Supplementary Materials

Supplementary Material. Validation of Infantile Colic Definition

Validation of the definition of infantile colic as at least 1 diagnosis of International Classification of Diseases 10th version (ICD-10) codes of R10.4 or R68.1 was done by reviewing the electronic medical records (EMR) in the Bundang CHA medical center and the Kangdong Sacred heart hospital. We reviewed the EMR of patients with a main diagnosis of ICD-10 R10.4 or R64.1 codes who visited the pediatric outpatient or emergency room at the age of 5 weeks to 4 months between 2008 and 2009. All records were reviewed by 2 separate physicians. A total of 187 infants was enrolled. To be diagnosed as infantile colic, the infants had to have a history of persistent, full-force crying with no apparent reason, no specific physical examination findings, not acute ill-looking, and a self-limited resolution course. In addition, it was diagnosed as infantile colic if the doctor who looked at the child wrote down the name of the diagnosis as infantile colic on the EMR. Infantile colic was finally diagnosed when both physicians agreed with the diagnosis of infantile colic. The mean age was 2.1 months, and the major chief complaints were irritability and/or excessive crying. Among of 187 enrolled infants, the diagnosis of 165 infants was finally confirmed as infantile colic. This protocol was reviewed and approved by the Institutional Review Board of Hallym University (2021-08-010) and CHA University (2018-10-005).

Reference

1. Baaleman DF, Di Lorenzo C, Benninga MA, Saps M. The effects of the Rome IV criteria on pediatric gastrointestinal practice. Curr Gastroenterol Rep 2020;22:1-7.
**Supplementary Table 1.** Checklist of Recommendations for Reporting of Observational Studies Using the Reporting of Studies Conducted Using Observational Routinely Collected Health Data Guidelines

| Item No. | Recommendation | Reported |
|----------|----------------|----------|
| **Title and abstract** | | |
| 1 | (1) Indicate the study’s design with a commonly used term in the title or the abstract.  
(2) Provide in the abstract an informative and balanced summary of what was done and what was found. | Abstract |
| **Introduction** | | |
| 2 | Explain the scientific background and rationale for the investigation being reported. | Introduction |
| 3 | State specific objectives, including any prespecified hypotheses. | Introduction |
| **Methods** | | |
| **Study design** | | |
| 4 | Present key elements of study design early in the paper. | Methods - Study design and Setting |
| 5 | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection. | Methods - Study Design and Setting, Data sources |
| **Participants** | | |
| 6 | (1) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up.  
(2) For matched studies, give matching criteria and number of exposed and unexposed. | Methods - Study population and Figure 1 |
| **Variables** | | |
| 7 | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable. | Methods - Data Sources; Exposure; Outcome; Covariates; Supplementary Table 5 |
| **Data sources/measurement** | | |
| 8 | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group. | Methods - Data Sources; |
| **Bias** | | |
| 9 | Describe any efforts to address potential sources of bias. | Methods - Covariates; Statistical analysis |
| **Study size** | | |
| 10 | Explain how the study size was arrived at. | Methods - Study population, Figure 1 |
| **Quantitative variables** | | |
| 11 | Explain how quantitative variables were handled in the analyses.  
If applicable, describe which groupings were chosen and why. | Methods - Statistical analysis |
| **Statistical methods** | | |
| 12 | (1) Describe all statistical methods, including those used to control for confounding.  
(2) Describe any methods used to examine subgroups and interactions.  
(3) Explain how missing data were addressed.  
(4) If applicable, explain how loss to follow-up was addressed.  
(5) Describe any sensitivity analyses. | Methods - Covariates; Statistical analysis, Table 1, Not applicable |


### Supplementary Table 1. Continued

| Item No. | Recommendation | Reported |
|----------|----------------|----------|
| **Results** | | |
| Participants | 13 | (1) Report numbers of individuals at each stage of study, eg, numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analyzed. | Results - Participants; Figure 1 |
| | | (2) Give reasons for non-participation at each stage. | Figure 1 |
| | | (3) Consider use of a flow diagram. | Figure 1 |
| Descriptive data | 14 | (1) Give characteristics of study participants (eg, demographic, clinical, social) and information on exposures and potential confounders. | Results - Participants; Table 1, Table 2, Supplementary Tables 3 and 4 |
| | | (2) Indicate number of participants with missing data for each variable of interest. | Methods - Table 1 |
| | | (3) Summarize follow-up time (eg, average and total amount). | Methods - Data sources |
| Outcome data | 15 | Report numbers of outcome events or summary measures over time | Results - Main outcome, Secondary outcome, Table 3, Table 4, Figure 3, and Supplementary Figure 1 |
| Main results | 16 | (1) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% CI). Make clear which confounders were adjusted for and why they were included. | Results - Main outcome, Secondary outcome, Table 3, Table 4, Figure 3, and Supplementary Figure 1 |
| | | (2) Report category boundaries when continuous variables were categorized. | Not applicable |
| | | (3) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period. | Not applicable |
| Other analyses | 17 | Report other analyses done, eg, analyses of subgroups and interactions, and sensitivity analyses. | Results - Figure 3, Supplementary Figure 1 |
| **Discussion** | | |
| Key result | 18 | Summarize key results with reference to study objectives. | Discussion |
| Limitation | 19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias | Discussion |
| Interpretation | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence. | Discussion |
| Generalizability | 21 | Discuss the generalizability (external validity) of the study results. | Discussion |
| **Other information** | | |
| Funding | 22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based. | Article information |
**Supplementary Table 2. Covariables in the Propensity Score Matching**

