Supplemental Table 1. Characteristics in middle childhood among cohort participants included and not included in the analysis

| Characteristic | *n* | Included1 |  | *n* | Not included1 |  | *p*2 |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  |  |  |  |  |  |
| Exposures |  |  |  |  |  |  |  |
| Infectious morbidity, days per year (IQR) |  |  |  |  |  |  |  |
| Diarrhea with vomiting | 1018 | 0.4 (0.0, 0.0) |  | 2066 | 0.3 (0.0, 0.0) |  | 0.18 |
| Cough with fever | 1018 | 1.1 (0.0, 1.0) |  | 2066 | 0.8 (0.0, 0.0) |  | 0.14 |
| Ear ache/discharge with fever | 1018 | 0.2 (0.0, 0.0) |  | 2066 | 0.2 (0.0, 0.0) |  | 0.82 |
| Fever | 1018 | 2.0 (0.0, 2.0) |  | 2066 | 1.6 (0.0, 2.0) |  | 0.37 |
| Inflammation biomarkers |  |  |  |  |  |  |  |
| White blood cell count, /mm3 | 893 | 7.1 ± 2.1 |  | 1806 | 7.1 ± 2.0 |  | 0.98 |
| C-reactive protein, mg/L | 924 | 1.4 ± 2.5 |  | 1868 | 1.4 ± 2.6 |  | 0.59 |
|  |  |  |  |  |  |  |  |
| Covariates |  |  |  |  |  |  |  |
| Sex, % boys | 1018 | 43.8 |  | 2184 | 51.3 |  | <0.0001 |
| Child’s age, y | 1018 | 8.5 ± 1.6 |  | 2174 | 8.9 ± 1.9 |  | <0.0001 |
| Height-for-age Z score3 | 997 | -0.8 ± 1.0 |  | 2103 | -0.8 ± 1.0 |  | 0.69 |
| BMI-for-age Z score3 | 995 | 0.1 ± 1.0 |  | 2101 | 0.1 ± 1.0 |  | 0.75 |
| Overweight, % BMI-for-age Z score >1 | 995 | 19.2 |  | 2101 | 17.8 |  | 0.34 |
| Iron deficiency4, % | 912 | 3.1 |  | 1836 | 3.3 |  | 0.78 |
| Anemia5, % | 932 | 3.0 |  | 1880 | 4.0 |  | 0.19 |
| Plasma vitamin B12, pmol/L | 897 | 331 ± 104 |  | 1819 | 325 ± 107 |  | 0.10 |
| Mother’s education, y | 987 | 9.0 ± 3.2 |  | 1716 | 8.5 ± 3.4 |  | 0.0003 |
| Mother’s height, cm | 994 | 157.6 ± 6.3 |  | 1865 | 157.8 ± 6.4 |  | 0.50 |
| Mother’s BMI, kg/m2 | 988 | 24.1 ± 3.7 |  | 1828 | 24.1 ± 3.8 |  | 0.30 |
| Food insecurity, % insecure | 1015 | 76.2 |  | 1933 | 75.4 |  | 0.20 |
| Socioeconomic status, % |  |  |  |  |  |  | 0.14 |
| 1 (lowest) | 58 | 5.7 |  | 148 | 6.9 |  |  |
| 2 | 313 | 30.8 |  | 724 | 33.6 |  |  |
| 3 | 575 | 56.5 |  | 1126 | 52.3 |  |  |
| 4 | 72 | 7.1 |  | 155 | 7.2 |  |  |
| Sibling groups in the study |  |  |  |  |  |  | 0.22 |
| No siblings | 915 | 94.7 |  | 1952 | 94.5 |  |  |
| Sibling pairs | 50 | 5.2 |  | 107 | 5.2 |  |  |
| Sibling triplets | 1 | 0.1 |  | 6 | 0.3 |  |  |
|  |  |  |  |  |  |  |  |

1 Mean ± SD unless noted otherwise

2 From Kruskal-Wallis and χ2 tests for continuous and categorical variables, respectively.

3 According to the World Health Organization growth reference for children and adolescents

4 Plasma ferritin <15 µg/L when CRP was ≤10 mg/L

5 Hemoglobin <12.7 g/dL (cut point adjusted for altitude)

Supplemental Table 2. Infectious morbidity symptoms in middle childhood and somatic complaints in adolescence among schoolchildren from Bogotá, Colombia

