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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.

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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 siblingdifference 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 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 ethnic¹⁶ and social class¹⁷ differences in breastfeeding practices, the impact of breastfeeding on gross and fine motor skills,¹⁸ and the impact of maternal employment on breastfeeding initiation¹⁹ and duration²⁰.

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 questionnaire²⁸ 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 height³⁰ 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 duration⁴⁸, 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 4⁵¹, while a smaller study found that caesarian delivery was not a significant predicator of first grade math or verbal scores⁵². There is also evidence that caesarean section has no impact on intelligence in adulthood⁵³ 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:

Cognitive Ability = β_1 Breastfeeding + $\beta_2 X + \varepsilon$ (1) Breastfeeding = $\gamma_1 C$ -Section + $\gamma_2 X + \eta$ (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 test⁵⁶. 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 "underidentified". 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 sample⁵⁸ while the estimated standard errors will also be biased⁵⁹. 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 satisfactory⁶⁰. 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 =-1.31SE=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 (β =0.28, SE=0.32 p<0.392, 5 (β =0.46, SE=0.28 p<0.098), 7 (β =-0.62, SE=6.24 p<0.920) and 11 (β =-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 selfefficacy, 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% (B=1.40, SE=0.26 p<0.001) and 7.0% (B=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 circumstances⁶⁶ 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 experimental⁶⁷ and quasiexperimental⁶⁸ 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 achievement⁶⁹. 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 behaviour⁷⁰ 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 neurodevelopment⁷¹. In addition, there is epigenetic evidence of the positive effects of licking and grooming by mother rats of their pups on neurocognitive development⁷², 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 ability⁷³. An experimental study finds that breast milk mediates IQ through its impact on brain growth and white matter growth in particular⁷⁴. 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 vitamins⁷⁷, can have a direct effect on neurodevelopment and subsequently IQ⁷⁸. 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 children⁷⁹. This is supported by recent findings that the relationship between breastfeeding and IQ is mediated by maternal confounding factors rather than LCPUFA⁸⁰. The literature on the mechanisms linking breastfeeding to IQ is therefore controversial and further research identifying the causal mechanisms is required.

	Not breastfed Breastfe		Breastfed >1 1	nonth	Odds ratio (95% CIs)	P value
	Mean (SD) or %	Ν	Mean (SD) or %	Ν		
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 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 %	Ν	Mean (SD) or %	Ν		
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 2 NCDS: Association of dependent variable and potential confounders by breastfeeding status

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

	OLS	5	Two-Stage Least Squares						
	Cognitive Score		Wks Breastfed		Cognitive Score				
	B(SE)	Р	B(SE)	Р	B(SE)	Р			
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	~ /				(0.00)				
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	~ /				(0.02)				
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			18.11		<u> </u>				
(Staiger-Stock)			(0.000						
Over-identification test			0.168						
(Sargan-Hansen J)	(0.682)								
Endogeneity test			0.436						
(Durbin-Wu-Hausman)		(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.

	OLS	5	Two-Stage Least Squares						
	Cognitive	Score	Wks Brea	astfed	Cognitive Score				
	B(SE)	Р	B(SE)	Р	B(SE)	Р			
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			26.44		1				
(Staiger-Stock)			(0.000						
Over-identification test			1.205						
(Sargan-Hansen J)			(0.272	,					
Endogeneity test (Durbin-Wu-Hausman)			2.554						
(Duroni- w u-mausinali)	(0.110)								

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

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.

	OLS	5	Two-Stage Least Squares				
	Cognitive	Score		Breastfed		Cognitive Score	
	B(SE)	Р	B(SE)	Р	B(SE)	Р	
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)	< 0.00	
Birth order	-1.62 (0.19)	< 0.001	-0.01 (0.01)	0.033	-1.64 (0.20)	< 0.00	
Birth Weight (kilos)	3.13 (0.41)	< 0.001	0.02 (0.02)	0.105	3.17 (0.44)	< 0.00	
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)	< 0.00	
Father's education	0.69 (0.11)	< 0.001	0.01 (0.00)	0.005	0.71 (0.13)	< 0.00	
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)	< 0.00	
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)	< 0.00	
Emergency c-section			-0.24 (0.05)	< 0.001			
Elective c-section			-0.13 (0.06)	0.028			
Weak-identification test			13.57		l		
(Staiger-Stock)			(0.000				
Over-identification test			0.614				
(Sargan-Hansen J)			(0.433	/			
Endogeneity test			0.130				
(Durbin-Wu-Hausman)			(0.718)			

