

## SUPPLEMENTARY MATERIALS

### Effects of exclusive breastfeeding on infant gut microbiota: a meta-analysis across studies and populations

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**Supplementary table 1. List of shared genera of seven included studies used in the Random Forest models to predict gut microbiota age.**

| Genera   | Relative importance |
|--|---------------------|
| k_bacteria.p_firmicutes.c_clostridia.o_clostridiales.f_lachnospiraceae.g_blautia                         | 3264.3029384        |
| k_bacteria.p_firmicutes.c_clostridia.o_clostridiales.f_lachnospiraceae.g_                                | 1905.2788811        |
| k_bacteria.p_bacteroidetes.c_bacteroidia.o_bacteroidales.f_prevotellaceae.g_prevotella                   | 935.6069474         |
| k_bacteria.p_firmicutes.c_clostridia.o_clostridiales.f.g_  | 903.0123160         |
| k_bacteria.p_firmicutes.c_bacilli.o_bacillales.f_staphylococcaceae.g_staphylococcus                      | 693.0597449         |
| k_bacteria.p_firmicutes.c_clostridia.o_clostridiales.f_veillonellaceae.g_dialister                       | 465.3432501         |
| k_bacteria.p_firmicutes.c_bacilli.o_lactobacillales.f_lactobacillaceae.g_lactobacillus                   | 430.9372453         |
| k_bacteria.p_proteobacteria.c_gammaproteobacteria.o_pasteurellales.f_pasteurellaceae.g_haemophilus       | 412.8020722         |
| k_bacteria.p_actinobacteria.c_actinobacteria.o_bifidobacteriales.f_bifidobacteriaceae.g_bifidobacterium  | 399.6333434         |
| k_bacteria.p_actinobacteria.c_actinomycetales.f_actinomycetaceae.g_actinomyces                           | 326.5063233         |
| k_bacteria.p_firmicutes.c_clostridia.o_clostridiales.f_lachnospiraceae.g_dorea                           | 232.9121374         |
| k_bacteria.p_firmicutes.c_bacilli.o_lactobacillales.f_enterococcaceae.g_enterococcus                     | 211.0289151         |
| k_bacteria.p_firmicutes.c_clostridia.o_clostridiales.f_lachnospiraceae.g_coprococcus                     | 184.2365345         |
| k_bacteria.p_firmicutes.c_bacilli.o_lactobacillales.f_streptococcaceae.g_streptococcus                   | 180.8771632         |
| k_bacteria.p_actinobacteria.c_coriobacteria.o_coriobacteriales.f_coriobacteriaceae.g_collinsella         | 157.8024889         |
| k_bacteria.p_firmicutes.c_clostridia.o_clostridiales.f_veillonellaceae.g_veillonella                     | 157.1312508         |
| k_bacteria.p_firmicutes.c_clostridia.o_clostridiales.f_clostridiaceae.g_clostridium                      | 132.3348777         |
| k_bacteria.p_firmicutes.c_clostridia.o_clostridiales.f_ruminococcaceae.g_oscillospira                    | 127.3175910         |
| k_bacteria.p_bacteroidetes.c_bacteroidia.o_bacteroidales.f_bacteroidaceae.g_bacteroides                  | 125.6500816         |
| k_bacteria.p_proteobacteria.c_gammaproteobacteria.o_pseudomonadales.f_pseudomonadaceae.g_pseudomonas     | 117.2762839         |
| k_bacteria.p_actinobacteria.c_actinobacteria.o_actinomycetales.f_micrococcaceae.g_rothia                 | 105.7002954         |
| k_bacteria.p_actinobacteria.c_coriobacteria.o_coriobacteriales.f_coriobacteriaceae.g_                    | 100.0155111         |
| k_bacteria.p_actinobacteria.c_coriobacteria.o_coriobacteriales.f_coriobacteriaceae.g_atopobium           | 66.9705451          |
| k_bacteria.p_proteobacteria.c_betaproteobacteria.o_neisseriales.f_neisseriaceae.g_neisseria              | 59.3097361          |
| k_bacteria.p_bacteroidetes.c_bacteroidia.o_bacteroidales.f_porphyromonadaceae.g_parabacteroides          | 54.3713192          |
| k_bacteria.p_proteobacteria.c_betaproteobacteria.o_burkholderiales.f_alcaligenaceae.g_sutterella         | 53.3836964          |
| k_bacteria.p_fusobacteria.c_fusobacteriia.o_fusobacteriales.f_fusobacteriaceae.g_fusobacterium           | 52.3247474          |
| k_bacteria.p_firmicutes.c_bacilli.o_gemellales.f_gemellaceae.g_  | 51.8088217          |
| k_bacteria.p_firmicutes.c_bacilli.o_lactobacillales.f_streptococcaceae.g_lactococcus                     | 44.6428095          |
| k_bacteria.p_bacteroidetes.c_bacteroidia.o_bacteroidales.f_rikenellaceae.g_                              | 32.7066309          |
| k_bacteria.p_cyanobacteria.c_chloroplast.o_streptophyta.f.g_   | 10.7313468          |
| k_bacteria.p_firmicutes.c_clostridia.o_clostridiales.f_veillonellaceae.g_acidaminococcus                 | 7.1897234           |
| k_bacteria.p_firmicutes.c_clostridia.o_clostridiales.f_lachnospiraceae.g_roseburia                       | 6.3092483           |
| k_bacteria.p_firmicutes.c_bacilli.o_lactobacillales.f_carnobacteriaceae.g_granulicatella                 | 4.2879708           |
| k_bacteria.p_firmicutes.c_bacilli.o_bacillales.f_paenibacillaceae.g_paenibacillus                        | 0.1393402           |
| k_bacteria.p_proteobacteria.c_alpha proteobacteria.o_sphingomonadales.f_sphingomonadaceae.g_sphingomonas | 0.1054538           |