| Characteristic                                      | Database           | Variables                                                                                                                                 |
|-----------------------------------------------------|--------------------|------------------------------------------------------------------------------------------------------------------------------------------|
| Demographics                                        | NHIS               | Age, sex, income quintile, residence at birth                                                                                             |
| NHIS-PIC 28 Questionnaire                           |                    | Birth weight, type of feeding (breastmilk, formula, mixed, or special milk) until 3-6 months of life, whether infant received additional complementary feeding before 3 months of age, visual sense, auditory sense, sleep on child's stomach?, child's bed or blanket soft?, child sleeps together in their parents' bed?, tummy time for baby? |
| Physical examination                                |                    | Whole body condition, head/forehead, face, eye, nose, ear, oral cavity/neck, lung, heart, abdomen, genital, extremity, spine, nerve, skin                                                                 |
| Comorbidities                                       |                    |                                                                                                                                         |
| Hospital utilization within 6 months of age         | NHIS               | Number of visiting to pediatrics, number of hospitalization, number of hospitalization in ICU, number of visiting ER                           |
| Certain conditions originating in the perinatal period | NHIS (ICD-10 code) | Fetus and newborn affected by maternal factors and by complications of pregnancy, labor and delivery                                          |
|                                                     | P00-P04            | Disorders related to length of gestation and fetal growth                                                                               |
|                                                     | P05-P08            | Birth trauma                                                                                                                             |
|                                                     | P20-P29            | Respiratory and cardiovascular disorders specific to the perinatal period                                                                  |
|                                                     | P35-P39            | Infections specific to the perinatal period                                                                                              |
|                                                     | P50-P61            | Hemorrhagic and hematological disorders of fetus and newborn                                                                              |
|                                                     | P70-P74            | Transitory endocrine and metabolic disorders specific to fetus and newborn                                                                |
|                                                     | P75-P78            | Digestive system disorders of fetus and newborn                                                                                           |
|                                                     | P80-P83            | Conditions involving the integument and temperature regulation of fetus and newborn                                                       |
|                                                     | P90-P96            | Other disorders originating in the perinatal period                                                                                       |
| Prevalent diseases diagnosed within 6 months of age  | NHIS (ICD-10 code) |                                                                                                                                         |
|                                                     | Z38.0              | Singleton, born in hospital                                                                                                              |
|                                                     | A08.4              | Viral intestinal infection, unspecified                                                                                                   |
|                                                     | A09.0              | Other and unspecified gastroenteritis and colitis of infectious origin                                                                    |
|                                                     | A09.9              | Gastroenteritis and colitis of unspecified origin                                                                                         |
|                                                     | B37.0              | Candidal stomatitis                                                                                                                      |
|                                                     | H10.0              | Mucopurulent conjunctivitis                                                                                                               |
|                                                     | H10.2              | Other acute conjunctivitis                                                                                                               |
|                                                     | H10.3              | Acute conjunctivitis                                                                                                                     |
|                                                     | H10.9              | Conjunctivitis, unspecified                                                                                                               |
|                                                     | H60.9              | Unspecified otitis externa                                                                                                                |
|                                                     | H66.0              | Acute suppurative otitis media                                                                                                            |
|                                                     | H66.9              | Otitis media, unspecified                                                                                                                 |
|                                                     | J00                | Acute nasopharyngitis                                                                                                                     |
|                                                     | J01.9              | Acute sinusitis, unspecified                                                                                                               |
|                                                     | J02.9              | Acute pharyngitis, unspecified                                                                                                            |
|                                                     | J03.9              | Acute tonsillitis, unspecified                                                                                                             |
|                                                     | J06.0              | Acute laryngopharyngitis                                                                                                                  |
|                                                     | J06.8              | Other acute upper respiratory infections of multiple sites                                                                             |
|                                                     | J06.9              | Acute upper respiratory infection, unspecified                                                                                             |
|                                                     | J18.9              | Pneumonia, unspecified                                                                                                                     |
|                                                     | J20.9              | Acute bronchitis                                                                                                                          |
|                                                     | J21.9              | Acute bronchiolitis                                                                                                                        |
|                                                     | J30.4              | Allergic rhinitis                                                                                                                         |
|                                                     | J45.9              | Other and unspecified asthma                                                                                                               |
|                                                     | K21.9              | Gastro-esophageal reflux disease without esophagitis                                                                                       |
| Characteristic | Database | Variables |
|---------------|----------|-----------|
| K30           |          | Functional dyspepsia |
| K52.9         |          | Noninfective gastroenteritis and colitis, unspecified |
| K59.0         |          | Constipation |
| K59.1         |          | Functional diarrhea |
| K59.9         |          | Functional intestinal disorder, unspecified |
| L01.0         |          | Impetigo [any organism] [any site] |
| L20.8         |          | Other atopic dermatitis |
| L20.9         |          | Atopic dermatitis |
| L21.1         |          | Seborrheic infantile dermatitis |
| L21.9         |          | Seborrheic dermatitis |
| L22           |          | Diaper dermatitis |
| L23.9         |          | Allergic contact dermatitis |
| L24.9         |          | Irritant contact dermatitis, unspecified cause |
| L30.9         |          | Dermatitis |
| L98.0         |          | Pyogenic granuloma |
| N39.0         |          | Urinary tract infection, site not specified |
| R11           |          | Nausea and vomiting |
| R50.9         |          | Fever, unspecified |