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

	OLS	5	Two-Stage Least Squares				
	Cognitive	Score	Breast	fed	Cognitive Score		
	B(SE)	Р	B(SE)	Р	B(SE)	Р	
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)	< 0.00	
Birth Weight (kilos)	3.05 (0.40)	< 0.001	0.00 (0.00)	0.105	3.17 (0.43)	< 0.00	
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)	< 0.00	
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)	< 0.00	
Father's education	1.06 (0.10)	< 0.001	0.01 (0.00)	0.005	1.12 (0.13)	< 0.00	
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)	< 0.00	
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)	< 0.00	
Parental social class IV	4.41 (0.88)	< 0.001	0.03 (0.03)	0.410	4.54 (0.89)	< 0.00	
Parental social class V	3.84 (0.70)	< 0.001	-0.01 (0.03)	0.805	3.81 (0.71)	< 0.00	
Parental social class VI	5.13 (1.28)	< 0.001	0.04 (0.05)	0.470	5.31 (1.31)	< 0.00	
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)	< 0.00	
Emergency c-section			-0.24 (0.05)	< 0.001			
Elective c-section			-0.13 (0.06)	0.028			
Weak-identification test	13.57						
(Staiger-Stock)			(0.000				
Overidentification test			0.412				
(Hansen J)			(0.521				
Endogeneity test			0.731				
(Durbin-Wu-Hausman)			(0.393	5)			

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

REFERENCES

1 Hoefer C, Hardy MC. Later development of breastfed and artificially fed infants. Comparison of physical and mental growth. J Am Med Assoc 1929;92:615-619.

2 Anderson JW, Johnstone BM, Remley DT. Breast feeding and cognitive development: A meta analysis. American Journal of Clinical Nutrition 1999; 70:525-535.

3 Drane DL. Logemann JA. A critical evaluation of the evidence on the association between type of infant feeding and cognitive development. Paediatric and Perinatal Epidemiology 2000;14:349-356.

4 Horta BL, Bahl R, Martines JC, Victora CG. Evidence on the long-term effects of breastfeeding: Systemic reviews and meta-analyses. World Health Organisation 2007.

5 Petryk A, Harris S.R, Jongbloed L. Breastfeeding and neurodevelopment: A literature review. Infants and Young Children 2007;20(2):120-134.

6 Jain A, Concato J, Leventhal JM. How good is the evidence linking breastfeeding and intelligence? Pediatrics 2002;109(6):1044-53.

7 Jacobson SW, Jacobson JL. Breastfeeding and intelligence in children: Mediated by mother's intelligence rather than better nutrition. BMJ 2006;333:929–30.

8 Angelsen NK, Vik T, Jacobsen G, Bakketeig LS. Breastfeeding and cognitive development at age one and five years. Arch Dis Child. 2001;85:183-188.

9 Kramer MS, Aboud F, Mironova E, et al. Breastfeeding and child cognitive development: New evidence from a large randomized trial. Arch Gen Psychiatry 2008;65(5):578-584.

10 Evenhouse E, Reilly S. Improved estimates of the benefits of breastfeeding using sibling comparisons to reduce selection bias. HSR: Health Services Research 2005;40(6):1781-1802.

11 Der G, Batty GD, Deary IJ. Effect of breast feeding on intelligence in children: prospective study, sibling pairs analysis, and meta-analysis. BMJ 2006;333(7575):929-930.

12 Greenland S. An introduction to instrumental variables for epidemiologists. International Journal of Epidemiology 2000;29:722-729.

13 Cameron AC, Trivedi PK. Microeconometrics. Cambridge University Press, 2005.

14 Plewis I. Millennium Cohort Study: technical report on sampling. London: Institute of Education, University of London, 2004.

