### SUPPLEMENTARY APPENDIX

This appendix provides readers additional information about the study protocol, the literature search and results.

Supplement to: "Early-life Exposures and Risk of Inflammatory Bowel Disease: a Systematic Review and Meta-analysis "

### SUPPLEMENTARY APPENDIX

## Appendix A: Study Protocol and Literature Search

- 1. Study identification
- 2. Eligibility criteria
- 3. Study selection and data abstraction
- 4. Risk of bias and study quality
- 5. Qualitative and quantitative analysis
- 6. Literature search and results

## **Appendix B: Supplementary Tables**

**Supplementary Tables 1** a–j: Extracted data from studies on the association between early life exposures and inflammatory bowel disease

- a. Maternal health and exposures during pregnancy
- b. Perinatal factors
- c. Birth month and related factors
- d. Breastfeeding
- e. Hygiene-related factors
- f. Social factors
- g. Immigration
- h. Infections
- i. Antibiotics and other medications
- j. Passive exposure to tobacco smoke

# Supplementary Table 2: Newcastle Ottawa Scale grading of all included studies

- 2a: Newcastle Ottawa Scale grading of case-control studies
- 2b: Newcastle Ottawa Scale grading of cohort studies

**Appendix C: Supplementary Figures 1-33** 

#### **APPENDIX A – STUDY PROTOCOL AND LITERATURE SEARCH**

#### 1. Study identification

We conducted the identification and retrieval of studies in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. We developed and executed a comprehensive search strategy in collaboration with a medical librarian (CS). We searched Embase (Ovid), MEDLINE ALL (Ovid), and Global Health (Ovid) databases from the date of database inception though May 23, 2019. We repeated the search from January 2019 until July 14, 2020 to identify the more recent studies. We did not apply any language or date restriction at the initial search. We applied a filter for observational studies, adapted from the Observational Studies search filter developed by the Scottish Intercollegiate Guidelines Network (SIGN). The search was designed using a combination of free-text terms and subject headings specific to each database, EMBASE Emtree subject headings, MEDLINE Medical Subject Headings (MeSH), and Global Health CABI subject headings. We also searched references of all included studies as well as pertinent reviews. The full search query for all biomedical platforms is available in Appendix A. Search results were exported into the Covidence platform and de-duplicated. The review protocol was registered with PROSPERO (CRD42019134980). The following are deviations from the registered protocol: given that several important exposures were reported in smaller cohort and case-control studies, including exposures that cannot be ascertained in population-based administrative data, we extended the review beyond population-based studies. While we did not plan quantitative review at the outset due to heterogeneity overall, we added quantitative synthesis to the review in order to add further objectivity and granularity. We included all studies, including non-English at the initial search. Given the number of studies to be screened, and lack of relevant non-English studies, we excluded non-English studies during abstract screening.

### 2. Eligibility criteria

We included case-control and cohort studies that determined the association of early-life environmental risk factors with CD, UC or IBD overall. Early-life was defined as extending from prenatal period to 5 years of age. Based on prior literature review (MA, JS), we included all relevant nongenetic exposures and categorized them into (1) maternal exposures and health during pregnancy, (2) perinatal factors (3) birth month and related-factors (4) breastfeeding, (5) hygiene-related factors, (6) social factors, (7) immigration, (8) antibiotics and other medications, (9) offspring health, including infections, and (10) passive smoking. We excluded studies if the timing of the exposure was not clearly defined at  $\leq$ 5 years of age. If studies reported data on both  $\leq$ 5 and  $\geq$ 5 years of age, we included only the former subset of patients. If multiple studies reported data from the same cohort, we included the most recent study, the one with the longest duration of follow-up, or the one with the largest sample size, in this order of priority. Studies published in a language other than English were excluded.

#### 3. Study selection and data abstraction

Study selection and data extraction were performed by two of seven investigators (MA, JS, CFG, JA, SCS, TL and JT) independently using the Covidence platform. Any conflict during abstract or full-text screening was resolved by review of the pertinent study jointly, with an additional arbiter when needed. Data were extracted per the Cochrane Consumers and Communication Review Group's template. The following elements were recorded: the name and year of the study, the country and region where it was conducted, study period and design, exposure(s) and outcome(s) and estimates.

#### 4. Risk of bias and study quality

The risk of bias and quality of studies were evaluated by two investigators independently, and jointly in case of discrepancy, using either the cohort or case-control studies instrument of the Newcastle-Ottawa Scale (NOS) (5). Studies

were evaluated in three domains: selection, comparability, and outcome, and were awarded a maximum of four, two or three points, respectively. A total score of seven or higher indicated a high-quality study.

# 5. Qualitative and quantitative analysis

We conducted random-effects meta-analyses to determine pooled estimates with 95% confidence intervals (CI) for homogenous exposures reported in  $\geq$ 2 studies with comparable study design (cohort or case-control) and outcome (CD, UC or IBD). As recent meta-analyses have been conducted for exposures breastfeeding and mode of delivery, we deferred meta-analyzing data for these exposures. We report meta-analyses for the following exposures: maternal age at pregnancy, prenatal exposure to tobacco smoke, perinatal factors including preterm birth and birth weight, rural versus urban living, passive exposure to tobacco smoke during childhood, measles vaccination, otitis media and antibiotic exposure during the first year of life. Adjusted estimates were used when available. When relevant data were available from cohort studies, we calculated odds ratios in order to be able to pool with odds ratios from case-control studies. When feasible, case-control and cohort studies estimates were pooled and meta-regression performed to determine if there were differences based on study type. Heterogeneity was evaluated using the l<sup>2</sup> score. Meta-analyses were performed using the Comprehensive Meta-Analysis (version 2.0; Biostat, Englewood, NJ).

For exposure categories that were not analyzed quantitatively, we extracted relevant data and performed a systematic review.

## 6. Literature search and results

Literature search was run on Friday, May 24th 2019 and repeated on July 14, 2020.

# Embase Classic+Embase 1947 to 2019 May 23

15351 references

- 1. exp migrant/
- 2. exp migration/
- 3. exp ethnology/
- 4. (emigra\* or immigra\* or migrant\* or migrat\* or ethnolog\* or transient\*).tw,kw.
- 5. or/1-4
- 6. exp antibiotic agent/
- 7. exp nonsteroid antiinflammatory agent/
- 8. oral contraception/ or exp oral contraceptive agent/ or hormonal contraception/
- 9. ((oral\* or hormon\*) adj3 contracept\*).tw,kw.
- 10. (antibiotic\* or penicillin\* or cephalosporin\* or tetracycline\* or doxycycline\* or minocycline\* or fluoroquinolone\* or macrolide\* or sulfonamide\* or metronidazole\* or vancomycin\*).tw,kw.
- 11. (nsaid\* or ocp\*).tw,kw.

12. ((nonsteroid\* or non-steroid\*) adj3 (antiinflammator\* or anti-inflammator\* or (anti adj2 inflammator\*))).tw,kw.

- 13. or/6-12
- 14. exp helicobacter/
- 15. exp Campylobacter/
- 16. Helicobacter\*.tw,kw.
- 17. Campylobacter\*.tw,kw.
- 18. (H adj2 pylori).tw,kw.
- 19. cagA.tw,kw.
- 20. ((cytotoxin-associated or (cytotoxin adj2 associated)) adj4 A).tw,kw.

- 21. VacA.tw,kw.
- 22. (Vacuolating adj2 cytotoxin\*).tw,kw.
- 23. exp disease elimination/
- 24. (eradication or elimination).tw,kw.
- 25. or/14-24
- 26. exp instrumental delivery/ or vaginal delivery/
- 27. (c?esarean\* or c-section\* or csection\*).tw,kw.
- 28. (mode adj4 deliver\*).tw,kw.
- 29. or/26-28
- 30. exp vaccine/
- 31. vaccin\*.tw,kw.
- 32. appendectomy/
- 33. (appendectom\* or appendicectom\* or appendicitis).tw,kw.
- 34. appendix.tw,kw.
- 35. exp tonsillectomy/
- 36. tonsillectom\*.tw,kw.
- 37. or/30-36
- 38. exp "physical activity, capacity and performance"/
- 39. exp sport/
- 40. (physical adj4 activit\*).tw,kw.
- 41. (exercis\* or sport\*).tw,kw.
- 42. or/38-41
- 43. environmental exposure/
- 44. exp domestic animal/
- 45. exp farm animal/
- 46. urban rural difference/
- 47. urban hygiene/
- 48. rural hygiene/ or rural population/
- 49. urban population/
- 50. "crowding (area)"/
- 51. population density/ or population abundance/ or population size/
- 52. family size/
- 53. birth order/
- 54. environmental sanitation/ or exp microbial contamination/ or pollution control/ or pollution transport/ or exp water management/
- 55. refrigerator/
- 56. exp food preservation/
- 57. exp socioeconomics/
- 58. exp "pollution and pollution related phenomena"/
- 59. sun exposure/
- 60. exp ultraviolet radiation/
- 61. exp vitamin D/ or folic acid/
- 62. exp child abuse/
- 63. (environmental adj4 (factor\* or exposure\*)).tw,kw.
- 64. (protect\* adj3 factor\*).tw,kw.

65. (early adj3 life).tw,kw.

66. ((domestic\* or farm\*) adj4 animal\*).tw,kw.

67. (pet or pets or dog\* or cat or cats).tw,kw.

68. (famil\* adj4 size\*).tw,kw.

69. (birth adj4 order).tw,kw.

70. (sanitation or refrigerat\* or pasteuriz\* or pollut\* or (food adj4 preserv\*)).tw,kw.

71. (urban\* or rural\*).tw,kw.

72. socioeconomic\*.tw,kw.

73. ((parent\* adj3 occupation) or (social adj3 mixing)).tw,kw.

74. latitude/

75. (sun or ultraviolet\* or UV or UVs or (vitamin adj4 D) or folate or (folic adj3 acid\*) or latitude).tw,kw.

76. or/43-75

77. maternal stress/

78. exp maternal care/ or prenatal exposure/

79. maternal smoking/

80. ((maternal or mother\* or pregnan\* or postpartum or post-partum or prenatal\* or pre-natal\* or postnatal\* or postnatal\* or perinatal\* or peri-natal\* or peripartum or peri-partum or prepartum or pre-partum) adj5 (diet\* or nutrition\* or infection\* or smok\* or stress\*)).tw,kw.

81. ((maternal or mother\* or pregnan\* or postpartum or post-partum or prenatal\* or pre-natal\* or postnatal\* or postnatal\* or perinatal\* or peri-natal\* or peripartum or peri-partum or prepartum or pre-partum) adj5 (risk adj4 factor\*)).tw,kw.

82. or/77-81

83. exp child nutrition/

84. weaning/

85. (breastfeeding or breast-feeding or breastfed\* or lactation or formula\* or colostrum or (human adj3 milk\*) or emulsifier\*).tw,kw.

86. ((breast or bottle\* or infant\* or child\*) adj4 feeding).tw,kw.

87. weaning.tw,kw.

88. or/83-87

89. exp parasite/

90. exp helminth/

91. exp hygiene/

92. hygiene hypothesis/

93. exp parasitosis/

94. exp smoking/

95. tobacco/

96. parasit\*.tw,kw.

97. (helminth\* or nematode\* or tapeworm\* or ascaria\* or flatworm\* or cestod\* or trematod\*).tw,kw.

98. hygien\*.tw,kw.

99. infestation.tw,kw.

100. (smok\* or tobacco\*).tw,kw.

101. (diet\* or nutrition\* or food\*).tw,kw.

102. or/89-101

103. exp child/

104. exp pediatrics/

105. (Infan\* or newborn\* or new-born\* or perinat\* or neonat\* or baby\* or babies or toddler\* or minors\* or boy or boys or boyfriend or boyhood or girl\* or kid or kids or child\* or schoolchild\* or school-child\*).mp.

106. (p?ediatric\* or peadiatric\* or prematur\* or preterm\*).mp.

- 107. school\*.tw,kw.
- 108. or/103-107
- 109. 102 and 108
- 110. 5 or 13 or 25 or 29 or 37 or 42 or 76 or 82 or 88 or 109
- 111. exp inflammatory bowel disease/
- 112. (inflammatory adj4 bowel adj4 disease\*).tw,kw.
- 113. ((ulcerative or ulcerous or mucosal or Idiopathic) adj3 (colitis or proctocolitis or colorectitis)).tw,kw.
- 114. (colitis adj3 (gravis or ulcerativa or ulcerosa)).tw,kw.
- 115. ((Crohn\* or granulomatous) adj3 (disease\* or enteritis or ileitis or ileitides or colitis or enterocolitis)).tw,kw.
- 116. ((regional or terminal) adj3 (enteritis or ileitis or ileitides or colitis or enterocolitis)).tw,kw.
- 117. (morbus adj3 crohn\*).tw,kw.
- 118. or/111-117
- 119. Clinical study/
- 120. exp Case control study/
- 121. Family study/
- 122. Longitudinal study/
- 123. Retrospective study/
- 124. Prospective study/ or exp incidence/ or exp prevalence/
- 125. Randomized controlled trials/ or intervention study/
- 126. 124 not 125
- 127. Cohort analysis/
- 128. (Case control adj3 (study or studies)).mp.
- 129. (observational adj3 (study or studies)).mp.
- 130. (epidemiologic\* adj3 (study or studies)).mp.
- 131. (cross sectional adj3 (study or studies)).mp.
- 132. (cohort or prospective or retrospective or population based or longitudinal).mp.
- 133. or/119-123,126-132
- 134. 110 and 118 and 133

# Ovid MEDLINE (R) ALL 1946 to May 23, 2019

6315 references

- 1. "Transients and Migrants"/
- 2. exp Human Migration/
- 3. Ethnology/
- 4. (emigra\* or immigra\* or migrant\* or migrat\* or ethnolog\* or transient\*).tw,kf.
- 5. or/1-4
- 6. exp anti-bacterial agents/ or exp antifungal agents/
- 7. exp Anti-Inflammatory Agents, Non-Steroidal/
- 8. exp Contraception/
- 9. ((oral\* or hormon\*) adj3 contracept\*).tw,kf.

10. (antibiotic\* or penicillin\* or cephalosporin\* or tetracycline\* or doxycycline\* or minocycline\* or fluoroquinolone\* or macrolide\* or sulfonamide\* or metronidazole\* or vancomycin\*).tw,kf.

- 11. (nsaid\* or ocp\*).tw,kf.
- 12. ((nonsteroid\* or non-steroid\*) adj3 (antiinflammator\* or anti-inflammator\* or (anti adj2 inflammator\*))).tw,kf.
- 13. or/6-12
- 14. exp Helicobacter/
- 15. exp Campylobacter/
- 16. Helicobacter\*.tw,kf.
- 17. Campylobacter\*.tw,kf.
- 18. (H adj2 pylori).tw,kf.
- 19. cagA.tw,kf.
- 20. ((cytotoxin-associated or (cytotoxin adj2 associated)) adj4 A).tw,kf.
- 21. VacA.tw,kf.
- 22. (Vacuolating adj2 cytotoxin\*).tw,kf.
- 23. exp Disease Eradication/
- 24. (eradication or elimination).tw,kf.
- 25. or/14-24
- 26. exp Delivery, Obstetric/
- 27. (c?esarean\* or c-section\* or csection\*).tw,kf.
- 28. (mode adj4 deliver\*).tw,kf.
- 29. or/26-28
- 30. exp Vaccines/
- 31. vaccin\*.tw,kf.
- 32. Appendectomy/
- 33. (appendectom\* or appendicectom\* or appendicitis).tw,kf.
- 34. appendix.tw,kf.
- 35. Tonsillectomy/
- 36. tonsillectom\*.tw,kf.
- 37. or/30-36
- 38. exp Exercise/
- 39. exp Sports/
- 40. (physical adj4 activit\*).tw,kf.
- 41. (exercis\* or sport\*).tw,kf.
- 42. or/38-41
- 43. exp Environmental Exposure/
- 44. exp Animals, Domestic/
- 45. exp Hygiene/
- 46. exp Population/
- 47. exp population health/ or maternal health/
- 48. population density/
- 49. Family Characteristics/
- 50. birth order/ or "social determinants of health"/
- 51. Sanitation/
- 52. Refrigeration/
- 53. exp Food Handling/

- 54. child health/ or infant health/ or maternal health/ or exp socioeconomic factors/
- 55. exp Environmental Pollution/

56. sunlight/

- 57. ultraviolet rays/
- 58. exp Vitamin D/ or exp Vitamin D Deficiency/ or exp Folic Acid/
- 59. exp Child Abuse/
- 60. (environmental adj4 (factor\* or exposure\*)).tw,kf.
- 61. (protect\* adj3 factor\*).tw,kf.
- 62. (early adj3 life).tw,kf.
- 63. ((domestic\* or farm\*) adj4 animal\*).tw,kf.
- 64. (pet or pets or dog\* or cat or cats).tw,kf.
- 65. (famil\* adj4 size\*).tw,kf.
- 66. (birth adj4 order).tw,kf.
- 67. (sanitation or refrigerat\* or pasteuriz\* or pollut\* or (food adj4 preserv\*)).tw,kf.
- 68. (urban\* or rural\*).tw,kf.
- 69. socioeconomic\*.tw,kf.
- 70. ((parent\* adj3 occupation) or (social adj3 mixing)).tw,kf.
- 71. (sun or ultraviolet\* or UV or UVs or (vitamin adj4 D) or folate or (folic adj3 acid\*) or latitude).tw,kf.

72. or/43-71

- 73. exp Maternal Behavior/
- 74. Prenatal Exposure Delayed Effects/

75. ((maternal or mother\* or pregnan\* or postpartum or post-partum or prenatal\* or pre-natal\* or postnatal\* or postnatal\* or perinatal\* or peri-natal\* or peripartum or peri-partum or prepartum or pre-partum) adj5 (diet\* or nutrition\* or infection\* or smok\* or stress\*)).tw,kf.

76. ((maternal or mother\* or pregnan\* or postpartum or post-partum or prenatal\* or pre-natal\* or postnatal\* or postnatal\* or perinatal\* or peri-natal\* or peripartum or peri-partum or prepartum or pre-partum) adj5 (risk adj4 factor\*)).tw,kf.

77. or/73-76

78. child nutritional physiological phenomena/ or exp infant nutritional physiological phenomena/ or exp maternal nutritional physiological phenomena/

79. exp Lactation/

80. (breastfeeding or breast-feeding or breastfed\* or lactation or formula\* or colostrum or (human adj3 milk\*) or emulsifier\*).tw,kf.

81. ((breast or bottle\* or infant\* or child\*) adj4 feeding).tw,kf.

- 82. weaning.tw,kf.
- 83. or/78-82
- 84. exp helminths/
- 85. parasites/
- 86. exp hygiene/
- 87. hygiene hypothesis/
- 88. exp Parasitic Diseases/
- 89. exp "tobacco use"/
- 90. parasit\*.tw,kf.

91. (helminth\* or nematode\* or tapeworm\* or ascaria\* or flatworm\* or cestod\* or trematod\*).tw,kf.

92. hygien\*.tw,kf.

93. infestation.tw,kf.

- 94. (smok\* or tobacco\*).tw,kf.
- 95. (diet\* or nutrition\* or food\*).tw,kf.

96. or/84-95

97. exp child/ or exp infant/ or minors/

98. exp Pediatrics/

99. (Infan\* or newborn\* or new-born\* or perinat\* or neonat\* or baby\* or babies or toddler\* or minors\* or boy or boys or boyfriend or boyhood or girl\* or kid or kids or child\* or schoolchild\* or school-child\*).mp.

100. (p?ediatric\* or peadiatric\* or prematur\* or preterm\*).mp.

- 101. school\*.tw,kf.
- 102. or/97-101
- 103.96 and 102
- 104. 5 or 13 or 25 or 29 or 37 or 42 or 72 or 77 or 83 or 103
- 105. exp Inflammatory Bowel Diseases/
- 106. (inflammatory adj4 bowel adj4 disease\*).tw,kf.

107. ((ulcerative or ulcerous or mucosal or Idiopathic) adj3 (colitis or proctocolitis or colorectitis)).tw,kf.

- 108. (colitis adj3 (gravis or ulcerativa or ulcerosa)).tw,kf.
- 109. ((Crohn\* or granulomatous) adj3 (disease\* or enteritis or ileitis or ileitides or colitis or enterocolitis)).tw,kf.
- 110. ((regional or terminal) adj3 (enteritis or ileitis or ileitides or colitis or enterocolitis)).tw,kf.
- 111. (morbus adj3 crohn\*).tw,kf.
- 112. or/105-111
- 113. Clinical study/ or observational study/ or comparative study/ or Observational Studies as Topic/

114. controlled before-after studies/ or cross-sectional studies/ or historically controlled study/ or interrupted time series analysis/

- 115. exp case-control studies/
- 116. epidemiologic studies/ or epidemiologic methods/
- 117. longitudinal studies/
- 118. retrospective studies/
- 119. Prospective Studies/ or incidence/ or prevalence/
- 120. randomized controlled trial/
- 121. 119 not 120
- 122. cohort studies/
- 123. (Case control adj3 (study or studies)).mp.
- 124. (observational adj3 (study or studies)).mp.
- 125. (epidemiologic\* adj3 (study or studies)).mp.
- 126. (cross sectional adj3 (study or studies)).mp.
- 127. (cohort or prospective or retrospective or population based or longitudinal).mp.

128. or/113-118,121-127

129. 104 and 112 and 128

# Global Health 1910 to 2019 Week 19

1396 references

1. exp migrants/

2. migration/

3. (emigra\* or immigra\* or migrant\* or migrat\* or ethnolog\* or transient\*).tw,kw.

- 4. or/1-3
- 5. exp antibiotics/
- 6. exp non-steroidal antiinflammatory agents/
- 7. exp oral contraceptives/ or exp contraceptives/
- 8. ((oral\* or hormon\*) adj3 contracept\*).tw,kw.

9. (antibiotic\* or penicillin\* or cephalosporin\* or tetracycline\* or doxycycline\* or minocycline\* or fluoroquinolone\* or macrolide\* or sulfonamide\* or metronidazole\* or vancomycin\*).tw,kw.

- 10. (nsaid\* or ocp\*).tw,kw.
- 11. ((nonsteroid\* or non-steroid\*) adj3 (antiinflammator\* or anti-inflammator\* or (anti adj2 inflammator\*))).tw,kw.
- 12. or/5-11
- 13. exp helicobacter/
- 14. exp campylobacter/
- 15. Helicobacter\*.tw,kw.
- 16. Campylobacter\*.tw,kw.
- 17. (H adj2 pylori).tw,kw.
- 18. cagA.tw,kw.
- 19. ((cytotoxin-associated or (cytotoxin adj2 associated)) adj4 A).tw,kw.
- 20. VacA.tw,kw.
- 21. (Vacuolating adj2 cytotoxin\*).tw,kw.
- 22. disease control/
- 23. (eradication or elimination).tw,kw.
- 24. or/13-23
- 25. caesarean section/ or exp birth/
- 26. (c?esarean\* or c-section\* or csection\*).tw,kw.
- 27. (mode adj4 deliver\*).tw,kw.
- 28. or/25-27
- 29. exp vaccines/
- 30. vaccin\*.tw,kw.
- 31. (appendectom\* or appendicectom\* or appendicitis).tw,kw.
- 32. appendix.tw,kw.
- 33. tonsillectom\*.tw,kw.
- 34. or/29-33
- 35. exp physical activity/
- 36. exp sport/
- 37. (physical adj4 activit\*).tw,kw.
- 38. (exercis\* or sport\*).tw,kw.
- 39. or/35-38
- 40. exposure/
- 41. exp domestic animals/
- 42. pets/
- 43. exp hygiene/
- 44. rural population/
- 45. urban population/
- 46. population density/ or overpopulation/

- 47. exp crowding/
- 48. family size/
- 49. sanitation/ or food sanitation/ or sewage/ or waste disposal/
- 50. refrigerators/ or refrigeration/
- 51. exp food preservation/ or microbial contamination/ or food contamination/ or food hygiene/
- 52. socioeconomics/
- 53. exp pollution/ or pollution control/
- 54. solar radiation/
- 55. ultraviolet radiation/
- 56. exp vitamin d/ or folic acid/
- 57. child abuse/
- 58. (environmental adj4 (factor\* or exposure\*)).tw,kw.
- 59. (protect\* adj3 factor\*).tw,kw.
- 60. (early adj3 life).tw,kw.
- 61. ((domestic\* or farm\*) adj4 animal\*).tw,kw.
- 62. (pet or pets or dog\* or cat or cats).tw,kw.
- 63. (famil\* adj4 size\*).tw,kw.
- 64. (birth adj4 order).tw,kw.
- 65. (sanitation or refrigerat\* or pasteuriz\* or pollut\* or (food adj4 preserv\*)).tw,kw.
- 66. (urban\* or rural\*).tw,kw.
- 67. socioeconomic\*.tw,kw.
- 68. ((parent\* adj3 occupation) or (social adj3 mixing)).tw,kw.
- 69. latitude/
- 70. (sun or ultraviolet\* or UV or UVs or (vitamin adj4 D) or folate or (folic adj3 acid\*) or latitude).tw,kw.
- 71. or/40-70
- 72. lactating women/ or pregnant women/
- 73. exp prenatal period/
- 74. maternal nutrition/

75. ((maternal or mother\* or pregnan\* or postpartum or post-partum or prenatal\* or pre-natal\* or postnatal\* or postnatal\* or perinatal\* or peri-natal\* or peripartum or peri-partum or prepartum or pre-partum) adj5 (diet\* or nutrition\* or infection\* or smok\* or stress\*)).tw,kw.

76. ((maternal or mother\* or pregnan\* or postpartum or post-partum or prenatal\* or pre-natal\* or postnatal\* or postnatal\* or perinatal\* or peri-natal\* or peripartum or peri-partum or prepartum or pre-partum) adj5 (risk adj4 factor\*)).tw,kw.

77. or/72-76

78. exp child nutrition/ or child feeding/ or exp infant feeding/

79. weaning/

80. (breastfeeding or breast-feeding or breastfed\* or lactation or formula\* or colostrum or (human adj3 milk\*) or emulsifier\*).tw,kw.

- 81. ((breast or bottle\* or infant\* or child\*) adj4 feeding).tw,kw.
- 82. weaning.tw,kw.
- 83. or/78-82
- 84. parasites/ or animal parasitic nematodes/
- 85. helminths/
- 86. toilets/

- 87. parasitoses/
- 88. tobacco smoking/
- 89. passive smoking/
- 90. parasit\*.tw,kw.
- 91. (helminth\* or nematode\* or tapeworm\* or ascaria\* or flatworm\* or cestod\* or trematod\*).tw,kw.
- 92. hygien\*.tw,kw.
- 93. infestation.tw,kw.
- 94. (smok\* or tobacco\*).tw,kw.
- 95. (diet\* or nutrition\* or food\*).tw,kw.
- 96. or/84-95
- 97. exp children/
- 98. paediatrics/

99. (Infan\* or newborn\* or new-born\* or perinat\* or neonat\* or baby\* or babies or toddler\* or minors\* or boy or boys or boyfriend or boyhood or girl\* or kid or kids or child\* or schoolchild\* or school-child\*).mp.