NHIS, National Health Insurance Service; NHSPIC, National Health Screening Program of Infants and Children; ICU, intensive care unit; ER, emergency room; ICD-10, International Classification of Diseases 10th version.
**Supplementary Table 3.** Operating Characteristics of the Diagnostic Codes Used to Define the Diseases

| Diseases     | Definition                                                                 | ICD-10 codes used in the study | N (%) in NICKs cohort (n = 917 707) | N (%) in this cohort (n = 368 556) |
|--------------|-----------------------------------------------------------------------------|--------------------------------|-------------------------------------|-----------------------------------|
| Exposure     |                                                                             |                                |                                     |                                   |
| Infantile colic | Individuals with at least relevant diagnosis codes from the age of 5 weeks to 4 months | R10.4X or R68.1                | 19 492 (2.12)                      | 8787 (2.38)                      |
| Outcomes     |                                                                             |                                |                                     |                                   |
| IBS          | Individuals with more than twice diagnosis of IBS after the age of 4 years   | K58.X                          | 139 571 (15.21)                    | 57 420 (15.58)                   |

ICD-10, International Classification of Diseases 10th version; NICKs, National Investigation of Birth Cohort in Korea study; IBS, irritable bowel syndrome.
**Supplementary Table 4. Results of the Questionnaires and Physical Examinations of the First Round of the National Health Screening Program of Infants and Children in the Cohort**

|                                | Observed data (n = 368 556) | Weighted data (n = 723 370) |
|--------------------------------|-----------------------------|-----------------------------|
|                                | n (%)                       | Weighted data n (%)          |
|                                | Control group (n = 359 769) | Control group (n = 363 528) |
|                                | Infantile colic group (n = 8787) | Infantile colic group (n = 359 842) |
|                                | Standardized difference (%) | Standardized difference (%) |

### Questionnaire

**Visual sense**

- **Appropriate**: 355 231 (98.7) vs. 358 957 (98.7)
  - Weighted: 355 461 (98.8)
  - Standardized difference: 0.8

- **Suspected disease**: 4502 (1.3) vs. 4570 (1.3)
  - Weighted: 4381 (1.2)
  - Standardized difference: 0.1

**Auditory sense**

- **Appropriate**: 354 804 (98.6) vs. 358 654 (98.7)
  - Weighted: 355 461 (98.8)
  - Standardized difference: 1.9

- **Suspected disease**: 4810 (1.3) vs. 4873 (1.3)
  - Weighted: 4609 (1.3)
  - Standardized difference: 0.1

**Additional feeding except breastmilk or powdered milk?**

- **Yes**: 204 394 (56.8) vs. 207 996 (57.2)
  - Weighted: 204 634 (56.9)
  - Standardized difference: 0.8

- **No**: 152 961 (42.5) vs. 155 532 (42.8)
  - Weighted: 155 208 (43.1)
  - Standardized difference: 0.0

**Sleep on child’s stomach?**

- **Yes**: 123 186 (34.2) vs. 124 782 (34.3)
  - Weighted: 123 548 (34.3)
  - Standardized difference: 4.9

- **No**: 234 566 (65.2) vs. 238 746 (65.7)
  - Weighted: 236 294 (65.7)
  - Standardized difference: 0.0

**Child’s bed or blanket soft?**

- **Yes**: 116 164 (32.3) vs. 117 758 (32.4)
  - Weighted: 118 134 (32.8)
  - Standardized difference: 1.7

- **No**: 241 823 (67.2) vs. 245 769 (67.6)
  - Weighted: 241 708 (67.2)
  - Standardized difference: 0.1

**Child sleeps together in their parents’ bed?**

- **Yes**: 221 691 (61.6) vs. 224 981 (61.9)
  - Weighted: 222 190 (61.7)
  - Standardized difference: 1.1

- **No**: 135 278 (37.9) vs. 138 547 (38.1)
  - Weighted: 137 652 (38.3)
  - Standardized difference: 0.1

**Tummy time for baby?**

- **Yes**: 327 435 (91.0) vs. 333 461 (91.7)
  - Weighted: 329 739 (91.6)
  - Standardized difference: 2.1

- **No**: 29 597 (8.2) vs. 30 067 (8.3)
  - Weighted: 30 104 (8.4)
  - Standardized difference: 0.0

### Physical examination

**Whole body condition**

- **Appropriate**: 359 642 (100.0) vs. 363 492 (100.0)
  - Weighted: 359 809 (100.0)
  - Standardized difference: 1.8

- **Suspected abnormal**: 35 (0.0) vs. 33 (0.0)
  - Weighted: 33 (0.0)
  - Standardized difference: 0.0

**Head/Fontanel**

- **Appropriate**: 359 460 (99.9) vs. 363 304 (99.9)
  - Weighted: 359 560 (99.9)
  - Standardized difference: 0.4

- **Suspected abnormal**: 220 (0.1) vs. 224 (0.1)
  - Weighted: 228 (0.1)
  - Standardized difference: 0.2

**Face**

- **Appropriate**: 359 622 (100.0) vs. 363 201 (100.0)
  - Weighted: 359 815 (100.0)
  - Standardized difference: 0.5