15 Dex S, Joshi H. Babies of the New Millennium. London: Policy Press, 2005.

16 Griffiths LJ, Tate AR, Dezateux C. The Millennium Cohort Study Child Health Group. The contribution of parental and community ethnicity to breastfeeding practices: evidence from the Millennium Cohort Study. International Journal of Epidemiology 2005;34:1378–1386.

17 Kelly Y, Watt R. Breast feeding initiation and exclusive duration at 6 month by social class: Results from the Millennium Cohort Study. Public Health Nutr. 2005;8:417-421.

18 Sacker A, Quigley MA, Kelly YJ. Breastfeeding and developmental delay: Findings from the Millennium Cohort Study. Pediatrics 2006;118:682-689.

19 Hawkins SS, Griffiths LJ, Dezateux C, Law C. The Millennium Cohort Study Child Health Group. Maternal employment and breast-feeding initiation: findings from the Millennium Cohort Study. Paediatric and Perinatal Epidemiology 2007;21:242–247.

20 Hawkins SS, Griffiths LJ, Dezateux C, Law C. The Millennium Cohort Study Child Health Group. The impact of maternal employment on breast-feeding duration in the UK Millennium Cohort Study. Public Health Nutrition 2007;10(9):891–896.

21 Power C, Elliot J. Cohort profile: 1958 British birth cohort (National Child Development Study). Int J Epidemiol 2006;35:34-41.

22 Bracken BA. Bracken Basic Concept Scale. Chicago: The Psychological Corporation, 1984.

23 Panter, J. Validity of the Bracken Basic Concept Scale-Revised for predicting performance on the metropolitan readiness test-sixth edition. Journal of Psychoeducational Assessment 2000;18:104-110.

24 Southgate V. Southgate group reading tests: manual of instructions. London: University of London Press, 1962.

25 Goodenough FL. The measurement of intelligence by drawings. New York: World Book Company, 1926.

26 Douglas JWB. The home and the school. London: MacGibbon and Kee, 1964.

27 Li R, Scanlon KS, Serdula MK. The validity and reliability of maternal recall of breastfeeding practices. Nutrition Reviews 2005;63:102-110.

28 Rutter M, Tizard J, Whitmore K. Education, Health, and Behaviour. London: Longmans, 1970.

29 Caldwell BM, Bradley RH. Home observation for measurement of the home environment (Rev, ed). Littlerock: University of Arkansas, 1984.

30 Case A, Paxson C. Stature and status: height, ability, and labor market outcomes. Journal of Political Economy 2008; 116(3):499-532.

31 Mennemayer ST. Can econometrics rescue epidemiology? Annals of Epidemiology 1997;7(4): 249-250.

32 Zahoori N, Savitz DA. Econometric approaches to epidemiologic data: relating endogeneity and unobserved heterogeneity to confounding. Annals of Epidemiology 1997;7(4):251-257.

33 Posner MA, Ash AS, Freund KM, Moskowitz MA, Schwartz M. Comparing standard regression, propensity score matching, and instrumental variables for determining the influence of mammography on stage of diagnosis. Health Services & Outcomes Research Methodology 2001;2: 279-290.

34 Davey Smith G, Sterne J, Fraser A, Tynelius P, Lawlor DA, Rasmussen F. The association between BMI and mortality using offspring BMI as an indicator of own BMI: large intergenerational mortality study. BMJ 2009;339:b5043.

35 Cebu Study Team. A child health production function estimated from longitudinal data. Journal of Development Economics 1992;38: 323-351.

36 VanDerslice J, Popkin B, Briscoe J. Drinking-water quality, sanitation, and breastfeeding: their interactive effects on infant health. Bulletin of WHO 1994;72(4): 589-60.

37 Zahoori N. Does endogeneity matter? A comparison of empirical analyses with and without control for endogeneity. Annals of Epidemiology 1997;7(4):258-266.

38 Perez-Escamilla R, Pollitt E, Lonnerdal B, Dewey KG. Infant feeding policies in maternity wards and their effect on breast-feeding success: an analytic overview. American Journal of Public Health 1994;84:89–97.

39 Rowe-Murray HJ, Fisher J. Baby Friendly Hospital Practices: Caesarean section is a persistent barrier to early initiation of breastfeeding. Birth 2002;29(2):124-131.