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Number of days with symptoms per year1 | CBCL | | | |  | YSR | | | |
| n | Mean ± SD | Unadjusted difference2  (95% CI) | Adjusted difference3  (95% CI) |  | n | Mean ± SD | Unadjusted difference2  (95% CI) | Adjusted difference3  (95% CI) |
|  |  |  |  |  |  |  |  |  |  |
| Diarrhea with vomiting |  |  |  |  |  |  |  |  |  |
| None | 708 | 61.2 ± 8.2 | Reference | Reference |  | 882 | 56.8 ± 7.2 | Reference | Reference |
| Moderate | 60 | 62.1 ± 9.8 | 0.9 (-1.6, 3.4) | 1.2 (-1.4, 3.7) |  | 69 | 57.4 ± 8.5 | 0.5 (-1.5, 2.6) | 0.6 (-1.5, 2.8) |
| High | 50 | 61.7 ± 7.0 | 0.5 (-1.5, 2.4) | 0.1 (-2.0, 2.1) |  | 65 | 57.9 ± 7.8 | 1.1 (-0.9, 3.0) | 1.4 (-0.7, 3.5) |
| *p*, trend4 |  |  | 0.52 | 0.73 |  |  |  | 0.25 | 0.17 |
|  |  |  |  |  |  |  |  |  |  |
| Cough with fever |  |  |  |  |  |  |  |  |  |
| None | 600 | 60.9 ± 8.0 | Reference | Reference |  | 743 | 56.8 ± 7.1 | Reference | Reference |
| Moderate | 113 | 61.8 ± 8.9 | 0.9 (-0.9, 2.6) | 0.8 (-1.1, 2.6) |  | 135 | 57.3 ± 7.8 | 0.4 (-1.0, 1.9) | 0.4 (-1.1, 1.9) |
| High | 105 | 63.0 ± 8.9 | 2.0 (0.2, 3.8) | 2.4 (0.6, 4.3) |  | 138 | 57.1 ± 8.3 | 0.3 (-1.2, 1.8) | 0.2 (-1.5, 1.8) |
| *p*, trend |  |  | 0.03 | 0.01 |  |  |  | 0.68 | 0.81 |
|  |  |  |  |  |  |  |  |  |  |
| Ear ache / discharge with fever |  |  |  |  |  |  |  |  |  |
| None | 754 | 61.0 ± 8.1 | Reference | Reference |  | 938 | 56.8 ± 7.3 | Reference | Reference |
| Moderate | 33 | 65.1 ± 11.1 | 4.0 (0.2, 7.8) | 4.2 (0.6, 7.8) |  | 39 | 59.5 ± 8.0 | 2.7 (0.2, 5.2) | 2.8 (0.4, 5.2) |
| High | 31 | 64.2 ± 9.0 | 3.1 (-0.1, 6.3) | 2.1 (-1.0, 5.1) |  | 39 | 57.5 ± 7.7 | 0.7 (-1.7, 3.1) | 0.5 (-2.2, 3.1) |
| *p*, trend |  |  | 0.02 | 0.05 |  |  |  | 0.27 | 0.32 |
|  |  |  |  |  |  |  |  |  |  |
| Fever |  |  |  |  |  |  |  |  |  |
| None | 456 | 60.8 ± 7.9 | Reference | Reference |  | 561 | 56.8 ± 6.9 | Reference | Reference |
| Low | 120 | 62.2 ± 8.1 | 1.4 (-0.2, 3.0) | 0.7 (-1.0, 2.4) |  | 149 | 57.6 ± 7.8 | 0.8 (-0.6, 2.1) | 0.4 (-1.0, 1.9) |
| Moderate | 136 | 61.8 ± 9.5 | 1.0 (-0.8, 2.7) | 1.3 (-0.6, 3.1) |  | 160 | 56.9 ± 8.4 | 0.1 (-1.3, 1.5) | 0.0 (-1.5, 1.5) |
| High | 106 | 62.2 ± 8.5 | 1.4 (-0.3, 3.2) | 1.0 (-0.9, 2.8) |  | 146 | 56.8 ± 7.2 | -0.1 (-1.4, 1.2) | -0.2 (-1.6, 1.3) |
| *p*, trend |  |  | 0.11 | 0.26 |  |  |  | 0.83 | 0.79 |
|  |  |  |  |  |  |  |  |  |  |

**Footnotes to Supplemental Table 2**

CBCL: Child Behavior Checklist (parent report); YSR: Youth Self-Report

1 Moderate and high number of days per year correspond to values < vs. ≥ the median for children with rates >0. Medians (days per year) are 4.6, 6.6, and 3.9 for diarrhea with vomiting, cough with fever, and ear ache / discharge with fever, respectively. For fever, low, moderate, and high are tertiles of the distribution among children with rates >0 and correspond to cutpoints (days per year) 4.7 and 13.5, respectively.

2 From linear regression models with somatic complaints score as the continuous outcome and indicator variables for each combination of symptoms as predictors. Robust estimates of variance were used in all models to account for correlations between siblings.

3 From linear regression models adjusted for child’s sex, age, iron deficiency, anemia, and low vitamin B12 at baseline, mother’s education, household food insecurity with hunger, and low socioeconomic status. Robust estimates of variance were used in all models to account for correlations between siblings.

4 Wald test for a variable representing the median value of each ordinal category introduced into the linear regression model as a continuous predictor.

Supplemental Table 3. Infectious morbidity symptoms in middle childhood and anxious/depressed behavior in adolescence among schoolchildren from Bogotá, Colombia