- 100. (p?ediatric\* or peadiatric\* or prematur\* or preterm\*).mp.
- 101. school\*.tw,kw.
- 102. or/97-101
- 103.96 and 102
- 104. 4 or 12 or 24 or 28 or 34 or 39 or 71 or 77 or 83 or 103
- 105. exp inflammatory bowel diseases/
- 106. (inflammatory adj4 bowel adj4 disease\*).tw,kw.
- 107. ((ulcerative or ulcerous or mucosal or Idiopathic) adj3 (colitis or proctocolitis or colorectitis)).tw,kw.
- 108. (colitis adj3 (gravis or ulcerativa or ulcerosa)).tw,kw.
- 109. ((Crohn\* or granulomatous) adj3 (disease\* or enteritis or ileitis or ileitides or colitis or enterocolitis)).tw,kw.
- 110. ((regional or terminal) adj3 (enteritis or ileitis or ileitides or colitis or enterocolitis)).tw,kw.
- 111. (morbus adj3 crohn\*).tw,kw.
- 112. or/105-111
- 113. case studies/
- 114. case-control studies/
- 115. longitudinal studies/
- 116. retrospective studies/
- 117. epidemiology/ or disease prevalence/ or epidemiological surveys/
- 118. cohort studies/
- 119. (Case control adj3 (study or studies)).mp.
- 120. (observational adj3 (study or studies)).mp.
- 121. (epidemiologic\* adj3 (study or studies)).mp.
- 122. (cross sectional adj3 (study or studies)).mp.
- 123. (cohort or prospective or retrospective or population based or longitudinal or prevalence or incidence).mp.
- 124. or/113-123
- 125. 104 and 112 and 124

## **APPENDIX B: Supplementary Tables**

**Supplementary Tables 1** a–j: Extracted data from studies on the association between early life exposures and inflammatory bowel disease

- a. Maternal health and exposures during pregnancy
- b. Perinatal factors
- c. Birth month and related factors
- d. Breastfeeding
- e. Hygiene-related factors
- f. Social factors
- g. Immigration
- h. Antibiotics and other medications
- i. Offspring health and infections
- j. Passive exposure to tobacco smoke

Effect estimates	Symbol
OR	*
aOR	**
HR	†
aHR	††
IRR	‡
alRR	<b>‡</b> ‡
MD	¶
RR	§
aRR	§§
SIR	#

Supplementary Table 2: Newcastle Ottawa Scale grading of all included studies

2a: Newcastle Ottawa Scale grading of all included case-control studies

2b: Newcastle Ottawa Scale grading of all included cohort studies

Study Type	Study	Study location	Study Time Period	Exposure Description	Total sample size (n)	Outcome	Period of exposure	Effect estimate value	Confidence interval (specify of different from 95% CI)	Comments
Cohort Studies		1	1				r			T
				Maternal smoking during pregnancy (any compared with none)	274390		Pregnancy	0.73	0.58-0.94	
					274390		Pregnancy	0.7	0.56-0.86	4
				Maternal age (25-34 vs < 25)	1250224		Perinatal Perinatal	0.87	0.69-1.10	-
	Aspberg, S. et al. 2006	Sweden	1987-2000	mucha age (15 54 65 4 25)	1249949		Perinatal	0.77	0.63-0.94	Adjusting variables not reported
					1110822		Perinatal	0.98	0.71-1.32	
				Maternal age (25-34 vs > 35)	1110583		Perinatal	1.03	0.77-1.39	
					1110689		Perinatal	0.86	0.65-1.13	
				Preeclampsia	1436235		Perinatal	0.85	0.42-1.72	
	Blomster, T.M. et al. 2014	Finland	1966	Smoking during pregnancy	6685	IBD	Pregnancy	1.7 <sup>6</sup>	1.2-2.5	Unadjusted estimates reported
				Antibiotics during pregnancy	6685		Pregnancy	1.65	1-2.4	
	Burnett, D. et al. 2020	Canada	1988-2014	Maternal age (clinical cohort)	262705		Perinatal	Not Sigr		
				Maternal age (administrative cohort) Maternal age	42906 2218789		Perinatal	Not Sigr Not Sigr		
				Maternal age Air pollutant, nitrogen dioxide	2218789 2218789		Perinatal Pregnancy	NOT SIG	0.96-1.03	
	Elten, M. et al. 2020	Canada	April 1st 1991 to March 31st 2014	Air pollutant, fine particulate matter	2218789		Pregnancy Pregnancy	0.91**	0.98-1.03	-
	Enter, M. et dl. 2020	Cunidad	April 13, 1991 to March 913, 1914	Air pollutant, nile particulate matter	2218789		Pregnancy	0.91	0.73-1.04	Adjusted for sex, maternal IBD, rural/urban area of residence at birth, median neighborhood household income
		1		Air pollutant, oxidant capacity	2218789		Prenatal	1.12**	0.79-1.59	1
	Greenbaum, S. et al. 2018	Israel	1991-2014	Maternal smoking during pregnancy	242342		Pregnancy	1.12	1.2-3.9	Unadjusted estimates reported
	,			Maternal age (20-29 vs 30-39)	117976		Perinatal	0.62**	0.44-0.87	
	Konijeti, G. et al. 2013	USA	1976-2008	Maternal age (20-29 vs > 40)	117976		Perinatal	0.87**	0.43-1.75	Adjusted for age, BMI, tobacco use, regular use of oral contraceptives, exposure to parental smoking, birth weight, history of being breast fed, and being born preterm
	Lange, A. et al. 2014	Denmark	1995-2009	Maternal smoking	979039		Infancy	0.8 <sup>††</sup>		Adjusting variables not reported
					827239		Pregnancy	1.93**	1.06-3.5	
	Ortqvist, A.K. et al. 2017	Sweden	2006-2013	Antibiotics during pregnancy	827239		Pregnancy	2.48	1.01-6.08	Adjusted for maternal and paternal history of IBD, parental education, maternal and paternal country of birth, and mode of delivery
					827239	UC	Pregnancy	1.25**	0.47-3.26	
				Maternal age (< 25 vs 26-28)	513740	CD	Perinatal	1.29	0.89-1.85	
	Ponsonby, A.L. et al. 2009	Australia	1983-1998	Maternal age (< 25 vs 29-32)	565218		Perinatal	1.48	1.05-2.08	Adjusted for sex, abormality, interventional birth, urban, married, SES, maternal age and year of birth
	,,			Maternal age (< 25 vs > 33)	495539		Perinatal	1.41	0.97-2.05	
				Past spontaneous abortion (No vs Yes)	998655	CD	Perinatal	1.03	0.77-1.39	
se-Control Studies		1	1	1						L
	Bernstein, C.N. et al. 2017	Counda	1984-2010	Maternal infection within 9 mo before delivery	12159		Pregnancy	0.96	0.84-1.09	
	Bernstein, C.N. et al. 2017	Canada	1984-2010	Maternal infection within 30d before delivery	12159		Pregnancy	0.97	0.82-1.14	Adjusted for urban vs rural residence, SES, age, and sex
				Maternal infection peripartum Maternal age (25-29 vs < 25)	12159		Perinatal Perinatal	0.85	0.58-1.09	
				Maternal age (25-29 vs 25-3) Maternal age (25-29 vs 30-34)	1247		Perinatal	0.76**	0.51-1.14	
	Canova, C. et al. 2020	Italy	1989-2012	Maternal age (25-29 vs 35-39)	906		Perinatal	0.74	0.43-1.27	Adjusted for sex, year of birth, season of birth, having older sibilings, number of births, birth weight, gestational age, Apgar score at 1 minute, maternal age and mother's education
				Maternal age (25-29 vs >= 40)	655		Perinatal	1.55	0.61-3.91	
					771		Perinatal	0.4	-1,8	
	Ekbom, A. et al. 1990	Sweden	1924-1957	Maternal age	771	CD	Perinatal	0.7 <sup>¶</sup>	-2,8	Unadjusted estimates reported
					771	UC	Perinatal	0.3 <sup>1</sup>	-2,4	
	Gruber, M. et al. 1996	USA	Not Reported	Mother smoking during pregnancy	144	CD	Pregnancy	0.604	0.29-1.3	Unadjusted estimates reported
	Han. D.Y. et al. 2010	New Zealand	Not Reported	Maternal smoking	727		Pregnancy	1.44	0.97-2.15	Unadjusted estimates reported
				Mother takes any regular medication during her pregnancy	851		Pregnancy	2.02*	1.09-3.75	
	Holmes, E.A. et al. 2019	Australia	2010-2013	Mother smoking when pregnant	495	IBD	Pregnancy	Not Re	ported	
				Gestational hypertension, preeclampsia, or eclampsia	2825	IBD	Pregnancy	17	1-2.8	Adjusted for sex, race, maternal age, maternal smoking, maternal diabetes, known or suspected fetal abnormality, maternal IBD, maternal infection, and placental or amniotic problems
	Hutfless, S. et al. 2012	USA	1996-2006	Placental or amniotic problems	2825	IBD	Pregnancy	1	0.7-1.5	Adjusted for sex, race, maternal age, maternal smoking, maternal diabetes, known or suspected fetal abnormality, maternal IBD, maternal infection, and gestational hypertension
				Maternal infection, inpatient or outpatient visit	2825	IBD	Pregnancy	0.9		Adjusted for sex, race, maternal age, maternal smoking, maternal diabetes, known or suspected fetal abnormality, maternal IBD, placental or anniotic problems, and gestational hypertension
	Mahid, S.S. et al. 2007	USA	Not Reported	Prenatal smoke exposure	495	CD	Perinatal	1.72	1.1-2.71	Adjusted for an
	manu, 3.5. et al. 2007	NC0	Not Reported	rienatai sinuke expusure	419		Perinatal	1.53	0.93-2.49	Adjusted for age
	Malmborg, P. et al. 2012	Sweden	1973-2006	Maternal UTI during pregnancy	16975		Pregnancy	1.27	1.01-1.59	Unadjusted estimates reported
					2229	IBD	Pregnancy	Not rep	ported	
	Radon, K. et al. 2007	Germany	March 2006 to August 2006	Smoking during pregnancy	2229	CD.	Pregnancy	0.5	0.3-0.8	Adjusted for age, gender, region, parental education, maternal and paternal history of IBD, nutrition other than breast milk at <5mo, birth weight < 2500 g, > 2 older siblings, rhinitis, and livi
					2229		Pregnancy Pregnancy	0.9	0.6-1.3	urban area
	Russell, R.K. et al. 2005	Scotland	Not Reported	Maternal smoking during pregnancy	124		Pregnancy Pregnancy	4.46	1.16-17.1	Vadjusted estimates reported
					1834		Pregnancy	1.519	0.905-2.551	
	Sonntag, B. et al. 2007	Germany	2003-2004	Disease During Pregnancy	1548		Pregnancy	1.267	0.735-2.183	Adjusted for disease during 1st year, preterm birth, maternal IBD, appendectomy, ever smoking, sex
	Strisciuglio, C, et al. 2017	Italy	2000-2014	Diseases during pregnancy (Risk of premature delivery, hormonal treatment, diabetes, hypertension, infections)	467		Pregnancy	Not rep		
	Thompson, N.P. et al. 2000		1946-1958		287		Pregnancy	1.27	0.26-5.31	Unadjusted estimates reported
	mompson, N.P. et al. 2000	UK.	1940-1938	Infection during pregnancy	287	UC	Pregnancy	0.84	0.12-4.35	
	Thorsen, S.U. et al. 2016	Denmark	1981-2004	Maternal age at delivery 25–35 compared with <25 years	384	IBD	Perinatal	1.27	0.89-1.80	Adjusted for 25(OH)D, gender, ethnicity, birth weight (categorical), gestational age (categorical) and mother's age (categorical)
			2004	Maternal age at delivery ≥35 compared with <25 years	384		Perinatal	1.29	0.71-2.36	
	van der Sloot, K. et al. 2020	Netherlands	Not Reported	Prenatal smoking	1671		Pregnancy	1.89	1.38-2.59	Adjusted for age, sex, and history of smoking
					1669		Pregnancy	1.62	1.17-2.24	
	Van Limbergen, J.E. et al. 2009	Scotland	Not Reported	Parental smoking during pregnancy, at birth	252		Neonatal	Not rep		4
	Velosa, M. et al. 2019	Israel	1964-1976	Mother's age at the time of delivery	1744		Perinatal	Not rep		
	Yoles, I. et al. 2018	Israel	1991-2014	Maternal Group B Streptococcus (GBS) colonization	195457		Pregnancy	1.29 <sup>†</sup>	1.03-1.6	Adjusting variables not reported
	Yu, I. et al. 2016	Ireland	2012-2015	Maternal smoking during pregnancy	209		Pregnancy	Not rep		4
		1			187	UL	Pregnancy	Not rep	ported	1