40 Perez-Escamilla R,Maulen-Radovan I,Dewey KG. The association between caesarean delivery and breast-feeding outcomes among Mexican women. American Journal of Public Health 1996;86(6):832-836.

41 Pérez-Ríos N, Ramos-Valencia G, Ortiz AP. Cesarean delivery as a barrier for breastfeeding initiation: The Puerto Rican experience. J Hum Lact 2008;24(3):293-302.

42 Chien LY, Tai CJ. Effect of delivery method and timing of breastfeeding initiation on breastfeeding outcomes in Taiwan. Birth 2007;34(2):123-130.

43 Rajan L. The impact of obstetric procedures and analgesia/anaesthesia during labour and delivery on breast feeding. Midwifery 1994;10:87-103.

44 DiMatteo MR, Lepper HS, Damush TM, Morton SC, Carney MF, Pearson M, Kahn KL. Cesarean childbirth and psychosocial outcomes: A meta-analysis. Health Psychology 1996;15(4):303-314.

45 Winberg J. Mother and newborn baby: mutual regulation of physiology and behavior--a selective review. Developmental Psychobiology 2005;47(3):217–29.

46 Varendi H, Porter RH, Winberg J. Does the newborn baby find the nipple by smell?. Lancet 1994;344:989–90.

47 Mikiel-Kostyra K, Mazur J, Boltruszko I. Effect of early skin-to-skin contact after delivery on duration of breastfeeding: a prospective cohort study. Acta Paediatr 2002;91:1301-1306.

48 Moore ER, Anderson GC, Bergman N. Early skin-to-skin contact for mothers and their healthy newborn infants. Cochrane Database of Systematic Reviews 2007, Issue 3.

49 Klingaman K, Ball H. Anthropology of caesarean section birth and breastfeeding: Rationale for evolutionary medicine on the postnatal ward. Durham Anthropology Journal 2007;14(1).

50 Manhire KM, Hagan AE, Floyd SA.A descriptive account of New Zealand mothers' responses to open-ended questions on their breast feeding experiences. Midwifery 2007;23(4): 372-381.

51 Broman SH, Nichols PL, Kennedy WA. Preschool IQ: Prenatal and Early Developmental Correlates. Hillsdale, New Jersey, Lawrence Erlbaum Associates, 1975.

52 Entwisle DR, Alexander KL. Long-term effects of caesarean delivery on parents' beliefs and children's schooling. Developmental Psychology 1987;23(5): 676-682.

53 Nilsen ST. Bergsjø P. Males born by caesarean section examined 18 years after delivery. Acta Obstetricia et Gynecologica Scandinavica. 1985;64(3):237-240.

54 Sussmann JE, McIntosh AM, Lawrie SM, Johnstone EC. Obstetric complications and mild to moderate intellectual disability. British Journal of Psychiatry 2009;194:224–228.

55 Ounsted M, Moar VA, Cockburn J, Redman CWG. Factors associated with the intellectual ability of children born to women with high risk pregnancies. BMJ 1984;288:1038-1041.

56 Cameron A.C. P.K. Trivedi. Microeconometrics. Cambridge University Press, 2005.

57 Hansen LP. Large sample properties of generalised method of moments estimators. Econometrica 1982;50:1029–1054.

58 Bound J, Jaeger DA, Baker RM. Problems with instrumental variable estimation when the correlation between the instruments and the endogenous explanatory variable is weak. Journal of the American Statistical Association 1995;90:443-450.

59 Nelson CR, Startz R. The distribution of the instrumental variable estimator and its t-ratio when the instrument is a poor one. Journal of Business 1990;63:S125-S140.

60 Staiger D, Stock JH. Instrumental variable regression with weak instruments Econometrica 1997;65:557-586.

61 Gale CR, Marriott LD, Martyn CN, Limond J, Inskip HM, Godfrey KM, Law CM, Cooper C, West C, Robinson SM. Breastfeeding, the use of docosahexaenoic acid-fortified formulas in infancy and neuropsychological function in childhood. Arch Dis Child, Published Online First: 4 February 2010.

