 (n=4923)

	OLS		Two-Stage Least Squares			
	Cognitive Score		Breastfed		Cognitive Score	
	B(SE)	P	B(SE)	P	B(SE)	P
Non-exclusively breastfed	1.37 (0.39)	<0.001			-0.62 (6.24)	0.920
Male	-1.68 (0.39)	<0.001	-0.02 (0.01)	0.107	-1.72 (0.41)	<0.001
Birth order	-1.62 (0.19)	<0.001	-0.01 (0.01)	0.033	-1.64 (0.20)	<0.001
Birth Weight (kilos)	3.13 (0.41)	<0.001	0.02 (0.02)	0.105	3.17 (0.44)	<0.001
Days of gestation	-0.01 (0.02)	0.512	0.00 (0.00)	0.021	-0.01 (0.02)	0.676
Mother's age at child's birth	0.15 (0.06)	0.020	0.00 (0.00)	0.031	0.14 (0.07)	0.061
Father's age at child's birth	0.10 (0.06)	0.083	0.00 (0.00)	0.020	0.11 (0.06)	0.093
Mother's education	0.73 (0.14)	<0.001	0.02 (0.01)	<0.001	0.77 (0.20)	<0.001
Father's education	0.69 (0.11)	<0.001	0.01 (0.00)	0.005	0.71 (0.13)	<0.001
Mother's height	-0.04 (0.03)	0.233	0.00 (0.00)	0.193	-0.03 (0.03)	0.314
Father's height	0.063 (0.03)	0.022	0.02 (0.00)	0.032	0.07 (0.03)	0.031
Mother smokes	-0.30 (0.43)	0.489	-0.10 (0.02)	<0.001	-0.48 (0.73)	0.507
Household amenities	0.86 (0.29)	0.003	0.02 (0.01)	0.013	0.90 (0.32)	0.005
Parental social class II	0.48 (0.74)	0.512	-0.04 (0.03)	0.165	0.41 (0.77)	0.592
Parental social class III	0.88 (0.62)	0.154	-0.01 (0.02)	0.629	0.86 (0.62)	0.164
Parental social class IV	2.29 (0.87)	0.008	0.03 (0.03)	0.410	2.34 (0.88)	0.008
Parental social class V	2.66 (0.72)	<0.001	-0.01 (0.03)	0.805	2.65 (0.73)	<0.001
Parental social class VI	3.41 (1.28)	0.008	0.04 (0.05)	0.470	3.48 (1.30)	0.007
Parental social class VII	2.55 (2.27)	0.262	0.02 (0.09)	0.837	2.60 (2.25)	0.249
Mother's parental investment	-0.77 (0.27)	0.004	0.02 (0.01)	0.048	-0.74 (0.30)	0.013
Father's parental investment	0.99 (0.21)	<0.001	0.00 (0.01)	0.733	0.98 (0.21)	<0.001
Emergency c-section			-0.24 (0.05)	<0.001		
Elective c-section			-0.13 (0.06)	0.028		
Weak-identification test (Staiger-Stock)	13.57 (0.000)					
Over-identification test (Sargan-Hansen J)	0.614 (0.433)					
Endogeneity test (Durbin-Wu-Hausman)	0.130 (0.718)					

Table 6 NCDS: Breastfeeding & Cognitive Ability at age 11 (n=4923)

	OLS		Two-Stage Least Squares			
	Cognitive Score		Breastfed		Cognitive Score	
	B(SE)	P	B(SE)	P	B(SE)	P
Non-exclusively breastfed	1.61 (0.37)	<0.001			-3.41 (5.83)	0.558
Male	-1.37 (0.37)	<0.001	-0.02 (0.01)	0.107	-1.48 (0.39)	<0.001
Birth order	-2.66 (0.18)	<0.001	-0.01 (0.01)	0.033	-2.71 (0.19)	<0.001
Birth Weight (kilos)	3.05 (0.40)	<0.001	0.00 (0.00)	0.105	3.17 (0.43)	<0.001
Days of gestation	-0.01 (0.02)	0.646	0.00 (0.00)	0.021	0.00 (0.02)	0.995
Mother's age at child's birth	0.45 (0.06)	<0.001	0.00 (0.00)	0.031	0.42 (0.07)	<0.001
Father's age at child's birth	0.07 (0.06)	0.214	0.00 (0.00)	0.020	0.09 (0.06)	0.146
Mother's education	1.00 (0.14)	<0.001	0.02 (0.01)	<0.001	1.11 (0.19)	<0.001
Father's education	1.06 (0.10)	<0.001	0.01 (0.00)	0.005	1.12 (0.13)	<0.001
Mother's height	-0.02 (0.03)	0.422	0.00 (0.00)	0.193	-0.02 (0.03)	0.648
Father's height	0.07 (0.03)	0.006	0.01 (0.00)	0.032	0.08 (0.03)	0.006
Mother smokes	-1.62 (0.41)	<0.001	-0.10 (0.02)	<0.001	-2.09 (0.68)	0.002
Household amenities	1.65 (0.25)	<0.001	0.02 (0.01)	0.013	1.76 (0.29)	<0.001
Parental social class II	1.25 (0.70)	0.074	-0.04 (0.03)	0.165	1.07 (0.74)	0.148
Parental social class III	2.15 (0.58)	<0.001	-0.01 (0.02)	0.629	2.10 (0.58)	<0.001
Parental social class IV	4.41 (0.88)	<0.001	0.03 (0.03)	0.410	4.54 (0.89)	<0.001
Parental social class V	3.84 (0.70)	<0.001	-0.01 (0.03)	0.805	3.81 (0.71)	<0.001
Parental social class VI	5.13 (1.28)	<0.001	0.04 (0.05)	0.470	5.31 (1.31)	<0.001
Parental social class VII	2.23 (2.02)	0.270	0.02 (0.09)	0.837	2.35 (1.98)	0.235
Mother's parental investment	-0.52 (0.25)	0.037	0.02 (0.01)	0.048	-0.43 (0.28)	0.120
Father's parental investment	0.95 (0.20)	<0.001	0.00 (0.01)	0.733	0.93 (0.20)	<0.001
Emergency c-section			-0.24 (0.05)	<0.001		
Elective c-section			-0.13 (0.06)	0.028		
Weak-identification test (Staiger-Stock)	13.57 (0.000)					
Overidentification test (Hansen J)	0.412 (0.521)					
Endogeneity test (Durbin-Wu-Hausman)	0.731 (0.393)					

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