RESEARCH LETTER

The Nutritional and Social Environment-Related Effects of Breastfeeding on Intelligence

While various studies document a positive association between duration of breastfeeding and the child’s intelligence, there is an ongoing discussion about the mechanisms behind that association.1,2 The usual approach to distinguish between nutritional and confounding environment-related effects is to control for observable environmental factors in the analysis. Varying availability and measures of control variables make comparisons across studies difficult and lead to different results concerning the partial correlation between duration of breastfeeding and intelligence.1,2 This study provides a new empirical test of the purely nutritional effect of breastfeeding on the child’s intelligence and does not rely on the availability of control variables.

Methods | The literature on the nutritional benefits of breastfeeding3,4 suggests that if the main sources of the association between duration of breastfeeding and intelligence are direct nutritional effects, this association should be monotonic. This proposition should especially hold true for breastfeeding in the first weeks of life.3 Accordingly, children who were breastfed for a short duration would be expected to be more intelligent than children who were not breastfed. For some newborns, breastfeeding is not possible for health reasons and thus they cannot receive the nutritional benefits of breastfeeding, but a stimulating social environment (eg, secure attachment, intellectual stimuli) can still be provided. Therefore, this study proposes to test for nonmonotonicity in the association between the duration of breastfeeding and the child’s intelligence at a duration of 0 (ie, when the newborn is not breastfed). As an empirical illustration of this idea, recent data on the Pelotas 1982 Birth Cohort5 are used. Data on IQ at age 30 were collected from June 4, 2012, to February 28, 2013. Data on breastfeeding were collected in 1984 and 1986. The Ethical Review Board of the Faculty of Medicine of the Federal University of Pelotas approved the study. Data analysis was conducted between April 9 and August 28, 2015. The following model was estimated:

\[
IQ = \beta_0 + \beta_{\text{break}} d_i + \sum_{m=1}^{M} \beta_m x_i^m + \epsilon_i
\]

where \(d_i\) is a dummy variable of 1 if the child was not breastfed and 0 if the child was breastfed, \(x_i\) indicates the individual breastfeeding duration, and \(M\) indicates the degree of polynomials used to approximate the association. \(\beta_{\text{break}}\) captures a potential nonmonotonicity in the association at a duration of 0; it indicates the difference between the actual mean IQ of children who were not breastfed and their predicted IQ based on the monotonic approximations. To precisely capture the shape of the association close to a duration of 0, the sample is restricted to durations smaller than 1 month (736 of 3493 observations [21.1%]) and polynomials up to the degree of 3 are used. Results of ordinary least-squares estimations are displayed in the Figure.

Results | The actual mean IQ of individuals who were not breastfed is significantly higher than the predictions based on the 3 monotonic approximations. The estimated \(\beta_{\text{break}}\) coefficients indicate significant upward shifts for children who were not breastfed (2-sided t tests, n = 736; linear model: \(P = .03\); quadratic model: \(P = .02\); cubic model: \(P = .08\)). Point estimates and 95% CIs are displayed in the Table.

Discussion | The identified pattern of a nonmonotonic association contradicts the interpretation of pure nutritional effects as the main source of the raw correlation between duration of breastfeeding and the child’s intelligence. Therefore, there must also be social environment-related factors associated with breastfeeding from which children who are not breastfed can also benefit. Combining the research strategy of this study with the usual approach of adding control variables to isolate nutritional effects bears the potential for new evidence in the debate on the existence of nutritional effects of breastfeeding on...
intelligence. If $\beta_{\text{break}}$ indicates a statistically significant upward shift in a carefully calibrated estimation model, which also includes all plausible and available environmental controls, there is strong evidence that the resulting partial regression coefficient of duration of breastfeeding is still not reflecting pure nutritional effects.

The pattern shown in this study also helps explain why studies comparing children who have ever been breastfed and those who have never been breastfed find no difference in intelligence.6

**Fabian Kosse, Dr rer pol**

**Author Affiliation:** Institute for Applied Microeconomics, University of Bonn, Bonn, Germany.

**Corresponding Author:** Fabian Kosse, Dr rer pol, Institute for Applied Microeconomics, University of Bonn, Adenaueralle 24-42, 53113 Bonn, Germany (kosse@uni-bonn.de).