Study Type	Study	Study location	Study Time Period	Exposure Description	Total sample size (n)	Outcome	Period of exposure (prenatal/ perinatal/ infancy/2-5 years of age)	Effect Estimate value	Confidence Interval (specify of different from 95% CI)	Comments
	Andersen, V. et al. 2013	Denmark	1977-2009	C-section C-section (boys) C-section (gifts)	2672708   1984758   1984758   1984758   1984758	CD UC IBD	Perinatal Perinatal Perinatal Perinatal Perinatal	1.07 <sup>°</sup> 1.1 <sup>##</sup> 1.18 <sup>##</sup> 1.26 <sup>##</sup> 1.06 <sup>##</sup>	1.02-1.12 0.99-1.22 1.08-1.28 1.15-1.37 0.97-1.15	Adjusted for birth order, maternal age, gestational age, SGA, maternal IBD, paternal IBD, hospital admissions due to infection, maternal sincking, antibiotic treatment during programoy
1	Aspberg, S. et al. 2006	Sweden	1987-2000	Birth weight (< 2500g vs > 2500g) Prematurity	1479216   1479216		Perinatal Perinatal	1.05"	0.65-1.72 0.80-1.72	Adjusting variables not reported
1		Denmark Scotland	1995-2008 1993-2007	C-section C-section	2098039 I 40145 I		Perinatal Perinatal	1.14 <sup>11</sup> 0.82 <sup>11</sup>		Adjusted for age, calendar-year, sex, birth weight, birth order, and country of birth Adjusting variables not reported
	Black, M. et al. 2015	Scotland	1993-2007	C-section	265272	BD	Perinatal	1.3#	0.62-2.73	Adjusted for maternal age, gestation at birth, maternal Carstairs decile, maternal smoking status, birth weight, year of delivery, male infant, and breastfeeding at 5 weeks
	Burnett, D. et al. 2017	Canada	1988-2014	C-section C-section (clinical cohort)	262729 I 262705 I	BD BD	Perinatal Perinatal	1.07 <sup>11</sup>	0.82-1.42 0.76-1.31	Adjusted for maternal age, parity, area-level income, rural residence, smoking, weight status, and birth weight for gestational age
				C-section (administrative cohort) C-section (clinical cohort)	42906 1		Perinatal Perinatal	1.11 <sup>‡‡</sup> 1.07 <sup>‡‡</sup>	0.77-1.59	Adjusted for maternal pre-pregnancy weight status, maternal age at birth, parity. Quintile of Annual income per person equivalent (QAIPPE), area of residence, and smoking during pregnancy
				C-section (administrative cohort)	42906	CD	Perinatal	Not F 0.88 <sup>11</sup>	Reported	Adjusted for maternal pre-pregnancy weight status, maternal age at birth, parity, Quintle of Annual income per person equivalent (QAIPPE), area of residence, and smoking during pregnancy
1	Burnett, D. et al. 2020	Canada	1988-2014	C-section (clinical cohort) C-section (administrative cohort)	262705 U 42906 U	nc	Perinatal Perinatal	Not F	Reported	Adjusted for maternal pre-pregnancy weight status, maternal age at onth, pamy, Quintie of Annual income per person equivalent (QAIP-PE), area of residence, and smoking during pregnancy
				Birth weight (small for gestational age) - clinical cohort Birth weight (small for gestational age) -administrative cohort	262705 I 42906 I	BD BD	Perinatal Perinatal	Not S Not S	Significant Significant	
				Birth weight (large for gestational age) - clinical cohort Birth weight (large for gestational age) - administrative cohort	262705 I 42905 I	BD	Perinatal Perinatal	Not S	Significant	
ı F	Elten, M. et al. 2020	Canada	April 1st, 1991 to March 31st, 2014	Birth weight	2218789	BD	Perinatal	Not S	Significant	
, F				Prematurity	2218789		Perinatal		Significant	
				Birth weight (2.3-3.175 vs < 2.26)	143681	CD	Perinatal	1.29 <sup>11</sup>	0.79-2.11	
				5 min Weight (2.5-5-17-5-42 - 2.2.5)	143681	nc	Perinatal	0.91**	0.55-1.49	
								1#	0.74-1.34	
				Birth weight (2.3-3.175 vs 3.2-4.54)	143681	CD	Perinatal	1	0.74-1.34	-
	Khalili, H. et al. 2013	USA	1991- June 1, 2007 (NHSII) and 1992- June 1, 2008 (NHSI)		143681	nc	Perinatal	0.98 <sup>11</sup>	0.75-1.27	Adjusted for age (months), cohort (NHSI vs. NHSII), BMI (<20, 20-24.9, 25-29.9, ≥ 30 kg/m2), smoking (never, past, current), history of diabetes in the mother (yes, no), maternal smoking during pregnancy (yes, no, unknown), ever use of oral contraceptives (yes, no), prematurity (yes, no), and having been breastfed (yes, no).
					143681	CD	Perinatal	1.05**	0.71-1.58	4. A. C. M. C. M. C. M. Manager, and M. Martinek Manager, M. Martinek Topological Application Management Management Management Management (Management Management Management Management Management Management Management Management Management Management Management Management Management Management Man Management Management Management Management Management Management Management Management Management Management Management Management Management Management Management Management Management Management Management Man Management Management M Management Management Management Management Ma
				Birth weight (2.3-3.175 vs > 4.54)						4
					143681	nc	Perinatal	1.02 <sup>11</sup>	0.71-1.37	
				Prematurity	143681	CD	Perinatal	0.69 <sup>‡‡</sup>	0.37-1.29	
					143681		Perinatal	0.81**	0.46-1.43	
, P	Konijeti, G. et al. 2013 Lange, A. et al. 2014	USA Denmark	1976-2008	Paternal age C-section	117976 0 979 039 0	CD	Perinatal Perinatal	1.3	Significant 0.9-1.8	Unadiusted estimates recorted
	Lange, A. et al. 2014	Denmark	1995-2009	Prematurity Elective C-section	972 188 765 840	CD	Perinatal Perinatal	1.2 <sup>†</sup> 1.67 <sup>†</sup>	0.7-2.1	Unadjusted estimates reported
				Birth weight (< 1500 g vs 2500-3999)	837 353 0	CD	Perinatal	0.65 <sup>11</sup>	0.16-2.62	
				Birth weight (1500-2499g vs 2500-3999) Birth weight (> 4000g vs 2500-3999)	875 767 0 942 058 0	CD	Perinatal Perinatal	0.68 <sup>11</sup> 0.87 <sup>11</sup>	0.36-1.28 0.59-1.28	-
·	Ponsonby, A.L. et al. 2009	Australia	19831998	Single vs multiple birth Prematurity (Gestational age > 37w vs < 27w)	998877 0 934633 0		Perinatal Perinatal	0.46 <sup>11</sup>	0.17-1.22 0.13-6.73	Adjusted for sex, abormality, interventional birth, urban, married, SES, maternal age, and year of birth
				Prematurity (Gestational age > 37w vs 28-36w)	989685	CD	Perinatal	0.88 <sup>††</sup>	0.53-1.46	
				Apgar score (10 vs 9) Apgar score (10 vs 5-8)	917739 0 539147 0	CD	Perinatal Perinatal	0.93 <sup>††</sup> 1.04 <sup>††</sup>	0.72-1.19 0.67-1.62	
ŀ	Steiner, N. et al. 2019	Southern Israel	1991-2014	Apgar score (10 vs 0-4) Birth weight (SGA < 5% centile for gestational age)	469091 215804 I	CD BD	Perinatal Perinatal	0.64 <sup>††</sup> 1.23	0.09-4.58	Adjusted for maternal age
Case-Control Studies	Ananthakrishanan, A.N. et al. 2015			C-section	895		Perinatal		Significant	rayanan na maanan aga
f	Ananthakrishanan, A.N. et al. 2015 Baron, S. et al. 2005	Boston	Not Reported	C-section Disease during pregnancy and risk of prematurity	444		Perinatal			4
									Reported	
E	Bernstein, C.N. et al. 2016	Canada		C-section	120 U 12159 I	UC	Perinatal Perinatal	4.67 <sup>°</sup>	1.3-16.1	Unadjusted estimates reported Adjusted for urban vs rural residence and socioeconomic status (quintiles)
	Bernstein, C.N. et al. 2016		1984-2010	C-section C-section	12159 6824 I	UC BD BD	Perinatal	4.67	1.3-16.1 0.89-1.24 0.86-1.32	
	Bernstein, C.N. et al. 2016		1984-2010	C-section C-section Birth weight	12159   6824   6824   6824	UC BD BD BD BD	Perinatal Perinatal	4.67 1.05 1.06 1 1.09	1.3-16.1 0.89-1.24 0.86-1.32 1-1 0.86-1.39	
	Bernstein, C.N. et al. 2016		1984-2010	C-section C-section	12159 6824 6824	UC BD BD BD CD	Perinatal Perinatal Perinatal Perinatal	4.67 1.05 1.06 1	1.3-16.1 0.89-1.24 0.86-1.32 1-1	
E	Bernstein, C.N. et al. 2016 Bernstein, C.N. et al. 2019		1984-2010	C-section C-section Brin weight Apgar score 1 min (> 7 vs < 7)	12159   6824   6824   6824   6824   6824   6824   6824	UC BD BD BD CD UC BD	Perinatal Perinatal Perinatal Perinatal Perinatal Perinatal Perinatal	4.67 1.05 1.06 1 1.09 1.42 0.78 1.07	1.3-16.1 0.89-1.24 0.86-1.32 1-1 0.86-1.39 1.02-1.96 0.55-1.11 0.49-2.33	
		Canada	1884-2010	C-section C-section Birth weight	12159 6824 6824 6824 6824 6824 6824 6824 6824	UC BD BD BD CD CD CD CD CD CD CD UC	Perinatal Perinatal Perinatal Perinatal Perinatal Perinatal	4.67 1.05 1.06 1 1.09 1.42 0.78 1.07 1.33 1.04	1.3-16.1 0.89-1.24 0.86-1.32 1-1 0.86-1.39 1.02-1.96 0.55-1.11 0.49-2.33 0.38-4.61 0.37-2.89	Adjuste for urban vs runil residence and socioeconomic status (guintites)
		Canada	1884-2010	C-section C-section Brin weight Apgar score 1 min (> 7 vs < 7)	12159 6824 6824 6824 6824 6824 6824 6824 6824	UC BD BD BD CD CD UC BD UC BD CD CD CD	Perinatal	4.67 1.05 1.06 1.09 1.42 0.78 1.07 1.33 1.04 1.04 1.04 1.04 1.04	1.3-16.1 0.89-1.24 0.86-1.32 1.1 0.86-1.39 1.02-1.96 0.55-1.11 0.49-2.33 0.38-4.61 0.37-2.89 0.95-1.06 0.94-1.08	Adjuste for urban vs runil residence and socioeconomic status (guintites)
1		Canada	1884-2010	C saction Casadion Median weight Apgar score 1 min (> 7 vs < 7) Apgar 5 min (> 7 vs < 7) Gestational age	12159 6824 6824 6824 6824 6824 6824 6824 6824	UC BD BD BD CD UC CD UC CD UC CD UC CD UC	Perinatal	4.67 1.05 1.06 1' 1.09 1.42 0.78 1.07 1.33 1.04 1.004 1.004 1.004	1.3-16.1 0.89-1.24 0.66-1.32 1-1 0.86-1.39 1.02-1.96 0.55-1.11 0.49-2.33 0.38-4.61 0.37-2.89 0.95-1.06	Adjuste for urban vs runil residence and socioeconomic status (guintites)
-		Canada	1884-2010	C estroton C estroton Birth wayst Apgar score 1 mm (> 7 ve < 7) Apgar score 5 min (> 7 ve < 7) Gestational age Birth ways() (2000 ve < 2000) Birth wayst (> 2000 ve < 2000)	12159 6824 6824 6824 6824 6824 6824 6824 6824	UC IBD IBD IBD IBD ICD IDC IDC IBD ICC IBD IBD IBD IBD	Perinatal Perinatal Perinatal Perinatal Perinatal Perinatal Perinatal Perinatal Perinatal Perinatal Perinatal Perinatal Perinatal Perinatal Perinatal Perinatal	4.67 1.05 1.06 1 1.09 1.42 0.78 1.07 1.33 1.04 1.0	1.3-16.1 0.89-1.24 0.86-1.32 1.4 0.86-1.39 1.02-1.96 0.55-1.11 0.49-2.33 0.38-4.61 0.37-2.89 0.95-1.06 0.94-1.08 0.91-1.08 0.42-3.00 0.48-4.19	Adjuste for urban vs runil residence and socioeconomic status (guintites)
-	Bernstein, C.N. et al. 2019	Canada Canada	1966-2010	C socion C socion Beth weight Agger socie 1 min (+ 7 vs < 7) Agger 5 min (+ 7 vs < 7) Cestational age Beth weight (= 2000 vs < 2000)	12159 6824 6824 6824 6824 6824 6824 6824 6824	UC IBD IBD IBD IBD IBD IBD IBD IBD	Perinatal Perina	4.67 1.05 1.05 1' 1.09 1.42 0.78 1.07 1.33 1.04 1.004 1.004 1.01 1.004 1.01 1.01 1.12 1.44 1.26 0.96 1.12 1.44 1.26 0.96 1.26 0.96 1.26 0.99 1.12 1.44 1.26 0.99 1.12 1.44 1.26 0.99 1.12 1.26 0.99 1.12 1.26 0.99 1.12 1.26 0.99 1.12 1.26 0.99 1.12 1.26 1.12 1.26 1.12	1.3-16.1 0.89-1.24 0.86-1.32 1.1 0.86-1.39 1.02-1.96 0.45-1.31 0.45-2.33 0.38-4.61 0.37-2.89 0.95-1.06 0.94-1.08 0.91-1.08 0.42-3.300 0.42-3.300 0.42-3.19 0.40-4.03 0.47-1.96	Adjusted for urban is normal residence and socioeconomic status (guintles)
e e	Bernstein, C.N. et al. 2019 Canova, C. et al. 2020 Decker, E. et al. 2010	Canada Canada Italy Germany	1984-2010 1975-2010 1989-2012 May 2008 and May 2009	C excelon C excelon Birth weight Aggar score 1 min (> 7 vs < 7) Aggar 5 min (> 7 vs < 7) Gestational age Birth weight (> 2000 vs < 2000) Single vs multiple Soft Aggar Song (> 200 vs < 200) Single vs multiple Soft Castolina (> 7 vs < 7) C excelon	12159 6824 6824 6824 6824 6824 6824 6824 6824	UC 180 180 180 180 180 180 180 180	Porinatal Porinatal Porinatal Porinatal Porinatal Porinatal Porinatal Porinatal Porinatal Porinatal Porinatal Porinatal Porinatal Porinatal Porinatal Porinatal Porinatal Porinatal	4.67 1.05 1.05 1.05 1.09 1.42 0.78 1.07 1.33 1.04 1.004 1.004 1.01 0.99 1.12 1.44 1.25 1.25	1.3-16.1 0.89-1.24 0.66-1.32 1.0 0.86-1.39 1.02-1.96 0.55-1.11 0.45-2.33 0.36-4.61 0.37-2.89 0.95-1.08 0.94-1.08 0.94-1.08 0.42-3.00 0.49-4.19 0.49-4.19 0.49-4.19 0.49-4.13 0.49-4.14 0.49-4.14 0.49-4.14 0.49-4.14 0.49-4.14 0.49-4.14 0.49-4.14 0.4	Adjusted for urban is normal residence and socioeconomic status (guintles)
e e	Bernstein, C.N. et al. 2019 Canova, C. et al. 2020 Decker, E. et al. 2010	Canada Canada Raly	1984-2010 1970-2010 1989-2012	C 480000 C 480000 Birth wayt Aggar score 1 min (> 7 vs < 7) Aggar score 1 min (> 7 vs < 7) Gestational aga Birth wayt (> 2000 vs < 2000) Birth wayt (> 2000 vs < 2000) Birth wayt (> 2000 vs < 30) Aggar score (> r < s < 7)	12159 6824 6824 6824 6824 6824 6824 6824 6824	UC BD BD BD BD BD DD UC DD UC DD UC DD UC BD BD BD BD BD BD BD BD BD BD BD BD BD	Perinatal Perina	4.67 1.06 1.06 1.06 1.07 1.42 1.07 1.07 1.07 1.04 1.04 1.04 1.04 1.04 1.04 1.05 1.12 1.05 1.05 1.05 1.05 1.05 1.12 1.05 1.12 1.05 1.05 1.05 1.12 1.05 1.05 1.12 1.05 1.12 1.05 1.12 1.12 1.14 1.05 1.14 1.05 1.14 1.05 1.14 1.05 1.14 1.05 1.14 1	1.3-16.1 0.89-1.24 0.86-1.32 1.4 0.86-1.39 1.02-1.98 1.02-1.98 0.55-1.11 0.45-2.33 0.38-4.61 0.37-2.89 0.95-1.08 0.94-1.08 0.42-3.00 0.42-3.00 0.42-4.19 0.42-3.00 0.42-3.01 0.42-3.00 0.42-3.01 0.4	Adjusted for visit vis rund residence and sociooconomic status (guintles) Usadjusted estimates reported Usadjusted estimates reported Adjusted for sex, year of birth, season of birth, having older sbilling, number of births, birth weight, gestational age, Apgar score at 1 minute, maternal age, and mother's education
e e	Bernstein, C.N. et al. 2019 Canova, C. et al. 2020 Decker, E. et al. 2010	Canada Canada Italy Germany	1984-2010 1975-2010 1989-2012 May 2008 and May 2009	C excelon C excelon Birth weight Aggar score 1 min (> 7 vs < 7) Aggar 5 min (> 7 vs < 7) Gestational age Birth weight (> 2000 vs < 2000) Single vs multiple Soft Aggar Song (> 200 vs < 200) Single vs multiple Soft Castolina (> 7 vs < 7) C excelon	12199 6824 6824 6824 6824 6824 6824 6824 6824	UC 000000000000000000000000000000000000	Perinatal Perina	4.67 1.06 1.06 1.06 1.09 1.09 1.09 1.09 1.07 1.04 1.04 1.04 1.04 1.04 1.04 1.04 1.04 1.04 1.04 1.04 1.04 1.04 1.04 1.05 1.15 1.05 1.15 1	1.3-16.1 0.89-1.24 0.89-1.32 1.1 0.69-1.32 0.69-1.39 1.02-1.99 1.02-1.99 1.02-1.99 1.02-1.91 0.49-2.33 0.38-4.61 0.37-2.89 0.99-1.06 0.91-1.08 0.49-1.08 0.49-1.08 0.49-1.08 0.49-1.09 0.49-4.19 0.40-4.03 0.45-1.38 0.55-1.38 0.55-1.38 0.55-1.38	Adjusted for situan vs rund residence and socioeconomic status (guintities) Ukudijusted estimates reported Ukudijusted estimates reported Adjusted for sex, year of birth, season of birth, having older sibling, number of birthe, birth weight, gestational age, Adgar score at 1 minute, maternal age, and mother's education
6 - - - -	Bernstein, C.N. et al. 2019 Canova, C. et al. 2020 Decker, E. et al. 2010	Canada Canada Italy Germany	1984-2010 1975-2010 1989-2012 May 2008 and May 2009	C 400000 C 400000 Bith weight Aggar score 1 min (> 7 vs < 7) 	12199 6824 6824 6824 6824 6824 6824 6824 6824 6824 6824 6824 6824 6824 6824 6824 1804 1804 1804 1978 1977 1977 1977 7771	UC	Perindal Per	4.67 1.06 1.06 1.06 1.06 1.09 1.09 1.09 1.09 1.04 1.00 1.04 1.04 1.04 1.04 1.04 1.04 1.04 1.04 1.05 1.04 1.05 1.14 1.15 1.05 1.14 1.15 1.15 1.14 1.55 1.14 1.15 1.15 1	1.3.16.1 0.89.132 0.89.132 1.1 0.86.132 1.2 0.56.111 0.462.233 0.334.461 0.334.461 0.372.499 0.441.08 0.951.108 0.494.108 0.494.139 0.494.1494.139 0.494.149.149 0.494.149	Adjusted for situan vs rund residence and socioeconomic status (guintities) Ukudijusted estimates reported Ukudijusted estimates reported Adjusted for sex, year of birth, season of birth, having older sibling, number of birthe, birth weight, gestational age, Adgar score at 1 minute, maternal age, and mother's education
6 - - - -	Bernstein, C.N. et al. 2019 Canova, C. et al. 2020 Decker, E. et al. 2010 Dopá, J.B. et al. 2017	Canada Canada Italy Germany Nothern Ireland	1994-2010 1970-2010 1989-2012 May 2008 and May 2009 1977-1998	C socion C socion Beth weight Aggar score 1 min (+ 7 vs < 7) Aggar 5 min (+ 7 vs < 7) Gestational age Beth weight (+ 2000 vs < 2500) Single vm Augles torn Aggar score (+ 2 vs < 7) C socion C socion	12159 6824 6824 6824 6824 6824 6824 6824 6824	UC BD BD BD BD BD CD DC DC DC DC DC DC DC DC DC DC DC DC	Perinatal Perina	4.67 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.07 1.00 1.12 0.08	1.3-16.1 0.89-1.24 0.89-1.24 0.89-1.32 1-1 0.86-1.32 1.02-1.96 0.56-1.11 0.49-2.33 0.38-4.61 0.37-2.89 0.49-1.08 0.49-1.08 0.49-1.09 0.49-4.19 0.49-4.19 0.49-4.19 0.49-4.19 0.49-1.38 0.53-1.58 0.53-1.58 0.53-1.58 0.53-1.58	Adjusted for urban is nutril residence and asoleoconomic status (guintities)  Usudjusted estimates reported  Adjusted estimates reported  Adjusted estimates reported  Usudjusted estimates reported  Usudjusted estimates reported
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- - - - - - - - - - - - - 	Bernstein, C.M. et al. 2019 Canova, C. et al. 2020 Decker, E. et al. 2010 Doyle, J.B. et al. 2017 Ekborn, A. et al. 1990	Canada Canada Italy Germany Nothern Ireland Sweden	1964-2010 1970-2010 1989-2012 May 2008 and May 2009 1977-1980 1924-1997	C 480000 C 480000 Birth waght Aggar score 1 mm (+ 7 ve < 7) Aggar score 1 mm (+ 7 ve < 7) Gestational age Birth waght (> 2000 ve < 2000) Birth waght (> 2000 ve < 2000) C 48000 C 48000 mm C 4800	12109 0024 0024 0024 0024 0024 0024 0024 00	UG BD BD BD BD BD BD BD BD BD BD BD BD BD	Periodal Period	4 467 1 067 1 067 1 067 1 07 1 07 1 07 1 07 1 07 1 07 1 07 1 07 1 07 1 004 1 00	1.3.16.1 0.89.1.24 0.89.1.24 1.1 0.66.1.32 1.1 0.62.1.39 0.32.4.39 0.32.4.39 0.32.4.39 0.32.4.39 0.32.4.39 0.32.4.39 0.32.4.30 0.42.4.30 0.42.4.30 0.42.4.30 0.42.4.30 0.42.4.4 0.39.4.4.30 0.42.4.30 0.42.4.4.4 0.39.4.4.4 0.44.4.4 0.44.4.4 0.44.4.4 0.44.4.4 0.44.4.4 0.45.4.30 0.42.4.30 0.44.4.4 0.44.4.4 0.44.4.4 0.44.4.4 0.44.4.4 0.44.4.4 0.44.4.4 0.45.4.30 0.45.4.30 0.44.4.4 0.44.4.4 0.44.4.4 0.44.4.4 0.44.4.4 0.45.4.4 0.45.4.4 0.45.4.4 0.45.4.4 0.45.4.4 0.45.4.4 0.45.4.4 0.45.4.4 0.45.4.4 0.45.4.4 0.45.4.4.4 0.45.4.4.4 0.45.4.4.4.4 0.45.4.4.4.4.4.4.4.4.4.4.4.4.4.4.4.4.4.4	Adjusted for urban is nutril residence and ecoloeconomic status (guintities)
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	Bernstein, C.N. et al. 2019 Canova, C. et al. 2020 Decker, E. et al. 2010 Dopk, J.B. et al. 2010 Ekkom, A. et al. 1990 Glat, T. et al. 1997 Huffless, S. et al. 2012 Kken, I. et al. 1998	Canada Canada Canada Rahy Germany Hothern testend Soveden P countries (Europe, USA) Nothern California Izrael	1994-2010 1975-2010 1975-2010 1989-2012 1989-2012 1924-1957 1924-1957 1996-2006 1995-1993	C 40000 C 40000 Birth wagit Aggar score 1 mm (+ 7 vs < 7) Aggar score 3 mm (+ 7 vs < 7) Gestational age Birth wagit (> 2200 vs < 2200) Singly vs mulgites bit Gestational age (> 30 vs < 30) Aggar score (> 7 vs < 7) C 4000 Birth wagit ( Permuturity Permuturity C 4000 Birth wagit (> 2500g) Gestational age (> 27 vs < 36w) Birth wagit (< 2500g)	11109           6824           6825           6826           6827           6828           6829           6829           6829           6829           6829           6829           889           898     <	UG 880 880 880 880 880 880 880 880 880 88	Periodal Period	4 457 1 05 1 05	1.3.14.1 0.85.1.24 0.85.1.24 1.1 0.85.1.22 1.1 0.95.1.22 0.25.1.26 0.25.1.26 0.25.1.26 0.25.1.26 0.25.1.26 0.25.1.26 0.45.1.26 0.	Adjeated for urban is nutril residence and asolesconories status (guintities)
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	Bernstein, C. M. et al. 2019 Canova, C. et al. 2020 Decker, E. et al. 2010 Dople, J. B. et al. 2017 Ekkom, A. et al. 1990 Glat, T. et al. 1997 Huffless, S. et al. 2012 Klein, I. et al. 1998 Levy, L. C. et al. 2012	Canada Canada Canada Rahy Garmany Nothern Iseland 9 countries (Europe, UEA) Nothern California Incast UB cohort	1994-2010 1970-2010 1970-2010 1989-2012 1989-2012 1997-1998 1924-1957 1924-1957 1926-2005 1992-1993 Nef Reported	C 45000 C 45000 Birth weight Aggar score 1 min (> 7 vs < 7) Aggar score 1 min (> 7 vs < 7) Gestational age Birth weight (> 2500 vs < 2500) Singiu vs nutgies Soft Aggar Sone (> 7 vs < 7) C 45000 Birth weight (> 2500 vs < 2500) Birth weight (> 2500 vs < 2500 v	1110         110           6224         6224           771         771           771         771           771         771           777         6225           32200         32200           32200         32200           32200         3220           32200         3220           32200 <td></td> <td>Periodal Periodal Per</td> <td>4 407 4 407 1 05 1 05 1 05 1 05 1 05 1 05 1 05 1 07 1 107 1 127 1 146 1 127 1 127 1 146 1 147 1 147</td> <td>1.3.16.1 0.89.1.24 0.89.1.24 1.1 0.86.1.32 1.1 0.95.1.38 0.05.1.38 0.05.1.38 0.05.1.38 0.03.24.48 0.03.24.97 0.03.24.97 0.03.24.97 0.03.24.97 0.03.24.97 0.04.2.30 0.42.30 0.44.10 0.44.30 0.44.10 0.4</td> <td>Adjusted for unternal age, gestational hypertension, placentel or anniolic problems, lich weight, gestational age Adjusted for rate, ses, maternal age, gestational hypertension, placentel or anniolic problems, lich weight, gestational age Adjusted for rate, ses, maternal age, gestational hypertension, placentel or anniolic problems, lich weight, gestational age Adjusted for rate, ses, maternal age, gestational hypertension, placentel or anniolic problems, lich weight, gestational age Adjusted for rate, ses, maternal age, gestational hypertension, placentel or anniolic problems, lich weight, gestational age Adjusted for rate, ses, maternal age, gestational hypertension, placentel or anniolic problems, lich weight, gestational age Adjusted for rate, ses, maternal age, gestational hypertension, placentel or anniolic problems, lich weight, gestational age</td>		Periodal Per	4 407 4 407 1 05 1 05 1 05 1 05 1 05 1 05 1 05 1 07 1 107 1 127 1 146 1 127 1 127 1 146 1 147 1 147	1.3.16.1 0.89.1.24 0.89.1.24 1.1 0.86.1.32 1.1 0.95.1.38 0.05.1.38 0.05.1.38 0.05.1.38 0.03.24.48 0.03.24.97 0.03.24.97 0.03.24.97 0.03.24.97 0.03.24.97 0.04.2.30 0.42.30 0.44.10 0.44.30 0.44.10 0.4	Adjusted for unternal age, gestational hypertension, placentel or anniolic problems, lich weight, gestational age Adjusted for rate, ses, maternal age, gestational hypertension, placentel or anniolic problems, lich weight, gestational age Adjusted for rate, ses, maternal age, gestational hypertension, placentel or anniolic problems, lich weight, gestational age Adjusted for rate, ses, maternal age, gestational hypertension, placentel or anniolic problems, lich weight, gestational age Adjusted for rate, ses, maternal age, gestational hypertension, placentel or anniolic problems, lich weight, gestational age Adjusted for rate, ses, maternal age, gestational hypertension, placentel or anniolic problems, lich weight, gestational age Adjusted for rate, ses, maternal age, gestational hypertension, placentel or anniolic problems, lich weight, gestational age
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	Bernstein, C.N. et al. 2019 Canova, C. et al. 2020 Decker, E. et al. 2010 Doyle, J.B. et al. 2017 Ekkom, A. et al. 1990 Glait, T. et al. 1997 Huffless, S. et al. 2012 Kenn, I. et al. 1998 Levy, J.C. et al. 2012 Radon, K. et al. 2007	Canada Canada Canada Raity Gammany Nothen Ireland Sweden 9 countries (Europe, USA) Nothern California Israel UG oxhert Sweden Gammany	1994-2010 1970-2010 1970-2010 1970-2010 1970-2010 1971-1980 1972-1980 1972-1980 1922-1993 1922-1993 1962-199 1962-199 1962-199 1962-199 1962-199 1962-199 1962-199 1962-199 1962-199 1962-199 1962-199 1962-199 1962-199 196 196 196 196 196 196 196 196 196	C 40000 C 40000 Bith weight Agar 5 min (> 7 vs < 7) Agar 5 min (> 7 vs < 7) Gestational age Bith weight (> 2000 + 2000) Bith weight (> 2000 + 2000) Gestational age (> 30 vs - 200) Agar 4000 (> 7 vs < 7) C 40000 C 40000 Bith weight (> 2000) C 40000 Bith weight (> 2000) C 40000 Bith weight (> 2000) C 40000 Bith weight (> 2000) C 40000 Bith weight (> 2000) Bith weight (> 2000	11100           6624           6625           6626           6627           6628           6624           6624           6625           6626           6626           6626           6627           6628           6629           6624           6624           6625           6626           6627           900           900           901           902           903           904           905           905           906           907           907           908           909           909           909           900           900           900           900           900           900           900           900           900           900           900           900           900           900           900           90		Periodal Per	4 47 4 47 1 06 1 06 1 07 1 07	1.3.161 1.3.161 0.891.12 1.1 0.861.12 1.1 1. 0.861.12 1.1 1.0 0.92.13 0.051.13 0.951.13 0.92.1 0.92.13 0.92.1 0.92	Adjusted for unternal age, gestational hypertension, placential or anniodic problems, licits weight, gestational age.
	Bernstein, C.N. et al. 2019 Canova, C. et al. 2020 Decker, E. et al. 2010 Doyle, J.B. et al. 2017 Ekkom, A. et al. 1990 Glait, T. et al. 1997 Huffless, S. et al. 2012 Kenn, I. et al. 1998 Levy, J.C. et al. 2012 Radon, K. et al. 2007	Canada Canada Canada Rahy Germany Nethem Initiand Seeden 9 countries (Europe, USA) Notherm California UE cobert Seeden	1995-2010 1999-2012 1999-2012 1999-2012 1999-2012 1999-2012 1999-2012 1999-2012 1999-2012 1999-2009 1992-1993 Not Reported 1992-1993 Not Reported 1993-2009	C 401001 C 401001 C 401001 Bith weight Agger 5 min (> 7 vs < 7) Agger 5 min (> 7 vs < 7) Gestational agie Bith weight (> 2000 vs < 2000) Bith weight (< 2000) C 401001 Bith weight (< 2000) Bith weig	1110         110           6224         6224           6224 <td></td> <td>Periodal Period</td> <td>4 467 4 467 1 0.6 1 0.6 1 0.6 1 0.6 1 0.6 1 0.7 1 0.7 1</td> <td>1.3.16.1 0.89.1.24 0.89.1.24 1.1 0.80.1.22 1.1 0.90.1.30 0.05.1.10 0.05.1.10 0.05.1.10 0.05.1.10 0.03.4.47 0.03.4.47 0.04.2.30 0.04.4.10 0.42.3.00 0.44.3.00 0.44.3.00 0.44.3.00 0.44.10 0.45.3.00 0.44.10 0.45.3.00 0.45.4.10 0.45.3.00 0.45.4.00 0.45.4.00 0.45.3.00 0.45.4.00 0.45.3.00 0.45.4.00 0.45.3.00 0.45.4.00 0.45.3.00 0.45.4.00 0.45.3.00 0.45.4.00 0.45.3.00 0.45.4.00 0.45.3.00 0.45.4</td> <td>Adjusted for rates in our in existing each or and excloseconomic index.  Adjusted estimates reported  Adjusted estimates reported  Adjusted for sex, year of birth, teasion of birth, having other shilling, number of births, birth weight, gestational age, Apgar score at 1 minute, maternal age, and mother's education  Adjusted estimates reported  Usedjusted estimates reported  Adjusted for race, sex, maternal age, gestational hyperformation, placental or annotic problems, birth weight, gestational age  Adjusted for race, sex, maternal age, gestational hyperformation, placental or annotic problems, birth weight, gestational age  Adjusted for maternal infection and ecoloseconomic index  Adjusted for maternal infection and ecoloseconomic index  Adjusted for maternal infection and ecoloseconomic index  Adjusted for particular infection and ecoloseconomic index</td>		Periodal Period	4 467 4 467 1 0.6 1 0.6 1 0.6 1 0.6 1 0.6 1 0.7 1	1.3.16.1 0.89.1.24 0.89.1.24 1.1 0.80.1.22 1.1 0.90.1.30 0.05.1.10 0.05.1.10 0.05.1.10 0.05.1.10 0.03.4.47 0.03.4.47 0.04.2.30 0.04.4.10 0.42.3.00 0.44.3.00 0.44.3.00 0.44.3.00 0.44.10 0.45.3.00 0.44.10 0.45.3.00 0.45.4.10 0.45.3.00 0.45.4.00 0.45.4.00 0.45.3.00 0.45.4.00 0.45.3.00 0.45.4.00 0.45.3.00 0.45.4.00 0.45.3.00 0.45.4.00 0.45.3.00 0.45.4.00 0.45.3.00 0.45.4.00 0.45.3.00 0.45.4	Adjusted for rates in our in existing each or and excloseconomic index.  Adjusted estimates reported  Adjusted estimates reported  Adjusted for sex, year of birth, teasion of birth, having other shilling, number of births, birth weight, gestational age, Apgar score at 1 minute, maternal age, and mother's education  Adjusted estimates reported  Usedjusted estimates reported  Adjusted for race, sex, maternal age, gestational hyperformation, placental or annotic problems, birth weight, gestational age  Adjusted for race, sex, maternal age, gestational hyperformation, placental or annotic problems, birth weight, gestational age  Adjusted for maternal infection and ecoloseconomic index  Adjusted for maternal infection and ecoloseconomic index  Adjusted for maternal infection and ecoloseconomic index  Adjusted for particular infection and ecoloseconomic index
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	Bernstein, C. N. et al. 2019 Canova, C. et al. 2020 Decker, E. et al. 2010 Dode, J.B. et al. 2017 Ekborn, A. et al. 1990 Glist, T. et al. 1997 Huffess, S. et al. 2012 Kian, I. et al. 1998 Levy, I.C. et al. 2012 Radon, K. et al. 2017 Radon, K. et al. 2007 Sonntag, B. et al. 2007	Canada Canada Canada Raity Commany Nothern Ireland Seeden 9 countries (Europe, UEA) Nothern California Israal UE cohort Seeden Germany Germany	1964-2010 1970-2010 1970-2010 1970-2010 1989-2012 1989-2012 1924-1980 1924-1987 1924-1987 1924-1987 1926-2008 1995-208 1955-208 1955-208 1955-208 1955-208 1955-208 1955-208 195	C 40000 C 40000 Extra surget Appar score 1 mir (+ 7 vs < 7) Appar score 1 mir (+ 7 vs < 7) C 40000 C 40000 + 7 vs < 7) C 40000 C 40000 + 7 vs < 7) C 40000 C 40000 C 40000 Exth velopit Premahulty Premahulty C 40000 Exth velopit C 40000 Exth ve	11109           6824           6825           6826           6827           6828           6828           6829           6824           6825           6826           6826           6827           6828           6829           6824           6825           6826           6826           6827           1004           1004           1007           101707           101707		Periodal Per	4 447 4 447 1 0.67 1 0.67 1 0.78 1 0.78 1 0.78 1 0.78 1 0.78 1 0.77 1 0.78 1 0.77 1 0.78 1 0.77 1 0.97 1 0.97	1.3.141 0.891.24 0.891.24 0.891.24 0.891.24 0.951.12 0.951.13 0.951.11 0.952.13 0.951.13 0.954.10 0.954.1	Adjusted for inten is nut it existing each or and excloseconomic istatio (guintifies)
	Bernstein, C.N. et al. 2019 Canova, C. et al. 2020 Decker, E. et al. 2010 Doyle, J.B. et al. 2017 Ekkom, A. et al. 1990 Glait, T. et al. 1997 Huffless, S. et al. 2012 Kenn, I. et al. 1998 Levy, J.C. et al. 2012 Radon, K. et al. 2007	Canada Canada Canada Raity Gammany Nothen Ireland Sweden 9 countries (Europe, USA) Nothern California Israel UG oxhert Sweden Gammany	1994-2010 1970-2010 1970-2010 1970-2010 1970-2012 1980-2012 1920-1980 1920-1980 1920-1980 1920-1983 Net Reported 1973-2006 March 2008 and August 2008 Amuny 2003 and March 2004 2150-1988	C 40000 C 40000 Bith weight Agger 5 min (~ 7 vs < 7) Agger 5 min (~ 7 vs < 7) Gestational age Bith weight (> 2000 a. 2000) Statistical age (> 2000 a. 2000) Catalition age (> 200 a. 2000) Catalition age (> 2000) Catalition a	11100           6624           6625           6626           6627           6628           6624           6624           6625           6626           6626           6627           6628           6629           6624           6624           6625           1004           1004           1007           1017           7771           7771           7771           7771           7771           7771           3200		Periodal Per	4 47 4 47 1 05 1 05 1 05 1 05 1 07 1 10 0 07 1 07	1.3.141 0.891.24 0.891.24 0.891.24 0.891.24 0.891.24 0.951.10 0.951.10 0.951.10 0.952.10 0.954.10 0.972.07 0.934.41 0.972.07 0.934.41 0.972.07 0.934.41 0.972.07 0.934.41 0.934.41 0.934.07 0.934.07 0.931.38 0.932.39 0.931.38 0.932.39 0.931.38 0.932.39 0.931.38 0.932.39 0.932.39 0.932.39 0.932.39 0.932.39 0.932.39 0.932.39 0.932.39 0.932.3	Adjusted for rates in our in existing each or and ecoloeconomic istable (guintifies)  Adjusted existinates reported  Adjusted existinates reported  Adjusted for race, sex, maternal age, gestational hypertension, placential or anniotic problems, birth weight, gestational age  Adjusted for race, sex, maternal age, gestational hypertension, placential or anniotic problems, birth weight, gestational age  Adjusted for race, sex, maternal age, gestational hypertension, placential or anniotic problems, birth weight, gestational age  Adjusted for race, sex, maternal age, gestational hypertension, placential or anniotic problems, birth weight, gestational age  Adjusted for race, sex, maternal age, gestational hypertension, placential or anniotic problems, birth weight, gestational age  Adjusted for race, sex, maternal age, gestational hypertension, placential or anniotic problems, birth weight, gestational age  Adjusted for race, sex, maternal age, gestational hypertension, placential or anniotic problems, birth weight, gestational age  Adjusted for race, sex, maternal age, gestational hypertension, placential or anniotic problems, birth weight, gestational age  Adjusted for race, sex, maternal age, gestational hypertension, placential or anniotic problems, birth weight, gestational age  Adjusted for race, sex, maternal age, gestational hypertension, placential or anniotic problems, birth weight, gestational age  Adjusted for race, sex, maternal age, gestational hypertension, placential or anniotic problems, birth weight, gestational age  Adjusted for race, sex, maternal age, gestational hypertension, placential or anniotic problems, birth weight, gestational age  Adjusted for race, sex, maternal age, gestational for placential or anniotic problems, birth weight, for placential age  Adjusted for race, sex, maternal age, gestational for placential or anniotic problems, birth weight, for placential age  Adjusted for age, gender, regon, and general exclusion and modulady adjusted for pany affinitis.
	Berndain, C. N. et al. 2019 Canova, C. et al. 2020 Decker, E. et al. 2010 Doyle, J. B. et al. 2017 Ekkon, A. et al. 1990 Giat, T. et al. 1997 Huffless, S. et al. 2012 Huffless, S. et al. 2012 Robin, I. et al. 1998 Levy, J. C. et al. 2012 Radon, K. et al. 2007 Somntag, B. et al. 2007 Thompson, N.P. et al. 1995	Canada Canada Canada Rahy Gaermany Hothern Heland Sweden F countries (Europe, UBA) Israel UIS cohort Sweden Germany Germany England	1964-2010 1976-2010 1976-2010 1976-2010 1977-2010 1977-1998 1922-1995 Not Reported 1992-1993 Not Reported 1992-1993 Not Reported 1973-2006 March 2008 and August 2008 January 2003 and March 2004 2004 2004	C 40000 C 40000 Extra surget Appar score 1 mir (+ 7 vs < 7) Appar score 1 mir (+ 7 vs < 7) C 40000 C 40000 + 7 vs < 7) C 40000 C 40000 + 7 vs < 7) C 40000 C 40000 C 40000 Exth velopit Premahulty Premahulty C 40000 Exth velopit C 40000 Exth ve	11109           6824           6825           6824           6825           6824           6825           771           771           771           771           771           771           771           771           771           771           771           771           771           771           771           771		Periodal Per	4 47 4 47 1 06 1 06 1 07 1 07 1 07 1 07 1 07 1 07 1 07 1 07 1 07 0 07 0 07 1 07 1 07 0 07 1 07	1.3.16.1         0.301.23           0.801.24         1.0.19           0.11.10         0.42.23           1.0.1.16         0.55.11           0.62.23         1.0.23           0.25.1.16         0.394.43           0.25.1.17         0.394.43           0.25.1.16         0.42.30           0.25.1.07         0.42.30           0.42.30         0.42.30           0.42.30         0.42.30           0.42.30         0.42.30           0.42.30         0.42.30           0.42.30         0.42.30           0.44.10         0.44.30           0.55.1.38         0.55.1.38           0.55.1.30         0.55.1.38           0.55.1.31         0.55.1.30           0.52.10         0.53.1.30           0.51.10         0.71.4           0.52.11         0.53.1           0.51.12         0.53.1           0.71.6         0.71.4           0.71.6         0.52.2           0.52.20         0.52.2           0.52.21         0.52.2           0.52.21         0.52.2           0.52.21         0.52.1.37           0.52.1.37         0.52.1.37	Adjusted for rates is not a solution and assistance status (quintiles)
	Bernstein, C. N. et al. 2019 Canova, C. et al. 2020 Decker, E. et al. 2010 Dode, J.B. et al. 2017 Ekborn, A. et al. 1990 Glist, T. et al. 1997 Huffless, S. et al. 2012 Kkien, I. et al. 1998 Levy, I.C. et al. 2012 Radon, K. et al. 2017 Radon, K. et al. 2007 Sonntag, B. et al. 2007	Canada Canada Canada Raity Commany Nothern Ireland Seeden 9 countries (Europe, UEA) Nothern California Israal UE cohort Seeden Germany Germany	1964-2010 1970-2010 1970-2010 1989-2012 1989-2012 1999-2012 1924-1997 1924-1997 1924-1997 1924-1997 1924-1997 1925-1993 Net Reported 1925-1993 Net Reported 1973-2006 March 2008 and August 2008 January 2003 and March 2004 1955-1964	C 40000 C 40000 Bith weight Agar son 1 mit (> 7 vs < 7) Agar 5 mit (> 7 vs < 7) Gestational age Bith weight (> 2000 vs = 2000) Single varinges both Gestational age (> 30 vs = 200) Agar 4000 (> 7 vs < 7) C 40000 C 40000 C 40000 Bith weight (> 2000 ys = 200) C 40000 Bith weight (> 2000 ys = 200) Bith weight (> 2000 ys = 200) C 40000 Bith weight (> 2000 ys = 2000 + 4000	11109           6824           6824           6824           6824           6824           6824           6824           6824           6824           6824           6824           6824           6824           6825           6826           6827           6828           6829           6829           6829           6829           6829           6829           6829           6829           701           771           771           771           771           771           771           771           771           771           771           771           771           771           771           771           9200           3200           3200           3200           3200           3200           3200           3200		Periodal Per	4 47 4 47 1 06 1 07 1 07 1 07 1 33 1 00 1 12 1 07 1 33 1 00 1 12 1 34 1 00 1 12 1 35 1 00 1 12 1 12	1.3.161 1.3.161 1.3.161 0.891.32 0.891.34 0.891.34 0.891.32 1.1 1.0.13 0.951.11 0.492.33 0.551.11 0.492.33 0.551.13 0.941.08 0.94	Adjusted for rates in rule and acciseconsenie status (quintiles)
	Berndain, C. N. et al. 2019 Canova, C. et al. 2020 Decker, E. et al. 2010 Doyle, J. B. et al. 2017 Ekkon, A. et al. 1990 Giat, T. et al. 1997 Huffless, S. et al. 2012 Huffless, S. et al. 2012 Robin, I. et al. 1998 Levy, J. C. et al. 2012 Radon, K. et al. 2007 Somntag, B. et al. 2007 Thompson, N.P. et al. 1995	Canada Canada Canada Rahy Gaermany Hothern Heland Sweden F countries (Europe, UBA) Israel UIS cohort Sweden Germany Germany England	1964-2010 1976-2010 1976-2010 1976-2010 1977-2010 1977-1998 1922-1995 Not Reported 1992-1993 Not Reported 1992-1993 Not Reported 1973-2006 March 2008 and August 2008 January 2003 and March 2004 2004 2004	C 40000 C 40000 Bith weight Agger 5 min (~ 7 vs < 7) Agger 5 min (~ 7 vs < 7) Gestational age Bith weight (> 2000 a. ~ 2000) Catalitoria (age) T-Bit vs ~ 30) Agger 5000 (~ 2000) a. ~ 2000) Catalitoria (age) T-Bit vs ~ 30) Agger 5000 (~ 2000) Catalitoria (age) T-Bit vs ~ 7) C 4000 C 4000 Bith weight Permuturly Bith weight C 4000 Bith weight (~ 2000g) C 4000 Bith weight (~ 2000g) C 4000 Bith weight (~ 2000g) C 4000 Bith weight (~ 2000g) C 4000 D 4000 (~ 2000g) C 4000 C 4000 Bith weight (~ 2000g) C 4000 C 4000 D 4000 (~ 2000g) C 4000 C 4000 D 4000 (~ 2000g) C 4000 Bith weight (~ 2000g) C 4000 C	11109           6824           6825           6824           6825           6826           6826           6827           6828           6829           6824           6824           6825           6826           6826           6827           1004           1004           1007           10170           10170		Periodal Per	4 467 4 467 1 067 1 067 1 07 1 07	1.3.141 0.891.24 0.891.24 0.891.24 0.891.24 0.891.24 0.951.10 0.951.11 0.92.23 0.951.10 0.92.20 0.42.30 0.42.30 0.42.30 0.42.30 0.42.30 0.42.30 0.42.30 0.44.10 0.42.30 0.44.10 0.42.30 0.44.10 0.42.30 0.44.10 0.42.30 0.44.10 0.42.30 0.44.10 0.42.30 0.44.10 0.42.30 0.44.10 0.42.30 0.44.10 0.42.30 0.44.10 0.42.30 0.44.10 0.42.30 0.44.10 0.42.30 0.44.10 0.42.30 0.44.10 0.42.30 0.44.10 0.42.30 0.44.10 0.42.30 0.44.10 0.42.30 0.44.10 0.42.30 0.45.1	Adjusted for rates is not a solar advance and acciseconomic lates (guintified)  Unadjusted estimates reported  Adjusted estimates reported
	Berndain, C. N. et al. 2019 Canova, C. et al. 2020 Decker, E. et al. 2010 Doyle, J.B. et al. 2017 Ektorn, A. et al. 1990 Giat, T. et al. 1997 Huffess, B. et al. 2012 Huffess, B. et al. 2012 Redon, I. et al. 1998 Levy, I. C. et al. 2012 Radon, K. et al. 2007 Sonntag, B. et al. 2007 Thompson, N.P. et al. 1995 Thompson, S. U. et al. 2016	Canada Canada Canada Raiy Bary Germany Nothern Reland Sweden 9 countries (Europe, USA) Nothern Cationia Israel Urael Germany Germany England Denmark	1884-2010 1895-2012 1895-2012 1895-2012 1892-1997 1824-1997 Not Reported 1995-2006 1995-2006 1995-2006 March 2006 and August 2008 March 2006 and August 2008 January 2003 and March 2004 1881-2004	<u>C 480000</u> <u>C 480000</u> Birth wagit Aggar score 1 mm (+ 7 vs + 7) Aggar score 1 mm (+ 7 vs + 7) Gestational age Birth wagit (> 2200 vs + 2200) Singly vs mulgites bin Gestational age (> 31 vs - 33) Aggar score (+ 7 vs + 7) C 48000 C 48000 Birth wagit (> 2200 vs + 2200) Birth wagit (> 2200 vs + 2200 v	11109           6824           6825           7771           7771           7771           7771           7771           7771           7771           7771           7771           7771           7771           7771           7771           7771           7771		Periodal Per	4 47 4 47 1 05 1 05 1 05 1 05 1 05 1 05 1 05 1 07 1 07	1.3.14.1 0.88.1.24 0.88.1.24 1.1 0.86.1.32 1.1 0.96.1.32 1.1 0.96.2.33 0.05.1.10 0.05.1.10 0.05.1.10 0.05.1.01 0.05.1.01 0.05.1.01 0.05.1.01 0.05.1.01 0.04.1.03 0.44.3.00 0.44.3.00 0.44.3.00 0.44.4.10 0.40.4.03 0.44.4.10 0.40.4.03 0.44.4.10 0.40.4.03 0.45.1.0	Adjusted for rate, sex, maternal age, gestational hypertinesion, placential or annotes problems, birth weight, gestational age Adjusted estimates reported Unadjusted estimates reported Unadjusted estimates reported Adjusted for race, sex, maternal age, gestational hypertinesion, placential or annotes problems, birth weight, gestational age Adjusted for race, sex, maternal age, gestational hypertinesion, placential or annotes problems, birth weight, gestational age Adjusted for race, sex, maternal age, gestational hypertinesion, placential or annotes problems, birth weight, gestational age Adjusted for race, sex, maternal age, gestational hypertinesion, placential or annotes problems, birth weight, gestational age Adjusted for race, sex, maternal age, gestational hypertinesion, placential or annotes problems, birth weight, gestational age Adjusted for race, sex, maternal age, gestational hypertinesion, placential or annotes problems, birth weight, gestational age Adjusted for race, sex, maternal age, gestational hypertinesion, placential or annotes problems, birth weight, gestational age Adjusted for faces exity and interval infection and mutually adjusted for parental BD, nale gender, rundition other hair braast mik < 5 mo, maternal anolog, 1 2 abling, finitisk, forg adjusted estimates reported Adjusted for disease during tayler, pergramery diseases, maternal BD, ageordisclomy, ever smaking, sex Unadjusted estimates reported Adjusted for disease during tayler, pergramery diseases, maternal BD, ageordisclomy, ever smaking, sex
	Berndain, C. N. et al. 2019 Canova, C. et al. 2020 Decker, E. et al. 2010 Doyle, J. B. et al. 2017 Ekkon, A. et al. 1990 Giat, T. et al. 1997 Huffless, S. et al. 2012 Huffless, S. et al. 2012 Robin, I. et al. 1998 Levy, J. C. et al. 2012 Radon, K. et al. 2007 Somntag, B. et al. 2007 Thompson, N.P. et al. 1995	Canada Canada Canada Rahy Gaermany Hothern Heland Sweden F countries (Europe, UBA) Israel UIS cohort Sweden Germany Germany England	1964-2010 1976-2010 1976-2010 1976-2010 1977-2010 1977-2008 and May 2009 1977-1998 1924-1957 Not Reported 1995-2006 1995-1993 Not Reported 1973-2006 March 2008 and August 2008 January 2003 and March 2004 2004 2004	C 40000           C 40000           Gendlam           Birth warght           Apgar score 1 mm (+ 7 vs < 7)	11109           6824           771           771           771           771           771           771           771           771           771           771           771           771           771           771           771           771           9200		Periodal Per	4 467 4 467 1 067 1 067 1 07 1	1.3.141 0.391 1.34 0.66 1.32 1.1 1.0 0.65 1.32 1.1 1.0 0.55 1.11 0.45 2.33 0.55 1.11 0.45 2.33 0.55 1.11 0.45 2.33 0.55 1.13 0.45 3.00 0.45 4.00 0.45 4.00 0.4	Adjusted for rates is not a solar advance and acciseconomic lates (guintified)  Unadjusted estimates reported  Adjusted estimates reported
	Berndain, C. N. et al. 2019 Canova, C. et al. 2020 Decker, E. et al. 2010 Doyle, J.B. et al. 2017 Ektorn, A. et al. 1990 Giat, T. et al. 1997 Huffess, B. et al. 2012 Huffess, B. et al. 2012 Redon, I. et al. 1998 Levy, I. C. et al. 2012 Radon, K. et al. 2007 Sonntag, B. et al. 2007 Thompson, N.P. et al. 1995 Thompson, S. U. et al. 2016	Canada Canada Canada Raiy Bary Germany Nothern Reland Sweden 9 countries (Europe, USA) Nothern Cationia Israel Urael Germany Germany England Denmark	1884-2010 1895-2012 1895-2012 1895-2012 1892-1997 1824-1997 Not Reported 1995-2006 1995-2006 1995-2006 March 2006 and August 2008 March 2006 and August 2008 January 2003 and March 2004 1881-2004	<u>C 480000</u> <u>C 480000</u> Birth wagit Aggar score 1 mm (+ 7 vs + 7) Aggar score 1 mm (+ 7 vs + 7) Gestational age Birth wagit (> 2200 vs + 2200) Singly vs mulgites bin Gestational age (> 31 vs - 33) Aggar score (+ 7 vs + 7) C 48000 C 48000 Birth wagit (> 2200 vs + 2200) Birth wagit (> 2200 vs + 2200 v	1110           6224           6225           6226           6226           6226           6226           6226           6227		Periodal Per	4 467 4 467 1 0.67 1 0.67 1 0.67 1 0.78 1 0.78 1 0.77 1 3.33 1 0.67 1 3.33 1 0.67 1 3.35 1 0.67 1 3.25 1 0.78 1 3.25 1 3.25	1.3.14.1 0.89.1.24 0.89.1.24 0.89.1.24 0.89.1.24 0.89.1.20 0.89.1.20 0.55.1.11 0.49.2.33 0.55.1.11 0.49.2.33 0.334.45 0.334.45 0.334.45 0.334.45 0.334.45 0.334.45 0.334.45 0.334.45 0.334.45 0.334.45 0.45.3.00 0.44.10 0.45.3.00 0.44.10 0.45.3.00 0.44.10 0.45.3.00 0.45.4.000 0.45.4.0000000000	Adjusted for rate, sex, maternal age, gestational hypertinesion, placential or annotes problems, birth weight, gestational age Adjusted estimates reported Unadjusted estimates reported Unadjusted estimates reported Adjusted for race, sex, maternal age, gestational hypertinesion, placential or annotes problems, birth weight, gestational age Adjusted for race, sex, maternal age, gestational hypertinesion, placential or annotes problems, birth weight, gestational age Adjusted for race, sex, maternal age, gestational hypertinesion, placential or annotes problems, birth weight, gestational age Adjusted for race, sex, maternal age, gestational hypertinesion, placential or annotes problems, birth weight, gestational age Adjusted for race, sex, maternal age, gestational hypertinesion, placential or annotes problems, birth weight, gestational age Adjusted for race, sex, maternal age, gestational hypertinesion, placential or annotes problems, birth weight, gestational age Adjusted for race, sex, maternal age, gestational hypertinesion, placential or annotes problems, birth weight, gestational age Adjusted for faces exity and interval infection and mutually adjusted for parental BD, nale gender, rundition other hair braast mik < 5 mo, maternal anolog, 1 2 abling, finitisk, forg adjusted estimates reported Adjusted for disease during tayler, pergramery diseases, maternal BD, ageordisclomy, ever smaking, sex Unadjusted estimates reported Adjusted for disease during tayler, pergramery diseases, maternal BD, ageordisclomy, ever smaking, sex