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Number of days with symptoms per year1 | CBCL | | | |  | YSR | | | |
| n | Mean ± SD | Unadjusted difference2  (95% CI) | Adjusted difference3  (95% CI) |  | n | Mean ± SD | Unadjusted difference2  (95% CI) | Adjusted difference3  (95% CI) |
|  |  |  |  |  |  |  |  |  |  |
| Diarrhea with vomiting |  |  |  |  |  |  |  |  |  |
| None | 708 | 56.2 ± 7.2 | Reference | Reference |  |  |  |  |  |
| Moderate | 60 | 57.9 ± 8.4 | 1.7 (-0.5, 3.9) | 1.7 (-0.6, 4.0) |  | 882 | 55.7 ± 6.7 | Reference | Reference |
| High | 50 | 57.1 ± 7.4 | 0.8 (-1.3, 2.9) | 0.4 (-1.7, 2.5) |  | 69 | 56.2 ± 7.7 | 0.5 (-1.4, 2.5) | 0.3 (-1.5, 2.2) |
| *p*, trend4 |  |  | 0.27 | 0.46 |  | 65 | 55.7 ± 6.6 | 0.0 (-1.7, 1.7) | 0.1 (-1.8, 2.0) |
|  |  |  |  |  |  |  |  | 0.90 | 0.83 |
| Cough with fever |  |  |  |  |  |  |  |  |  |
| None | 600 | 56.2 ± 7.1 | Reference | Reference |  |  |  |  |  |
| Moderate | 113 | 56.4 ± 7.3 | 0.2 (-1.2, 1.7) | 0.1 (-1.3, 1.5) |  | 743 | 55.7 ± 6.9 | Reference | Reference |
| High | 105 | 57.7 ± 8.4 | 1.5 (-0.2, 3.2) | 1.9 (0.1, 3.7) |  | 135 | 55.3 ± 6.2 | -0.4 (-1.5, 0.8) | -0.8 (-2.0, 0.3) |
| *p*, trend |  |  | 0.09 | 0.04 |  | 138 | 56.1 ± 6.7 | 0.5 (-0.8, 1.7) | 0.5 (-0.8, 1.9) |
|  |  |  |  |  |  |  |  | 0.51 | 0.52 |
| Ear ache / discharge with fever |  |  |  |  |  |  |  |  |  |
| None | 754 | 56.4 ± 7.3 | Reference | Reference |  |  |  |  |  |
| Moderate | 33 | 55.6 ± 7.7 | -0.7 (-3.4, 1.9) | -0.6 (-3.2, 1.9) |  | 938 | 55.7 ± 6.8 | Reference | Reference |
| High | 31 | 57.9 ± 8.0 | 1.6 (-1.3, 4.4) | 1.4 (-1.7, 4.6) |  | 39 | 56.1 ± 6.7 | 0.4 (-1.8, 2.5) | 0.4 (-1.7, 2.6) |
| *p*, trend |  |  | 0.37 | 0.49 |  | 39 | 55.8 ± 5.9 | 0.2 (-1.7, 2.0) | 0.7 (-1.5, 3.0) |
|  |  |  |  |  |  |  |  | 0.80 | 0.47 |
| Fever |  |  |  |  |  |  |  |  |  |
| None | 456 | 55.9 ± 7.1 | Reference | Reference |  | 561 | 55.7 ± 7.0 | Reference | Reference |
| Low | 120 | 56.5 ± 6.9 | 0.6 (-0.9, 2.0) | 0.2 (-1.3, 1.7) |  | 149 | 55.9 ± 6.5 | 0.2 (-1.0, 1.4) | -0.1 (-1.4, 1.1) |
| Moderate | 136 | 56.6 ± 7.5 | 0.7 (-0.8, 2.1) | 0.6 (-0.9, 2.1) |  | 160 | 55.4 ± 6.1 | -0.3 (-1.4, 0.8) | -0.4 (-1.6, 0.9) |
| High | 106 | 58.0 ± 8.1 | 2.1 (0.4, 3.8) | 1.7 (0.1, 3.4) |  | 146 | 56.0 ± 6.8 | 0.3 (-0.9, 1.5) | 0.2 (-1.2, 1.5) |
| *p*, trend |  |  | 0.01 | 0.05 |  |  |  | 0.74 | 0.84 |
|  |  |  |  |  |  |  |  |  |  |

**Footnotes to Supplemental Table 3**

CBCL: Child Behavior Checklist (parent report); YSR: Youth Self-Report

1 Moderate and high number of days per year correspond to values < vs. ≥ the median for children with rates >0. Medians (days per year) are 4.6, 6.6, and 3.9 for diarrhea with vomiting, cough with fever, and ear ache / discharge with fever, respectively. For fever, low, moderate, and high are tertiles of the distribution among children with rates >0 and correspond to cutpoints (days per year) 4.7 and 13.5, respectively.

2 From linear regression models with anxious/depressed behavior score as the continuous outcome and indicator variables for each combination of symptoms as predictors. Robust estimates of variance were used in all models to account for correlations between siblings.

3 From linear regression models adjusted for child’s sex, age, iron deficiency, anemia, and low vitamin B12 at baseline, mother’s education, household food insecurity with hunger, and low socioeconomic status. Robust estimates of variance were used in all models to account for correlations between siblings.

4 Wald test for a variable representing the median value of each ordinal category introduced into the linear regression model as a continuous predictor.

Supplemental Table 4. Infectious morbidity symptoms in middle childhood and withdrawn/depressed behavior in adolescence among schoolchildren from Bogotá, Colombia

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Number of days with symptoms per year1 | CBCL | | | |  | YSR | | | |
| n | Mean ± SD | Unadjusted difference2  (95% CI) | Adjusted difference3  (95% CI) |  | n | Mean ± SD | Unadjusted difference2  (95% CI) | Adjusted difference3  (95% CI) |
|  |  |  |  |  |  |  |  |  |  |
| Diarrhea with vomiting |  |  |  |  |  |  |  |  |  |
| None | 708 | 56.1 ± 6.5 | Reference | Reference |  | 882 | 55.6 ± 6.4 | Reference | Reference |
| Moderate | 60 | 56.9 ± 6.3 | 0.8 (-0.8, 2.5) | 1.0 (-0.7, 2.8) |  | 69 | 56.3 ± 6.3 | 0.7 (-0.9, 2.2) | 0.6 (-1.1, 2.3) |
| High | 50 | 55.6 ± 5.9 | -0.5 (-2.2, 1.2) | -1.1 (-2.7, 0.5) |  | 65 | 55.2 ± 6.5 | -0.4 (-2.0, 1.2) | -0.4 (-2.0, 1.2) |
| *p*, trend4 |  |  | 0.73 | 0.83 |  |  |  | 0.76 | 0.79 |
|  |  |  |  |  |  |  |  |  |  |
| Cough with fever |  |  |  |  |  |  |  |  |  |
| None | 600 | 56.0 ± 6.5 | Reference | Reference |  | 743 | 55.6 ± 6.6 | Reference | Reference |
| Moderate | 113 | 55.6 ± 5.7 | -0.4 (-1.6, 0.8) | -0.5 (-1.7, 0.6) |  | 135 | 55.6 ± 5.9 | 0.0 (-1.1, 1.1) | -0.1 (-1.2, 1.0) |
| High | 105 | 57.1 ± 7.1 | 1.1 (-0.4, 2.5) | 1.3 (-0.3, 3.0) |  | 138 | 55.5 ± 6.1 | -0.1 (-1.3, 1.0) | 0.0 (-1.2, 1.2) |
| *p*, trend |  |  | 0.18 | 0.14 |  |  |  | 0.82 | 0.97 |
|  |  |  |  |  |  |  |  |  |  |
| Ear ache / discharge with fever |  |  |  |  |  |  |  |  |  |
| None | 754 | 56.1 ± 6.5 | Reference | Reference |  | 938 | 55.5 ± 6.5 | Reference | Reference |
| Moderate | 33 | 55.5 ± 5.7 | -0.6 (-2.6, 1.3) | -0.5 (-2.5, 1.5) |  | 39 | 57.0 ± 6.0 | 1.5 (-0.5, 3.4) | 1.5 (-0.5, 3.4) |
| High | 31 | 57.5 ± 6.9 | 1.4 (-1.0, 3.9) | 1.1 (-1.6, 3.8) |  | 39 | 56.2 ± 5.9 | 0.6 (-1.3, 2.5) | 1.2 (-0.9, 3.3) |
| *p*, trend |  |  | 0.35 | 0.53 |  |  |  | 0.32 | 0.15 |
|  |  |  |  |  |  |  |  |  |  |
| Fever |  |  |  |  |  |  |  |  |  |
| None | 456 | 55.8 ± 6.2 | Reference | Reference |  | 561 | 55.5 ± 6.6 | Reference | Reference |
| Low | 120 | 56.0 ± 6.4 | 0.2 (-1.1, 1.5) | -0.1 (-1.4, 1.2) |  | 149 | 55.7 ± 6.2 | 0.2 (-0.9, 1.3) | 0.0 (-1.3, 1.2) |
| Moderate | 136 | 57.1 ± 7.3 | 1.2 (-0.1, 2.6) | 1.1 (-0.3, 2.6) |  | 160 | 56.2 ± 6.6 | 0.7 (-0.5, 1.8) | 0.6 (-0.6, 1.8) |
| High | 106 | 56.3 ± 6.3 | 0.5 (-0.8, 1.8) | 0.3 (-1.1, 1.8) |  | 146 | 55.2 ± 5.7 | -0.3 (-1.4, 0.8) | -0.3 (-1.4, 0.8) |
| *p*, trend |  |  | 0.30 | 0.46 |  |  |  | 0.71 | 0.78 |
|  |  |  |  |  |  |  |  |  |  |