- **Suspected abnormal**: 58 (0.0) vs. 60 (0.0)
  - Weighted: 27 (0.0)
  - Standardized difference: 0.0

**Eye**

- **Appropriate**: 359 069 (99.8) vs. 362 915 (99.8)
  - Weighted: 359 233 (99.8)
  - Standardized difference: 1.2

- **Suspected abnormal**: 611 (0.2) vs. 613 (0.2)
  - Weighted: 609 (0.2)
  - Standardized difference: 0.2

**Nose**

- **Appropriate**: 359 251 (99.9) vs. 363 100 (99.9)
  - Weighted: 359 384 (99.9)
  - Standardized difference: 2.0

- **Suspected abnormal**: 429 (0.1) vs. 428 (0.1)
  - Weighted: 458 (0.1)
  - Standardized difference: 0.1

**Ear**

- **Appropriate**: 358 863 (99.7) vs. 362 706 (99.8)
  - Weighted: 358 950 (99.8)
  - Standardized difference: 1.3

- **Suspected abnormal**: 817 (0.2) vs. 882 (0.2)
  - Weighted: 891 (0.2)
  - Standardized difference: 0.4

**Oral cavity/neck**

- **Appropriate**: 359 359 (99.9) vs. 363 201 (99.9)
  - Weighted: 359 470 (99.9)
  - Standardized difference: 0.7

- **Suspected abnormal**: 321 (0.1) vs. 327 (0.1)
  - Weighted: 372 (0.1)
  - Standardized difference: 0.1
### Supplementary Table 4. Continued

| Body Part | Observed data (n = 368 556) | Weighted data (n = 723 370) |
|-----------|-----------------------------|----------------------------|
|           | n (%) | Control group (n = 359 769) | Infantile colic group (n = 8787) | n (%) | Control group (n = 363 528) | Infantile colic group (n = 359 842) |
| Lung      |       |                             |                             |       |                             |                             |
| Appropriate | 359 457 (99.9) | 8782 (99.9) | 1.8 | 363 306 (99.9) | 359 606 (99.9) | 0.3 |
| Suspected abnormal | 222 (0.1) | 2 (0.0) | | 222 (0.1) | 235 (0.1) | |
| Heart     |       |                             |                             |       |                             |                             |
| Appropriate | 359 404 (99.9) | 8778 (99.9) | 0.2 | 363 247 (99.9) | 359 548 (99.9) | 0.0 |
| Suspected abnormal | 276 (0.1) | 6 (0.1) | | 280 (0.1) | 294 (0.1) | |
| Abdomen   |       |                             |                             |       |                             |                             |
| Appropriate | 359 552 (99.9) | 8783 (100.0) | 1.6 | 363 399 (100.0) | 359 786 (100.0) | 0.0 |
| Suspected abnormal | 128 (0.0) | 1 (0.0) | | 129 (0.0) | 56 (0.0) | |
| Genital   |       |                             |                             |       |                             |                             |
| Appropriate | 358 579 (99.7) | 8761 (99.7) | 0.6 | 362 416 (99.7) | 358 623 (99.7) | 0.2 |
| Suspected abnormal | 1188 (0.3) | 23 (0.3) | | 1112 (0.3) | 1219 (0.3) | |
| Extremity |       |                             |                             |       |                             |                             |
| Appropriate | 358 795 (99.7) | 8762 (99.7) | 0.2 | 362 627 (99.8) | 358 951 (99.8) | 0.2 |
| Suspected abnormal | 884 (0.2) | 22 (0.3) | | 901 (0.2) | 891 (0.2) | |
| Spine     |       |                             |                             |       |                             |                             |
| Appropriate | 359 585 (99.9) | 8780 (99.9) | 1.2 | 363 430 (100.0) | 359 756 (100.0) | 0.1 |
| Suspected abnormal | 94 (0.0) | 4 (0.0) | | 98 (0.0) | 85 (0.0) | |
| Nerve     |       |                             |                             |       |                             |                             |
| Appropriate | 359 615 (100.0) | 8782 (99.9) | 0.4 | 363 463 (100.0) | 359 791 (100.0) | 0.0 |
| Suspected abnormal | 64 (0.0) | 2 (0.0) | | 65 (0.0) | 51 (0.0) | |
| Skin      |       |                             |                             |       |                             |                             |
| Appropriate | 355 538 (98.8) | 8702 (99.0) | 2.1 | 359 375 (98.9) | 355 936 (98.9) | 0.1 |
| Suspected abnormal | 4117 (1.1) | 82 (0.9) | | 4153 (1.1) | 3886 (1.1) | |

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*Unless otherwise specified, all variables were assessed at the age of four to 6 months.*

*Weighted using inverse probability of exposure weighting based on the propensity score. The propensity score was estimated using multivariable logistic regression with 97 previously covariates, as defined in Supplementary Table 2. Participants in the reference group were weighted as (propensity score/[1-propensity score]). This method produces a weighted pseudosample of participants in the reference group with the same distribution of measured covariates as the exposure group.*

*Values are reported as n (%) unless otherwise indicated.*

*As the reference group, the control group consisted of children who had not been diagnosed with infantile colic at 5 weeks to 4 months of age.*

*The infantile colic group consists of children who have been diagnosed with infantile colic at least once between 5 weeks and 4 months of age.*