						1			Confidence interva	
Study type	Study	Study location	Study Time Period	Exposure Description	Total sample size (	n) Outcom	Period of exposure	Effect estimate value	(specify of differen from 95% CI)	Comments
									from 95% CI)	
Cohort studies						I4 CD	Birth	2"	1.37-2.4	Unadiusted estimates reported
				Month of birth January		14 UC	Birth	1.21"	0.76-1.65	Indiuste sames reported
						I4 CD	Birth	1.36"	1.11-2.13	Unadjusted estimates reported
				Month of birth February	84	I4 UC	Birth	0.69"	0.33-1.05	Unadjusted estimates reported
				Month of birth April		I4 CD	Birth	0.61"	0.24-0.82	Unadjusted estimates reported
	Chowers, Y et al. 2004	Israel	Not Reported			I4 UC	Birth	1.12"	0.66-1.58	Unadjusted estimates reported
				Month of birth May	-	14 CD	Birth	0.68	0.30-0.90	Unadjusted estimates reported
						14 UC 14 CD	Birth	1.37" 1.23"	0.87-1.87	Unadjusted estimates reported Unadjusted estimates reported
				Month of birth November		14 UC	Birth	0.9"	0.50-1.29	Inadjusted estimates reported
						14 CD	Birth	1.18"	1.07-1.99	Unadjusted estimates reported
				Month of birth December	84	I4 UC	Birth	1.02"	0.61-1.42	Unadjusted estimates reported
						14 CD	Rieth	1.0255	0.66-1.58	Adjusted for age (Month), body mass index (<21, 21e24.9, 25e29.9, \$30 kg/m2), ancestry (Southern European, Scandinavian, other Caucasian, non-white), oral contraceptive use (never, past, current), hormonal replacement therapy (never, past, current, premenopause), smoking (never, past, present)
			IBD diagnosis between June 1976 to June	Residence at Southern latitude (south of 379 N) compared with Northern (north of north of 41- 429)			birtii		0.80-1.29	Adjusted for age (Month), body mass index (<21, 21e24.9, 25e29.9, \$30 kg/m2), ancestry (Southern European, Scandinavian, other Caucasian, non-white), oral contraceptive use (never, past, current), hormonal
	Khalili, H. et al. 2012	USA	2002 (NHS I), between June 1989 to June		84	I4 UC	Birth	1.0255	0.80-1.29	replacement therapy (never, past, current, premenopause), smoking (never, past, present) Adjusted for age (Month), body mass index (<21, 21e24.9, 25e29.9, \$30 kg/m2), ancestry (Southern European, Scandinavian, other Caucasian, non-white), oral contraceptive use (never, past, current), hormonal
			2003 in NHS II	Poridones at Middle Initiaties compared with Northern Initiation	84	I4 CD	Birth	0.9155	0.70-1.19	replacement therapy (never, past, current, premenopause), smoking (never, past, present)
				Residence at Middle latitudes compared with Northern latitudes	0,	IA LIC	Birth	0.6955	0.44-1.07	Adjusted for age (Month), body mass index (<21, 21e24.9, 25e29.9, \$30 kg/m2), ancestry (Southern European, Scandinavian, other Caucasian, non-white), oral contraceptive use (never, past, current), hormonal replacement therapy (never, past, current, premenopause), smoking (never, past, present)
					5492751	LO IBD	Birth		reported	-chanement enricht freier's hent enreut he meruhannelt wuond freier. Hant he enrit
	Sonnenberg, A. et al. 2009	England	Born between April 1997 and March 2006	Seasonality/Month of birth	549275		Birth		reported	
					5492753	LO UC	Birth	Not	reported	
	Ponsonby A.L. et al. 2009	Victoria, Australia	Born between 1983–1998	Spring birth compared with others	25350	DO CD	Birth	0.99"	0.75-1.30	Adjusting variables not reported
					1571000	IBD	Birth		significant	
	Card T.R. et al. 2002	England	1978-1998	Month of birth October	1571000		birth		significant	
					1571000		Birth Birth		significant reported	
	Ekbom, A. et al. 1991	Sweden	1924-1957	Spring Birth compared with others	61065	-	Birth		reported	
Case-control studies					0100.	500	birtii			l
				Season of birth: January-March	119 78	B6 IBD	Birth	0.98	0.93-1.02	Unadjusted estimates reported
	Shaw, S.Y. et al. 2014	Canada	1984 to 2010	Season of birth: April-June	119 78	B6 IBD	Birth	1.07*	1.02-1.12	Unadjusted estimates reported
	5104, 51. Ct 0. 2024	cunada	1504 10 10 10	Season of birth: July-September	119 78	-	Birth	0.95	0.91-1.00	Unadjusted estimates reported
				Season of birth: October-December	119 78		Birth	1.01	0.96-1.05	Unadjusted estimates reported
	Haslam, N. et al. 2000	ик	Diagnosed with CD between 1972 and 1989	Month of birth: January-June Year of birth: Odd year	Controls NR, 928 IB Controls NR, 928 IB	-	Birth Birth	1.14 <sup>9</sup> 0.98 <sup>9</sup>	1.01-1.30 0.84-1.14	Unadjusted estimates reported Unadjusted estimates reported
				rear of birth: Odd year		D CD 95 IBD	0-2 years	0.98 1	0.68-1.49	Unalgisted estimates reported
				Sun exposure in Summer	-	95 IBD	3-5 years	0.8	0.53-1.22	Unadjusted estimates reported
	Holmes, E.A. et al. 2019	Australia	2010-2013			95 IBD	0-2 years	ı	0.66-1.51	Unadjusted estimates reported
				Sun exposure in Winter	49	95 IBD	3-5 years	0.7	0.44-1.10	Unadjusted estimates reported
	Thorsen, S.U. et al. 2016	Denmark	Born bewteen 1981–2004	Perinatal Vitamin D	76	58 IBD	Perinatal	1.12"	0.88-1.42	Variables adjusted for: 25(OHID, gender, ethni- city, birth weight (categorical), gestational age (categorical) and mother's age (categorical)
	Van Ranst, M. et al. 2005	Belgium	Born between January 1, 1935 and December 31, 1990	Seasonality/Month of birth	6 15	60 CD	Birth	0.64	0.45-0.91	Unadjusted estimates reported
				Season of birth- Winter	35	59 CD	Birth	1.2	0.2-3.2	Unadjusted estimates reported
		1		Scale of an en' Willer		24 UC	Birth	1.2	0.3-2.8	Unadjusted estimates reported
				Season of birth- Spring		59 CD	Birth	0.8	0.3-3.4	Unadjusted estimates reported
	Lopez-Serrano, P. et al. 2010	Spain	2004			24 UC	Birth	0.8	0.3-2.4	Unadjusted estimates reported
				Season of birth- Summer		59 CD 24 UC	Birth	0.9	0.5-2.8	Unadjusted estimates reported Unadjusted estimates reported
						24 UC 59 CD	Birth	1 0.9 <sup>°</sup>	0.5-3.4	Unadjusted estimates reported
		1		Season of birth- Autumn	-	24 UC	Birth	1	0.5-2.8	Unadjusted estimates reported
		1		Month of birth January	32 275 97		Birth	1.06	1.01-1.11	Unadjusted estimates reported
				Month of birth February	32 275 97	-	Birth	1.04	0.99-1.09	Unadjusted estimates reported
				Month of birth April	32 275 97	77 CD	Birth	0.96	0.91-1.01	Unadjusted estimates reported
	Disanto, G. et al. 201	Scotland, England	1997 to 2009		32 275 97		Birth	1.06	1.02-1.11	Unadjusted estimates reported
				Month of birth August	32 275 97	_	Birth	1.04	0.99-1.10	Unadjusted estimates reported
					32 275 97	_	Birth	0.97*	0.93-1.02	Unadjusted estimates reported Unadjusted estimates reported
				Month of birth October	32 275 97 32 275 97		Birth	0.92	0.87-0.97	Unajuste estimate reported
					17 246 15	-	Birth	1.042	1.009-1.076	Uniquistic summers reported Uniquistic summers reported Uniquistic summers reported
	Lee, J. et al. 2020	South Korea	January 1997 and August 2015	Birth Month	17 246 15		Birth	1.032	1.011-1.053	Unadjusted estimates reported
	Canova, C. et al. 2020	Italy	Born between 1982 and 2012	Birth season (October-April vs May-September)	1 80	14 IBD	Birth	1.19"	0.86-1.65	Adjusted for sex, year of birth, season of birth, having older sibilins, number of births, birth weight, gestational age; Apgar score at 1 minute, maternal age and mother's education