**Footnotes to Supplemental Table 4**

CBCL: Child Behavior Checklist (parent report); YSR: Youth Self-Report

1 Moderate and high number of days per year correspond to values < vs. ≥ the median for children with rates >0. Medians (days per year) are 4.6, 6.6, and 3.9 for diarrhea with vomiting, cough with fever, and ear ache / discharge with fever, respectively. For fever, low, moderate, and high are tertiles of the distribution among children with rates >0 and correspond to cutpoints (days per year) 4.7 and 13.5, respectively.

2 From linear regression models with withdrawn/depressed behavior score as the continuous outcome and indicator variables for each combination of symptoms as predictors. Robust estimates of variance were used in all models to account for correlations between siblings.

3 From linear regression models adjusted for child’s sex, age, iron deficiency, anemia, and low vitamin B12 at baseline, mother’s education, household food insecurity with hunger, and low socioeconomic status. Robust estimates of variance were used in all models to account for correlations between siblings.

4 Wald test for a variable representing the median value of each ordinal category introduced into the linear regression model as a continuous predictor.

Supplemental Table 5. Infectious morbidity symptoms in middle childhood and rule breaking behavior in adolescence among schoolchildren from Bogotá, Colombia

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Number of days with symptoms per year1 | CBCL | | | |  | CBCL | | | |
| n | Mean ± SD | Unadjusted difference2  (95% CI) | Adjusted difference3  (95% CI) |  | n | Mean ± SD | Unadjusted difference2  (95% CI) | Adjusted difference3  (95% CI) |
|  |  |  |  |  |  |  |  |  |  |
| Diarrhea with vomiting |  |  |  |  |  |  |  |  |  |
| None | 708 | 55.0 ± 5.3 | Reference | Reference |  | 882 | 54.4 ± 4.9 | Reference | Reference |
| Moderate | 60 | 55.7 ± 5.9 | 0.7 (-0.8, 2.3) | 1.2 (-0.4, 2.7) |  | 69 | 54.2 ± 5.2 | -0.2 (-1.5, 1.0) | -0.0 (-1.4, 1.3) |
| High | 50 | 54.7 ± 4.9 | -0.2 (-1.7, 1.2) | -0.4 (-2.0, 1.1) |  | 65 | 53.7 ± 4.1 | -0.7 (-1.8, 0.3) | -0.7 (-1.9, 0.5) |
| *p*, trend4 |  |  | 0.95 | 0.90 |  |  |  | 0.18 | 0.26 |
|  |  |  |  |  |  |  |  |  |  |
| Cough with fever |  |  |  |  |  |  |  |  |  |
| None | 600 | 55.0 ± 5.2 | Reference | Reference |  | 743 | 54.4 ± 4.9 | Reference | Reference |
| Moderate | 113 | 54.6 ± 5.1 | -0.4 (-1.4, 0.6) | -0.3 (-1.3, 0.7) |  | 135 | 54.2 ± 5.0 | -0.2 (-1.1, 0.7) | -0.4 (-1.3, 0.5) |
| High | 105 | 55.4 ± 6.1 | 0.4 (-0.9, 1.6) | 1.0 (-0.4, 2.4) |  | 138 | 53.9 ± 4.9 | -0.5 (-1.4, 0.4) | -0.1 (-1.1, 0.9) |
| *p*, trend |  |  | 0.60 | 0.17 |  |  |  | 0.26 | 0.82 |
|  |  |  |  |  |  |  |  |  |  |
| Ear ache / discharge with fever |  |  |  |  |  |  |  |  |  |
| None | 754 | 55.0 ± 5.3 | Reference | Reference |  | 938 | 54.3 ± 4.9 | Reference | Reference |
| Moderate | 33 | 53.6 ± 5.2 | -1.4 (-3.2, 0.4) | -1.3 (-3.0, 0.4) |  | 39 | 55.0 ± 4.7 | 0.7 (-0.8, 2.2) | 0.6 (-0.9, 2.1) |
| High | 31 | 55.9 ± 6.4 | 0.9 (-1.4, 3.1) | 0.6 (-2.1, 2.9) |  | 39 | 54.0 ± 4.2 | -0.3 (-1.7, 1.0) | -0.3 (-1.8, 1.3) |
| *p*, trend |  |  | .69 | 0.94 |  |  |  | 0.83 | 0.95 |
|  |  |  |  |  |  |  |  |  |  |
| Fever |  |  |  |  |  |  |  |  |  |
| None | 456 | 54.9 ± 5.2 | Reference | Reference |  | 561 | 54.4 ± 4.9 | Reference | Reference |
| Low | 120 | 55.5 ± 5.5 | 0.5 (-0.5, 1.6) | 0.4 (-0.7, 1.5) |  | 149 | 54.3 ± 5.2 | -0.1 (-1.0, 0.8) | -0.5 (-1.4, 0.5) |
| Moderate | 136 | 54.8 ± 5.4 | -0.1 (-1.1, 0.9) | 0.3 (-0.8, 1.3) |  | 160 | 54.7 ± 5.0 | 0.3 (-0.6, 1.2) | 0.4 (-0.5, 1.4) |
| High | 106 | 55.1 ± 5.5 | 0.2 (-0.9, 1.4) | 0.3 (-1.0, 1.5) |  | 146 | 53.6 ± 4.3 | -0.8 (-1.6, 0.0) | -0.5 (-1.5, 0.4) |
| *p*, trend |  |  | 0.81 | 0.70 |  |  |  | 0.10 | 0.40 |
|  |  |  |  |  |  |  |  |  |  |