*The difference between the groups divided by the pooled standard deviation; a value greater than 10% is interpreted as a meaningful difference.*
| Clinical characteristics                                                                 | Observed data (n = 368,556) | Weighted data (n = 723,370) |
|-----------------------------------------------------------------------------------------|------------------------------|----------------------------|
|                                                                                  | n (%)                        | n (%)                        |
| Control group (n = 359,769)                                                          |                              | Control group (n = 363,328)  |
|-child group (n = 8787)                                                                |                              | Infantile colic group (n = 359,842) |
| Hospital utilization within 6 months of age                                            |                              |                              |
| No. of visits to pediatricians                                                       | 341,551 (94.9)               | 345,435 (95.0)               |
|                                                                                     | 8688 (98.9)                  | 342,290 (95.1)               |
| No. of hospitalizations                                                               | 54,711 (15.2)                | 55,468 (15.3)                |
|                                                                                     | 1519 (17.3)                  | 55,961 (15.6)                |
| No. of hospitalizations in ICU                                                        | 740 (0.2)                    | 751 (0.2)                    |
|                                                                                     | 20 (0.2)                     | 747 (0.2)                    |
| No. of visits to ER                                                                   | 15,903 (4.4)                 | 16,843 (4.6)                 |
|                                                                                     | 1174 (13.4)                  | 18,281 (5.1)                 |
| Certain conditions (ICD-10 codes) originating in the perinatal period                 |                              |                              |
| Fetus and newborn affected by maternal factors and by complications of pregnancy, labor and delivery | 6727 (1.9)                   | 6811 (1.9)                   |
| Disoders related to length of gestation and fetal growth                              | 2414 (0.7)                   | 2438 (0.7)                   |
| Birth trauma                                                                          | 3104 (0.9)                   | 3142 (0.9)                   |
| Respiratory and cardiovascular disorders specific to the perinatal period              | 14,603 (4.1)                 | 14,845 (4.1)                 |
| Infections specific to the perinatal period                                           | 49,707 (13.8)                | 50,342 (13.8)                |
| Hemorrhagic and Hematological disorders of fetus and newborn                           | 112,149 (31.2)               | 113,338 (31.2)               |
| Transitory endocrine and metabolic disorders specific to fetus and newborn            | 10,010 (2.8)                 | 10,155 (2.8)                 |
| Digestive system disorders of fetus and newborn                                       | 10,079 (2.8)                 | 10,283 (2.8)                 |
| Conditions involving the integument and temperature regulation of fetus and newborn   | 13,213 (3.7)                 | 13,366 (3.7)                 |
| Other disorders originating in the perinatal period                                    | 20,116 (5.6)                 | 20,447 (5.6)                 |
| Prevalent diseases (ICD-10 codes) diagnosed within 6 months of age                   |                              |                              |
| Singleton, born in hospital                                                           | 245,264 (68.2)               | 247,791 (68.2)               |
| Viral intestinal infection, unspecified                                                | 9,741 (2.7)                  | 10,064 (2.8)                 |
| Infectious gastroenteritis and colitis of infectious origin                            | 5,416 (1.5)                  | 5,524 (1.5)                  |
| Other and unspecified gastroenteritis and colitis of infectious origin                | 18,362 (5.1)                 | 18,802 (5.2)                 |
| Gastroenteritis and colitis of unspecified origin                                      | 20,055 (5.6)                 | 20,541 (5.7)                 |
| Candidal stomatitis                                                                  | 6,325 (1.8)                  | 6,402 (1.8)                  |
| Mucopurulent conjunctivitis                                                           | 5,620 (1.6)                  | 5,674 (1.6)                  |
| Other acute conjunctivitis                                                            | 6,863 (1.9)                  | 6,934 (1.9)                  |
| Acute conjunctivitis                                                                 | 13,848 (3.8)                 | 14,011 (3.9)                 |
| Conjunctivitis, unspecified                                                           | 14,776 (4.1)                 | 14,961 (4.1)                 |
| Unspecified otitis externa                                                            | 4,455 (1.2)                  | 4,511 (1.2)                  |
| Acute suppurative otitis media                                                        | 14,873 (4.1)                 | 15,000 (4.1)                 |
| Otitis media, unspecified                                                             | 7,989 (2.2)                  | 8,038 (2.2)                  |
| Acute nasopharyngitis                                                                | 104,381 (29.0)               | 105,974 (29.2)               |
| Acute sinusitis, unspecified                                                          | 12,585 (3.5)                 | 12,707 (3.5)                 |
| Acute pharyngitis                                                                    | 37,920 (10.5)                | 38,483 (10.6)                |
| Acute tonsillitis, unspecified                                                        | 18,232 (5.1)                 | 18,441 (5.1)                 |
| Acute laryngopharyngitis                                                             | 9,189 (2.6)                  | 9,276 (2.6)                  |
### Supplementary Table 5. Continued