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**Outcomes of Respiratory Syncytial Virus Immunoprophylaxis in Infants Using an Abbreviated Dosing Regimen of Palivizumab**

Respiratory syncytial virus (RSV) is the most common cause of lower respiratory tract infections in infants younger than 1 year. Premature infants, infants with chronic lung disease, infants with major congenital heart diseases, or infants with severe immunodeficiencies are at highest risk of hospital admission for RSV. Palivizumab, a monoclonal antibody, reduces pulmonary viral replication by 100-fold on serum drug levels greater than 40 mg/mL in the cotton rat model.1 On the basis of randomized clinical trials, monthly administration of 15 mg/kg of palivizumab reduces hospitalizations by approximately 55% in these infants.2 However, the costliness of this drug restrains its broader use. The American Academy of Pediatrics recommends a maximum of 5 palivizumab doses in selected risk groups during the RSV season,3 although pharmacokinetic analyses suggest that equivalent antibody protection may be sustainably achieved with fewer doses.3,4

**Methods** | In British Columbia, administration of palivizumab necessitates central approval through the British Columbia RSV Immunoprophylaxis Program, and eligible infants are closely followed up by program-coordinated clinics across the province. The RSV season extends from November to April, with the first and last palivizumab doses given the closest day to November 15 and on April 15, respectively. All infants receive a maximum of 3 or 4 doses based on criteria listed in the Table, with maximal dose intervals of 28 days after the first dose and 35 days after the second and subsequent approved doses (prospectively defined as the scheduled dosing period). Hospitalizations in the preceding month are assessed in program clinics before each dose and up to April 30 each year. Program data were linked to the Discharge Abstract Database of the British Columbia Health Authorities to confirm hospitalizations, according to 7 diagnostic codes for RSV bronchiolitis or acute respiratory infection of unspecified cause using the *International Classification of Diseases, Tenth Revision,* and *International Classification of Diseases, Tenth Revision, Clinical Modification.* The study was approved by the Children’s & Women's Research Ethics Board. Written informed consent was obtained from all participants in whom blood samples were obtained for RSV neutralizing antibody measures.

**Table. Administration Criteria for Respiratory Syncytial Virus Immunoprophylaxis in British Columbia**

<table>
<thead>
<tr>
<th>Indication</th>
<th>Maximum No. of Doses</th>
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<tr>
<td>BPD or CLD requiring oxygen or continuous positive airway pressure at &gt;28 days of age and &lt;1 year of age by November 1 AND receiving supplemental oxygen on or after July 1</td>
<td>4</td>
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<tr>
<td>Born at &lt;29 weeks of gestation and discharged home on or after September 1</td>
<td>4</td>
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<tr>
<td>Tracheostomy, receiving home oxygen, or receiving home ventilatory support on or after November 1 and &lt;2 years of age by November 1</td>
<td>4</td>
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<tr>
<td>Multiples (twins or triplets) of approved child and born on or after November 1, 2012</td>
<td>Same as approved sibling</td>
</tr>
<tr>
<td>Hemodynamically significant CHD and &lt;2 years of age by November 1</td>
<td>4</td>
</tr>
<tr>
<td>Severe immunodeficiency (eg, stem cell transplantation) and &lt;2 years of age by November 1</td>
<td>4</td>
</tr>
<tr>
<td>Cystic fibrosis with lung disease and born on or after January 1</td>
<td>4</td>
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<tr>
<td>Trisomy 21 without hemodynamically significant CHD and discharged home on or after October 1 and with a risk factor score ≥24 points*</td>
<td>4</td>
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<tr>
<td>Significant pulmonary disability (pulmonary hypertension, pulmonary malformations, severe BPD, progressive neuromuscular disease, other) and &lt;2 years of age by November 1</td>
<td>4</td>
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<tr>
<td>Infants born between 29 and &lt;35 completed weeks of gestation without BPD or CLD and discharged home on or after October 1 and with a risk factor score ≥24 points*</td>
<td>3</td>
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</table>

Abbreviations: BPD, bronchopulmonary dysplasia; CHD, congenital heart disease; CLD, chronic lung disease.

* Risk factor score is calculated as follows: Infant attends day care regularly during first 3 months after discharge (22 points); discharged home in December, January, or February (20 points); discharged home in November or March (10 points); gestational age at birth of 29 weeks to less than 31 weeks of completed gestation (10 points); more than 5 people living in household (12 points); sibling younger than 5 years (14 points); remote community, travel of more than 1 hour or of more than 100 km required to the nearest hospital (10 points); girl not receiving breast milk, or boy (8 points); birth weight less than 10th percentile (8 points); and 2 or more smokers in household (8 points).