**Footnotes to Supplemental Table 5**

CBCL: Child Behavior Checklist (parent report); YSR: Youth Self-Report

1 Moderate and high number of days per year correspond to values < vs. ≥ the median for children with rates >0. Medians (days per year) are 4.6, 6.6, and 3.9 for diarrhea with vomiting, cough with fever, and ear ache / discharge with fever, respectively. For fever, low, moderate, and high are tertiles of the distribution among children with rates >0 and correspond to cutpoints (days per year) 4.7 and 13.5, respectively.

2 From linear regression models with total rule breaking behavior score as the continuous outcome and indicator variables for each combination of symptoms as predictors. Robust estimates of variance were used in all models to account for correlations between siblings.

3 From linear regression models adjusted for child’s sex, age, iron deficiency, anemia, and low vitamin B12 at baseline, mother’s education, household food insecurity with hunger, and low socioeconomic status. Robust estimates of variance were used in all models to account for correlations between siblings.

4 Wald test for a variable representing the median value of each ordinal category introduced into the linear regression model as a continuous predictor.

Supplemental Table 6. Infectious morbidity symptoms in middle childhood and aggressive behavior in adolescence among schoolchildren from Bogotá, Colombia

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Number of days with symptoms per year1 | CBCL | | | |  | YSR | | | |
| n | Mean ± SD | Unadjusted difference2  (95% CI) | Adjusted difference3  (95% CI) |  | n | Mean ± SD | Unadjusted difference2  (95% CI) | Adjusted difference3  (95% CI) |
|  |  |  |  |  |  |  |  |  |  |
| Diarrhea with vomiting |  |  |  |  |  |  |  |  |  |
| None | 708 | 58.7 ± 7.8 | Reference | Reference |  | 882 | 56.2 ± 7.2 | Reference | Reference |
| Moderate | 60 | 59.0 ± 9.2 | 0.2 (-2.1, 2.6) | 0.7 (-1.7, 3.1) |  | 69 | 57.0 ± 8.7 | 0.8 (-1.3, 2.9) | 1.1 (-1.1, 3.4) |
| High | 50 | 59.3 ± 8.2 | 0.6 (-1.8, 2.9) | 0.1 (-2.3, 2.6) |  | 65 | 54.9 ± 6.6 | -1.3 (-3.0, 0.4) | -1.2 (-3.1, 0.7) |
| *p*, trend4 |  |  | 0.61 | 0.80 |  |  |  | 0.21 | 0.38 |
|  |  |  |  |  |  |  |  |  |  |
| Cough with fever |  |  |  |  |  |  |  |  |  |
| None | 600 | 58.7 ± 7.8 | Reference | Reference |  | 743 | 56.3 ± 7.3 | Reference | Reference |
| Moderate | 113 | 58.2 ± 7.3 | -0.5 (-2.0, 1.0) | -0.7 (-2.2, 0.8) |  | 135 | 55.8 ± 7.0 | -0.5 (-1.8, 0.8) | -0.7 (-2.1, 0.6) |
| High | 105 | 59.9 ± 9.2 | 1.2 (-0.6, 3.1) | 1.6 (-0.4, 3.6) |  | 138 | 55.9 ± 7.5 | -0.4 (-1.7, 1.0) | 0.4 (-1.1, 1.9) |
| *p*, trend |  |  | 0.22 | 0.15 |  |  |  | 0.54 | 0.68 |
|  |  |  |  |  |  |  |  |  |  |
| Ear ache / discharge with fever |  |  |  |  |  |  |  |  |  |
| None | 754 | 58.6 ± 7.8 | Reference | Reference |  | 938 | 56.1 ± 7.3 | Reference | Reference |
| Moderate | 33 | 58.7 ± 8.3 | 0.0 (-2.8, 2.9) | -0.0 (-2.7, 2.8) |  | 39 | 57.9 ± 8.4 | 1.8 (-0.8, 4.4) | 1.9 (-0.7, 4.5) |
| High | 31 | 62.1 ± 9.9 | 3.4 (0.0, 6.9) | 2.0 (-2.0, 5.9) |  | 39 | 56.6 ± 7.1 | 0.5 (-1.7, 2.8) | 1.0 (-1.7, 3.7) |
| *p*, trend |  |  | 0.07 | 0.36 |  |  |  | 0.41 | 0.26 |
|  |  |  |  |  |  |  |  |  |  |
| Fever |  |  |  |  |  |  |  |  |  |
| None | 456 | 58.6 ± 7.8 | Reference | Reference |  | 561 | 56.3 ± 7.3 | Reference | Reference |
| Low | 120 | 58.8 ± 8.0 | 0.2 (-1.4, 1.8) | -0.2 (-1.9, 1.5) |  | 149 | 56.1 ± 7.4 | -0.1 (-1.5, 1.2) | -0.6 (-2.0, 0.8) |
| Moderate | 136 | 58.7 ± 8.0 | 0.1 (-1.4, 1.7) | 0.2 (-1.4, 1.9) |  | 160 | 56.7 ± 7.6 | 0.4 (-0.9, 1.8) | 0.8 (-0.7, 2.2) |
| High | 106 | 59.6 ± 8.3 | 1.0 (-0.7, 2.7) | 0.6 (-1.2, 2.5) |  | 146 | 55.4 ± 6.9 | -0.8 (-2.1, 0.4) | -0.3 (-1.8, 1.1) |
| *p*, trend |  |  | 0.28 | 0.47 |  |  |  | 0.26 | 0.86 |
|  |  |  |  |  |  |  |  |  |  |

