Supplementary Online Content

Flohr C, Henderson AJ, Kramer MS, et al. Effect of an intervention to promote breastfeeding on asthma, lung function, and atopic eczema at age 16 years: follow-up of the PROBIT randomized trial. *JAMA Pediatr*. Published online November 13, 2017. doi:10.1001/jamapediatrics.2017.4064

- eTable 1. Characteristics of 12,183 Participants With Valid Lung Function Data
- eTable 2. Lung Function in Those Who Reported a Diagnosis of Asthma and Wheezing
- **eTable 3.** Instrumental Variable and Observational Associations of Duration and Exclusivity of Breastfeeding (\geq 3 Months vs. <3 Months) With Lung Function Outcomes
- **eTable 4.** Intention-to-Treat Analysis With Multiple Imputation, Comparing Intervention vs Control Groups (N = 17,046)

This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Characteristics of 12,183 participants with valid lung function data

| | N (%) | | | |
|--|----------------------|----------------------------|-----------------------|--|
| Characteristic | Total (n = 12183) | Intervention (n = 6360) | Control (n = 5823) | |
| Measured at child's birth | , | | , | |
| Maternal age, y | | | | |
| <20 | 1649 (13.5) | 893 (14.0) | 756 (13.0) | |
| 20-34 | 10038 (82.4) | 5209 (81.9) | 4829 (82.9) | |
| ≥35 | 496 (4.1) | 258 (4.1) | 238 (4.1) | |
| Maternal education | | | | |
| Completed university | 1653 (13.6) | 905 (14.2) | 748 (12.8) | |
| Advanced secondary or partial university | 6221 (51.1) | 3009 (47.3) | 3212 (55.2) | |
| Common secondary | 3881 (31.9) | 2174 (34.2) | 1707 (29.3) | |
| Incomplete secondary | 428 (3.5) | 272 (4.3) | 156 (2.7) | |
| Paternal education | | | | |
| Completed university | 1584 (13.0) | 853 (13.4) | 731 (12.6) | |
| Advanced secondary or partial university | 5565 (45.7) | 2600 (40.9) | 2965 (50.9) | |
| Common secondary | 4384 (36.0) | 2553 (40.1) | 1831 (31.4) | |
| Incomplete secondary or unknown | 650 (5.3) | 354 (5.6) | 296 (5.1) | |
| Stratum-level variable | | | | |
| East/Urban | 3682 (30.2) | 1950 (30.7) | 1732 (29.7) | |
| East/Rural | 1947 (16.0) | 980 (15.4) | 967 (16.6) | |
| West/Urban | 3174 (26.1) | 2130 (33.5) | 1044 (17.9) | |
| West/Rural | 3380 (27.7) | 1300 (20.4) | 2080 (35.7) | |
| Number children in household | | | | |
| 0 | 6923 (56.8) | 3750 (59.0) | 3173 (54.5) | |
| 1 | 4252 (34.9) | 2123 (33.4) | 2129 (36.6) | |
| 2+ | 1008 (8.3) | 487 (7.7) | 521 (8.9) | |
| Maternal smoking during pregnancy | | | | |
| No | 11940 (98.0) | 6207 (97.6) | 5733 (98.5) | |
| Yes | 243 (2.0) | 153 (2.4) | 90 (1.5) | |

| Characteristic | N (%) | | |
|---|----------------------|----------------------------|-----------------------|
| Child at birth | Total (n = 12183) | Intervention (n = 6360) | Control (n = 5823) |
| Child sex | | | |
| Female | 6288 (51.6) | 3252 (51.1) | 3036 (52.1) |
| Male | 5895 (48.4) | 3108 (48.9) | 2787 (47.9) |
| Birthweight, mean (SD), kg | 3.44 (0.42) | 3.44 (0.42) | 3.44 (0.42) |
| Gestation length, mean (SD), weeks | 39.4 (1.0) | 39.4 (1.0) | 39.3 (1.0) |
| Measured in child's first year | | | |
| Duration of exclusive breastfeeding, mo | | | |
| <3 | 8870 (73.3) | 3465 (55.1) | 5405 (92.9) |
| 3-<6 | 2794 (23.1) | 2429 (38.6) | 365 (6.3) |
| ≥6 | 437 (3.6) | 391 (6.2) | 46 (0.8) |
| Duration of breastfeeding, mo | | | |
| <3 | 4207 (34.8) | 1872 (29.8) | 2335 (40.2) |
| 3-<6 | 2785 (23.0) | 1417 (22.5) | 1368 (23.5) |
| ≥6 | 5111 (42.2) | 3000 (47.7) | 2111 (36.3) |