| Study type Study   | Study location  
   | Study Time Period   
  | Exposure Description   | Total sample size (n)  | Outcome  
   | Period of exposure  
   | Effect estimate type (odds ratio, relative   | Effect estimate value   | Confidence interval (specify of<br>different from 95% CI)   | p-value  
  | Comments  |
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hert Studies		
   |   
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   |   
   | risk, rate ratio etc)  |   | different from 95% CI)  | ,  
  |   |
|  |   
   |   
  | Breastfeeding (yes/no)   | 1676264 person-years   | CD   
   | infancy   
   | MV-adjusted HR   | 0.99''  | 0.76-1.30   | NS   
  | Adjusted for smoking, BMI, birthweight, preterm birth, history of diabetes in the mother, maternal history of smoking during preganancy and oral contraceptive use.   |
|  |   
   |   
  | breastneeding (yes/mo)   | 1676264 person-years   | uc   
   | infancy   
   | MV-adjusted HR   | 1.03"   | 0.81-1.31   | NS   
  | Adjusted for smoking, BMI, birthweight, preterm birth, history of diabetes in the mother, maternal history of smoking during pregarancy and oral contraceptive use.<br>Adjusted for smokins. BMI, birthweight, creterm birth, history of diabetes in the mother, maternal history of smokine durine creasanancy and oral contraceptive use.   |
|  |   
   |   
  | Breastfed S3 months (compared with no breastfeeding)   | 1676264 person-years<br>1676264 person-years   | CD<br>UC   
   | infancy   
   | MV-adjusted HR<br>MV-adjusted HR   | 1.26''<br>1.09''  | 0.83-1.93<br>0.73-1.72  | NS<br>NS   
  | Adjusted for smoking, BMI, birthweight, preterm birth, history of diabetes in the mother, maternal history of smoking during preganancy and onal contraceptive use.<br>Adjusted for smoking, BMI, birthweight, preterm birth, history of diabetes in the mother, maternal history of smoking during preganancy and onal contraceptive use.  |
| Khalili, H. et al. 2013  | Boston, USA   
   | 1976-2008   
  | Breastfed 4-8 mos (compared with no breastfeeding)   | 1676264 person-years   | 00   
   | Infancy   
   | MV-adjusted HR   | 0.94"   | 0.66-1.32   | NS   
  | Adjusted for smoking, BMI, birthweight, preterm birth, history of diabetes in the mother, maternal history of smoking during preganancy and oral contraceptive use.   |
|  |   
   |   
  |  | 1676264 person-years   | UC<br>CD   
   | infancy   
   | MV-adjusted HR<br>MV-adjusted HR   | 0.97"   | 0.65-1.46   | NS<br>NS   
  | Adjusted for smoking, BMI, birthweight, preterm birth, history of diabetes in the mother, maternal history of smoking during preganancy and onal contraceptive use.<br>Adjusted for smoking, BMI, birthweight, preterm birth, history of diabetes in the mother, maternal history of smoking during preganancy and onal contraceptive use.  |
|  |   
   |   
  | Breastfed 29 months (compared with no breastfeeding)   | 1676264 person-years<br>1676264 person-years   | uc   
   | infancy   
   | MV-adjusted HR   | 0.90"   | 0.56-1.46   | NS NS  
  | Augustee too smooring, box, on the weight, preterm birth, history of outbreas in the mother, maternal instory or smooring during pregamency and onal contraceptive use.<br>Adjusted for smooring, BMI, birthweight, preterm birth, history of diabetes in the mother, maternal history of smoking during pregamency and onal contraceptive use.   |
| Burnett, D. et al. 2017  | Nova Soctia, Canada   
   | 1988-2014   
  | Breastfeeding  | 262 729  | IBD  
   | Infancy   
   | aHR  | 1.09"   | 0.84-1.41   | NS   
  | Adjusted for maternal age, parity, area-level income, rural residence, smoking, weight status, and birth weight for gestational age   |
| e-Control Studies  |   
   | 1   
  | 1  | 1238   | CD   
   | infancy   
   | aOR  | 0.55"   | 0.41-0.74   | Not reported   
  | Adjusted for family history of IBD, smoking, age at recruitment, social class at birth, ethnic identity and ser; BF significant when >3 months  |
| Gearry, R.B. et al. 2010   | Canterbury, New Zealand   
   | June 2003 to May 2005   
  | Breastfeeding  | 1253   | uc   
   | infancy   
   | aOR  | 0.71"   | 0.52-0.96   | Not reported   
  | Adjusted for family history of IBD, smoking, age at recruitment, social class at birth, ethnic identity and sex; BF significant when >3 months  |
|  |   
   |   
  |  | 607  | CD   
   | Infancy   
   | crude OR   | 1'  | 0,5-2.2   | Not reported   
  | Unadjusted estimates reported   |
| Ekbom, A. et al. 1990  | Uppsala county, Sweden  
   | 1924-1957   
  | Exclusive breastfeeding  | 678  | UC<br>IBD  
   | infancy   
   | crude OR<br>crude OR   | 0.8   | 0,5-1,4   | Not reported   
  | Unadjusted ostimates reported<br>Unadjusted ostimates records   |
| Baron, S. et al. 2005  | Northern France   
   | 1988-1997   
  | Breastfeeding  | 444  | 0  
   | Infancy   
   | aOR  | 2.1   | 13-3.4  | 0,003  
  | Adjusted for mother's educational level   |
|  |   
   |   
  | Breastfeeding birth-6 mos  | 388  | CD   
   | infancy   
   | aOR  | 1.1   | 0.7-1.9   | Not reported   
  | Adjusted for age, gender, family history of IBD, maternal smoking and social class  |
| Amre, D.K. et al. 2006   | Montreal, Canada  
   | 1995-2004   
  | Breastfeeding 7-12 mos<br>Breastfeeding >1 year  | 388  | CD<br>CD   
   | infancy   
   | aOR<br>aOR   | 1.3"<br>1.6"  | 0.7-2.6<br>0.5-5.1  | Not reported<br>Not reported   
  | Adjusted for age, gender, family history of IBD, maternal smoking and social class<br>Adjusted for age, gender, family history of IBD, maternal smoking and social class  |
| Basson, A. et al. 2014   | Western Cape, South Africa  
   | September 2011-January 2013   
  | Breastfed as an infant   | 407  | CD   
   | infancy   
   | aDR  | 0.74"   | 0.39-1.41   | <0,05  
  | Adjusted for age at study enrolment, gender and ethnicity   |
| Radon, K. et al. 2007  | Germany   
   | March 2006 to August 2006   
  | Nutrition other than breastmilk at 5 months  | 1931   | CD   
   | Infancy   
   | aDR  | 0.9   | 0.7-1.3   | Not reported   
  | Adjusted for age, gender, region, and parental education and mutually adjusted for IBD parental history, birth weight, maternal smoking during pregnancy, siblings, rhinitis and residence in urban area  |
|  |   
   |   
  |  | 1791   | UC   
   | Infancy   
   | aOR  | 0.7"  | 0.5-0.9   | Not reported   
  | Adjusted for age, gender, region, and parental education and mutually adjusted for IBD parental history, birth weight, maternal smoking during pregnancy, siblings, rhinitis and residence in urban area  |
| Salgado, V.C. et al. 2017  | Brazil  
   | Not Reported  
  | Breastfeeding  | 308  | CD   
   | Infancy   
   | aHR  | 0.77"   | 0.28-2.09   | 0,616  
  | Adjusted for sex, age, race, educational level, family income, residence, housing conditions, family size in adulthood and childhood, pets, exposure to untreated water, vaccination (childhood), viral diseases (childho<br>helmintic infections, exposure to enteric pathogens, previous appendicatomy, tobacco exposure and family history   |
| Russel, M.G. et al. 1998   | Netherlands   
   | October 1991 to July 1997   
  | Breastfeeding  | Not reported   | CD<br>UC   
   | infancy   
   | Not reported<br>OR   | Not re<br>2'  | 10-3.9  | NS<br>NS   
  | The authors only report that breastleading was not associated with the development of IBD, except in patients with pancolitis (see below)<br>Only OR reported is in patients with ulcerative pancolitis   |
|  |   
   |   
  |  | Not reported<br>457  | CD UC  
   | Infancy   
   | RR   | 2<br>Not re   |   | No reported  
  | Unity UK reported is in patients with ukerative pancetitis<br>BR of CD associated with breastfeeding was close to unity (data not shown)  |
| Persson, P.G. et al. 1993  | Stockholm   
   | 1984-1987   
  | Breastfeeding  | 250  | UC   
   | infancy   
   | RR   | Not re  | ported  | Not reported   
  | Same for RC (close to unity; data not shown)  |
| Corrao, G. et al. 1998   | Italy   
   | 1989-1992   
  | Breastfeeding  | 450  | CD<br>UC   
   | infancy   
   | 0R<br>08   | 1.9   | 11-33   | <0.05  
  | Unadjusted estimates reported. 81.3% CD vs 86.7% in controls<br>Unadjusted estimates reported. 81.3% UC vs 86.4% in controls  |
| Jiang, L. et al. 2007  | China   
   | 2004  
  | Breastfeeding  | 1188<br>354  | uc   
   | Infancy   
   | OR   | 1.5 <sup>°</sup><br>0.8 <sup>°</sup>  | 0.47-1.37   | <0.05  
  | Unadjusted estimates reported. 81.3% UC vs 86.4% in controls<br>Unadjusted estimates reported.  |
| Jakobsen, C. et al. 2013   | Denmark   
   | 2007-2009   
  | Breastfeeding > 3 months compared with <3 months   | 592  | IBD  
   | infancy   
   | aOR  | 0.5   | 0.3-1.0   | 0,058  
  | Adjusted for age, gender, ethnicity, area of residence and socioeconomic status   |
|  |   
   |   
  |  | 533  | UC<br>CD   
   | infancy   
   | aOR<br>aOR   | 0.5"  | 0.2-1.0   | 0,06   
  | Adjusted for age, gender, ethnicity, area of residence and socioeconomic status<br>Adjusted for smokim at diamosis, contact with cats in childhood, and scorts activity in childhood  |
| Harry T and MA   | (Terration  
   | 2000 2000   
  | Breastfeeding 0-5 months   | 545  | uc   
   | infancy   
   | aDR  | 2.716   | 1.072-2.801   | 0,041  
  | Adjusted for smoking at diagnosis, contact with cats in childhood, and sports activity in childhood<br>Adjusted for sports activity and family size in childhood  |
| Hlavaty, T. et al. 2013  | Slovalca  
   | 2008-2009   
  | Breastfeeding 6-12 months  | 545  | CD   
   | infancy   
   | Not reported   | Not re  | ported  | Not reported   
  | 34% CD vs 56% controls  |
| Ham, D.Y. et al. 2010  | New Zeland  
   | Not Reported  
  | Breastfeeding  | 503<br>851   | UC<br>CD   
   | infancy   
   | Not reported   | Not n<br>0.97   | 0.58-1.61   | Not reported   
  | 43% vs 56% controls<br>Uhadjustad extimates reported.   |
| time, p. r. w. m. acade  | New Local C   
   | nos neportero   
  | and an and a second  | 534  | IBD  
   | infancy   
   | OR   | 1.07  | 0.52-2.16   | NS   
  | Unadjusted estimates reported.  |
|  |   
   |   
  | Breastfeeding  | 534  | CD   
   | Infancy   
   | OR   | 1.8   | 0.6-5.38  | NS   
  | Unadjusted estimates reported.  |
| Hansen, T.S. et al. 2011   | Denmark   
   | 2003-2004   
  |  | 534  | UC IBD   
   | infancy   
   | 08   | 0.7   | 0.2-1.84<br>0.23-1.11   | NS<br>NS   
  | Unadjusted estimates reported.<br>Unadjusted estimates reported.  |
|  |   
   |   
  | Breastfeeding more than 6 months   | 534  | 00   
   | infancy   
   | OR   | 0.63  | 0.2-1.91  | NS   
  | Unadjusted estimates reported.  |
|  |   
   |   
  |  | 534  | UC   
   | infancy   
   | OR   | 0.4   | 0.13-1.28   | NS   
  | Unadjusted estimates reported.  |
| Thompson, N.P. et al. 1995   | ик  
   | 1950-1968   
  | Breastfeeding  | 2792<br>1426   | CD<br>UC   
   | infancy   
   | OR<br>OR   | 1.04  | 0.88-1.25<br>0.90-1.50  | Not reported<br>Not reported   
  | Unadjusted estimates reported.<br>Unadjusted estimates reported.  |
| Thompson, N.P. et al. 2000   | ик  
   | 1946-1958   
  | Breastfed  | 287  | CD   
   | infancy   
   | OR   | 0.4   | 0.5-1.03  | 0,06   
  | Unadjusted estimates reported.  |
| inompion, n.r. et al. 2000   | UK.   
   | 1346-1358   
  | breastree  | 287  | UC   
   | Infancy   
   | OR   | 2.76  | 0.86-9.81   | 0,1  
  | Unadjusted estimates reported.  |
|  |   
   |   
  |  | 1126   | CD   
   | infancy   
   | aOR  | 0.086"  | 0.03-0.243  | significant at p<0.0006 level after Bonferroni adjustment.   
  | Adjusted for sex, age and country income based on GNI. †5   |
|  |   
   |   
  |  | 1100   | 110  
   | Infancy   
   |  |   |   |  
  |   |
| Ng, S.C. et al. 2015   | Asia and Australia  
   | April 2011 to March 2013  
  | Breastfeeding for 7-12 mos, compared with 0-6 mos  | 1196<br>1126   | UC<br>CD   
   | infancy   
   | aOR<br>aOR   | 0.142""<br>0.542"   | 0.073-0.277<br>0.310-0.949  |  
  | Adjusted for sex, age and country income based on GNL 15<br>Adjusted for sex, age and country income based on GNL 15  |
| Ng. S.C. et al. 2015   | Asia and Australia  
   | April 2011 to March 2013  
  | Breastfeeding for 7-12 mos, compared with 0-6 mos<br>Breastfeeding for >12 mos, compared with 0-6 mos  | 1126<br>1196   | CD<br>UC   
   | Infancy   
   | aOR<br>aDR<br>aOR  | 0.142**<br>0.542**<br>1.05**  | 0.073-0.277<br>0.310-0.949<br>0.708-1.557   | significant at p=0.0006 level after Bonferroni adjustment.<br>0,032<br>0,809   
  | Advance for user, age and country income hand on 601. 15<br>Advance for sax, age and country income hand on 601. 15<br>Advance for use, age and country income hand on 601. 15  |
|  |   
   | April 2011 to March 2013  
  | Breastfeeding for >12 mos, compared with 0-6 mos   | 1126<br>1196<br>334  | CD<br>UC<br>UC   
   | infancy<br>infancy<br>infancy   
   | aOR<br>aOR<br>aOR<br>OR  | 0.142""<br>0.542"   | 0.073-0.277<br>0.310-0.949  | significant at p<0.0006 level after Bonferroni adjustment.<br>0,032  
  | Adjusted for sex, age and country income based on GNA. 15<br>Adjusted for sex, age and country income based on GNA. 15  |
| Ng. S.C. et al. 2015<br>Lamoutocin, S.M. et al. 1991   | Asia and Australia<br>Uppsala county, Sweden  
   |   
  |  | 1126<br>1196   | CD<br>UC   
   | Infancy   
   | aOR<br>aDR<br>aOR  | 0.142''<br>0.542''<br>1.05''<br>1.2'  | 0.073-0.277<br>0.310-0.949<br>0.708-1.557<br>0.31-2.78  | significant at p=0.0006 level after Bonferroni adjustment.<br>0,032<br>0,809<br>NS   
  | Adjusted for sex, age and examtly inseme based on ONL 'S<br>Adjusted for sex, age and examtly inseme based on ONL 'S<br>Adjusted for sex, age and examtly inseme based on ONL 'S<br>Designed edimeted ange and.   |
|  |   
   |   
  | Breastfeeding for >12 mos, compared with 0.6 mos<br>Wearing before 14 days<br>Breastfeeding frequency  | 1126<br>1196<br>334<br>334<br>334<br>1497  | CD<br>UC<br>UC<br>Extensive UC<br>Non-progressive UC<br>IBD  
   | infancy<br>infancy<br>infancy<br>infancy<br>infancy<br>infancy  
   | aOR<br>aOR<br>OR<br>OR<br>OR<br>OR<br>OR<br>Not reported   | 0.142"<br>0.542"<br>1.05"<br>1.2"<br>1.67<br>Not n<br>Not n   | 0.073-0.277<br>0.310-0.949<br>0.708-1.557<br>0.31-2.78<br>0.35-2.86<br>0.40-6.98<br>ported  | significant at pc0.0006 lovel after Boeferroei adjustment.<br>0,012<br>0,000<br>NS<br>NS<br>NS<br>NS<br>NS   
  | Adabatik trava, sag pand cardon konsen kasad on 604. 15.<br>Adabatik trava, sag pand cardon konsen kasad on 604. 15.<br>Adjuster for san, sag pand quarty konsen kasad on 604. 15.<br>Adjuster for san, sag pand quarty konsen kasad on 604. 15.<br>Adjuster for san, sage and quarty konsen kasad on 604. 15.<br>Adjuster for san, sage and quarty konsen kasad on 604. 15.<br>Adjuster for san, sage and quarty konsen kasad on 604. 15.<br>Adjuster for san, sage and quarty konsen kasad on 604. 15.<br>Adjuster for san, sage and quarty konsen kasad on 604. 15.<br>Adjuster for san, sage and quarty konsen kasad on 604. 15.<br>Adjuster for sam, sage and quarty konsen kasad on 604. 15.<br>Adjuster for sam, sage and quarty konsen kasad on 604. 15.<br>Adjuster for sam, sage and quarty konsen kasad on 604. 15.<br>Adjuster for sam, sage and quarty konsen kasad on 604. 15.<br>Adjuster for sam, sage and quarty konsen kasad on 604. 15.<br>Adjuster for sam, sage and quarty konsen kasad on 604. 15.<br>Adjuster for sam, sage and quarty konsen kasad on 604. 15.<br>Adjuster for sam, sage and quarty konsen kasad on 604. 15.<br>Adjuster for sam, sage and quarty konsen kasad on 604. 15.<br>Adjuster for sam, sage and quarty konsen kasad on 604. 15.<br>Adjuster for sam, sage and quarty konsen kasad on 604. 15.<br>Adjuster for sam, sage and quarty konsen kasad on 604. 15.<br>Adjuster for sam, sage and quarty konsen kasad on 604. 15.<br>Adjuster for sam, sage and quarty konsen kasad on 604. 15.<br>Adjuster for sam, sam, sam, sam, sam, sam, sam, sam,  |
| lamution, SM, et al. 1991  | Uppsala county, Sweden  
   | 2045-1964   
  | Breastfeeding for >12 mos, compared with 0-6 mos<br>Weaning before 14 days   | 1126<br>1196<br>334<br>334<br>334  | CD<br>UC<br>UC<br>Extensive UC<br>Non-progressive UC   
   | Infancy<br>Infancy<br>Infancy<br>Infancy<br>Infancy   
   | 40R<br>40R<br>00R<br>00R<br>00R<br>00R   | 0.142"<br>0.542"<br>1.05"<br>1.2"<br>1'<br>1.67 <sup>°</sup>  | 0.073-0.277<br>0.310-0.349<br>0.706-1.557<br>0.31-2.78<br>0.35-2.86<br>0.40-6.98<br>ported<br>ported  | ingoificant at p=0.0006 level after Bonferroni adjustment.<br>0,032<br>0,089<br>NS<br>NS<br>NS   
  | Adjatate for sax, age and constry income Seade on ON, 55<br>Adjatate for sax, age and constry income Seade on ON, 55<br>Adjatate for sax, age and constry income Seade on ON, 55<br>Undigitate distinuous segurate.<br>Disdigitate adjatates segurate.  |
|  |   
   | 2045-1964   
  | Deveatereding for >12 may, compared with 0.6 mos<br>Wearing before 34 days<br>breastleeding heaponcy<br>Breastleeding davation<br>frequency of formula leading<br>Tropic of formula leading  | 1126<br>1196<br>334<br>334<br>1497<br>1497<br>1497<br>1497   | CD<br>UC<br>Extensive UC<br>Non-progressive UC<br>IBD<br>IBD<br>IBD<br>IBD   
   | Infancy<br>Infancy<br>Infancy<br>Infancy<br>Infancy<br>Infancy<br>Infancy<br>Infancy<br>Infancy   
   | NGA<br>NGA<br>NGA<br>NG<br>NG<br>NG<br>NGA<br>NGA<br>NGA<br>NGA<br>NGA   | 0.142"*<br>0.542"*<br>1.05"<br>1.2"<br>1.67"<br>Not re<br>Not re<br>Not re  | 0.073-0.277<br>0.310-0.949<br>0.708-1.557<br>0.31-2.78<br>0.35-2.86<br>0.40-6.98<br>ported<br>ported  | Significant at pel 2005 (eval after Benferreis Aljusteen),<br>6,009<br>165<br>165<br>165<br>165<br>165<br>165<br>165<br>165<br>165   
  | Adabati for size, age and canoty invense based on 504. 55<br>Adjusted for size, age and canoty invense based on 504. 55<br>Adjusted for size, age and canoty invense based on 504. 55<br>Dandgusted andimates appende.<br>Dandgusted andimates appende.<br>Dandgus  |
| lamution, SM, et al. 1991  | Uppsala county, Sweden  | 2045-1964  | Invasteeding for 52 mos, compared with 0.6 mos<br>Wearing before 54 days<br>Braasteeding through the second second<br>Researchering datation<br>Frequency of formula feeding<br>Type of formula feeding<br>Datation Second Seco   | 1126<br>1196<br>334<br>334<br>334<br>349<br>1497<br>1497<br>1497<br>1497   | CD<br>UC<br>Extensive UC<br>IBD<br>IBD<br>IBD<br>IBD<br>IBD  | Infancy<br>Infancy<br>Infancy<br>Infancy<br>Infancy<br>Infancy<br>Infancy<br>Infancy<br>Infancy<br>Infancy  | NG4<br>NG4<br>NG4<br>NG<br>NG<br>NG<br>NG4<br>NG4<br>NG4<br>NG4<br>NG4   | 0.142"<br>0.542"<br>1.05"<br>1.2"<br>1.67<br>Not re<br>Not re<br>Not re<br>Not re   | 0.073.0.277<br>0.310.349<br>0.208.1557<br>0.33.2.78<br>0.35.2.86<br>0.406.58<br>ported<br>ported<br>ported<br>ported<br>ported  | significant at pel 2003 (well after bitwheren's significant<br>0.037<br>0.087<br>0.087<br>165<br>165<br>165<br>165<br>165<br>165<br>165<br>165  | Aduata for say, age and earder investment and en 00. %<br>Schlarter forms, age on of earder investment and en 00. %<br>Adjuate forms, age and earder investment and en 00. %<br>Schlarter forms, age and earder investment and en 00. %<br>Schlarter forms, age and earder investment and en 00. %<br>Schlarter forms, age and earder investment and earder investment and earder investment<br>Schlarter forms, age and earder investment and earder investment and earder investment<br>Schlarter forms, age and earder investment and earder investment<br>Schlarter forms, age an   |
| lamution, SM, et al. 1991  | Uppsala county, Sweden  
   | 2045-1964   
  | Invasifieding for >12 mix, compared with 0.6 mix.<br>Wraning before 34 days.<br>Invasifieding browney<br>Invasifieding drogeney<br>Invasifieding drogeney<br>Tayor of fromsile fielding<br>Tayor of fromsile fielding<br>Addres sagars for formsile fielding<br>apr of starting mixed freedings  | 1126<br>1196<br>334<br>334<br>1497<br>1497<br>1497<br>1497   | CD<br>UC<br>Extensive UC<br>Non-progressive UC<br>IBD<br>IBD<br>IBD<br>IBD   
   | Infancy<br>Infancy<br>Infancy<br>Infancy<br>Infancy<br>Infancy<br>Infancy<br>Infancy<br>Infancy   
   | NGA<br>NGA<br>NGA<br>NG<br>NG<br>NG<br>NGA<br>NGA<br>NGA<br>NGA<br>NGA   | 0.142"<br>0.542"<br>1.05"<br>1.2"<br>1.67<br>Not re<br>Not re<br>Not re<br>Not re   | 0.073.0.277<br>0.150.589<br>0.0761.557<br>0.33-2.78<br>0.35-2.86<br>0.40.6.58<br>ponted<br>ponted<br>ponted<br>ponted<br>ponted   | Significant at pel 2005 (eval after Benferreis Aljusteen),<br>6,009<br>165<br>165<br>165<br>165<br>165<br>165<br>165<br>165<br>165   
  | Adabati for size, age and canoty invense based on 504. 55<br>Adjusted for size, age and canoty invense based on 504. 55<br>Adjusted for size, age and canoty invense based on 504. 55<br>Dandgusted andimates appende.<br>Dandgusted andimates appende.<br>Dandgus  |
| lamatus, 5.M. et al. 1991<br>clas, T. et al. 1947  | Uppsala county, Sweden  | 2545-1964  | Invasteeding for 52 mos, compared with 0.6 mos<br>Wearing before 54 days<br>Braasteeding through the second second<br>Researchering datation<br>Frequency of formula feeding<br>Type of formula feeding<br>Datation Second Seco   | 1126<br>314<br>314<br>314<br>314<br>314<br>314<br>1407<br>1407<br>3407<br>3407<br>3407<br>244<br>228   | CD<br>UC<br>Extensive UC<br>Hon-progressive UC<br>IBD<br>IBD<br>IBD<br>IBD<br>IBD<br>IBD<br>UC<br>CD   | Infancy<br>Infancy<br>Infancy<br>Infancy<br>Infancy<br>Infancy<br>Infancy<br>Infancy<br>Infancy<br>Infancy<br>Infancy<br>Infancy<br>Infancy<br>Infancy<br>Infancy<br>Infancy  | 60.<br>102.<br>102.<br>103.<br>104.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>1 | 0.442"<br>0.542"<br>1.05"<br>1.2"<br>1.2"<br>1.67'<br>Not n<br>Not n<br>Not n<br>Not n<br>Not n   | 0.073 0.277<br>0.130 0.389<br>0.026 1.557<br>0.33-2.78<br>0.35-2.86<br>0.40 6.58<br>ported<br>ported<br>ported<br>ported<br>Not reported<br>Not reported<br>Not reported  | Significant at pel 2005 level after transmission<br>0,003<br>0,000<br>165<br>165<br>165<br>165<br>165<br>165<br>165<br>165<br>165<br>165  | Aduata for say, age and earder investment and en 00. %<br>Schlarter forms, age on of earder investment and en 00. %<br>Adjuate forms, age and earder investment and en 00. %<br>Schlarter forms, age and earder investment and en 00. %<br>Schlarter forms, age and earder investment and en 00. %<br>Schlarter forms, age and earder investment and earder investment and earder investment<br>Schlarter forms, age and earder investment and earder investment and earder investment<br>Schlarter forms, age and earder investment and earder investment<br>Schlarter forms, age an   |
| lamution, SM, et al. 1991  | Uppsala county, Sweden  | 2045-1964  | Invasifieding for >12 mix, compared with 0.6 mix.<br>Wraning before 34 days.<br>Invasifieding browney<br>Invasifieding drogeney<br>Invasifieding drogeney<br>Tayor of fromsile fielding<br>Tayor of fromsile fielding<br>Addres sagars for formsile fielding<br>apr of starting mixed freedings  | 1128<br>1156<br>134<br>334<br>1407<br>1407<br>1407<br>1407<br>1407<br>1407<br>1407<br>205<br>225<br>204  | CD<br>UC<br>UC<br>Ettmise UC<br>IBD<br>IBD<br>IBD<br>IBD<br>IBD<br>IBD<br>IBD<br>UC<br>CD<br>UC  | infancy<br>Infancy<br>Infancy<br>Infancy<br>Infancy<br>Infancy<br>Infancy<br>Infancy<br>Infancy<br>Infancy<br>Infancy<br>Infancy<br>Infancy<br>Infancy<br>Infancy<br>Infancy  | 00.<br>00.<br>00.<br>00.<br>00.<br>00.<br>00.<br>00.<br>00.<br>00.   | 0.142"<br>0.542"<br>1.05"<br>1.2"<br>1.6"<br>Not n<br>Not n | 0.079.0.277 0.310.0.549 0.704.1.557 0.312.7.28 0.35.2.86 0.40.6.38 ported ported ported Nat reported Nat reported Nat reported Nat reported Nat reported  | significant at per 30000 werd after the transmission of 40000 services of 400000 services of 40000 ser  | Aduata for say, age and earder investment and en 00. %<br>Schlarter forms, age on of earder investment and en 00. %<br>Adjuate forms, age and earder investment and en 00. %<br>Schlarter forms, age and earder investment and en 00. %<br>Schlarter forms, age and earder investment and en 00. %<br>Schlarter forms, age and earder investment and earder investment and earder investment<br>Schlarter forms, age and earder investment and earder investment and earder investment<br>Schlarter forms, age and earder investment and earder investment<br>Schlarter forms, age an   |
| lamatus, 5.M. et al. 1991<br>clas, T. et al. 1947  | Uppsala county, Sweden  
   | 2545-1964   
  | Invasifieding for >12 mox, compared with 0.6 mox.<br>Waaring before 14 days.<br>Invasifieding browney<br>Invasifieding daysian<br>Topor of normals feeding<br>Topor of normals feeding<br>App of storting mixed feedings.<br>Invasifieding<br>Invasifieding  | 1126<br>314<br>314<br>314<br>314<br>314<br>314<br>1407<br>1407<br>3407<br>3407<br>3407<br>244<br>228   | CD<br>UC<br>Extensive UC<br>Hon-progressive UC<br>IBD<br>IBD<br>IBD<br>IBD<br>IBD<br>IBD<br>UC<br>CD   
   | Infancy<br>Infancy<br>Infancy<br>Infancy<br>Infancy<br>Infancy<br>Infancy<br>Infancy<br>Infancy<br>Infancy<br>Infancy<br>Infancy<br>Infancy<br>Infancy<br>Infancy<br>Infancy  
   | 60.<br>102.<br>102.<br>103.<br>104.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>105.<br>1 | 0.142"<br>0.542"<br>1.05"<br>1.2"<br>1.6"<br>Not n<br>Not n | 0.073 0.277<br>0.130 0.389<br>0.026 1.557<br>0.33-2.78<br>0.35-2.86<br>0.40 6.58<br>ported<br>ported<br>ported<br>ported<br>Not reported<br>Not reported<br>Not reported  | Significant at pel 2005 level after transmission<br>0,003<br>0,000<br>165<br>165<br>165<br>165<br>165<br>165<br>165<br>165<br>165<br>165  | ApJatha Ervan, sag and entrof visions baard on 60. %             
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| lamostion, 5.56 et al. 1991<br>citaç T. et al. 3987<br>shlorwel, P.J. et al. 1979  | Lippsala county, Seeden international IBD Study group Southampton, UK   
   | 1945-1964<br>Not Reported   
  | Brazelfeeding for +12 mos, compared with 0.6 mos<br>Virazing before 34 days<br>examinating transvery<br>brazelfeeding transvery<br>Tape of formular hering<br>Tape of formular hering<br>Tape of formular hering<br>and of score (monthwith<br>Brazelfeeding<br>Encloseding<br>Encloseding   | 138<br>138<br>334<br>344<br>347<br>347<br>347<br>347<br>347<br>347<br>347<br>347   | CD<br>UC<br>UC<br>Extensive UC<br>18D<br>18D<br>18D<br>18D<br>18D<br>18D<br>18D<br>18D<br>0<br>0<br>0<br>0<br>0<br>0<br>0<br>0<br>0<br>0<br>0<br>0<br>0<br>0<br>0<br>0<br>0<br>0<br>0  
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   | 40.<br>40.<br>40.<br>40.<br>40.<br>40.<br>40.<br>40.<br>40.<br>40.   |   | 0.070.277           0.336.499           0.336.499           0.364.507           6.15.27           0.55.28           0.964.58           0.964.58           operation           opera   | significant at pd. 2020 evel after break indexense indextonenti<br>Q.037<br>6.089<br>145<br>145<br>145<br>145<br>145<br>145<br>145<br>145  
  | Adabati for say, and notion insum and on 00. %5<br>Adabati for say, and notion insum based on 00. %5<br>Adabati for say, and notion insum based on 00. %5<br>Adabati for any and 00. %5<br>Adabati for any any and 00. %5<br>Adabati for any   |
| Samustani, S.M. et al. 3991<br>Sites, T. et al. 3987<br>Millioneul, F.J. et al. 1979<br>What al. et al. 1979   | Lippula county, Sweden Lippula county, Sweden International IBO Study group Southampton, UK China   
   | 2045-1364 2045-1364 Not Reported April 2007 to April 2010   
  | Invasiteding for >12 mos, compared with 0.6 mos<br>freaming before 14 days<br>Invasiteding duration<br>Frequency of formula feeding<br>Frequency of formula feeding<br>Addet super to formula/mith.<br>Addet super to formula/mith.<br>Exast feeding<br>Invasiteding<br>Invasiteding<br>Invasiteding<br>Invasiteding<br>Invasiteding   | 138<br>138<br>134<br>134<br>140<br>1407<br>1407<br>1407<br>1407<br>1407<br>1407<br>1407  | CD<br>UC<br>UC<br>Extensive UC<br>Hon-progressive UC<br>HBD<br>HBD<br>HBD<br>HBD<br>HBD<br>UC<br>CD<br>UC<br>CD<br>UC<br>CD<br>HBD<br>CD   
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 | 6.070.277     6.133.6499     6.333.6499     6.334.547     6.332.37     6.352.38     6.45.48     6.49    
6.49     6 | significant at pdl 2000 (well after bitwheresi signatures).<br>0,017<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,007<br>0,00  | Abataba Toras, aga not antri nomes and no 05. %           Abataba Toras, aga not antri nomes and no 05. %           Abataba Toras, aga not antri nomes and no 05. %           Abataba Toras, aga not antri nomes and no 05. %           Abataba Toras, aga not antri nomes and no 05. %           Abataba Toras, aga not antri nomes and no 05. %           Abataba Toras, aga not antri nomes and no 05. %           Abataba Toras, aga not antri nomes and no 05. %           Abataba Toras, aga not antri nomes and no 05. %           Abataba Toras, aga not antri nomes and no 05. %           Abataba Toras, aga not antri nomes and no 05. %           Abataba Toras, aga not antri nomes and no 05. %           Abataba Toras, aga not antri nomes antri no   |
| Samushian, S.M. et al. 1991<br>Gitaq, T. et al. 1987<br>Mourouel, P.J. et al. 1999<br>Heavy, Y.F. et al. 2013<br>Heavier J. E. et al. 2019<br>Heavier, I.E. et al. 2019  | Uppuls courty, Seeden           International 8D Study group           Deathamption, UC           Once           Solution III   
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  | Invasifieding for >12 mix, compared with 0.6 mix.<br>Varining larliers 24 days.<br>Invasifieding browsny<br>Invasifieding browsny<br>Invasifieding daviation<br>Tigue of domaka leading<br>Tigue of domaka leading<br>Age of storting mixed feesdings<br>Invasifieding<br>Invasifieding<br>Invasifieding<br>Invasifieding<br>Invasifieding<br>Invasifieding<br>Invasifieding<br>Invasifieding  | 138<br>138<br>334<br>344<br>347<br>347<br>347<br>347<br>347<br>347<br>347<br>347   | CD<br>UC<br>UC<br>Extensive UC<br>18D<br>18D<br>18D<br>18D<br>18D<br>18D<br>18D<br>18D<br>0<br>0<br>0<br>0<br>0<br>0<br>0<br>0<br>0<br>0<br>0<br>0<br>0<br>0<br>0<br>0<br>0<br>0<br>0  
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| Samustauri, 516 et al. 1991<br>Silar, T. et al. 1987<br>Monuel, F. J. et al. 1979<br>Mong, F. F. et al. 2013<br>Proc. Information, E. et al. 2009<br>Large, L. Et al. 2012<br>Monuelationski, O. et al. 2015   | Upputs county, Sweden           International BD Starty group           Exchampton, UK           Onion           Exclusion           UAA           UAA  
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Et al. 2012<br>Monuelationski, O. et al. 2015   | Upputs county, Sweden           International BD Starty group           Exchampton, UK           Onion           Exclusion           UAA           UAA  | 2845-1564 Ref Reported Ref Reported April 2020 to April 2020 Ref Reported Ref Reported Statistics  | Invastreding for 1.2 mos, compared with 0.6 mos<br>Variancy before 54 days<br>Invasing before 54 days<br>Invastreding druation<br>Inception of Inmuta Reding<br>Ingue of Inmuta Reding<br>Ingue of Inmuta Reding<br>Addie upper formula/hult<br>Addie upper formula/hult<br>Ad   | 138<br>138<br>134<br>134<br>140<br>1407<br>1407<br>1407<br>1407<br>1407<br>1407<br>1407<br>244<br>234<br>234<br>234<br>234<br>234<br>234<br>234  | CO           UC           UC           Marcine UC           Marcine UC           MO   | 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Internations, S.M. et al. 1991           Ellar, T. et al. 1987           Weburwell, P.J. et al. 1979           Hong, Y.F. et al. 2013           Para Indergen, I.E. et al. 2009           Annual A. C. et al. 2012           Machadomak, O. et al. 2016           Dople, I.R. et al. 2017           Decker, E. et al. 2010           Immathy, K. et al. 2010           Immathy and A. et al. 2016           Impartment, C. et al. 2016	Upputs county, Swethen           International BD Starky group           Data           China           China           Data           Other           Exclamational BD Starky group           China           China           Upputs county, Swethen           Other           Starken           Exclamation           Martinita, Countain           Stachbert county           Starkent county           Starkent county           Starkent county           Starkent county           Starkent county	2845-1564           2845-1564           Net Reported           April 2007 to April 2010           Wet Reported           March Reported           2027 2008 2010.2011           2027 2008 2010.2011           2027 2008 2010.2011           2027 2008 2010.2011           2027 2008 2010.2011           2025 2010 to May 2020           Net Reported           2026 2020 2011           2026 2020 2011           2026 2020 2011	Invastending for 12 mox, compared with 0.6 mos Variang before 34 days Invastending browsny resultation of the set region of movies heading Tops of starting mixed headings Addre starts the movies headings Addre starts the set Age of starting mixed headings Addre starts the set Addre starts the set	138 138 134 134 134 1487 1497	G0           UC           UC           Stemmas UC           B00	Maray Maray	OA			gipplent at pel 2000 rend after bankrass i dynamics 0,037 0,049 0,049 0,047 0,047 0,057	Adjank arva, spin divery investe value of 05 %     Adjank arva, spin divery investe value of 06 %     Adjank arva, spin divery investe value of 06 %     Adjank arva, spin divery investe value of 06 %     Adjank arva, spin divery investe value of 06 %     Adjank arva, spin divery investe value of 06 %     Adjank arva, spin divery investe value of 06 %     Adjank arva, spin divery investe value of 06 %     Adjank arva, spin divery investe value of 06 %     Adjank arva, spin divery investe value of 06 %     Adjank arva, spin divery investe value of 06 %     Adjank arva, spin divery investe value of 06 %     Adjank arva, spin divery investe value of 06 %     Adjank arva, spin divery investe value of 06 %
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Immunitation, S. M. et al. 1999         Elite, T. et al. 1987         Whorwell, P. J. et al. 1979         Whorwell, P. J. et al. 1979         Whorwell, P. J. et al. 1979         Whorwell, P. J. et al. 2071         Schurg, L. et al. 2020         Schurg, L. et al. 2021         Marchael, C. et al. 2026         Imageneration, C. M. et al. 2021         Valueli, H. et al. 2021         Natures, S., et al. 2022         Rain, L. et al. 2021	Upputs county, Swethen           International BD Starky group           Bachampton, UK           Onion           Bachampton, UK           Onion           Bachampton, UK           Otion           Bachampton, UK           Otion           Bachampton, UK	284-1564           Ref Reported           April 2021 to April 2020           April 2021 to April 2020           Ref Reported	baselseding for >12 mor, compared with 0.6 mor.  varing barfore 24 days  leasafiseding brogueary reading dardition regioner of more of the offee offe	1138 1138 134 134 134 134 1407 140	G0           UC           UC           Detended UC           Ring-regressive UC           Ring           Ring <td< td=""><td>Maray Maray</td><td>coli coli coli coli coli coli coli coli</td><td></td><td>6.070.277     6.070.277     6.033.699     6.334.597     6.334.597     6.352.86     6.08</td><td>significant affect Marken Sectores 4, department           0.01           0.02           0.03           0.03           0.04           0.05</td><td></td></td<>	Maray Maray	coli coli coli coli coli coli coli coli		6.070.277     6.070.277     6.033.699     6.334.597     6.334.597     6.352.86     6.08	significant affect Marken Sectores 4, department           0.01           0.02           0.03           0.03           0.04           0.05	
Inmunitation, S. M. et al. 1991	Upputs county, Swethen           International BD Starky group           Bachampton, UK           Onion           Bachampton, UK           Onion           Bachampton, UK           Otion           Bachampton, UK           Otion           Bachampton, UK	244-1564       244-1564       Net Reported       Approximation       Approximation <td>Insaffeding for 12 mor, compared with 0.6 mos.</td> <td>138 138 134 134 134 134 134 134 134 134</td> <td>G0           VC           VC           VE           VE           VE           Non-sequence           IR0           IR0</td> <td>Many Many Many Many Many Many Many Many</td> <td>ACA ACA ACA ACA ACA ACA ACA ACA</td> <td></td> <td></td> <td>significant affect Marken Sectores 4, department           0.01           0.02           0.03           0.03           0.04           0.05</td> <td>Appland Irans, ong ond androm isome and on 05. 15           Appland Irans, ong ond androm isome and on 05. 15           Appland Irans, ong ond androm isome and on 05. 15           Appland Irans, ong ond androm isome and on 05. 15           Appland Irans, ong ond androm isome and on 05. 15           Appland Irans, ong ond androm isome and on 05. 15           Appland Irans, ong ond androm isome and on 05. 15           Appland Irans, ong ond androm isome and on 05. 15           Appland Irans, ong ond androm isome and on 05. 15           Appland Irans, ong ond androm isome and on 05. 15           Appland Irans, ong ond androm isome and on 05. 15           Appland Irans, ong ond androm isome and on 05. 15           Appland Irans, ong ond androm isome and on 05. 15           Appland Irans, ong ond androm 05. 15           Appland Irans, ong ond 05. 15     &lt;</td>	Insaffeding for 12 mor, compared with 0.6 mos.	138 138 134 134 134 134 134 134 134 134	G0           VC           VC           VE           VE           VE           Non-sequence           IR0	Many Many Many Many Many Many Many Many	ACA ACA ACA ACA ACA ACA ACA ACA			significant affect Marken Sectores 4, department           0.01           0.02           0.03           0.03           0.04           0.05	Appland Irans, ong ond androm isome and on 05. 15           Appland Irans, ong ond androm isome and on 05. 15           Appland Irans, ong ond androm isome and on 05. 15           Appland Irans, ong ond androm isome and on 05. 15           Appland Irans, ong ond androm isome and on 05. 15           Appland Irans, ong ond androm isome and on 05. 15           Appland Irans, ong ond androm isome and on 05. 15           Appland Irans, ong ond androm isome and on 05. 15           Appland Irans, ong ond androm isome and on 05. 15           Appland Irans, ong ond androm isome and on 05. 15           Appland Irans, ong ond androm isome and on 05. 15           Appland Irans, ong ond androm isome and on 05. 15           Appland Irans, ong ond androm isome and on 05. 15           Appland Irans, ong ond androm 05. 15           Appland Irans, ong ond 05. 15     <
Internations, S. M. et al. 1991         Glar, T. et al. 1997         Monowell, P. J. et al. 1977         House, S. F. et al. 2013         House, S. F. et al. 2013         House, S. J. et al. 2017         House, S. J. et al. 2017         Decker, F. et al. 2018         House, S. J. et al. 2017         Decker, F. et al. 2018         Heurestowick, D. et al. 2016         House, S. et al. 2017         Decker, F. et al. 2018         Heurestowick, D. et al. 2015         House, S. et al. 2013         House, S. et al. 2012         House, S. et al. 2012         House, S. et al. 2017         House, S. et al. 2017	Upputs county, Swethen           International BD Starky group           Bachampton, UK           Onion           Bachampton, UK           Onion           Bachampton, UK           Otion           Bachampton, UK           Otion           Bachampton, UK										
  | 284-1564           284-1564           Aut: Reported  | Insafteding for 12 mor, compared with 0.6 mos.  
  | 138<br>138<br>134<br>134<br>134<br>134<br>134<br>134<br>134<br>134   | G0           VC           VC           December VC           Hone regressive VC           HO  
  | Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray<br>Maray | GA<br>GA<br>GA<br>GA<br>GA<br>GA<br>GA<br>GA<br>GA<br>GA<br>GA<br>GA<br>GA<br>G  
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	Authors and Year	Study location	Study Time Period	Exposure Description	Total sample size (n)	CD/UC/IBD	Period of	Effect estimate value	Confidence interval (specify of different from 95% CI)	Comments
Cohort Studies					1479216	70	0-5 yrs	1.15	0.95-1.40	Unalisated estimates recorded
	Aspberg, S. et al. 2006 Baser, P. et al. 2012	Sweden	1987-2000	parity 1 compared with ≥2	1479216 924749		0-5 yrs 0-2 yrs old	1.17 <sup>°</sup> 0.9 <sup>1</sup>	0.99-1.39 0.42-1.93	Unadjusted estimates reported Adjusted for ago, sex, calendar period, birth order, average gross annual income based on total household income, degree of urbanization, birth place of parents, and any parental diagnoses of the specific outcome.
		Denmark	1973-2008 Alberta: 1999-2008, Manitobi	Helmintic Infection (Filled prescription for Mebendazole)	9247491		3-5 years old	1.131	0.7-1.62 21 years (0.58-0.96), 22 years (0.59-0.96), 23 years (0.54-1.01), 24	Advanted for age, see, calendar period, birth order, average gross annual income based on total household income, degree of urbanization, birth place of parents, and any parental diagnoses of the specific outcome.
	Benchimol, E.I. et al. 2017	Canada	Alberta: 1999–2008, Manitobi and Ontario: 1999–2010, and Nova Scotia: 2000–2008		26331	80	0-5 years old	0.75-0.78	(0.59-0.96), 23 years (0.54-1.01), 24 years (0.50-1.00), and 25 years ( Cl 0.51-1.00)	n Adjusted for app, sex and mighborhood income
	Burnett, D. et al. 2020	Canada	1988-2014	Living area (Urban vs. Rural) Administrative cohort Living area (Urban vs. Rural) Clinical cohort	42906		0-5 yrs 0-5 yrs		Not signifcant Not signifcant	N/A N/A
	Elten, M. et al. 2020	Canada	April 1st, 1991 and March 31st 2014	Living area (Urban vs. Rural)	2218789		0-5 yrs Birth	1.1"	Not signifcant 0.91-1.32	NA Adjusted for gunder, place of origin, number of skillings and place of living
	Klement E. et al. 2008	brael	1998-2004	birth order (3 vs 1)	93164 I 35592 I	80	Birth	1.26"	1.02-1.55	Adjusted for gender, place of origin, number of siblings and place of living
				birth order (4 vs 1) birth order (25 vs 1) Urban life	20025 I 979039 0	80	Birth 0-5 yrs	2.35"	1.01-2.05 1.47-3.77 1.0-1.8	Adjusted for gender, place of origin, member of abilings and place of living Adjusted for gender, place of origin, member of abilings and place of living Unadjusted entimeters provid
	Lange, A, et al. 2014	Denmark	1995-2009	First born Living in urban area compared with not urban	979039	20	Infancy Perinatal	1.2 <sup>†</sup> 1.46 <sup>''</sup>	0.8-1.7	Unadjusted estimates reported
	Porsonby, A.L. et al. 2009	Victoria, Australia	1983-1998	Birth order (Later born vs firstborn) Livestock farm compared with city	998828	20	Perinatal	0.96"	0.74-1.25	Adjusted for sax, abornality, interventional birth, urban, married, SSS, maternal age and year of birth Adjusted for sax, abornality, interventional birth, urban, married, SSS, maternal age and year of birth
Case-Control Studies	Timm, S. 2014	Northern Europe	1945-1973	Village compared with city	10864 10864		0-5 yrs 0-5 yrs	0.75	0.31-0.98 0.52-1.10	Adjusted for age, sex, smoking and BMI Adjusted for age, sex, smoking and BMI
Case-Control Studies	Amre. D.K. et al. 2006	Montreal. Canada	1995-2004	Owning a pet during pregnancy Owning a pet between birth - 5 years of age	388 (		Pregnancy	0.9	0.5-1.6	Adjusted for age, gender, family history of BD, maternal smoking and maternal education
	Amre, D.S. et #. 2006	Montreal, Canada	1995-2004	Number of older siblings (0,1,22) Fiped or bottled water, compared with water from	388 ( 388 (	20 20	0-5 yrs 0-5 yrs	1.2"" Not Reported	0.7- 2.2 Not reported	Adjusted for age, gender, family history of IBD, maternal smoking and maternal education N(A
				outside sources Access to hot piped water	407 0		0-5 yrs 0-5 yrs	2.1" 1.18	1.2-4.0 0.71-2.0	Adjusted for age at study encolment, ethnicity and gender Adjusted for age at study encolment, ethnicity and gender
				Suburban or urban community compared with rural/farm/informal settlement s5 persons in household, compared with 26	407		0-5 yrs 0-5 yrs	1.21 <sup>""</sup> 0.68 <sup>""</sup>	0.71-2.1 0.43-1.09	Adjusted for age at study encolment, whinking and gender Adjusted for age at study encolment, whinking and gender
	Basson, A. et al. 2014	Western Cape, South Africa	September 2011 and January	s3 persons sharing bathroom compared with >4 persons >3 bedrooms compared with s2	407 407 407	20	0-5 yrs 0-5 yrs	0.55"	0.31-0.97 0.69-1.11	Projemier on page in zoop versioning en energies en genome Adjusted for age at study enrolment, ethnicity and gender Adjusted for age at study enrolment, ethnicity and gender
			2013	Flush toilet compared with bucket/pit latrine/no facility no pets compared with pets	407 0	20	0-5 yrs 0-5 yrs	1.35" 1.47"		Angioment mengken mangementanisme, seinanary ana ganakan Adjashad for aga se stady eventement, ethnicity and gander Adjashad for aga se stady eventement, ethnicity and gander
				No donkey/horse/cow/sheep on property compared with any present	407	30	0-5 yrs	1.67	0.83-3.45	Adjusted for age at study enrolment, ethnicity and gender
				no helminth infection compared with helminth infection No treatment for heminth infection compared with treatment	407 407		0-5 yrs 0-5 yrs	0.87"	0.53-1.42	Adjusted for age at study enrolment, ethnicity and gender Adjusted for age at study enrolment, ethnicity and gender
	Bernstein, C.N. et al. 2006	Manitoba, Canada	Not Reported	Living with pet cats before age 5	797 0		0-5 yrs	0.66"	0.46-0.96	Adjusted for upp and gender
	Bernstein, C.N. et al. 2019	Canada	1970-2010	Number of household residents before age 5 Rural vs urban	797 0	20	0-5 yrs Perinatal	0.9'	0.83-0.97 0.72-1.15	Accorde for a gain or gender Unadjustel extinutes regorted
	Boneberger, A. et al. 2011	Central South of Chile	June 2009 and February 2010	Rural place of living	226	JC .	Infancy 0-5 yrs	2.2"	Not reported	Adjusted for age (518 years/1018 years), see (make/lemain), and next place of living in the first year of life and motually adjusted for at least one parent with Mapuche descent, High paternal education and pets
	Doyle, J.B. et al. 2017	Northern Ireland	1971-1986	Household Size	67173 278 (	80 10	Neonatal 0-5 yrs	1.38	Not Significant 0.37-5.20	Phylatel to de ( Les Ferningen et les au june), ensue, ensue, en ensue et ren par un et en par un et en mousen paparer to en ensuoi partie ensue en renouter, registrer ne exclusion et est
				No older siblings	274	20	0-5 yrs 0-5 yrs	0.94	0.29-3.05 0.25-3.65	Unalfysted etimates reported Unalfysted etaimates reported
				One older sibling	274	20	0-5 yrs 0-5 yrs	1.25	0.43-3.59 0.48-6.16	Unadjusted estimates reported Unadjusted estimates reported
				Two older siblings Parson-to-room ratio in home	274	JC D	0-5 yrs 0-5 yrs	0.77	0.27-2.25	Ukadjusted etimates reported Ukadjusted etimates reported
	Feerer M A and 2000	11K	Not Roser		274	JC .	0-5 yrs 0-5 yrs	1.23 <sup>°</sup> 0.59 <sup>°</sup>	0.46-3.27 0.28-1.24	Undgistel etimates reported Undgistel etimates reported
	Feeney, M.A. et al. 2002	un.	Not Reported	Urban environment Cat in the home	274	JC D	0-5 yrs 0-5 yrs	0.96' 0.81'	0.41-2.23 0.41-1.63	Undjusted orimites reported Undjusted orimites reported
					274	JC D	0-5 yrs 0-5 yrs	1.27 <sup>'</sup> 0.65 <sup>'</sup>	0.71-2.26 0.34-1.24	Unadjusted estimates reported Unadjusted estimates reported
				Dog in the home	274	JC D	0-5 yrs 0-5 yrs	0.69 <sup>°</sup> 1.76 <sup>°</sup>	0.35-1.34 0.75-4.14	Unadjusted atrimates reported Unadjusted atrimates reported
				Bird in the home	274	JC D	0-5 yrs 0-5 yrs	0.99	0.46-2.09 0.43-1.81	Unaljusted orimites reported Unaljusted orimites reported
				Rodent in the home	274	JC D	0-5 yrs Infancy	0.6	0.25-1.44 0.61-1.13	Undjusted orkimates reported Adjusted for family history of IBD, smoking status, age at recruitment, social class at birth, ethnic identity and sex
				Town dwelling compared with city dwelling	1253 1238	ж	Infancy Infancy	1.11" 0.83"	0.82-1.51 0.6-1.13	Adjusted for fumily history of IBD, unoling status, age at recruitment, social class at birth, ethnic identity and soc Adjusted for fumily history of IBD, unoling status, age at recruitment, social class at birth, ethnic identity and soc
	Gearry, R.B. et al. 2010	Canterbury, New Zealand	June 1, 2003 and May 30, 200	S Country dwelling compared with city dwelling	1253	JC D	Infancy Infancy	1.24 <sup>**</sup> 0.49 <sup>**</sup>		Adjusted for fumily history of IBD, unoling status, age at recruitment, social class at birth, ethnic identity and sex Adjusted for fumily history of IBD, unoling status, age at recruitment, social class at birth, ethnic identity and sex
				Vegetable garden	1253	JC D	Infancy 0-5 yrs	0.66"		Adjusted for funity history of IBD, unoding status, age at recruitment, social class at birth, ethnic identity and sex Unadjusted estimates reported
				Water tap	728	x	0-5 yrs 0-5 yrs	0.9	0.5-1.7	deniqueme examinar reporter Unadjuted estimate reporter Unadjuted estimate reporter
				Hot Water tap	728	JC DI	0-5 yrs	1.3° 3.3°	0.7-2.2	Unadjusted estimates reported
	Gent, A.E. et al. 1994	ик	1988	Separate Bathroom	728	JC DI	0-5 yrs 0-5 yrs	1.3°	13-83	Unadjasted eximulas reported Unadjasted eximulas reported
				Flush toilet	728	JC .	0-5 yrs 0-5 yrs	1.1 1.4' 2.6'	0.5-2.6	Unalgisted of crimites reported Unalgisted of crimites reported Unalgisted of crimites reported
				Mains drainage Tap Water	728 0	JC	0-5 yrs 0-5 yrs	1.2'	0.9-7.3 0.7-2.1 0.53-1.66	Unalgisted ofinities reported Unalgisted ofinities reported Unalgisted of initiaties reported
	Hampe, J. et al. 2003	Germany	July 1996 to January 1998	Warm Tap Water Water Toilet	4615	80	0-5 yrs 0-5 yrs	1.25'	0.53-1.66 0.78-2.00 0.83-2.39	Unadjude ekstmaas sepontel Okadjustel ekstmaas sepontel
				birth rank 23 compared with <3 Pet Ownership	4615	80	0-5 yrs Birth	0.68	0.83-2.39 0.51-0.91 0.92-1.73	Unadjusted estimates reported
	Han, D.Y. et al. 2010	New Zealand	Not Reported	Regularly feed pets Had a sandpit in the garden	851 ( 851 ( 851 (	20	<6 yrs <6 yrs	0.82	0.92-1.73 0.55-1.22 0.8-1.45	Unalgiosted estimates reported Unalgiosted estimates reported
	Hansen, T.S. et al. 2011	Denmark		Running Water	534 ( 534 (	80	0-5 yrs Infancy Infancy	0.5	0.8-1.45 0.15-1.66 0.05-5.51	Unadjuted activities reported Adjusted for sensiting status, appendectums, tamilactums, scage of our contraceptions, and consumption of fibre, suppr, ceffex, and eggs and mutually adjusted with variables in analysis Adjusted for sensiting status, sependectums, terralitectums, super or and contraceptives, and communificion of fibre, suppr, ceffex, and eggs and mutually adjusted with variables in analysis
			2003-2004		534 0	JC .	infancy	0.5"	0.13-2.0 0.41-0.41	Application of a making spannerschaft, connections, using of our contraceptives, and consumption or new, using, contra, interger and mousing spannerschaft, contraction of mousing and an application of mousing spannerschaft, contraction of mousing spannerschaft, and application of mousing spannerschaft, using and mousing spannerschaft, using and mousing spannerschaft, using and mousing spannerschaft, using and mousing spannerschaft, contraction of the stage of an application of the stage of mousing spannerschaft, and application of the stage of mousing spannerschaft, using spannerschaft, using and mousing spannerschaft, using and mousing spannerschaft and spannerschaft
				Rural dweller in Middle Eastern Migrants	795 0	JC DI	Infancy Infancy 0-5 yrs	0.09"	0.04-0.24	Adjusted for age, sex, cigarrete smoking and family history of IBD
	1				795 0 795 0 795 0	JC DI	0-5 yrs 0-5 yrs Infancy	0.12"	0.18-0.68 0.05-0.30 0.13-0.64	Alpitato for gas, san, gipernes maning and family history of 180 Alpitato for gas, san, gipernes maning and family history of 180 Alpitato for gas, san, gipernes maning and family history of 180
				Pet ownership in Middle Eastern Migrants	795	JC	Infancy	0.28	0.02-0.93	Adjusted for age, sex, cigarrete smoking and family history of IBD
					795 ( 795 ( 795 (	JC DI	0-5 yrs 0-5 yrs Infancy	0.24	0.13-0.57	Adjatato for gas, sax, digaretas ending and lemih Yolany of BD Adjatato for gas, sax, digaretas ending and lemih Yolany of BD Adjatato for gas, sax, generas ending and lemih Yolany of BD
	1			Farm animal ownership in Middle Eastern Migrants	795 0 795 0 795 0	JC	Infancy	0.12	0.04-0.44	Adjusted for age, sex, cigarrete smoking and family history of IBD
	Ko, Y.; et al. 2015	Australia	Not Reported		795	ж	0-5 yrs 0-5 yrs Infancy	0.1	0.04-0.40	Aljunte for age, se, cigentes sensitio and fumity history of BD Aljunte for age, se, cigentes analogi and fumity history of BD Aljunte for age, se cigentes analogi and fumity history of BD
				Sharing bedroom in Middle Eastern Migrants	795	JC D	Infancy Infancy	0.47"	0.21-1.04 0.28-1.3	Adjusted for age, see, cigarreta unoking and family history of BD Adjusted for age, see, cigarreta unoking and family history of BD
	1				795	JC D	0-5 yrs 0-5 yrs	0.4"	0.16-0.80 0.19-0.97 0.04-0.37	Adjusted for age, sex, cigarrete emologi and family history of IBD Adjusted for age, sex, cigarrete emologi and family history of IBD Adjusted for sex new citationation and IBP.
				Pet feeding in Middle Eastern Migrants	795	JC D	Infancy Infancy	0.12"	0.05-0.46	Adjusted for age, see, cigarreta unoking and family history of BD Adjusted for age, see, cigarreta unoking and family history of BD
					795 0	JC D	0-5 yrs 0-5 yrs	0.1"	0.03-0.30 0.05-0.35	Adjusted for age, see, cigarrete smoking and tumity history of BD Adjusted for age, see, cigarrete smoking and tumity history of BD Adjusted for undersone see and the adjust and tumity history of BD
				Access to Hot Water in Middle Eastern Migrants	795 0	JC D	Infancy Infancy	1.71" 1.85"	0.68-4.30 0.78-4.36	Adjusted for ago, sax, Gjarrete smoking and family history of IBD Adjusted for ago, sax, Gjarrete smoking and family history of IBD
				Refrigerator	795	ж	0-5 yrs 0-5 yrs	1.56 <sup>''</sup> 1.69 <sup>''</sup>		Adjusted for age, sex, cigarrete annoting and family history of 180 Adjusted for age, sex, cigarrete annoting and family history of 180 un
	Levy, L.C. et al. 2012 Malekzadeh, F. et al. 2009	South India	Not Reported	Refrigerator receiving deworming treatment Home refrigerator and freezer	634 I 634 I	8D	≪Syrs ≪Syrs		Not reported	NA NA 
	warenzacieth, F. et al. 2009	ee-ban, mah	1998 to 2004	Pets	405 0	20	0-5 yrs Infancy	2.08"		Adjusted for sextsbacco use and current age Adjusted for study region, age in quarties, gender, duration of exclusive breastleeding, parental history of IBD, number of edder siblings, highest parental education and maternal sensing during pregnancy
	Radon, K. et al. 2007	Germany		Farm animals	1791 1931 (	20	Infancy Infancy	0.9"	0.6-1.2 0.3-0.9	Adjusted for study region, age in quarties, gender, duration of exclusive breastfeeding, parental history of IBD, number of older siblings, highest parental education and maternal smoking during prepriancy Adjusted for study region, age in quarties, gender, duration of acclusive breastfeeding, parental history of IBD, number of older siblings, highest parental education and maternal smoking during prepriancy
			March 2006 and August 2006	Cpen Well	1791 304 (	00	Infancy 0-5 yrs	0.4"		Adjusted for study region, age in quarties, gender, duration of exclusive breastfeeding, parental history of 180, number of older siblings, highest parental education and maternal smoking during pregnancy Adjusting variables not reported
		South India		Applying Cow dung to Floor	330 304 (	00	0-5 yrs 0-5 yrs	0.55	0.30-0.99	Adjusting variables not reported Adjusting variables not reported
	Ramakrishna, B.S. et al. 2012		Not Reported	Personal Towel	330 304 (	0	0-5 yrs 0-5 yrs	3.13"	Not reported 1.48-6.60	Adjusting variables not reported Adjusting variables not reported
				Well Water	330 ( 832 (	20	0-5 yrs 0-5 yrs	0.271"	Not reported 0.087-0.084	Adjusting variables not reported Adjusting variables not reported
		US cohort		Mouth Wash	626 I 626 I	JC	0-5 yrs 0-5 yrs			Adjusting variables not reported Adjusting variables not reported
	Sahu, M.K. et al. 2010	South India	Not Reported	Urban (compared with Rural) residence	415 (	ic	Neonatal Neonatal		Not reported Not reported	N/A N/A
			reos neported	(somparett with nural) residence	415	ю.	0-3 years 0-3 years	L	Not reported	N/A N/A
	Samuelsson, S.M. et al. 1991	Uppsala county, Sweden	1945-1964	Birth order (did not specify further)	334 334	JC Extensive UC	Perinatal Perinatal	1.01' 1'	0.92-1.12 0.88-1.11	Unadjustad estimatas reported Dinadjustad estimatas reported
	Strisciuglio, C. et al. 201	Italy	2000-2014	Birth order (did not specify further) Increased number of toilets	334 1 663 0 663 1	10	Perinatal Neonatal Neonatal	1.06' 1.73' 2.17'	0.89-1.25 Not reported Not reported	Unadjusted extinsas regoried Unadjusted extinsas regoried
	Thompson, N.P. et al. 1995	England and Wales	2000-2014	Urban/rural maternal residence	663 2966 1578	20	Neonatal	1.01 1.17	0.65-1.55 0.91-1.50	Unsighted antimates reported Dadgisted extinuities reported Da
	Thompson, N.P. et al. 2000	ик	1950-1968 1946-1958	First born	287 287	20 JC	Neonatal Birth Birth	0.92	0.34-2.47 0.57-3.17	Unadjusted estimates reported Unadjusted estimates reported
				Living area (rural vs large village)	1671 ( 1669 (	JC .	0-5 yrs 0-5 yrs	0.61	0.44-0.84 0.80-1.45	Unadjusted estimates reported Adjusted for age, gender and smoking status at diagnosis
	van der Sloot. K. et al. 2020	Netherlands	Not Reported	Living area (rural vs urban)	1671 ( 1669 (	JC D	0-5 yrs 0-5 yrs	1.67 <sup>°</sup> 1.2 <sup>°</sup>	1.19-2.36 0.98-2.05	Adjusted for age, gender and smoking status at diagnosis Adjusted for age, gender and smoking status at diagnosis
				Household Pets (< 1yr)	1671 0 1669 0	JC D	Infancy Infancy	0.3"	0.22-0.40 0.24-0.44	Adjusted for age, gender and smoking status at diagnosis Adjusted for age, gender and smoking status at diagnosis
L				Household Pets (1-5 yrs)	1671 0 1669 0		1-5 yrs 1-5 yrs	0.37		Adjusted for age, gunder and smoking status at diagnosis Adjusted for age, gunder and smoking status at diagnosis
-				-		-			-	