**Footnotes to Supplemental Table 6**

CBCL: Child Behavior Checklist (parent report); YSR: Youth Self-Report

1 Moderate and high number of days per year correspond to values < vs. ≥ the median for children with rates >0. Medians (days per year) are 4.6, 6.6, and 3.9 for diarrhea with vomiting, cough with fever, and ear ache / discharge with fever, respectively. For fever, low, moderate, and high are tertiles of the distribution among children with rates >0 and correspond to cutpoints (days per year) 4.7 and 13.5, respectively.

2 From linear regression models with aggressive behavior score as the continuous outcome and indicator variables for each combination of symptoms as predictors. Robust estimates of variance were used in all models to account for correlations between siblings.

3 From linear regression models adjusted for child’s sex, age, iron deficiency, anemia, and low vitamin B12 at baseline, mother’s education, household food insecurity with hunger, and low socioeconomic status. Robust estimates of variance were used in all models to account for correlations between siblings.

4 Wald test for a variable representing the median value of each ordinal category introduced into the linear regression model as a continuous predictor.

Supplemental Table 7. Inflammatory biomarkers in middle childhood and somatic complaints in adolescence among schoolchildren from Bogotá, Colombia

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Inflammatory Biomarker | CBCL | | | |  | YSR | | | |
| n | Mean ± SD | Unadjusted difference1  (95% CI) | Adjusted difference2  (95% CI) |  | n | Mean ± SD | Unadjusted difference1  (95% CI) | Adjusted difference2  (95% CI) |
|  |  |  |  |  |  |  |  |  |  |
| White blood cell count |  |  |  |  |  |  |  |  |  |
| ≤10,000 /mm3 | 667 | 61.2 ± 8.4 | Reference | Reference |  | 830 | 56.9 ± 7.4 | Reference | Reference |
| >10,000 /mm3 | 49 | 63.3 ± 7.6 | 2.0 (-0.2, 4.2) | 2.1 (-0.2, 4.4) |  | 61 | 57.9 ± 7.4 | 0.9 (-1.0, 2.8) | 1.5 (-0.6, 3.5) |
| *p*3 |  |  | 0.08 | 0.08 |  |  |  | 0.34 | 0.17 |
|  |  |  |  |  |  |  |  |  |  |
| Per 1,000/mm3 | 716 |  | 0.0 (-0.2, 0.3) | 0.0 (-0.2, 0.3) |  | 891 |  | 0.0 (-0.2, 0.2) | 0.1 (-0.1, 0.3) |
| *p* |  |  | 0.77 | 0.75 |  |  |  | 0.88 | 0.45 |
|  |  |  |  |  |  |  |  |  |  |
| C-reactive protein |  |  |  |  |  |  |  |  |  |
| ≤3.0 mg/L | 682 | 61.4 ± 8.4 | Reference | Reference |  | 844 | 57.1 ± 7.5 | Reference | Reference |
| >3.0 mg/L | 59 | 61.9 ± 8.2 | 0.5 (-1.6, 2.7) | 0.1 (-2.2, 2.4) |  | 78 | 56.4 ± 7.6 | -0.7 (-2.4, 1.1) | -1.0 (-3.0, 0.9) |
| *p* |  |  | 0.62 | 0.92 |  |  |  | 0.45 | 0.30 |
|  |  |  |  |  |  |  |  |  |  |
| Per 100% difference | 741 |  | 0.2 (-0.2, 0.6) | 0.1 (-0.2, 0.5) |  | 922 |  | 0.0 (-0.3, 0.3) | -0.1 (-0.4, 0.2) |
| *p* |  |  | 0.29 | 0.50 |  |  |  | 0.90 | 0.69 |
|  |  |  |  |  |  |  |  |  |  |

CBCL: Child Behavior Checklist (parent report); YSR: Youth Self-Report

1 From linear regression models with somatic complaints score as the continuous outcome and indicator variables for each inflammatory biomarker as predictors. Robust estimates of variance were used in all models to account for correlations between siblings.

2 From linear regression models adjusted for child’s sex, age, iron deficiency, anemia, and low vitamin B12 at baseline, mother’s education, household food insecurity with hunger, and low socioeconomic status. Robust estimates of variance were used in all models to account for correlations between siblings.