SD = standard deviation

eTable 2. Lung function in those who reported a diagnosis of asthma and wheezing

| | Wheezing in past 12 months | | | | | |
|------------------------|------------------------------|--------------|-------------------------------|---------|---------------------|---------|
| | Yes | No | | | | |
| | n=767 | n=11382 | Cluster adjust | ted | Further adjust | ed* |
| Outcome | Mean | (SD) | β (95% CI) p-value β (95% CI) | | β (95% CI) | p-value |
| FEV1 z-score | -0.59 (1.44) | -0.41 (1.40) | -0.13 (-0.23,-0.04) | 0.01 | -0.14 (-0.23,-0.04) | 0.004 |
| FVC z-score | -0.49 (1.26) | -0.35 (1.19) | -0.05 (-0.13, 0.04) | 0.27 | -0.05 (-0.13, 0.03) | 0.26 |
| FEV1/FVC ratio z-score | 0.02 (1.61) | 0.12 (1.62) | -0.19 (-0.29,-0.09) | 0.01 | -0.19 (-0.29,-0.09) | 0.0003 |
| | Ever asthma | | | | | |
| | Yes | No | | | | |
| | n=204 | n=11941 | Cluster adjusted | | Further adjusted* | |
| Outcome | Mean (SD) | | β (95% CI) | p-value | β (95% CI) | p-value |
| FEV1 z-score | -0.77 (1.34) | -0.42 (1.40) | -0.24 (-0.41,-0.06) | 0.01 | -0.26 (-0.44,-0.08) | 0.004 |
| FVC z-score | -0.44 (1.14) | -0.36 (1.20) | -0.08 (-0.24, 0.07) | 0.29 | -0.08 (-0.24, 0.07) | 0.29 |
| FEV1/FVC ratio z-score | -0.35 (1.65) | 0.12 (1.62) | -0.31 (-0.50,-0.11) | 0.01 | -0.34 (-0.53,-0.14) | 0.001 |
| | Asthma attack past 12 months | | | | | |
| | Yes | No | | | | |
| | n=49 | n=12092 | Cluster adjusted | | Further adjusted* | |
| Outcome | Mean (SD) | | β (95% CI) | p-value | β (95% CI) | p-value |
| FEV1 z-score | -0.85 (1.60) | -0.42 (1.40) | -0.21 (-0.57, 0.15) | 0.26 | -0.26 (-0.61, 0.10) | 0.16 |
| FVC z-score | -0.39 (1.22) | -0.36 (1.20) | 0.00 (-0.31, 0.31) | >0.99 | -0.01 (-0.32, 0.30) | 0.94 |
| FEV1/FVC ratio z-score | -0.43 (1.91) | 0.12 (1.62) | -0.30 (-0.69, 0.09) | 0.13 | -0.34 (-0.73, 0.05) | 0.08 |