| Clinical characteristics                                      | Observed data (n = 368 556) | Weighted data (n = 723 370) |
|---------------------------------------------------------------|-----------------------------|----------------------------|
|                                                               | n (%) | Weighted difference (%) | n (%) | Weighted difference (%) |
|                                                               | Control group (n = 359 769) | Infantile colic group (n = 8787) | Control group (n = 363 528) | Infantile colic group (n = 359 842) |
| Other acute upper respiratory infections of multiple sites    | 9292 (2.6) | 265 (3.0) | 2.9 | 9427 (2.6) | 9916 (2.78) | 0.3 |
| Acute upper respiratory infection, unspecified               | 81 665 (22.7) | 2198 (25.0) | 5.1 | 82 711 (22.8) | 84 377 (23.4) | 0.5 |
| Pneumonia, unspecified                                      | 66 304 (18.4) | 1634 (18.6) | 0.6 | 66 995 (18.4) | 66 559 (18.5) | 0.7 |
| Acute bronchitis                                             | 48 798 (13.6) | 1129 (12.8) | 2.2 | 49 176 (13.5) | 50 601 (14.1) | 0.7 |
| Allergic rhinitis                                            | 8795 (2.4) | 208 (2.4) | 0.1 | 8833 (2.4) | 8289 (2.3) | 0.7 |
| Other and unspecified asthma                                 | 8334 (2.3) | 181 (2.1) | 1.9 | 8384 (2.3) | 8510 (2.4) | 0.2 |
| Gastroesophageal reflux disease without esophagitis         | 8416 (2.3) | 333 (3.8) | 8.6 | 8617 (2.4) | 8590 (2.4) | 0.4 |
| Functional dyspepsia                                         | 7635 (2.1) | 315 (3.6) | 8.7 | 7834 (2.2) | 8289 (2.3) | 0.2 |
| Noninfective gastroenteritis and colitis, unspecified        | 16 372 (4.6) | 561 (6.4) | 8.2 | 16 709 (4.6) | 18 306 (5.1) | 0.8 |
| Constipation                                                 | 15 365 (4.3) | 574 (6.5) | 9.9 | 15 699 (4.3) | 16 272 (4.5) | 0.7 |
| Functional diarrhea                                          | 5223 (1.5) | 205 (2.3) | 6.1 | 5360 (1.5) | 5375 (1.5) | 0.0 |
| Functional intestinal disorder, unspecified                  | 10 060 (2.8) | 357 (4.1) | 7.3 | 10 248 (2.8) | 10 274 (2.9) | 0.1 |
| Impetigo [any organism] [any site]                          | 5586 (1.6) | 146 (1.7) | 1.2 | 5641 (1.6) | 5642 (1.6) | 0.0 |
| Other atopic dermatitis                                      | 20 095 (5.6) | 479 (5.5) | 1.1 | 20 245 (5.6) | 19 907 (5.5) | 0.3 |
| Atopic dermatitis                                           | 57 318 (15.9) | 1507 (17.2) | 3.4 | 58 007 (16.0) | 56 019 (15.6) | 0.0 |
| Seborrheic infantile dermatitis                              | 9003 (2.5) | 253 (2.9) | 2.7 | 9124 (2.5) | 9301 (2.6) | 0.6 |
| Seborrheic dermatitis                                        | 7460 (2.1) | 199 (2.3) | 1.3 | 7563 (2.1) | 7599 (2.1) | 0.2 |
| Diaper dermatitis                                            | 27 123 (7.5) | 784 (8.9) | 5.1 | 27 525 (7.6) | 27 099 (7.5) | 0.4 |
| Allergic contact dermatitis                                  | 16 542 (4.6) | 479 (5.5) | 3.7 | 16 794 (4.6) | 17 709 (4.9) | 0.1 |
| Irritant contact dermatitis, unspecified cause               | 6867 (1.9) | 220 (2.3) | 4.1 | 6974 (1.9) | 7213 (2.0) | 0.2 |
| Dermatitis                                                   | 13 542 (4.3) | 480 (5.3) | 5.6 | 13 630 (4.3) | 13 785 (4.4) | 0.1 |
| Pyogenic granuloma                                           | 4750 (1.3) | 131 (1.5) | 1.1 | 4820 (1.3) | 4498 (1.3) | 0.0 |
| Urinary tract infection, site not specified                  | 7731 (2.1) | 231 (2.6) | 3.1 | 7861 (2.2) | 8302 (2.3) | 0.1 |
| Nausea and vomiting                                          | 10 334 (2.9) | 495 (5.6) | 13.6 | 10 699 (2.9) | 11 869 (3.3) | 0.5 |
| Fever, unspecified                                           | 18 237 (5.1) | 524 (6.0) | 4.1 | 18 507 (5.1) | 21 594 (5.9) | 0.1 |

**Drug (drug classification code) used within 6 months of age**

| Sedative-hypnotics                                          | 10 825 (3.0) | 524 (6.0) | 14.3 | 11 172 (3.1) | 11 444 (3.2) | 0.5 |
| Antiepileptics                                              | 64 (0.0) | 4 (0.0) | 1.1 | 68 (0.0) | 74 (0.0) | 0.4 |
| Antipyretics                                                | 126 399 (35.1) | 3410 (38.8) | 7.5 | 127 985 (35.2) | 134 985 (37.5) | 4.4 |
| Psycho-nervous system drug                                  | 23 677 (6.6) | 687 (7.8) | 4.7 | 23 987 (6.6) | 23 820 (6.6) | 0.5 |
| Antispasmodics                                              | 8222 (2.3) | 638 (7.3) | 23.1 | 8741 (2.4) | 9205 (2.6) | 0.5 |
| Antihistamine                                               | 168 646 (46.9) | 4231 (48.2) | 2.4 | 179 449 (49.4) | 168 537 (46.8) | 0.7 |
| Other allergic drug                                         | 2175 (0.6) | 65 (0.7) | 1.8 | 2205 (0.6) | 2021 (0.6) | 1.2 |
| Circulatory system drugs                                    | 2058 (0.6) | 53 (0.6) | 0.7 | 2086 (0.6) | 2121 (0.6) | 0.2 |
| Respiratory system drugs                                    | 195 021 (54.2) | 4905 (55.8) | 3.3 | 197 134 (54.2) | 198 425 (55.1) | 2.8 |
| Digestive system drugs                                      | 188 764 (52.5) | 5899 (67.1) | 30.3 | 191 926 (52.8) | 191 892 (53.3) | 0.8 |
| Hormone drugs                                               | 17 352 (4.8) | 432 (4.9) | 0.5 | 17 530 (4.8) | 16 764 (4.7) | 0.6 |
| Steroid                                                     | 17 026 (4.7) | 425 (4.8) | 0.5 | 17 200 (4.7) | 16 463 (4.6) | 0.5 |