Reference #	Authors	Study location	Study Time Period	Exposure Description	Total sample size (n)	CD/UC/IBD	Period of exposure	Effect estimate value	Confidence interval (specify of different from 95% Cl)	Comments
Cohort Studies		[			1479216	CD	0-5 vrs	1.09	0.66-1.81	Unadjusted estimates reported
				Maternal education (Comprehensive school compared with continuation school)	1479216	UC	0-5 yrs	0.97	0.69-1.37	enterpaire commerce repaired
	Aspberg, S. et al. 2006	Sweden	1987-2000		1479216	CD	0-5 yrs	1.24	0.84-1.84	Unadjusted estimates reported
				Maternal education (University or equivalent compared with continuation school)	1479216	UC	0-5 yrs	0.99	0.74-1.34	Unadjusted estimates reported
				Marrital status (not married vs married mother)	998877		Perinatal	1.73 <sup>t†</sup>	1.10-2.71	Adjusted for sex, abormality, interventional birth, urban, married, SES, maternal age and year of birth
	Ponsonby, A.L. et al. 2009	Australia	1983-1998	SES index mid compared with low SES index high compared with low	252084		Perinatal	1.12 <sup>t†</sup>	0.78-1.61	Adjusted for sex, abornality, interventional birth, urban, married, SES, maternal age and year of birth
				SES index righ compared with low SES index very high compared with low	248158 248492		Perinatal	1.06"	0.73-1.53	Adjusted for sex, abormality, interventional birth, urban, married, SES, maternal age and year of birth Adjusted for sex, abormality, interventional birth, urban, married, SES, maternal age and year of birth
Case-Control Studies					240452	CD	Felilididi	1.44	1.04*2.07	Pepere la se, ucamany, ma tenena ana ini ucan, manan, oco, maana uga ang ten o an
				Daycare birth-6 mos	388	CD	Infancy	4.5	1.4-13.7	Adjusted for age, gender, family history of IBD, maternal smoking and social class (via maternal education)
				Daycare 7-12 mos	388	CD	Infancy	1.5	0.8-2.9	Adjusted for age, gender, family history of IBD, maternal smoking and social class (via maternal education)
	Amre, D.K. et al. 2006	Montreal, Canada	1995-2004	Daycare1-3 years	388		0-5 yrs	1.1	0.5-1.6	Adjusted for age, gender, family history of IBD, maternal smoking and social class (via maternal education)
				Matemal education (none-grade 4, secondary, college/technical, university)	388		0-5 yrs		eported	NA Na
				Paternal education (none-grade 4, secondary, college/technical, university) Family income	388 388		0-5 yrs Birth		eported eported	N/A
	Basson, A. et al. 2014	South Africa	September 2011 to January 2013		407		Infancy	0.61"		Adjusted for age at study enrolment, gender and ethnicity
		a .		Socioeconomic status Q4	12159		Perinatal	1.37	1.06-1.77	Unadjusted estimates reported
	Bernstein, C.N. et al. 2019	Canada	1970-2010	Socioeconomic status Q5	12159	IBD	Perinatal	1.35	1.01-1.79	Unadjusted estimates reported
	Boneberger, A. et al. 2011	Central South of Chile	June 2009 to February 2010	High paternal education	226	UC	0-5 yrs	2.1"	1.0-4.5	Adjusted for age (<18 years/N18 years), sex (male/female), and rural place of living in the first year of life and mutually adjusted for Mapuche descent, high paternal education, pets, at least one older sibling
				Day care	226		Infancy		eported	Adjusted for age (s18 years/N18 years), sex (male/female), and rural place of living in the first year of life and mutually adjusted for Mapuche descent, high paternal education, pets, at least one older sibling
1	Canova, C. et al. 2020	Italy	1989-2012	Maternal education (Primary vs High school)	1 586		Perinatal	1.23" 0.96"	0.87-1.76	Adjusted for sex, year of birth, season of birth, having older sibilins, number of births, birth weight, gestational age; Apgar score at 1 minute, maternal age and mother's education Adjusted for sex, year of birth, season of birth, having older sibilins, number of births, birth weight, gestational age; Apgar score at 1 minute, maternal age and mother's education
1	Doyle, J.B. et al. 2017	Northern Ireland	1971-1986	Maternal education (Primary vs University) Socioeconomic Status	946 67173		Perinatal Neonatal		0.53-1.76 phificant	nayonon na von, ynan or nann, onason or onen, nammig ower sommin, nammer or onen, omen weigen, gesialtorial age, Apgar score at i minute, materna age and mother's equidation
1				Matemal education	801		0-5 yrs		eported	Adjustment not reported/not applicable. Higher education was associated with lower odds of CD
1	Eslahpazir, J. et al. 2017	Montreal, Canada	1980-2010	Paternal education	801		0-5 yrs		eported	Adjustment not reported/not applicable. Higher education was associated with lower odds of CD
1					278		0-5 yrs	0.78	0.18-3.40	Unadjusted estimates reported
1				Social class 1 or 2	274		0-5 yrs	2.49	0.65-9.54	Unadjusted estimates reported
1					278		0-5 yrs	0.49	0.14-1.78	Unadjusted estimates reported
				Social class 3 (M) or (N)	274		0-5 yrs	1.71	0.46-6.36	Unadjusted estimates reported
				Control along A and F	278 274		0-5 yrs	0.5	0.14-1.83	Unadjusted estimates reported Unadjusted estimates reported
				Social class 4 or 5	274		0-5 yrs 0-5 yrs	0.63	0.31-4.56	onadjuste esimales reported
				Attended nursery	270		0-5 yrs	0.5	0.22-1.16	Unadjusted estimates reported
					278		0-5 yrs	1.92	0.87-4.22	Unadjusted estimates reported
	Feeney, M.A et al. 2002	LIK.	Not Reported	Seldom use of swimming pool	274	uc	0-5 yrs	1.48	0.75-2.91	Unadjusted estimates reported
	r cency, morer al. 2002	on and a second s	nor reported		278		0-5 yrs	2.9	1.21-6.91	Unadjusted estimates reported
				Frequent use of swimming pool	274		0-5 yrs	1.19	0.55-2.58	Unadjusted estimates reported
					278 274		0-5 yrs	1.62 <sup>°</sup>	0.57-4.58	Unadjusted estimates reported Unadjusted estimates reported
				No family car in 0-5 yrs	274		0-5 yrs 0-5 yrs	0.44	0.15-1.31	Unadjuste desimates reported
				One family car in 0-5 vrs	270		0-5 yrs	0.53	0.25-1.14	Unadjusted estimates reported
					278	CD	0-5 yrs	1.39	0.64-3.00	Unadjusted estimates reported
				No house moves	274	UC	0-5 yrs	0.8	0.34-1.87	Unadjusted estimates reported
					278		0-5 yrs	1.78	0.79-4.01	Unadjusted estimates reported
				One house move	274		0-5 yrs	0.92	0.45-1.87	Unadjusted estimates reported
					1238 1253		Birth Birth	0.55"	0.41-0.75	Adjusted for family history of IBD, smoking status, age at recruitment, social class at birth, ethnic identity and sex Adjusted for family history of IBD, smoking status, age at recruitment, social class at birth, ethnic identity and sex
				Social class at birth- class 3-4 (ref class 1-2)	1233		Birth	0.03	0.46-0.66	Adjusted for family history of IBD, smoking status, age at recruitment, social class at birth, ethnic identity and sex
				Social class at birth- class 5-6 (ref class 1-2)	1253		Birth	0.59"	0.4-0.88	Adjusted for family history of IBD, smoking status, age at recruitment, social class at birth, ethnic identity and sex
	Gearry, R.B. et al. 2010	Canterbury, New Zealand	June 1, 2003 to May 30, 2005		1238	CD	Infancy	0.82"	0.62-1.08	Adjusted for family history of IBD, smoking status, age at recruitment, social class at birth, ethnic identity and sex
	Gearry, R.B. et al. 2010	Canterbury, New Zealand	June 1, 2003 to May 30, 2005	Home-heating- wood (presence vs absence)	1253	uc	Infancy	0.83"	0.63-1.09	Adjusted for family history of IBD, smoking status, age at recruitment, social class at birth, ethnic identity and sex
					1238		Infancy	1.12"	0.86-1.45	Adjusted for family history of IBD, smoking status, age at recruitment, social class at birth, ethnic identity and sex
1				Home-heating- coal (presence vs absence)	1253		Infancy	1.24"	0.96-1.61	Adjusted for family history of IBD, smoking status, age at recruitment, social class at birth, ethnic identity and sex
1				Hama baatian, alaattisitu (araaanaa uu chooona)	1238		Infancy	0.84"	0.65-1.08	Adjusted for family history of IBD, smoking status, age at recruitment, social class at birth, ethnic identity and sex Adjusted for family history of IBD, smoking status, age at recruitment, social class at birth, ethnic identity and sex
1				Home-heating- electricity (presence vs absence)	1253 1497		Infancy 0-5 yrs	0.72 Not n		nayanan an ianay inanay unina, aninang atalaa, age at terdininten, social kaasa at unin, enintrineninty atta sex NA
1				primary school in mothers	1497		0-5 yrs 0-5 yrs	lower odds	not reported	NA
1	Gilat, T. et al. 1987	International IBD Study group	Not Reported	primary school parents	1497		0-5 yrs	- 0.71	0.31-1.62	Unadjusted estimates reported. Negative estimate as reported in the study.
1				university/ college education of parents	1497		0-5 yrs	- 0.67	0.45-1.00	Unadjusted estimates reported. Negative estimate as reported in the study.
1	Hampe, J. et al. 2003	Germany	July 1996 to January 1998	Central heating	4615		0-5 yrs	1.31	0.8-2.12	Unadjusted estimates reported
1				Takeaway consumption	851		0-5 yrs	1.66	1.15-2.38	Unadjusted estimates reported Unadjusted estimates reported
1	Han, D.Y. et al. 2010	New Zealand	Not Reported	>50% home carpeted Lived in a house with a swimming pool for greater than one year	851 851		0-5 yrs	1.51 <sup>°</sup>	1-2.26	Unadjusted estimates reported Unadiusted estimates reported
1				Lived in a house with a swimming pool for greater than one year Preschool	851		0-5 yrs 0-5 yrs	1.29	0.35-1.35	Unadjusted estimates reported Unadjusted estimates reported
1				Father's education	495	00	Prenatal		eported	NA .
1	Holmes, E.A. et al. 2019	Australia	2010-2013	Mother's education	495		Prenatal			N/A. IBD with higher "Trade cert or other", lower "University qualification" or "Secondary school or less"
					795		Infancy	1.97		Adjusted for age, sex, cigarrele smoking and family history of IBD
	Ko, Y. et al. 2015	Australia	Not Reported	Takeaway consumption in middle eastern migrants	795		Infancy	1.22		Adjusted for age, sex, cigarrete smoking and family history of IBD
				-	795		0-5 yrs	2.65		Adjusted for age, sex, cigarrete smoking and family history of IBD
		ł			795		0-5 yrs	3.96		Adjusted for age, sex, cigarete smoking and family history of IBD Unadjusted estimates recorted
	Lopez-Serrano, P. et al. 2010	Spain	2004	Parental occupation (higher skill level)	783 783		0-5 yrs 0-5 yrs	1.83	1.14-2.95	Unagusted estimates reported Unadjusted estimates reported
	Benelikken B.B		Not Described	A Business A Business A	832		0-5 yrs	0.083		Adjusting variables not reported
	Ramakrishna, B.S. et al. 2012	USA and India	Not Reported	0-5 yrs daycare	626		0-5 yrs	-	eported	NA
					334		Birth	0.87	0.41-1.86	Unadjusted estimates reported
1			1945-1964				Birth	0.58	0.21-1.57	Unadjusted estimates reported
	Samuelsson, S.M. et al. 1991	Uppsala County, Sweden	1040-1004	Paternal SES (middle vs high)	334		Birth	2.8	0.56-13.88	Unadjusted estimates reported
1					334		Birth	0.66	0.30-1.42	Unadjusted estimates reported Unadjusted estimates reported
1				Paternal SES (low vs high)		Extensive UC Non-progressive UC	Birth Birth	6.13	0.09-0.75	Unadjusted estimates reported Unadjusted estimates reported
1	Strisciuglio, C. et al. 2017	Campania, Southern Italy	2000-2014	Maternal degree	305		0-5 yrs	5.5	2.5-11.6	Adjusted for breast feeding, father's employment, gluten introduction, no. Of siblings, autoimmune diseases, pets and bed sharing
·	•		•		250					