^{*}Adjusted for stratum-level variables (urban vs rural and East vs West Belarus residence), maternal and paternal education, and child sex, birth weight, gestation length, and age at follow-up

eTable 3. Instrumental Variable and Observational Associations of Duration and Exclusivity of Breastfeeding (≥3 Months vs. <3 Months) With Lung Function Outcomes

| | Instrumental v | Instrumental variable analysis Exclusive breastfeeding >= 3 vs. <3 months (control) | | Observational analysis | | |
|------------------------|----------------------|---|--------------------|----------------------------------|--|--|
| | | | | Exclusive breastfeeding >= 3 vs. | | |
| | <3 month | | | <3 months (control) | | |
| | Cluster-adjusted | Further adjusted * | Cluster-adjusted | Further adjusted * | | |
| Lung Function | β (95 | β (95% CI) | | β (95% CI) | | |
| FEV1 z-score | -1.14 (-2.31, 0.02) | -1.00 (-2.17, 0.18) | 0.03 (-0.03, 0.09) | 0.03 (-0.03, 0.10) | | |
| FVC z-score | -0.62 (-1.56, 0.32) | -0.49 (-1.61, 0.63) | 0.03 (-0.03, 0.08) | 0.03 (-0.02, 0.08) | | |
| FEV1:FVC ratio z-score | -0.41 (-2.06, 1.25) | -0.41 (-2.30, 1.47) | 0.01 (-0.06, 0.08) | 0.01 (-0.06, 0.08) | | |
| FEV1:FVC ratio x 100 | -5.34 (-17.76, 7.08) | -5.23 (-19.31, 8.85) | 0.09 (-0.44, 0.62) | 0.10 (-0.43, 0.62) | | |

^{*}Adjusted for stratum-level variables (urban vs. rural and East vs. West Belarus), and for child age at follow-up, sex, birthweight, and both maternal and paternal education. Asthma and lung function models were also adjusted for gestational age at birth.

eTable 4. Intention-to-treat analysis with multiple imputation, comparing intervention vs control groups (N = 17,046)

| | Group, No. (%) | | OR (95% CI) | |
|---|-----------------------|------------------|---------------------|---------------------|
| | Intervention (n=8865) | Control (n=8181) | Cluster-adjusted | Further adjusted* |
| Flexural eczema on skin examination | 29 (0.3) | 49 (0.6) | 0.57 (0.32, 1.00) | 0.55 (0.32, 0.95) |
| Flexural eczema past year | 41 (0.5) | 52 (0.6) | 0.66 (0.34, 1.27) | 0.66 (0.34, 1.27) |
| Sleep-disturbed flexural eczema past year | 18 (0.2) | 28 (0.3) | 0.63 (0.28, 1.39) | 0.65 (0.28, 1.52) |
| | Group, No. (%) | | OR (95% CI) | |
| | Intervention (n=8865) | Control (n=8181) | Cluster-adjusted | Further adjusted* |
| Ever asthma | 140 (1.6) | 136 (1.7) | 0.86 (0.56, 1.32) | 0.85 (0.56, 1.29) |
| Wheezing past 12 months | 542 (6.1) | 524 (6.4) | 0.77 (0.48, 1.22) | 0.71 (0.45, 1.10) |
| Asthma attack in the past 12 months | 37 (0.4) | 29 (0.4) | 1.09 (0.57, 2.06) | 1.09 (0.57, 2.06) |
| | Group, mean (SD) | | β (95% CI) | |
| | Intervention (n=8865) | Control (n=8181) | Cluster-adjusted | Further adjusted* |
| FEV1 z-score | -0.68 (1.53) | -0.23 (1.22) | -0.34 (-0.66,-0.01) | -0.29 (-0.60, 0.02) |
| FVC z-score | -0.46 (1.25) | -0.31 (1.14) | -0.19 (-0.51, 0.13) | -0.14 (-0.46, 0.17) |
| FEV1:FVC ratio z-score | -0.02 (2.75) | 0.32 (2.09) | -0.09 (-0.66, 0.49) | -0.09 (-0.65, 0.47) |
| FEV1:FVC ratio x 100* | 85.15 (15.2) | 88.38 (10.6) | -1.51 (-5.36, 2.34) | -1.49 (-5.26, 2.29) |

^{*}Adjusted for stratum-level variables (urban vs. rural and East vs. West Belarus), and for child age at follow-up, sex, birthweight, and maternal and paternal education. Asthma and lung function models were also adjusted for gestational age at birth.