3 Wald test.

Supplemental Table 8. Inflammatory biomarkers in middle childhood and anxious/depressed behavior in adolescence among schoolchildren from Bogotá, Colombia

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Inflammatory Biomarker | CBCL | | | |  | YSR | | | |
| n | Mean ± SD | Unadjusted difference1  (95% CI) | Adjusted difference2  (95% CI) |  | n | Mean ± SD | Unadjusted difference1  (95% CI) | Adjusted difference2  (95% CI) |
|  |  |  |  |  |  |  |  |  |  |
| White blood cell count |  |  |  |  |  |  |  |  |  |
| ≤10,000 /mm3 | 667 | 56.2 ± 7.0 | Reference | Reference |  | 830 | 55.6 ± 6.6 | Reference | Reference |
| >10,000 /mm3 | 49 | 58.0 ± 8.8 | 1.8 (-0.7, 4.2) | 1.3 (-1.3, 3.9) |  | 61 | 56.8 ± 8.1 | 1.2 (-0.9, 3.2) | 1.4 (-0.9, 3.7) |
| *p*3 |  |  | 0.18 | 0.33 |  |  |  | 0.27 | 0.23 |
|  |  |  |  |  |  |  |  |  |  |
| Per 1,000/mm3 | 716 |  | -0.1 (-0.3, 0.2) | -0.1 (-0.4, 0.2) |  | 891 |  | 0.1 (-0.2, 0.3) | 0.1 (-0.1, 0.4) |
| *p* |  |  | 0.63 | 0.55 |  |  |  | 0.62 | 0.36 |
|  |  |  |  |  |  |  |  |  |  |
| C-reactive protein |  |  |  |  |  |  |  |  |  |
| ≤3.0 mg/L | 682 | 56.5 ± 7.3 | Reference | Reference |  | 844 | 55.9 ± 6.8 | Reference | Reference |
| >3.0 mg/L | 59 | 55.0 ± 5.4 | -1.4 (-2.9, 0.0) | -1.6 (-3.2, 0.0) |  | 78 | 55.2 ± 7.0 | -0.7 (-2.4, 0.9) | -0.4 (-2.3, 1.5) |
| *p* |  |  | 0.06 | 0.06 |  |  |  | 0.37 | 0.66 |
|  |  |  |  |  |  |  |  |  |  |
| Per 100% difference | 741 |  | -0.2 (-0.5, 0.1) | -0.2 (-0.5, 0.2) |  | 922 |  | -0.1 (-0.4, 0.1) | -0.1 (-0.4, 0.1) |
| *p* |  |  | 0.23 | 0.28 |  |  |  | 0.36 | 0.33 |
|  |  |  |  |  |  |  |  |  |  |

CBCL: Child Behavior Checklist (parent report); YSR: Youth Self-Report

1 From linear regression models with anxious/depressed behavior score as the continuous outcome and indicator variables for each inflammatory biomarker as predictors. Robust estimates of variance were used in all models to account for correlations between siblings.

2 From linear regression models adjusted for child’s sex, age, iron deficiency, anemia, and low vitamin B12 at baseline, mother’s education, household food insecurity with hunger, and low socioeconomic status. Robust estimates of variance were used in all models to account for correlations between siblings.

3 Wald test.

Supplemental Table 9. Inflammatory biomarkers in middle childhood and withdrawn/depressed behavior in adolescence among schoolchildren from Bogotá, Colombia

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Inflammatory Biomarker | CBCL | | | |  | YSR | | | |
| n | Mean ± SD | Unadjusted difference1  (95% CI) | Adjusted difference2  (95% CI) |  | n | Mean ± SD | Unadjusted difference1  (95% CI) | Adjusted difference2  (95% CI) |
|  |  |  |  |  |  |  |  |  |  |
| White blood cell count |  |  |  |  |  |  |  |  |  |
| ≤10,000 /mm3 | 667 | 56.0 ± 6.3 | Reference | Reference |  | 830 | 55.5 ± 6.2 | Reference | Reference |
| >10,000 /mm3 | 49 | 57.3 ± 7.1 | 1.3 (-0.8, 3.3) | 1.6 (-0.5, 3.7) |  | 61 | 57.4 ± 8.3 | 1.9 (-0.2, 4.0) | 2.6 (0.2, 5.0) |
| *p*3 |  |  | 0.22 | 0.15 |  |  |  | 0.08 | 0.04 |
|  |  |  |  |  |  |  |  |  |  |
| Per 1,000/mm3 | 716 |  | 0.1 (-0.2, 0.3) | 0.1 (-0.1, 0.4) |  | 891 |  | 0.2 (0.0, 0.4) | 0.3 (0.02, 0.5) |
| *p* |  |  | 0.60 | 0.28 |  |  |  | 0.12 | 0.02 |
|  |  |  |  |  |  |  |  |  |  |
| C-reactive protein |  |  |  |  |  |  |  |  |  |
| ≤3.0 mg/L | 682 | 56.1 ± 6.5 | Reference | Reference |  | 844 | 55.6 ± 6.4 | Reference | Reference |
| >3.0 mg/L | 59 | 55.8 ± 5.7 | -0.4 (-1.9, 1.2) | 0.1 (-1.6, 1.9) |  | 78 | 55.6 ± 6.0 | 0.0 (-1.4, 1.4) | 0.1 (-1.4, 1.7) |
| *p* |  |  | 0.63 | 0.88 |  |  |  | 0.96 | 0.86 |
|  |  |  |  |  |  |  |  |  |  |
| Per 100% difference | 741 |  | -0.1 (-0.4, 0.2) | -0.1 (-0.4, 0.2) |  | 922 |  | 0.0 (-0.3, 0.2) | -0.1 (-0.3, 0.2) |
| *p* |  |  | 0.59 | 0.59 |  |  |  | 0.77 | 0.61 |
|  |  |  |  |  |  |  |  |  |  |

CBCL: Child Behavior Checklist (parent report); YSR: Youth Self-Report

1 From linear regression models with withdrawn/depressed behavior score as the continuous outcome and indicator variables for each inflammatory biomarker as predictors. Robust estimates of variance were used in all models to account for correlations between siblings.

2 From linear regression models adjusted for child’s sex, age, iron deficiency, anemia, and low vitamin B12 at baseline, mother’s education, household food insecurity with hunger, and low socioeconomic status. Robust estimates of variance were used in all models to account for correlations between siblings.