Study type	Study	Study Location	Study Time Period	Exposure Description	Total sample size (n)	Outcome	Period of Exposure	Effect estimate value	Confidence interval (specify if different from 95% CI)	Comment
			1977-1995		8700000		Birth	1.07**	0.8-1.43	
			1996-2003 2004-2009	Second-Generation Immigrants	8700000 8700000	IBD	Birth Birth	0.69 <sup>##</sup> 0.78‡‡	0.56-0.86 0.67-0.92	
			2010-2014 2015-2018		8700000 8700000	100	Birth Birth	0.96 <sup>11</sup> 1.13 <sup>11</sup>	0.85-1.08 1.01-1.26	-
				Second-Generation Female Immigrants Second-Generation Female Immigrants from country of Iow IBD risk	8700000 8700000		Birth Birth	0.89 <sup>##</sup> 0.84 <sup>##</sup>	0.81-0.98 0.59-1.19	Adjusted for sex, age (0–9, 10–14, 15–74 in 1-year intervals and ≥75 years) and calendar time (1-year
	Agrawal, M. et al. 2020	Denmark		Second-Generation Female Immigrants from country of moderate IBD risk	8700000	IBD	Birth	0.96**	0.87-1.00	intervals).
				Second-Generation Female Immigrants from country of high IBD risk Second-Generation Male Immigrants	8700000 8700000		Birth Birth	0.69 <sup>88</sup> 1.06 <sup>88</sup>	0.49-0.96 0.97-1.17	-
				Second-Generation Male Immigrants from country of low IBD risk Second-Generation Male Immigrants from country of moderate IBD risk	8700000 8700000		Birth Birth	1.06 <sup>11</sup> 1.02 <sup>11</sup>	0.76-1.48	
				Second-Generation Male Immigrants from country of Indicate his fish	8700000	IBD	Birth	0.7**	0.49-0.99	
			1977-2018 1977-2018	First Generation Immigrants	8700000		0-5 yrs 0-5 yrs	1.07## 0.95##	0.9-1.27 0.72-1.26	Adjusted for sex, age (0–9, 10–14, 15–74 in 1-year intervals and ≥75 years), calendar time (1-year intervals
			1977-2018	Maternal country of birth- Israel	8700000 1144213		0-5 yrs Birth	1.14## reference	0.92-1.42	and continent of birth
					1144213 1144213		Birth Birth	reference 1.2 <sup>99</sup>	1.09-1.32	
				Maternal region of birth- West	1144213 1144213	UC	Birth Birth	0.69 <sup>89</sup> 0.71 <sup>99</sup>	0.58-0.82	1
				Maternal country of birth- Former USSR	1144213		Birth	0.5555	0.43-0.67	
				Maternal country of birth- Asia	1144213 1144213		Birth Birth	0.61 <sup>55</sup> 0.71 <sup>55</sup>	0.5-0.73 0.60-0.82	-
				Maternal country of birth- North Africa	1144213 1144213		Birth Birth	0.75 <sup>55</sup> 0.47 <sup>55</sup>	0.66-0.85	
				Maternal country of birth- Ethiopia	1144213	CD	Birth	0.5255	0.43-0.62	Adjusting variables include age, gender and diagnosis. Other variables that were included by forward selection
	Ghersin, I. et al. 2019	Israel	2002-2016	Paternal country of birth- Israel	1144213 1144213		Birth Birth	0.49 <sup>89</sup> reference	0.33-0.67	country of origin (Israel, western countries, former US Asia, Africa, Ethiopia), num- ber of children in the
					1144213 1144213	UC	Birth Birth	reference 1.15 <sup>55</sup>	1.002-1.33	household (0-2, ≥3), and socioeconomic status (high, medium, low)
				Paternal region of birth- West	1144213	UC	Birth	0.77%	0.62-0.95	1
				Paternal country of birth- Former USSR	1144213 1144213	UC	Birth Birth	0.65 <sup>59</sup> 0.6 <sup>59</sup>	0.54-0.77 0.47-0.77	1
				Paternal country of birth- Asia	1144213 1144213		Birth Birth	0.59 <sup>55</sup> 0.66 <sup>55</sup>	0.49-0.71 0.52-0.84	
				Paternal country of birth- North Africa	1144213	CD	Birth	0.91 <sup>55</sup>	0.78-1.04	1
				Paternal country of birth- Ethiopia	1144213 1144213	UC CD	Birth Birth	0.67 <sup>°</sup> 0.41 <sup>55</sup>	0.52-0.85 0.27-0.63	
ŀ					1144213 2144660		Birth Birth	0.22 <sup>55</sup> 0.63 <sup>8</sup>	0.10-0.48 0.53-0.75	
				All second-generation immigrants compared with children of nonimmigrants	2144660	CD	Birth	0.49 <sup>8</sup>	0.38-0.63	
					2144660 2144660		Birth Birth	0.78 <sup>8</sup> 0.11 <sup>8</sup>	0.60-1.01 0.05-0.25	
				Second-generation East Asia and Pacific compared with with children of nonimmigrants	2144660 2144660		Birth Birth	0.13 <sup>8</sup> 0.1 <sup>8</sup>	0.05-0.34 0.03-0.41	-
				Second-generation Eastern Europe and Central Asia compared with children of	2144660 2144660		Birth Birth	0.6 <sup>#</sup>	0.36-0.99 0.14-0.82	1
				nonimmigrants	2144660	UC	Birth	0.66*	0.30-1.49	
				Second-generation Latin America and Caribbean compared with children of	2144660 2144660		Birth Birth	0.66 <sup>8</sup> 0.48 <sup>8</sup>	0.45-0.98 0.27-0.88	-
	Benchimol, E.I. et al. 2015	Canada	1994-2009	nonimmigrants	2144660 2144660	UC	Birth Birth	0.71 <sup>8</sup> 0.94 <sup>8</sup>	0.38-1.33 0.57-1.53	Adjusted for age and sex
	1015			Second-generation Middle East and North Africa compared with children of nonimmigrants	2144660		Birth	0.61*	0.27-1.35	1
				-	2144660 2144660		Birth Birth	1.63 <sup>8</sup> 0.83 <sup>8</sup>	0.87-3.05 0.63-1.09	-
				Second-generation South Asia compared with with children of nonimmigrants	2144660 2144660		Birth Birth	0.57 <sup>8</sup> 1.11 <sup>8</sup>	0.37-0.89 0.74-1.68	-
					2144660	IBD	Birth	0.63	0.37-1.09	1
				Second-generation Sub-Sahara Africa compared with children of nonimmigrants	2144660 2144660	UC	Birth Birth	0.59 <sup>8</sup> 0.68 <sup>8</sup>	0.28-1.24 0.28-1.64	
				Second-generation Western Europe and North America compared with children of	2144660 2144660		Birth Birth	1.15 <sup>8</sup> 1.15 <sup>8</sup>	0.77-1.72	-
	Montgomery, S.M. et			nonimmigrants Second-generation Indian/Pakistani/Bangladeshi	2144660 8432		Birth Birth	1.2 <sup>*</sup> 7.02 <sup>**</sup>	0.62-2.32	1
	al. 1999	United Kingdom	April 5-11, 1970	Second-generation mulan/Fanstaniyaangladesin Second-generation West Indian/Guyanese	8432		Birth	3.47**	0.47-25.87	Adjusted for sex and household crowding
				All second-generation immigrants		CD	Birth Birth	0.98"	0.94-1.02	4
				Second-generation from Denmark		CD	Birth	1.17	1.02-1.35	1
				Second-generation from Finland		UC CD	Birth Birth	1.09 <sup>#</sup> 0.83 <sup>#</sup>	0.95-1.24 0.77-0.90	
				-		UC CD	Birth Birth	1.07"	1.00-1.14 0.99-1.29	-
				Second-generation from Norway		UC	Birth	0.93*	0.81-1.06	1
				Second-generation from Greece		CD UC	Birth Birth	0.99 <sup>#</sup> 0.56 <sup>#</sup>	0.67-1.42 0.34-0.88	1
				Second-generation from Italy		CD UC	Birth Birth	1.30 <sup>°</sup> 0.81 <sup>°</sup>	0.87-1.85	1
				Second-generation from Spain		CD	Birth Birth	0.85"	0.45-1.46 0.33-1.18	}
				Second-generation from Great Britain and Ireland		CD	Birth	1.00*	0.67-1.44	1
						UC CD	Birth Birth	0.66 <sup>#</sup> 1.12 <sup>#</sup>	0.41-1.00 0.96-1.30	1
				Second-generation from Germany	-	UC CD	Birth Birth	0.99" 1.20"	0.85-1.15 0.81-1.72	}
	Li, X. et al. 2011	Sweden	1986-2007	Second-generation from Austria		UC	Birth	1.14*	0.79-1.59	Adjusted for age (in 5- year groups), gender, time per
				Second-generation from Yugoslavia		CD UC	Birth Birth	1.19" 0.60"	0.97-1.44 0.46-0.76	socio-economic status, and geographical region-spec
				Second-generation from Romania		CD UC	Birth Birth	1.39 <sup>#</sup> 0.65 <sup>#</sup>	0.76-2.34 0.26-1.35	4
				Second-generation from Estonia	-	CD	Birth	0.85"	0.62-1.13	1
				- Second-generation from Poland		UC CD	Birth Birth	1.09" 1.02"	0.85-1.38 0.77-1.32	1
						UC CD	Birth Birth	0.96 <sup>#</sup> 1.26 <sup>#</sup>	0.74-1.24 0.92-1.69	4
				Second-generation from Hungary		UC	Birth	0.87	0.61-1.20	1
				Second-generation from Chile		CD UC	Birth Birth	0.49 <sup>e</sup> 0.91 <sup>e</sup>	0.28-0.80 0.62-1.31	1
				- Second-generation from Turkey		CD UC	Birth Birth	0.89" 0.86"	0.68-1.15 0.65-1.12	4
				Second-generation from Lebanon		CD	Birth	1.20"	0.80-1.73	1
				- Second-generation from Iran		UC CD	Birth Birth	1.16"	0.60-1.64 0.87-150	1
						UC CD	Birth Birth	1.55 <sup>#</sup> 1.85 <sup>#</sup>	1.14-2.06 1.28-2.59	4
				Second-generation from Iraq		UC	Birth	1.19	0.72-1.83	1
-Control Studies	Bernstein, C.N. et al.	Manitoba, Canada	Not Reported	First generation Canadian (born in Canada), compared with controls	797	CD	Birth	0.33	0.17-0.62	Adjusted for age and gender
	2006 van der Sloot, K. et al.			First generation Canadian (born in Canada), compared with UC	797	CD	Birth 0-5 yrs	0.5 <sup>**</sup> 1.2 <sup>**</sup>	0.31-0.83 0.38-3.78	Adjusted for gender, age, and smoking status at diagn
	2020	Netherlands	Not Reported	Non-Western Migration (2nd generation)	1669	UC	0-5 yrs	1.2	0.46-4.38	[never/former/current]

Study tupe	Study	Study Location	Study Time Period	Exposure Description	Total sample size (n)	Outcome	Period of exposure	Effect estimate value	Confidence interval (specify if different from 95% CI)	Comments
Cohort Studies							-	•	-	
	Lange, A. et al. 2014	Denmark	1995-2009	Antibiotics or infections requiring hospitalization	979039	CD	Infancy	1.4††	1-1.8	Adjusted for family history of CD, mode of delivery, birth order, year of birth, gestational age, rural vs urban residence, maternal smoking, and NSAID use in infancy
Case-Control Studies										
	Amre, D.K. et al. 2006	Montreal, Canada	1995-2004	Physician-diagnosed childhood infections	388	CD	0-5 yrs	0.9**	0.6, 1.5	Adjusted for age, gender, family history of IBD, maternal smoking, and maternal education
	Axelrad J.E. et al. 2019	Sweden	2002-2014	Gastroenteritis	480721	IBD	0-5 yrs	1.09**	1.01–1.16	Adjusted for sex, age, birth year, place of residence, and previous gastrointestinal surgery, autoimmune disease, and family history of IBD
	Bernstein, C.N. et al. 2019	Manitoba, Canada	1970-2010	Infections	12159	IBD	Infancy	1.39*	1.09-1.79	Unadjusted estimates reported
	Ekbom, A. et al. 1990	Sweden	1924-1957	Postnatal infection	771	IBD	Perinatal	5.5¶	2.6-11.8	Unadjusted estimates reported
	Hildebrand, H. et al. 2008	Sweden	1973-1997	Otitis media	7648	CD	0-5 yrs	1.61**	0.89-2.92	Adjusted for maternal age
	Thidebrand, H. et al. 2008	Sweden	1973-1997	Pneumonia	7648	CD	0-5 yrs	3.56**	1.79-7.08	
					2671	IBD	0-5 yrs	2.8**	1.5-5.23	
	Shaw, S.Y. et al. 2013	Canada	1989-2008	Otitis media	2671	CD	0-5 yrs	2.69**	1.23-5.9	Adjusted for cumulative number of non–gastrointestinal-related physician v
					2671	UC	0-5 yrs	3.02**	1.07-8.5	
	Springmann, V. et al. 2014	Quebec Canada	1988-2005	Infection	2030	CD	0-5 yrs	0.98**	0.77-1.24	Adjusted for age, gender, and area of residence
	5pringmann, v. et al. 2014		1900 2009	Infection	2030	CD	Infancy	0.98**	0.74-1.3	
				Infections or hospitalizations	467	IBD	Infancy	Not Reported		
	Strisciuglio, C. et al. 2017	Italy	2000-2014	Infections such as measles, mumps, smallpox, rubella	467	IBD	U-3 yrs	Not Reported		
					2244	CD	Pregnancy (first trimester)	1,11	0.93-1.32*	
					2244	CD	Pregnancy (second trimester)	0,93	0.79-1.11*	
	Thompson, N.P. et al. 1995	United Kingdom	1950-1968	Exposure to measles	2244	CD	Pregnancy (third trimester)	0,95	0.8-1.13*	Unadjusted estimates reported
					2244	CD	At birth	0,88	0.74-1.06*	
					2244	CD	0-6 months	0,9	0.76-1.07*	
					2244	CD	Infancy	0,96	0.78-1.18*	
	Whorwell, P. J. et al. 1979	Southampton, United	Not Reported	Gastroenteritis	228	CD	Infancy	Not Reported		
		Kingdom			204	UC	Infancy	Not Reported		

Study deisgn Cohort Studies	Study	Study location	Study Time Period	Exposure Description	Total sample size (n)	Outcome	Period of exposure	Effect estimate value	Confidence interval (specify if different from 95% Cl)	Comments			
					968468	CD		1.34++	1.11-1.62				
				Antibiotics			ļ						
					968468		ł	1.10††	0.84-1.44				
	Nylund, C. et al. 2019	United States of America	Not Reported	Proton pump inhibitors	968468		0-6 mos	1.45††	0.86-2.42	Adjusting variables not reported			
					968468		ł	3.76++	2.28-6.17				
				H2 receptor antagonists	968468 968468		ł	1.34++ 1.23++	1.01-1.80 0.83-1.83				
	Lange, A. et al. 2014	Denmark	1991-2000; 2001-2010	Antibiotics or infections requiring hospitalization	979 039		Infancy	1.4++	1-1.8	Adjusted for family history of CD, mode of delivery, birth order, year of birth, gestational age, rural vs urban residence, maternal smoking, and NSAID use in			
				Antibiotics at ≤1 year of age	1072426	IBD	Infancy	5.51 <sup>++</sup>	1.66-18.28	infancy			
				1-2 courses of antiaerobic									
	Kronman, M.P. et al. 2012	United Kingdom	1994-2009	antibiotics	1072426		Infancy	3.33**	1.69-6.58	Adjusted for family history of IBD, gender, chronic granulomatous disease primary sclerosing cholangitis, and socioeconomic deprivation			
				>2 antiaerobic antibiotics	1072426		Infancy	4.77††	2.13-10.68	, ,			
				Antibiotics at ≤5 years of age	1072426		0-5 yrs	2.62 <sup>++</sup>	1.61-4.25				
	Ortquist A K at al. 2017	Swadan	2006-2013	Antibiotics	827239		Infancy	1.11 <sup>++</sup>	0.57-2.15	Adjusted for mother's and father's history of IBD, parental education, mother's			
	Ortqvist, A.K. et al. 2017	Sweden	2006-2013	Antibiotics	827239		Infancy	0.72 <sup>++</sup> 1.23 <sup>++</sup>	0.27-1.92	and father's country of birth and mode of delivery			
Case-Control					827239	UC	Infancy	1.23	0.45-3.39				
studies					-								
	Shaw S.Y. et al. 2010	Canada	1996-1997, 2007-2008	Antibiotics		IBD	Infancy	2.9 <sup>*</sup>	1.21-6.96	Unadjusted estimates reported			
					577627		0-2 mos	NA	1.08-3.15				
				Antibiotics use in the previous 3 months	577627		3-11 mos	3.32**	1.15-9.56				
				months	577627		Infancy	1.53**	0.15-15.46				
	Hviid, A. et al. 2010	Denmark	1995-2003		577627		2-3 yrs	3.73**	1.02-13.60	Adjusted for age (in 1-year intervals) and calendar period (in 1-year intervals)			
					577627 577627		0-2 mos	4.19** 1.04**	1.64-10.68 0.53-2.04				
				Antibiotic use >3 months previously	577627		3-11 mos Infancy	1.04**	0.53-2.04				
					577627		2-3 yrs	2.17**	0.32-2.33				
				Any regular medication	851		< 6 yrs	1.36*	0.65-2.83				
	Han, D.Y. et al. 2010	New Zealand	Not Reported	≥4 antibiotics/year	851		< 6 yrs	2.19*	1.41-3.40	Unadjusted estimates reported			
					5720		0-5 yrs	2.2**	0.75-6.43				
				Antibiotics (ever vs never users)	5720	UC	0-5 yrs	1.07**	0.41-2.79				
					5720	CD	0-5 yrs	2.92**	0.85-10				
				Antibiotics (1 prescription vs. none)	5720	UC	0-5 yrs	1**	0.28-3.52				
				Antibiotics (2-4 prescriptions vs.	5720	CD	0-5 yrs	2.37**	0.77-7.11				
	Troolson E at al 2020	United Kingdom	1998-2017	none)	5720	UC	0-5 yrs	1.01**	0.36-2.84	Adjusted for age (+/- 2 years), sex, general practice, and registration year in			
	Troelsen, F. et al. 2020	omea vingaom	1990-2017	Antibiotics (5-9 prescriptions vs.	5720	CD	0-5 yrs	2.39**	0.79-2.27	the registry			
				none)	5720	UC	0-5 yrs	1.05**	0.39-2.91				
				Antibiotics (10-19 prescriptions vs.	5720	CD	0-5 yrs	1.97**	0.63-6.12				
				none)	5720		0-5 yrs	1.06**	0.36-3.08				
				Antibiotics (≥20 prescriptions vs.	5720		0-5 yrs	0.54**	0.90-3.25				
				none)	5720		0-5 yrs	1.75**	0.47-6.50				
					1804		0-6 mos	1.45**	0.80-2.62				
					1804		0-6 mos	2.61**	1.17-5.81	Adjusted for sex; year of birth; season of birth; having older siblings; number			
	Canova, C. et al. 2020	Italy	1989-2012	Antibiotics	1804		0-6 mos	0.85**	0.29-2.52	of births; birth weight; gestational age; Apgar scores at 1 minute; maternal age; mother's formal education at the moment of birth and gastrointestinal			
					1804		Infancy	1.07**	0.64-1.79	age; mother's formal education at the moment of birth and gastrointestinal infections (hospital discharge record diagnosis).			
					1804		Infancy	1.72**	0.84-3.53				
					1804		Infancy	0.72**	0.28-1.86				
	Gearry, R.B. et al. 2010	New Zealand	2003-2005	antibiotic use >4 times/year	1238		Infancy	1.21**	0.78-1.58	Adjusting variables not reported			
	Gearry, R.B. et al. 2010	New Zealand	2003-2005	antibiotic use >4 times/year	1253		Infancy	0.94**	0.58-1.51	Adjusting variables not reported			

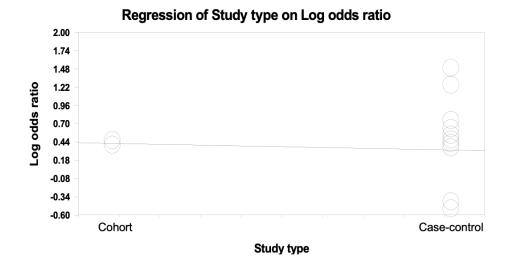
Study design	Study	Study Location	Study Time Period	Exposure Description	Total sample size (n)	Outcome	Period of exposure	Effect estimate value	Confidence interval (specify if different from 95% Cl)	Comments
<b>Case Control Studies</b>										
	Thompson, N.P. et al. 1995	England	1950-1968	Passive smoking	3073	CD	0-5 yrs	1.04	0.88-1.23	Unadjusted estimates reported. Note: total number of CD patients with controls.
	mompson, N.F. et al. 1995	England	1550-1508	Fassive smoking	1654	UC	0-5 yrs	1.1	0.90-1.50	Unadjusted estimates reported. Note: total number of UC patients with controls
	Han, D.Y. et al. 2010	New Zealand	Not Reported	Smoking Exposure	851	CD	0-5 yrs	1.19	0.89-1.59	Unadjusted estimates reported. There was no significant association with smokers at home during the adolescence, childhood, or preschool period (p > 0.05). Represented OR children < 6 yrs
	Basson, A. et al. 2014	Western Cape, South Africa	September 20	Passive smoking	407	IBD	0-5 yrs	1.71	1.01-2.94	Adjusted for age at study enrolment, gender and ethnicity

	•		Ca	ase-control S	tudies		r			
Study (name, year)			Selection			Comparability		Ехро	osure	
								2. Same		
	1.ls the	2.				Comparability of		method of ascertainm		
	case	z. Representa		4.	Total	cases and controls	1.	ent for	3. Non-	Total
	definition		3. Selection	 Definition	points for	on the basis of the		cases and	Response	points for
	adequate?	the cases (1	of Controls	of Controls	selection (4	design or analysis	of exposure	controls (1	rate (1	outcome (3
	(1 point)	point)	(1 point)	(1 point)	points)	(2 points)	(1 point)	point)	point)	points)
Amre, D.K. et al. 2006	1(a)	1(a)	0(b)	1(a)	3		1(b)	1(a)	1(a)	3
Ananthakrishnan, A.N. et al. 2015	0(c)	0(b)	0(c)	0(b)	0		0(c)	1(a)	0(c)	1
Axelrad, J. et al. 2019	1(a)	1(a)	1(a)	1(a)	4		1(a)	1(a)	0(c)	2
Bager, P. et al. 2012	0(b)	1(a)	1(a)	1(a)	3		0(d)	1(a)	1(a)	3
Baron, S. et al. 2005	1(a)	1(a)	1(a)	0(b)	3		1(b)	1(a)	1(a)	3
Basson, A. et al. 2014	1(a)	1(a)	1(a)	1(a)	4		0(c)	1(a)	1(a)	2
Bergstrand, O. et al. 1983	1(a)	0(b)	1(a)	0(b)	2		0(c)	1(a)	0(c)	1
Bernstein, C.N. et al. 2006	1(a)	1(a)	1(a)	0(b)	3		0(c)	1(a)	0(c)	1
Bernstein, C.N. et al. 2016	1(a) 1(a)	1(a) 1(a)	1(a) 1(a)	1(a) 1(a)	4		1(a) 1(a)	1(a) 1(a)	0(c) 1(a)	2
Bernstein, C.N. et al. 2017 Bernstein, C.N. et al. 2019	1(a) 1(a)	1(a) 1(a)	1(a) 0(c)	1(a) 1(a)	3		1(a) 1(a)	1(a) 1(a)	1(a)	3
Boneberger, A. et al. 2011	1(a) 1(a)	1(a)	0(b)	1(a)	3		0(c)	1(a)	0(b)	1
Canova, C. et al. 2020	0(b)	1(a)	1(a)	1(a)	3		1(a)	1(a)	1(a)	3
Corrao, G. et al. 1998	1(a)	1(a)	1(a)	1(a)	4		1(b)	1(a)	1(a)	3
Davis, R.L. et al. 2001	0(b)	0(b)	0(c)	1(a)	1		1(a)	1(a)	1(a)	3
Decker, E. et al. 2010	0(b)	0(b)	0(b)	0(b)	0		0(c)	1(a)	0(c)	1
Disanto G. et al. 2012	0(c)	0(b)	1(a)	1(a)	2		1(a)	1(a)	0(c)	2
Doyle, J.B. et al. 2017	1(a)	0(b)	1(a)	1(a)	3	0	1(a)	1(a)	1(a)	3
Ekbom, A. et al. 1990	1(a)	1(a)	0(b)	0(b)	2	2	1(a)	1(a)	1(a)	3
Eslahpazir J. et al. 2017	1(a)	0(b)	1(a)	1(a)	4		1(b)	1(a)	0(c)	2
Feeney, M. et al. 1997	1(a)	1(a)	1(a)	0(b)	3		0(d)	1(a)	0(c)	1
Feeney, M. et al. 2002	1(a)	1(a)	0(b)	1(a)	3		0(c)	1(a)	0(c)	1
Gearry, R.B. et al. 2010	1(a)	1(a)	1(a)	1(a)	4		1(b)	1(a)	1(a)	3
Gent, A.E. et al. 1994	1(a)	0(b)	0(b)	1(a)	2		0(c)	1(a)	1(a)	2
Gilat, T. et al. 1987	0(b)	0(b)	0(b)	1(a)	1		0(c)	1(a)	0(b)	1
Gruber, M. et al. 1996	0(b)	1(a)	1(a)	0(b)	2		0(d)	1(a)	0(c)	1
Hampe, J. et al. 2003	1(a)	1(a)	1(a)	1(a)	4		1(b)	1(a)	0(c)	2
Han, D.Y. et al. 2010	1(a)	1(a)	1(a)	0(b)	3		0(d)	1(a)	1(a)	2
Hansen, T.S. et al. 2011	1(a)	1(a)	0(b)	1(a)	3		0(d)	1(a)	1(a)	2
Haslam, N. et al. 2000	1(a)	0(b)	0(c)	0(b)	1		1(a)	1(a)	0(c)	2
Hildebrand, H. et al. 2008	1(a)	1(a)	1(a)	1(a)	4		1(a) 0(d)	1(a)	1(a)	3
Hlavaty, T. et al. 2013 Holmes, E.A. et al. 2019	1(a) 1(a)	1(a) 1(a)	1(a) 0(b)	1(a) 1(a)	3		0(d) 0(d)	1(a) 1(a)	0(c) 1(a)	2
Hutfless, S. et al. 2012	1(a) 1(a)	0(b)	1(a)	0(b)	2		1(a)	1(a) 1(a)	0(c)	2
Hviid, A. et al. 2011	1(a) 1(a)	1(a)	1(a) 1(a)	1(a)	4		1(a)	1(a) 1(a)	1(a)	3
Jakobsen, C. et al. 2013	1(0)	1(0)	1(a)	1(0)	-	2	1(0)		(d)	5
Jiang, L. et al. 2007	1(a)	1(a)	1(a)	1(a)	4		0(c)	1(a)	1(a)	2
Klein, I. et al. 1993	1(a)	1(a)	1(a)	0(b)	3	0	0(c)	1(a)	1(a)	2
Ko, Y. et al. 2015	1(a)	0(b)	1(a)	1(a)	3		0(d)	1(a)	1(a)	2
Lavy, A. et al. 2001	1(a)	1(a)	1(a)	1(a)	4	1	0(c)	1(a)	1(a)	3
Lee, J. et al. 2020	0(b)	1(a)	0(c)	0(b)	1	0	1(a)	1(a)	0(c)	2
Levy, L.C. et al. 2012	0(c)	0(b)	0(c)	0(b)	0	2	0(c)	0(b)	0(c)	0
Lopez-Serrano, P. et al. 2010	1(a)	1(a)	0(b)	1(a)	3	2	0(d)	1(a)	0(c)	1
Mahid, S.S. et al. 2007	1(a)	0(b)	1(a)	0(b)	2	1	0(e)	1(a)	1(a)	2
Malekzadeh, F. et al. 2009	1(a)	1(a)	0(b)	1(a)	3	2	1(b)	1(a)	0(c)	2
Malmborg, P. et al. 2012	1(a)	1(a)	1(a)	1(a)	4	1	1(a)	1(a)	0(c)	2
Ng, S.C. et al. 2015	1(a)	1(a)	1(a)	1(a)	4		0(c)	1(a)	1(a)	2
Niewiadomski, O. et al. 2016	1(a)	0(b)	1(a)	1(a)	3		0(c)	1(a)	1(a)	2
Persson, R.G. et al. 1993	1(a)	1(a)	1(a)	1(a)	4		0(d)	1(a)	1(a)	2
Radon, K. et al. 2007	1(a)	1(a)	1(a)	1(a)	4		0(d)	1(a)	1(a)	2
Ramakrishna B.S. et al. 2012	0(c)	0(b)	0(c)	0(b)	0		1(b)	0(b)	0(c)	1
Russel, M.G. et al. 1998	1(a)	1(a)	1(a)	1(a)	4		0(d)	1(a)	1(a)	2
Russell, R K. et al. 2005	0(c)	0(b)	0(c)	0(b)	0		0 (e)	0(b)	0(c)	0
Sahu M.K. et al. 2010 Salgado, V.C. et al. 2017	0(c)	0(b)	1(a) 0(b)	0(b)	3		1(b) 0(c)	0(b) 1(a)	0(c)	1
Salgado, V.C. et al. 2017 Samuelson, S.M. et al. 1991	1(a) 1(a)	1(a) 1(a)	0(b) 1(a)	1(a) 0(b)	3		0(c) 0(c)	1(a) 1(a)	1(a) 1(a)	2
Sanagapalli, S. et al. 2015	1(a) 1(a)	1(a) 1(a)	1(a) 1(a)	0(b) 1(a)	4		0(c) 0(c)	1(a) 1(a)	1(a) 0(c)	1
Shaw, S.Y. et al. 2010	1(a) 1(a)	0(b)	1(a) 1(a)	1(a) 1(a)	3		0(C) 1(a)	1(a) 1(a)	1(a)	3
Shaw, S.Y. et al. 2013	1(a) 1(a)	1(a)	1(a)	1(a)	4		0(d)	1(a) 1(a)	1(a)	3
Shaw, S.Y. et al. 2014	1(a)	1(a) 1(a)	1(a)	1(a) 1(a)	4		1(a)	1(a) 1(a)	1(a)	3
Shaw, S.Y. et al. 2015	1(a)	1(a)	1(a)	1(a)	4		1(a)	1(a)	0(c)	2
Sonntag, B. et al. 2007	1(a)	0(b)	0(c)	1(a)	2		1(a)	1(a)	0(c)	2
Springmann, V. et al. 2014	1(a)	1(a)	1(a)	1(a)	4		0(d)	1(a)	1(a)	3
Strisciuglio, C. et al. 2017	1(a)	0(b)	1(a)	1(a)	3		0(c)	1(a)	0(c)	1
Thompson, N.P. et al. 1995	0(b)	0(b)	1(a)	0(b)	1		0(d)	1(a)	0(c)	1
Thompson, N.P. et al. 2000	1(a)	1(a)	1(a)	0(b)	3	0	0(c)	1(a)	1(a)	2
	1(a)	1(a)	1(a)	1(a)	4		1(a)	1(a)	1(a)	3
Thorsen, S.U. et al. 2016	1(a)	41.3	1(a)	1(a)	3		1(a)	1(a)	0(c)	2
Troelsen, F.S. et al. 2019	0(b)	1(a)			4	0	0(d)	1(a)	1(a)	2
		1(a)	1(a)	1(a)	4		0(0)	-(0)		
Troelsen, F.S. et al. 2019 Urashima, H. et al. 1999 Vahedi, H. et al. 2011	0(b) 1(a) 1(a)	1(a) 0(b)	1(a) 0(b)	0(b)	1	2	0(c)	1(a)	0(c)	
Troelsen, F.S. et al. 2019 Urashima, H. et al. 1999 Vahedi, H. et al. 2011 van der Sloot, K.W.J. et al. 2020	0(b) 1(a) 1(a) 0(c)	1(a) 0(b) 1(a)	1(a) 0(b) 1(a)	0(b) 1(a)	1	2 1	0(c) 0 (c/d)	1(a) 1(a)	0(c) 1(a)	2
Troelsen, F.S. et al. 2019 Urashima, H. et al. 1999 Vahedi, H. et al. 2011 van der Sloot, K.W.J. et al. 2020 Van Limbergen, J.E. et al. 2009	0(b) 1(a) 1(a)	1(a) 0(b)	1(a) O(b) 1(a) O(c)	0(b)	1	2 1 2	0(c)	1(a) 1(a) 0(b)	0(c) 1(a) 0(c)	2
Troelsen, F.S. et al. 2019 Urashima, H. et al. 1999 Vahedi, H. et al. 2011 van der Sloot, K.W.J. et al. 2020 Van Limbergen, J.E. et al. 2009 Van Ranst, M. et al. 2005	0(b) 1(a) 1(a) 0(c) 0(c)	1(a) 0(b) 1(a) 0(b)	1(a) 0(b) 1(a) 0(c) 1(a)	0(b) 1(a) 0(b)	1 3 0	2 1 2 2	0(c) 0 (c/d) 0(c)	1(a) 1(a) 0(b) 1	0(c) 1(a) 0(c) (a)	2
Troelsen, F.S. et al. 2019 Urashima, H. et al. 1999 Vahedi, H. et al. 2011 van der Sloot, K.W.J. et al. 2020 Van Limbergen, J.E. et al. 2009 Van Ranst, M. et al. 2005 Vcev, A. et al. 2015	0(b) 1(a) 1(a) 0(c) 0(c) 1(a)	1(a) 0(b) 1(a) 0(b) 1(a)	1(a) 0(b) 1(a) 0(c) 1(a) 1(a)	0(b) 1(a) 0(b) 1(a)	1 3 0	2 1 2 2 0	0(c) 0 (c/d) 0(c) 0(c)	1(a) 1(a) 0(b) 1(a)	0(c) 1(a) 0(c) (a) 0(c)	200
Troelsen, F.S. et al. 2019 Urashima, H. et al. 1999 Vahedi, H. et al. 2011 van der Sloot, K.W.J. et al. 2020 Van Limbergen, J.E. et al. 2009 Van Ranst, M. et al. 2005 Vcev, A. et al. 2015 Velosa, M. et al. 2019	0(b) 1(a) 1(a) 0(c) 0(c) 1(a) 0(b)	1(a) 0(b) 1(a) 0(b) 1(a) 1(a)	1(a) 0(b) 1(a) 0(c) 1(a) 1(a)	0(b) 1(a) 0(b) 1(a) 1(a)	1 3 0 4 3	2 1 2 2 0 0 2	0(c) 0 (c/d) 0(c) 0(c) 1(a)	1(a) 1(a) 0(b) 1(a) 1(a)	0(c) 1(a) 0(c) (a) 0(c) 0(c)	2 0 1 2
Troelsen, F.S. et al. 2019 Urashima, H. et al. 1999 Vahedi, H. et al. 2011 van der Sloot, K.W.J. et al. 2020 Van Limbergen, J.E. et al. 2009 Van Ranst, M. et al. 2005 Vcev, A. et al. 2015 Velosa, M. et al. 2019 Villumsen M. et al. 2013	0(b) 1(a) 1(a) 0(c) 0(c) 1(a) 0(b) 1(a)	1(a) 0(b) 1(a) 0(b) 1(a) 1(a) 1(a)	1(a) 0(b) 1(a) 0(c) 1(a) 1(a) 1(a) 1(a)	0(b) 1(a) 0(b) 1(a) 1(a) 1(a)	1 3 0 4 3 4	2 1 2 2 0 0 2 2 2 2	0(c) 0 (c/d) 0(c) 0(c) 1(a) 1(a)	1(a) 1(a) 0(b) 1(a) 1(a) 1(a)	0(c) 1(a) 0(c) (a) 0(c) 0(c) 1(a)	1 2 0 1 1 2 3 3
Troelsen, F.S. et al. 2019         Urashima, H. et al. 1999         Vahedi, H. et al. 2011         van der Sloot, K.W.J. et al. 2020         Van Limbergen, J.E. et al. 2009         Van Ranst, M. et al. 2005         Vcev, A. et al. 2015         Velosa, M. et al. 2019         Villumsen M. et al. 2013         Wang, Y.F. et al. 2013	0(b) 1(a) 1(a) 0(c) 0(c) 1(a) 0(b) 1(a) 0(b)	1(a) 0(b) 1(a) 0(b) 1(a) 1(a) 1(a) 0(b)	1(a) 0(b) 1(a) 0(c) 1(a) 1(a) 1(a) 1(a) 1(a)	0(b) 1(a) 0(b) 1(a) 1(a) 1(a) 1(a)	1 3 0 4 3 4 2	2 1 2 2 0 0 2 2 2 2 2 2	0(c) 0 (c/d) 0(c) 0(c) 1(a) 1(a) 0(c)	1(a) 1(a) 0(b) 1(a) 1(a) 1(a) 1(a) 1(a)	0(c) 1(a) 0(c) (a) 0(c) 0(c) 1(a) 0(c)	2 0 1 2 3 3
Troelsen, F.S. et al. 2019 Urashima, H. et al. 1999 Vahedi, H. et al. 2011 van der Sloot, K.W.J. et al. 2020 Van Limbergen, J.E. et al. 2009 Van Ranst, M. et al. 2005 Vcev, A. et al. 2015 Velosa, M. et al. 2019 Villumsen M. et al. 2013	0(b) 1(a) 1(a) 0(c) 0(c) 1(a) 0(b) 1(a)	1(a) 0(b) 1(a) 0(b) 1(a) 1(a) 1(a)	1(a) 0(b) 1(a) 0(c) 1(a) 1(a) 1(a) 1(a)	0(b) 1(a) 0(b) 1(a) 1(a) 1(a)	1 3 0 4 3 4	2 1 2 2 0 0 2 2 2 2 2 2 0 0	0(c) 0 (c/d) 0(c) 0(c) 1(a) 1(a)	1(a) 1(a) 0(b) 1(a) 1(a) 1(a)	0(c) 1(a) 0(c) (a) 0(c) 0(c) 1(a)	