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1. Unless otherwise specified, all baseline characteristics were assessed in the first 6 months of age of the participants.
2. Weighted using inverse probability of exposure weighting based on the propensity score. The propensity score was estimated using multivariable logistic regression with 97 previously covariates, as defined in Supplementary Table 2. Participants in the reference group were weighted as (propensity score/[1-propensity score]). This method produces a weighted pseudo sample of participants in the reference group with the same distribution of measured covariates as the exposure group.
3. Results are reported as n (%) unless otherwise indicated.
4. As the reference group, the control group consists of children who had not been diagnosed with infantile colic at 5 weeks to 4 months of age.
5. The infantile colic group consists of children who have been diagnosed with infantile colic at least once between 5 weeks and 4 months of age.
6. Differences greater than 10% were interpreted as meaningful differences. All the standardized differences in the cohort values were < 0.05.
Supplementary Table 6. Subgroup Analysis of the Risk of Irritable Bowel Syndrome With Former Infantile Colic

| Subgroup                     | Unweighted data (n = 368 556) | Weighted data (n = 723 370) |
|------------------------------|-------------------------------|-----------------------------|
|                              | Control group<sup>b</sup> | Infantile colic group<sup>c</sup> | Control group<sup>b</sup> | Infantile colic group<sup>c</sup> | HR (95% CI)<sup>d</sup> |
| Breast feeding<sup>f</sup>    |                               |                             |                             |                              |
| Total number                 | 163 567 (3745)                | 165 601 (165 291)           |                               |                              |
| IBS<sup>e</sup> (n [%])      | 25 266 (15.5)                 | 25 598 (15.5)               | 28 972 (17.5)                 | 1.146 (1.119 to 1.174)       |
| No Breast feeding<sup>f</sup>|                               |                             |                             |                              |
| Total number                 | 194 696 (5009)                | 197 927 (194 551)           |                               |                              |
| IBS<sup>e</sup> (n [%])      | 30 392 (15.6)                 | 30 949 (15.6)               | 32 786 (16.9)                 | 1.087 (1.063 to 1.111)       |
| Birth weight < 3.26 kg<sup>g</sup> |                               |                             |                             |                              |
| Total number (%)             | 188 194 (4747)                | 190 155 (194 339)          |                               |                              |
| IBS<sup>e</sup> (n [%])      | 29 461 (15.7)                 | 29 802 (15.7)               | 34 154 (17.6)                 | 1.135 (1.110 to 1.160)       |
| Birth weight ≥ 3.26 kg<sup>g</sup> |                               |                             |                             |                              |
| Total number (%)             | 171 575 (4040)                | 173 373 (165 503)          |                               |                              |
| IBS<sup>e</sup> (n [%])      | 26 426 (15.4)                 | 26 746 (15.4)               | 27 604 (16.7)                 | 1.088 (1.006 to 1.114)       |
| Male<sup>h</sup>             |                               |                             |                             |                              |
| Total number (%)             | 182 802 (4456)                | 184 696 (183 696)          |                               |                              |
| IBS<sup>e</sup> (n [%])      | 28 974 (15.9)                 | 29 353 (15.9)               | 33 210 (18.1)                 | 1.147 (1.122 to 1.173)       |
| Female<sup>h</sup>           |                               |                             |                             |                              |
| Total number (%)             | 176 967 (4331)                | 178 831 (175 873)          |                               |                              |
| IBS<sup>e</sup> (n [%])      | 26 913 (15.2)                 | 27 194 (15.2)               | 28 549 (16.2)                 | 1.077 (1.052 to 1.102)       |
| Low economic status<sup>i</sup> |                               |                             |                             |                              |
| Total number (%)             | 175 705 (4371)                | 177 580 (177 466)          |                               |                              |
| IBS<sup>e</sup> (n [%])      | 27 577 (15.7)                 | 27 896 (15.7)               | 29 935 (16.9)                 | 1.081 (1.056 to 1.106)       |
| High economic status<sup>i</sup> |                               |                             |                             |                              |
| Total number (%)             | 171 860 (4128)                | 173 610 (170 267)          |                               |                              |
| IBS<sup>e</sup> (n [%])      | 26 413 (15.4)                 | 26 734 (15.4)               | 29 956 (16.7)                 | 1.158 (1.131 to 1.185)       |

<sup>a</sup>Weighted using inverse probability of exposure weighting based on the propensity score. The propensity score was estimated using multivariable logistic regression with 97 previously covariates, as defined in Supplementary Table 2. Participants in the reference group were weighted as (propensity score/[1-propensity score]). This method produces a weighted pseudosample of participants in the reference group with the same distribution of measured covariates as the exposure group.