62 Der G, Batty GD, Deary IJ. Effect of breast feeding on intelligence in children: prospective study, sibling pairs analysis, and meta-analysis. BMJ 2006;333(7575):929-930.

63 Gomez-Sanchiz M, Canete R, Rodero I, Baeza JE, Gonzalez JA. Influence of breast-feeding and parental intelligence on cognitive development in the 24-month-old child. Clin Pediatr 2004; 43:753–61.

64 Angelsen NK, Vik T, Jacobsen G, Bakketeig LS. Breastfeeding and cognitive development at age one and five years. Arch Dis Child. 2001;85:183-188.

65 Johnson DL, Swank PR, Howie VM, Baldwin CD, Owen M. Breast-feeding and children's intelligence. Psychol Rep. 1996;79:1179-1185.

66 Hawkes D, Plewis I. Modelling non-response in the National Child Development Study. Journal of the Royal Statistical Society Series A 2006;169(3):479-491.

67 Kramer MS, Aboud F, Mironova E, et al. Breastfeeding and child cognitive development: New evidence from a large randomized trial. Arch Gen Psychiatry 2008;65(5):578-584.

68 Evenhouse E, Reilly S. Improved estimates of the benefits of breastfeeding using sibling comparisons to reduce selection bias. HSR: Health Services Research 2005;40(6):1781-1802.

69 Rees DI, Sabia JJ. The effect of breast feeding on educational attainment: evidence from sibling data. Journal of Human Capital 2009;3:43-72.

70 Michaelsen KF, Lauritzen L, Mortensen EL. Goldberg G. Effects of breastfeeding on cognitive function. In Prentice A, Prentice A, Filteau S, Simondon K. (Eds.) Breast-Feeding: Early Influences on Later Health. Advances in Experimental Medicine and Biology, Vol. 639. Springer Netherlands, 2009: 199-215.

71 Feldman R, Eidelma AI. Direct and indirect effects of breast milk on the neurobehavioral and cognitive development of premature infants. Dev Psychobiol 2003;43: 109-119.

72 Weaver ICG, Cervoni N, Champagne FA, D'Alessio AC, Sharma S, Seckl JR, Dymov S, Szyf M, Meaney MJ. Epigenetic programming by maternal behaviour. Nature Neuroscience 2004;7(8):847-854.

73 Caspi A, Williams B, Kom-Cohen J, Craig I, Milne B, Poulton R, Schalkwyk LC, Taylor A, Werts H, Moffitt TE. Moderation of breastfeeding effects on the IQ by genetic variation in fatty acid metabolism. PNAS 2007;104(47):18860-18865.

74 Isaacs EB, Fischl BR, Quinn BT, Chong WK, Gadian DG, Lucas A. Impact of breast milk on IQ, brain size and white matter development. Pediatric Research 2009, Dec 22. Epub.

75 Xiang M, Alfven G, Blennow M, Trygg M, Zetterstrom R. Long-chain polyunsaturated fatty acids in human milk and brain growth during early infancy. Acta Paediatrica 2000;89:142-147.

76 Donovan SM, Odle J. Growth factors in milk as mediators of infant development. Annual Review of Nutrition 1994;14:127-167.

77 Cockburm F. Role of infant dietary long-chain polyunsaturated fatty acids, liposoluble vitamins, cholesterol and lecithin on psychomotor development. Acta Paediatrica Supplement 2003;442:19-33.

78 McCann JC, Ames BN. (2005) Is docosahexaenoic acid, an n-3 long chain polyunsaturated fatty acid, required for the development of normal brain function? An overview of evidence from cognitive and behavioral tests in humans and animals. Am J Clin Nutr 82:281-95.

79 Simmer K, Patole S, Rao SC. Longchain polyunsaturated fatty acid supplementation in infants born at term. Cochrane Database of Systematic Reviews 2008, Issue 1. Art. No.: CD000376.

80 Gale CR, Marriott LD, Martyn CN, Limond J, Inskip HM, Godfrey KM, Law CM, Cooper C, West C, Robinson SM. Breastfeeding, the use of docosahexaenoic acid-fortified formulas in infancy and neuropsychological function in childhood. Arch Dis Child, Published Online First: 4 February 2010.