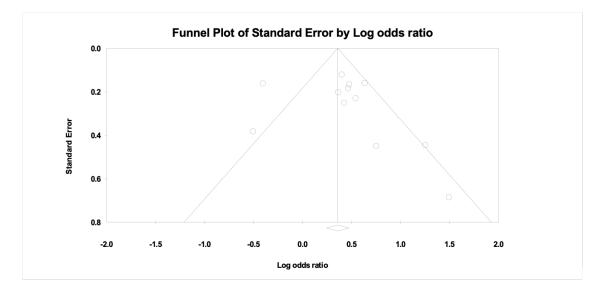
				Cohort stu	dies					
Study (name, year)			Selection			Comparability		Out	come	
				4. Demonstrati on that				2. Was follow-up		
	1.Represen tativeness of the exposed cohort (1	Selection	3. Ascertain ment of exposure	outcome of interest was not present at start of study (1	Total points for selection	Comparability of cohorts on the basis of the design or analysis (2	1. Assessmen t of outcome (1	long enough for outcomes	3. Adequacy of follow up (1	Total points for outcome
	point)	point)	(1 point)	point)	(4 points)	points)	point)	(1 point)	point)	(3 points)
Agrawal, M. et al. 2020	1(a)	1(a)	1(a)	1(a)	4	2	1(a)	1(a)	1(a)	3
Andersen, V. et al. 2013	1(a)	1(a)	1(a)	0(b)	3	2	1(b)	0(b)	0(d)	1
Andersen, V. et al. 2020	1(a)	1(a)	1(a)	1(a)	4	2	1(a)	1(a)	0(c)	2
Aspberg, S. et al. 2006	1(a)	1(a)	1(a)	1(a)	4	0	1(a)	1(a)	0(d)	2
Bager, P. et al. 2012	1(a)	1(a)	1(a)	0(b)	3	2	1(b)	1(a)	0(d)	2
Benchimol, E. et al. 2015	1(a)	1(a)	1(a)	1(a)	4	2	1(b)	1(a)	1(a)	3
Benchimol, E.I. et al. 2017	1(a)	1(a)	1(a)	1(a)	4	2	1(b)	0(b)	0(d)	1
Black, M. et al. 2015	1(a)	1(a)	0(a)	0(b)	2	2	1(b)	1(a)	0(c)	2
Black, M. et al. 2015	0(d)	1(a)	1(a)	1(a)	3	2	1(b)	1(a)	1(a)	3
Blomster, T.M. et al. 2014	1(a)	1(a)	1(b)	1(a)	4	2	1(b)	1(a)	1(b)	3
Burnett, D. et al. 2017	1(a)	1(a)	1(a)	1(a)	4	2	1(b)	1(a)	0(d)	2
Burnett, D. et al. 2020	1(a)	1(a)	1(a)	1(a)	4	2	1(b)	1(a)	0(c)	2
Card, T.R. et al. 2002	1(a)	1(a)	1(a)	1(a)	4	1	1(b)	1(a)	1(b)	3
Chowers, Y. et al. 2004	1(a)	1(a)	1(a)	1(a)	4	1	1(b)	1(a)	0(d)	2
Ekbom, A. et al. 1991	1(a)	1(a)	1(a)	1(a)	4	1	1(b)	1(a)	0(d)	2
Elten, M. et al. 2020	1(a)	1(a)	1(a)	0(b)	3	2	1(a)	1(a)	1(a)	3
Ghersin, I. et al. 2019	1(a)	1(a)	1(a)	1(a)	4	2	1(b)	0(b)	1(a)	2
Greenbaum, S. et al. 2018	1(a)	1(a)	0(d)	1(a)	3	2	0(d)	0(b)	0(d)	0
Khalili, H. et al. 2012	1(b)	1(a)	1(b)	1(a)	4	2	1(a)	1(b)	1(a)	3
Khalili, H. et al. 2013	1(a)	1(a)	1(a)	0(b)	3	2	1(b)	1(a)	1(b)	3
Klement, E. et al. 2008	1(a)	1(a)	1(b)	1(a)	4	2	1(b)	0(b)	1(b)	2
Konijeti, G. et al. 2013	1(a)	1(a)	1(b)	1(a)	4	2	1(b)	1(a)	1(b)	2
Kronman, M.P. et al. 2012	1(a)	1(a)	1(a)	1(a)	4	2	1(b)	1(a)	1(b)	3
Lange, A. et al. 2014	1(a)	1(a)	0(d)	0(b)	2		0(d)	1(a)	0(c)	1
Li, X. et al. 2011	1(a)	1(a)	1(a)	1(a)	4		1(b)	1(a)	1(b)	3
Montgomery, S.M. et al. 1999	1(a)	1(a)	1(a)	1(a)	4		1(a)1(b)	1(b)	1(a)	3
Morris, D.L. et al. 2000	1(a)	1(a)	1(b)	1(a)	4		1(b)	1(a)	1(b)	1
Nylund, C. et al. 2019	1(a)	1(a)	1(a)	0(b)	3		1(a)	1(a)	0(d) 1(b)	2
Ortqvist, A.K. et al. 2019 Ponsonby, A.L. et al. 2009	1(a) 1(a)	1(a) 1(a)	1(a) 1(a)	1(a) 0(b)	4		1(b) 1(b)	1(a) 1(a)	1(b) 0(d)	3
Seagroatt, V. et al. 2003	1(a) 1(a)	1(a) 1(a)	1(a) 1(a)	0(b) 1(a)	4		1(b) 1(a)	1(a) 1(a)	0(d) 0(d)	2
Sonnenberg, A. et al. 2009	1(a)	1(a) 1(a)	1(a)	1(a)	4		1(b)	1(a) 1(a)	1(b)	3
Steiner, N. et al. 2019	1(a)	1(a)	1(a)	1(a)	4		1(b)	1(a)	1(b)	3
Timm, S. et al. 2014	1(a)	1(a)	1(b)	1(a)	4		0(c)	1(a)	1(b)	2
Yoles, I. et al. 2018	1(b)	1(a)	1(a)	1(a)	4		1(b)	0(b)	0(d)	1

## **APPENDIX C: Supplementary Figures**

**Supplementary Figure 1:** Meta-regression of cohort vs case-control studies on the association between maternal smoking and subsequent IBD diagnosis in the offspring (P value of slope 0.45)



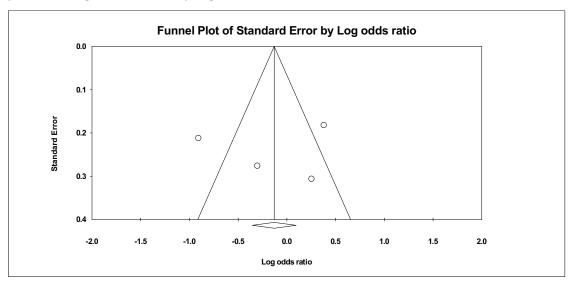
**Supplementary Figure 2:** Funnel plot to assess publication bias in studies on the association between maternal smoking and subsequent IBD diagnosis in the offspring (Egger's 2-sided p-value 0.451)



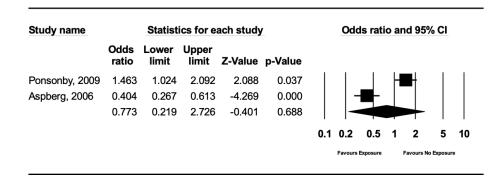
**Supplementary Figure 3:** Forest plot of the association between older maternal age and subsequent IBD diagnosis in the offspring (I<sup>2</sup> 87.06%)

Study name		Statist	ics for e	ach study	/	Odds ratio and 95% Cl
	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value	
Ponsonby, 2009	1.463	1.024	2.092	2.088	0.037	
Aspberg, 2006	0.404	0.267	0.613	-4.269	0.000	
Canova, 2020	0.740	0.431	1.272	-1.090	0.276	│ │ ┼∰┼ │ │ │
Thorsen, 2016	1.290	0.708	2.352	0.831	0.406	│ │ │ <mark>⊣</mark> ∰∔ │ │
	0.863	0.452	1.648	-0.445	0.656	
						0.1 0.2 0.5 1 2 5 10
						Favours Exposure Favours No Exposure

**Supplementary Figure 4:** Funnel plot to assess publication bias in studies on the association between older maternal age and subsequent IBD diagnosis in the offspring



**Supplementary Figure 5:** Forest plot of the association between older maternal age and subsequent CD diagnosis in the offspring (I<sup>2</sup> 95.27%)



**Supplementary Figure 6:** Forest plot of the association between low birth weight and subsequent IBD diagnosis (I<sup>2</sup> 76.75%)

Study name		Statist	ics for e	ach study	L	Odds ratio and 95% Cl
	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value	
Steiner, 2019	1.245	1.084	1.429	3.103	0.002	
Aspberg, 2006	1.094	0.674	1.776	0.364	0.716	
Khalili, 2013	1.101	0.699	1.733	0.414	0.679	
Ponsonby, 2009	0.741	0.393	1.395	-0.930	0.352	
Canova, 2020	1.120	0.419	2.993	0.226	0.821	
Thorsen, 2016	1.210	0.590	2.481	0.520	0.603	
Hutfless, 2012	1.600	0.687	3.728	1.089	0.276	
van der Sloot, 2020	0.980	0.666	1.442	-0.103	0.918	
van der Sloot, 2020*	1.060	0.730	1.540	0.306	0.760	
Malmborg, 2012	0.981	0.738	1.304	-0.133	0.894	
Radon, 2007	0.493	0.360	0.676	-4.401	0.000	
Radon, 2007*	0.468	0.321	0.683	-3.939	0.000	
	0.920	0.727	1.164	-0.695	0.487	
						0.1 0.2 0.5 1 2 5 10 Favours Exposure Favours No Exposure

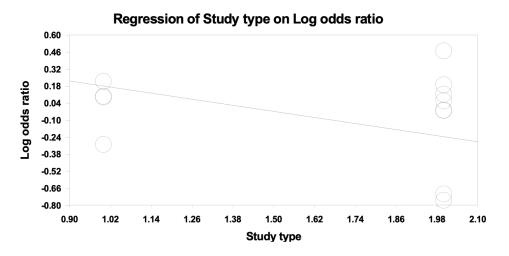
**Supplementary Figure 7:** Forest plot of the association between low birth weight and subsequent CD diagnosis (I<sup>2</sup> 70.72%)

Study name	Stat	stics for e	each stud	у	Odds ratio and 95% Cl
	Odds Low ratio lim			p-Value	
Khalili, 2013	1.101 0.6	99 1.733	3 0.414	0.679	-#=-
Ponsonby, 2009	0.741 0.3	93 1.395	5 -0.930	0.352	│ │ →■┼╸│ │ │
van der Sloot, 2020	0.980 0.6	66 1.442	2 -0.103	0.918	-♣-
Malmborg, 2012	0.981 0.7	38 1.304	-0.133	0.894	
Radon, 2007	0.493 0.3	60 0.676	6 -4.401	0.000	
Hutfless, 2012	2.700 0.7	00 10.407	7 1.443	0.149	│ │ │ <del>│ <b>│ </b> </del>
	0.875 0.6	24 1.225	5 -0.780	0.435	
					0.1 0.2 0.5 1 2 5 10
					Favours Exposure Favours No Exposure

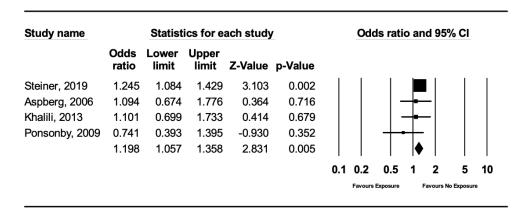
**Supplementary Figure 8:** Forest plot of the association between low birth weight and subsequent UC diagnosis (I<sup>2</sup> 81.66%)

Study name		Statist	Odds ratio and 95% CI									
	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value							
van der Sloot, 2020*	1.060	0.730	1.540	0.306	0.760				-	-		
Radon, 2007*	0.468	0.321	0.683	-3.939	0.000							
Hutfless, 2012	1.600	0.501	5.110	0.793	0.428				+	▰┼─	-	
	0.831	0.412	1.677	-0.515	0.606							
						0.1	0.2	0.5	1	2	5	10
							Favours	Exposure		Favours N	o Exposu	е

**Supplementary Figure 9:** Meta-regression of cohort vs case-control studies on the association between low birth weight and subsequent IBD diagnosis (P value of slope <0.001)



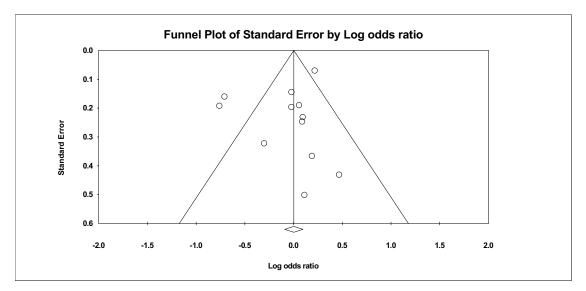
**Supplementary Figure 10:** Forest plot of the association between low birth weight and subsequent IBD diagnosis: cohort studies (I<sup>2</sup> 42.67%)



**Supplementary Figure 11:** Forest plot of the association between low birth weight and subsequent IBD diagnosis: case-control studies (I<sup>2</sup> 73.39%)

Study name		Statist	ics for e	ach study	Odds ratio and 95% Cl						
	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value						
Canova, 2020	1.120	0.419	2.993	0.226	0.821	│ │ ┼─╆─┼─ │ │					
Thorsen, 2016	1.210	0.590	2.481	0.520	0.603	│ │ │→╋┼ │ │					
Hutfless, 2012	1.600	0.687	3.728	1.089	0.276	│ │ │ <del>│ ■│ ■</del> │  │ │					
van der Sloot, 2020	0.980	0.666	1.442	-0.103	0.918	-∰-					
van der Sloot, 2020*	1.060	0.730	1.540	0.306	0.760	-╋-					
Malmborg, 2012	0.981	0.738	1.304	-0.133	0.894						
Radon, 2007	0.493	0.360	0.676	-4.401	0.000	-					
Radon, 2007*	0.468	0.321	0.683	-3.939	0.000	-∰-					
	0.852	0.627	1.157	-1.025	0.305						
						0.1 0.2 0.5 1 2 5 10					
						Favours Exposure Favours No Exposure					

**Supplementary Figure 12:** Funnel plot to assess publication bias in studies on the association between low birth weight and subsequent IBD diagnosis (Egger's 2-sided p-value 0.353)



**Supplementary Figure 13:** Forest plot of the association between premature birth and subsequent IBD diagnosis (I<sup>2</sup> 26.47%)

Study name		Statist	ics for e	ach study	L	Odds ratio and 95% CI
	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value	
Aspberg, 2006	1.200	0.818	1.759	0.934	0.350	│ │ │ ┼┳┼│ │ │
Khalili, 2013	0.801	0.458	1.400	-0.778	0.437	│ │ ┼╋┼ │ │ │
Khalili, 2013*	0.805	0.486	1.331	-0.846	0.397	│ │ ├──┼ │ │ │
Thompson, 1995	1.180	0.962	1.448	1.590	0.112	
Thompson, 1995*	1.086	0.819	1.441	0.574	0.566	🖶
Hutfless, 2012	0.600	0.300	1.200	-1.444	0.149	│ │ ─┼∎┼ │ │ │
Sonntag, 2007	1.059	0.724	1.548	0.296	0.767	.     -≢-
Sonntag, 2007*	0.941	0.642	1.379	-0.312	0.755	_♣-
Canova, 2020	1.260	0.397	3.999	0.392	0.695	│ │ ┼┼╋┼──│ │
Thorsen, 2016	0.840	0.351	2.013	-0.391	0.696	│ │ <del>│ ┩ </del> │ │ │
Ekbom, 1990	0.500	0.204	1.225	-1.516	0.129	
Baron, 2005	4.670	1.327	16.435	2.401	0.016	
	1.020	0.872	1.192	0.242	0.808	
						0.1 0.2 0.5 1 2 5 10 Favours Exposure Favours No Exposure

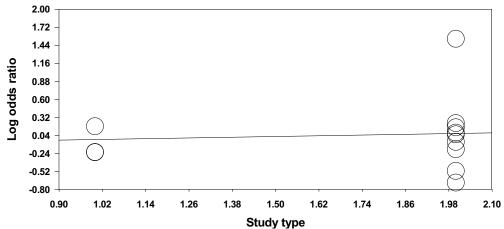
**Supplementary Figure 14:** Forest plot of the association between premature birth and subsequent CD diagnosis (I<sup>2</sup> 5.33%)

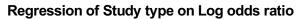
Study name		Statist	ics for e	Odds ratio and 95% Cl								
	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value							
Khalili, 2013	0.801	0.458	1.400	-0.778	0.437			+	■+-			
Hutfless, 2012	0.400	0.100	1.600	-1.295	0.195		+		+	-		
Sonntag, 2007	1.059	0.724	1.548	0.296	0.767			· ·		-		
Thompson, 1995	1.180	0.962	1.448	1.590	0.112					+		
Ekbom, 1990	0.700	0.191	2.572	-0.537	0.591		-			+		
	1.073	0.890	1.293	0.739	0.460				•			
						0.1	0.2	0.5	1	2	5	10
							Favours	Exposure	F	Favours N	o Exposu	re

**Supplementary Figure 15:** Forest plot of the association between premature birth and subsequent UC diagnosis (I<sup>2</sup> 46.91%)

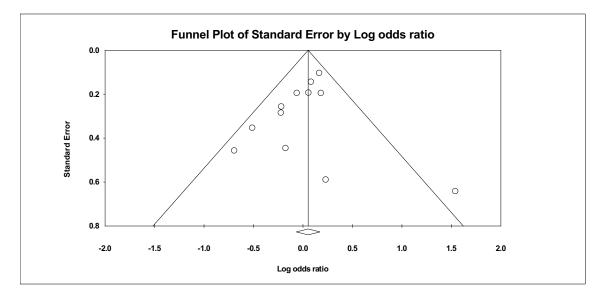
Study name		Statist	ics for e	ach study	Odds ratio and 95% Cl							
	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value							
Hutfless, 2012	0.600	0.190	1.897	-0.870	0.385	│ <del>│                                  </del>						
Sonntag, 2007	0.941	0.642	1.379	-0.312	0.755	-♣-						
Thompson, 1995	1.086	0.819	1.441	0.574	0.566							
Baron, 2005	4.670	1.327	16.435	2.401	0.016							
Ekbom, 1990	0.400	0.103	1.549	-1.326	0.185							
Khalili, 2013	0.805	0.486	1.331	-0.846	0.397	│ │ ├───┤ │ │						
	0.972	0.695	1.360	-0.165	0.869							
						0.1 0.2 0.5 1 2 5 10						
						Favours Exposure Favours No Exposure						

**Supplementary Figure 16:** Meta-regression of cohort vs case-control studies on the association between premature birth and subsequent IBD diagnosis (P value of slope 0.538)

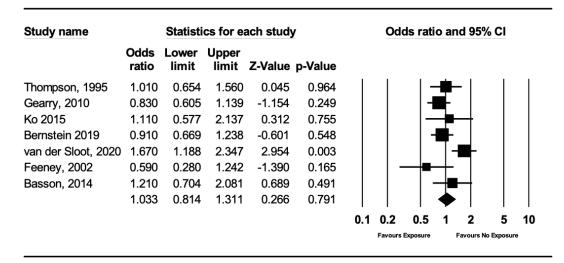




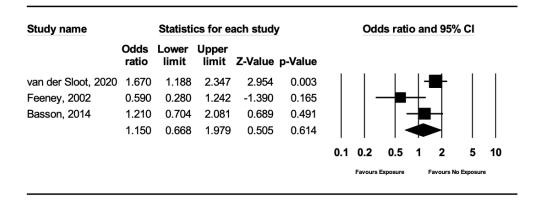
**Supplementary Figure 17:** Funnel plot to assess publication bias in studies on the association between premature birth and subsequent IBD diagnosis (Egger's 2-sided p-value 0.41)



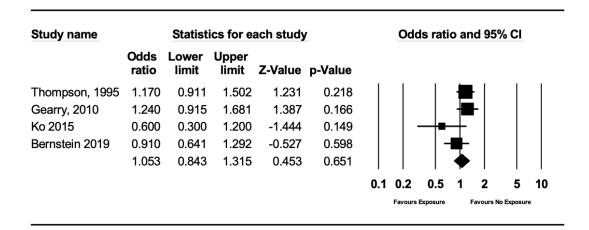
**Supplementary Figure 18:** Forest plot of the association between rural vs urban living and subsequent IBD diagnosis (I<sup>2</sup> 52.76%)



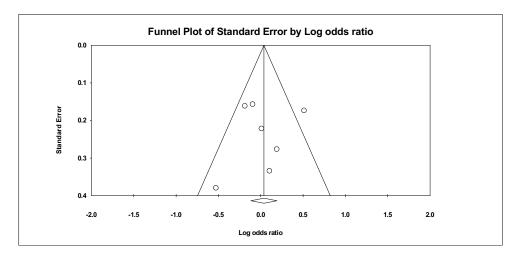
Supplementary Figure 19: Forest plot of the association between rural vs urban living and subsequent CD diagnosis (I<sup>2</sup> 68.81%)



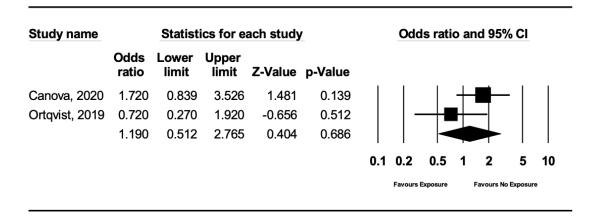
**Supplementary Figure 20:** Forest plot of the association between rural vs urban living and subsequent UC diagnosis (I<sup>2</sup> 38.33%)



**Supplementary Figure 21:** Funnel plot to assess publication bias in studies on the association between rural vs urban and subsequent IBD diagnosis



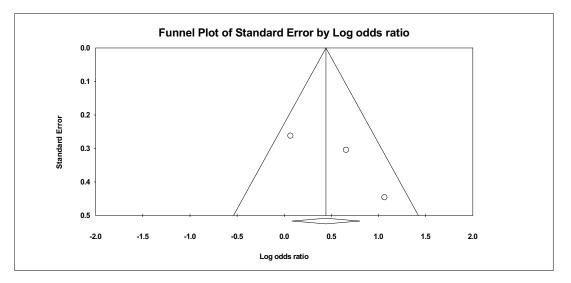
**Supplementary Figure 22:** Forest plot of the association between antibiotic exposure during infancy and subsequent CD diagnosis (I<sup>2</sup> 49.29%)



**Supplementary Figure 23:** Forest plot of the association between antibiotic exposure during infancy and subsequent UC diagnosis (I<sup>2</sup> 44.82%)

Study name		Statist	ics for e	ach study	Odds ratio and 95% Cl							
	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value							
Canova, 2020	1.230	0.448	3.376	0.402	0.688			+-		┠┼─	-	
Ortqvist, 2019	0.720	0.279	1.856	-0.680	0.496		-		∎┼─	—		
	0.925	0.464	1.845	-0.221	0.825				۲			
						0.1	0.2	0.5	1	2	5	10
							Favours	Exposure		Favours N	lo Exposu	e

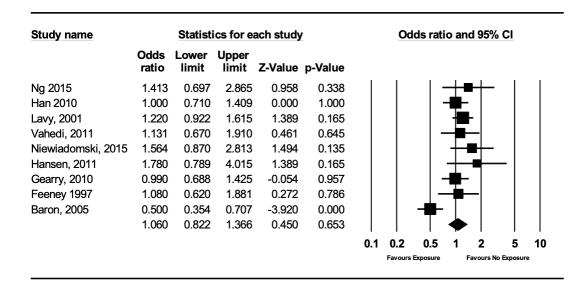
**Supplementary Figure 24:** Funnel plot to assess publication bias in studies on the association between antibiotic exposure during infancy and subsequent IBD diagnosis



**Supplementary Figure 25:** Forest plot of the association between measles vaccine and subsequent IBD diagnosis (I<sup>2</sup> 55.52%)

Study name		Statisti	ics for e	ach study	y	Odds ratio and 95% Cl
	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value	
eeney 1997	0.970	0.640	1.470	-0.144	0.886	-#-
Shaw 2015	1.500	0.506	4.450	0.731	0.465	│ │
/cev 2015	1.720	1.027	2.880	2.062	0.039	
Davis 2001	0.590	0.208	1.674	-0.992	0.321	│ │──┤╋─┼──│ │
Hansen, 2011	1.300	0.756	2.237	0.948	0.343	│ │ │ <del>│</del> ╋┼ │
Ng 2015	1.413	0.697	2.865	0.958	0.338	│ │ │ <del>│</del> ╋┼╸│
Han 2010	1.000	0.710	1.409	0.000	1.000	-♣-
_avy 2001	1.220	0.922	1.615	1.389	0.165	
Gearry 2010	0.990	0.688	1.425	-0.054	0.957	<b>-</b> ∎-
/ahedi 2011	1.131	0.670	1.910	0.461	0.645	
Niewiadomski 2015	1.564	0.870	2.813	1.494	0.135	│ │ │ <del>│ ■</del> ┼─ │
Baron 2005	0.500	0.354	0.707	-3.920	0.000	-♣-
.avy 2001*	0.970	0.748	1.257	-0.230	0.818	🖶
Searry 2010*	0.860	0.591	1.252	-0.787	0.431	
/ahedi 2011*	1.177	0.808	1.714	0.849	0.396	│ │ │ →■→│ │
liewiadomski 2015*	2.251	1.134	4.469	2.319	0.020	
	1.078	0.911	1.275	0.871	0.383	
						0.1 0.2 0.5 1 2 5 1 Favours Exposure Favours No Exposure

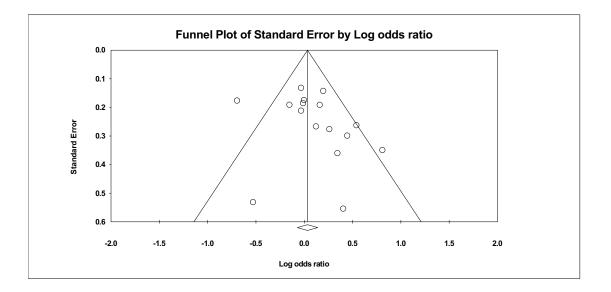
**Supplementary Figure 26:** Forest plot of the association between measles vaccine and subsequent CD diagnosis (I<sup>2</sup> 64.69%)



**Supplementary Figure 27:** Forest plot of the association between measles vaccine and subsequent UC diagnosis (I<sup>2</sup> 28.2%)

Study name		Statist	ics for e	ach study	1		Od	ds rat	atio and 95% Cl					
	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value									
Lavy, 2001	0.970	0.748	1.257	-0.230	0.818				٠					
Vahedi, 2011	1.177	0.808	1.714	0.849	0.396					⊢				
Niewiadomski, 2015	2.251	1.134	4.469	2.319	0.020				-	╼				
Hansen, 2011	1.000	0.478	2.092	0.000	1.000			-	-+-					
Gearry, 2010	0.860	0.591	1.252	-0.787	0.431			-	-					
Feeney 1997	0.840	0.443	1.592	-0.535	0.593			+	╺┼╴	-				
	1.046	0.844	1.296	0.407	0.684				•					
						0.1	0.2	0.5	1	2	5	10		
							Favours	Exposure		Favours N	o Exposur	e		

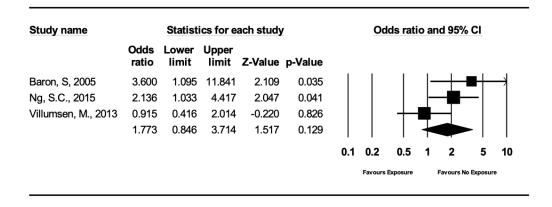
**Supplementary Figure 28:** Funnel plot to assess publication bias in studies on the association between measles vaccine and subsequent IBD diagnosis (Egger's 2-sided p-value = 0.206)



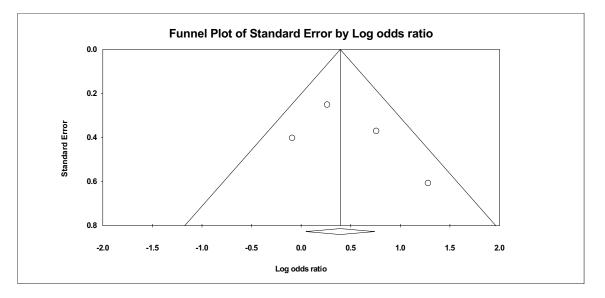
Supplementary Figure 29: Forest plot of the association between BCG vaccine and subsequent IBD diagnosis (1<sup>2</sup> 37.58%)

Study name	Statistics for each study					Odds ratio and 95% Cl						
	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value							
Baron, S, 2005	3.600	1.095	11.841	2.109	0.035				-			$\rightarrow$
Ng, S.C., 2015	2.136	1.033	4.417	2.047	0.041				-		—	
Ng, S.C., 2015*	1.302	0.796	2.130	1.050	0.293							
Villumsen, M., 2013	0.915	0.416	2.014	-0.220	0.826			+		_		
	1.549	0.969	2.477	1.828	0.068							
						0.1	0.2	0.5	1	2	5	10
						Favours Exposure				Favours No Exposure		

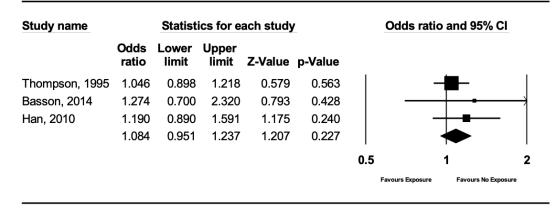
Supplementary Figure 30: Forest plot of the association between BCG vaccine and subsequent CD diagnosis (I<sup>2</sup> 53.17%)



**Supplementary Figure 31:** Funnel plot to assess publication bias in studies on the association between BCG vaccine and subsequent IBD diagnosis



**Supplementary Figure 32:** Forest plot of the association between passive exposure to tobacco smoke and subsequent CD diagnosis (I<sup>2</sup> 64.16%)



**Supplementary Figure 33:** Funnel plot to assess publication bias in studies on the association between passive exposure to tobacco smoke and subsequent CD diagnosis