<sup>b</sup>As the reference group, the control group comprises children who had not been diagnosed with infantile colic at 5 weeks to 4 months of age.

<sup>c</sup>The infantile colic group consists of children who have been diagnosed with infantile colic at least once between 5 weeks and 4 months of age. Infantile colic was defined with at least one diagnosis of International Classification of Diseases 10th version (ICD-10) code R10.4 (other and unspecified abdominal pain) or R68.1 (nonspecific symptoms peculiar to infancy).

<sup>d</sup>Hazard ratios (HRs) were assessed using a Cox proportional hazards model to examine the relationship between infantile colic history and the risk of irritable bowel syndrome (IBS) development and hospitalization in the cohort.

<sup>e</sup>IBS was defined as the diagnosis of ICD-10 codes K58.X (IBS) more than twice after 4 years of age.

<sup>f</sup>Subgroup divided according to the status of breastfeeding before 4 to 6 months of age. Missing data for all data = 1539.

<sup>g</sup>Subgroup divided according to the median value of birthweight.

<sup>h</sup>Subgroup divided according to the sex.

<sup>i</sup>Subgroup divided according to the economic status, defined as insurance premium acquired from the National Health Insurance Service (NHIS). Missing data for all data = 12 492.
### Supplementary Table 7. Subgroup Analysis for the Risk of Strict Irritable Bowel Syndrome With Former Infantile Colic

| Subgroup | Unweighted data (n = 368,556) | Weighted data (n = 723,370)* |
|----------|-------------------------------|------------------------------|
|          | Control group¹ | Infantile colic group¹ | Control group¹ | Infantile colic group¹ | HR (95% CI)¹ |
| Breast feeding | | | | | |
| Total number | 163,567 | 3745 | 165,601 | 165,291 | 1.306 (1.268 to 1.346) |
| IBS (n [%]) | 15,104 (9.2) | 467 (12.5) | 15,345 (9.3) | 19,505 (11.8) |
| No Breast feeding | | | | | |
| Total number | 194,696 | 5009 | 197,927 | 194,551 | 1.214 (1.182 to 1.247) |
| IBS (n [%]) | 19,214 (9.9) | 4631 (12.6) | 19,581 (9.9) | 22,741 (11.7) |
| Birth weight < 3.26 kg | | | | | |
| Total number | 188,194 | 4747 | 190,155 | 194,339 | 1.291 (1.256 to 1.327) |
| IBS (n [%]) | 18,322 (9.7) | 623 (13.1) | 18,561 (9.8) | 23,732 (12.2) |
| Birth weight ≥ 3.26 kg | | | | | |
| Total number | 171,575 | 4040 | 173,373 | 165,503 | 1.210 (1.175 to 1.246) |
| IBS (n [%]) | 16,154 (9.4) | 476 (11.8) | 16,364 (9.4) | 18,513 (11.2) |
| Male | | | | | |
| Total number | 182,802 | 4456 | 184,696 | 183,696 | 1.289 (1.254 to 1.325) |
| IBS (n [%]) | 17,887 (9.8) | 578 (13.0) | 18,127 (9.8) | 22,642 (12.3) |
| Female | | | | | |
| Total number | 176,967 | 4331 | 178,831 | 175,873 | 1.217 (1.182 to 1.253) |
| IBS (n [%]) | 16,589 (9.4) | 521 (12.0) | 16,798 (9.4) | 19,603 (11.2) |
| Low economic status | | | | | |
| Total number | 175,705 | 4371 | 177,580 | 177,466 | 1.196 (1.162 to 1.230) |
| IBS (n [%]) | 17,569 (10.0) | 537 (12.3) | 17,799 (10.0) | 20,807 (11.7) |
| High economic status | | | | | |
| Total number | 171,860 | 4128 | 173,610 | 170,267 | 1.333 (1.295 to 1.373) |
| IBS (n [%]) | 15,614 (9.1) | 523 (12.7) | 15,826 (9.1) | 20,055 (11.8) |

1Weighted using inverse probability of exposure weighting based on the propensity score. The propensity score was estimated using multivariable logistic regression with 97 previously covariates, as defined in Supplementary Table 2. Participants in the reference group were weighted as (propensity score/[1-propensity score]). This method produces a weighted pseudo sample of participants in the reference group with the same distribution of measured covariates as the exposure group.
2As the reference group, the control group comprises children who had not been diagnosed with infantile colic at 5 weeks to 4 months of age.
3The infantile colic group consists of children who have been diagnosed with infantile colic at least once between 5 weeks and 4 months of age. Infantile colic was defined with at least one diagnosis of International Classification of Diseases 10th version (ICD-10) code R10.4 (other and unspecified abdominal pain) or R68.1 (nonspecific symptoms peculiar to infancy).
4Hazard ratios (HRs) were assessed using a Cox proportional hazards model to examine the relationship between infantile colic history and the risk of irritable bowel syndrome (IBS) development and hospitalization in the cohort.
5IBS was defined as the diagnosis of ICD-10 codes K58.X (IBS) more than twice after 4 years of age.
6Subgroup divided according to the status of breastfeeding before 4 to 6 months of age. Missing data for all data = 1539.
7Subgroup divided according to the median value of birthweight.
8Subgroup divided according to the economic status, defined as insurance premium acquired from the National Health Insurance Service (NHIS). Missing data for all data = 12,492.