3 Wald test.

Supplemental Table 10. Inflammatory biomarkers in middle childhood and rule breaking behavior in adolescence among schoolchildren from Bogotá, Colombia

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Inflammatory Biomarker | CBCL | | | |  | YSR | | | |
| n | Mean ± SD | Unadjusted difference1  (95% CI) | Adjusted difference2  (95% CI) |  | n | Mean ± SD | Unadjusted difference1  (95% CI) | Adjusted difference2  (95% CI) |
|  |  |  |  |  |  |  |  |  |  |
| White blood cell count |  |  |  |  |  |  |  |  |  |
| ≤10,000 /mm3 | 667 | 54.9 ± 5.2 | Reference | Reference |  | 830 | 54.4 ± 4.9 | Reference | Reference |
| >10,000 /mm3 | 49 | 55.4 ± 5.4 | 0.5 (-1.1, 2.0) | 0.5 (-1.1, 2.1) |  | 61 | 54.7 ± 5.3 | 0.3 (-1.1, 1.7) | 0.9 (-0.6, 2.5) |
| *p*3 |  |  | 0.56 | 0.53 |  |  |  | 0.68 | 0.23 |
|  |  |  |  |  |  |  |  |  |  |
| Per 1,000/mm3 | 716 |  | 0.0 (-0.2, 0.2) | 0.0 (-0.2, 0.2) |  | 891 |  | 0.0 (-0.2, 0.1) | 0.0 (-0.1, 0.2) |
| *p* |  |  | 0.90 | 0.99 |  |  |  | 0.75 | 0.56 |
|  |  |  |  |  |  |  |  |  |  |
| C-reactive protein |  |  |  |  |  |  |  |  |  |
| ≤3.0 mg/L | 682 | 55.0 ± 5.2 | Reference | Reference |  | 844 | 54.5 ± 5.0 | Reference | Reference |
| >3.0 mg/L | 59 | 55.1 ± 5.9 | 0.1 (-1.5, 1.6) | -0.2 (-1.9, 1.5) |  | 78 | 54.0 ± 4.6 | -0.5 (-1.6, 0.6) | -0.7 (-1.8, 0.5) |
| *p* |  |  | 0.91 | 0.82 |  |  |  | 0.38 | 0.23 |
|  |  |  |  |  |  |  |  |  |  |
| Per 100% difference | 741 |  | 0.1 (-0.1, 0.3) | 0.1 (-0.2, 0.3) |  | 922 |  | 0.0 (-0.2, 0.2) | 0.00 (-0.2, 0.2) |
| *p* |  |  | 0.42 | 0.58 |  |  |  | 0.73 | 0.96 |
|  |  |  |  |  |  |  |  |  |  |

CBCL: Child Behavior Checklist (parent report); YSR: Youth Self-Report

1 From linear regression models with rule breaking behavior score as the continuous outcome and indicator variables for each inflammatory biomarker as predictors. Robust estimates of variance were used in all models to account for correlations between siblings.

2 From linear regression models adjusted for child’s sex, age, iron deficiency, anemia, and low vitamin B12 at baseline, mother’s education, household food insecurity with hunger, and low socioeconomic status. Robust estimates of variance were used in all models to account for correlations between siblings.

3 Wald test.

Supplementary Table 11. Inflammatory biomarkers in middle childhood and aggressive behavior in adolescence among schoolchildren from Bogotá, Colombia

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Inflammatory Biomarker | CBCL | | | |  | YSR | | | |
| n | Mean ± SD | Unadjusted difference1  (95% CI) | Adjusted difference2  (95% CI) |  | n | Mean ± SD | Unadjusted difference1  (95% CI) | Adjusted difference2  (95% CI) |
|  |  |  |  |  |  |  |  |  |  |
| White blood cell count |  |  |  |  |  |  |  |  |  |
| ≤10,000 /mm3 | 667 | 58.8 ± 7.9 | Reference | Reference |  | 830 | 56.2 ± 7.4 | Reference | Reference |
| >10,000 /mm3 | 49 | 58.9 ± 8.3 | 0.1 (-2.3, 2.5) | -0.1 (-2.6, 2.5) |  | 61 | 56.7 ± 7.7 | 0.5 (-1.5, 2.5) | 1.4 (-0.7, 3.6) |
| *p*3 |  |  | 0.94 | 0.96 |  |  |  | 0.62 | 0.20 |
|  |  |  |  |  |  |  |  |  |  |
| Per 1,000/mm3 | 716 |  | 0.0 (-0.3, 0.2) | -0.1 (-0.4, 0.2) |  | 891 |  | -0.1 (-0.3, 0.1) | 0.0 (-0.2, 0.3) |
| *p* |  |  | 0.79 | 0.64 |  |  |  | 0.47 | 0.97 |
|  |  |  |  |  |  |  |  |  |  |
| C-reactive protein |  |  |  |  |  |  |  |  |  |
| ≤3.0 mg/L | 682 | 58.8 ± 7.9 | Reference | Reference |  | 844 | 56.3 ± 7.4 | Reference | Reference |
| >3.0 mg/L | 59 | 58.5 ± 8.3 | -0.3 (-2.5, 1.8) | -1.1 (-3.4, 1.1) |  | 78 | 56.2 ± 7.6 | -0.1 (-1.8, 1.7) | -0.3 (-2.0, 1.5) |
| *p* |  |  | 0.76 | 0.34 |  |  |  | 0.94 | 0.75 |
|  |  |  |  |  |  |  |  |  |  |
| Per 100% difference | 741 |  | 0.1 (-0.2, 0.4) | 0.1 (-0.3, 0.4) |  | 922 |  | 0.1 (-0.1, 0.4) | 0.1 (-0.2, 0.4) |
| *p* |  |  | 0.59 | 0.77 |  |  |  | 0.34 | 0.55 |
|  |  |  |  |  |  |  |  |  |  |

CBCL: Child Behavior Checklist (parent report); YSR: Youth Self-Report

1 From linear regression models with aggressive behavior score as the continuous outcome and indicator variables for each inflammatory biomarker as predictors. Robust estimates of variance were used in all models to account for correlations between siblings.

2 From linear regression models adjusted for child’s sex, age, iron deficiency, anemia, and low vitamin B12 at baseline, mother’s education, household food insecurity with hunger, and low socioeconomic status. Robust estimates of variance were used in all models to account for correlations between siblings.

3 Wald test.