**Supplementary table 2. Meta-analysis of all seven included studies: gut bacterial taxa with differential relative abundances between non-exclusively breastfed vs. exclusively breastfed infants ≤6 months of age.**

| Bacterial taxa  | Pooled estimate<br>(log(OR)) | 95% Pooled<br>lower limit | 95% Pooled<br>upper limit | Pooled p-<br>value | FDR adjusted<br>pooled p-value |
|---|------------------------------|---------------------------|---------------------------|--------------------|--------------------------------|
| <b>Phylum</b>   |                              |                           |                           |                    |                                |
| k_bacteria.p_firmicutes   | 0.2477163                    | 0.1134765                 | 0.3819560                 | 0.0002983          | 0.0017898                      |
| k_bacteria.p_bacteroidetes  | 0.2079683                    | 0.0596613                 | 0.3562754                 | 0.0059883          | 0.0179648                      |
| <b>Order</b>  |                              |                           |                           |                    |                                |
| k_bacteria.p_firmicutes.c_clostridia.o_clostridiales  | 0.3015251                    | 0.1242695                 | 0.4787808                 | 0.0008559          | 0.0105564                      |
| k_bacteria.p_bacteroidetes.c_bacteroidia.o_bacteroidales  | 0.2100511                    | 0.0615603                 | 0.3585419                 | 0.0055625          | 0.0369277                      |
| k_bacteria.p_firmicutes.c_erysipelotrichi.o_erysipelotrichales                                      | 0.2005008                    | 0.0248186                 | 0.3761830                 | 0.0252963          | 0.1169955                      |
| <b>Family</b>   |                              |                           |                           |                    |                                |
| k_bacteria.p_firmicutes.c_clostridia.o_clostridiales.f_veillonellaceae                              | 0.2311548                    | 0.0632499                 | 0.3990596                 | 0.0069698          | 0.0756721                      |
| k_bacteria.p_bacteroidetes.c_bacteroidia.o_bacteroidales.f_bacteroidaceae                           | 0.2107748                    | 0.0526031                 | 0.3689465                 | 0.0090070          | 0.0855663                      |
| k_bacteria.p_firmicutes.c_erysipelotrichi.o_erysipelotrichales.f_erysipelotrichaceae                | 0.2005008                    | 0.0248186                 | 0.3761830                 | 0.0252963          | 0.1747746                      |
| k_bacteria.p_firmicutes.c_clostridia.o_clostridiales.f_clostridiaceae                               | 0.1652266                    | 0.0003203                 | 0.3301328                 | 0.0495566          | 0.3086619                      |
| <b>Genus</b>  |                              |                           |                           |                    |                                |
| k_bacteria.p_firmicutes.c_erysipelotrichi.o_erysipelotrichales.f_erysipelotrichaceae.g_eubacterium. | 0.3926058                    | 0.1501225                 | 0.6350890                 | 0.0015067          | 0.0561251                      |
| k_bacteria.p_firmicutes.c_clostridia.o_clostridiales.f_veillonellaceae.g_megasphaera                | 0.4000827                    | 0.1225438                 | 0.6776217                 | 0.0047227          | 0.1115318                      |
| k_bacteria.p_bacteroidetes.c_bacteroidia.o_bacteroidales.f_bacteroidaceae.g_bacteroides             | 0.2107748                    | 0.0526031                 | 0.3689465                 | 0.0090070          | 0.1220036                      |
| k_bacteria.p_firmicutes.c_clostridia.o_clostridiales.f_lachnospiraceae.g_clostridium                | 0.3454360                    | 0.0502793                 | 0.6405927                 | 0.0217997          | 0.2512768                      |
| k_bacteria.p_firmicutes.c_clostridia.o_clostridiales.f_veillonellaceae.g_veillonella                | 0.2136555                    | 0.0111645                 | 0.4161465                 | 0.0386374          | 0.3598107                      |

Only those with pooled p-values <0.05 are shown. OR: odds ratio; FDR: false discovery rate.

**Supplementary table 3. Meta-analysis of five studies that included a non-breastfeeding group: gut bacterial taxa with trend in relative abundance across exclusive breastfeeding, non-exclusive breastfeeding and non-breastfeeding groups.**

| Bacterial taxa   | Pooled estimate<br>(log(OR)) | 95% Pooled lower limit | 95% Pooled upper limit | Pooled p-value | FDR adjusted p-value |
|--|------------------------------|------------------------|------------------------|----------------|----------------------|
| <b>Phylum</b>  |                              |                        |                        |                |                      |
| k_bacteria.p_firmicutes  | 0.2891066                    | 0.1303173              | 0.4478959              | 0.0003590      | 0.0021542            |
| k_bacteria.p_verrucomicrobia   | 0.1902821                    | 0.0337017              | 0.3468625              | 0.0172274      | 0.0516822            |
| k_bacteria.p_bacteroidetes   | 0.2156141                    | 0.0236994              | 0.4075287              | 0.0276654      | 0.0553308            |
| <b>Order</b>   |                              |                        |                        |                |                      |
| k_bacteria.p_firmicutes.c_clostridia.o_clostridiales   | 0.3924806                    | 0.2685252              | 0.5164361              | 0.0000000      | 0.0000000            |
| k_bacteria.p_actinobacteria.c_coriobacteria.o_coriobacteriales   | 0.3158688                    | 0.2090123              | 0.4227252              | 0.0000000      | 0.0000001            |
| k_bacteria.p_proteobacteria.c_gammaproteobacteria.o_pasteurellales                                       | -0.2179258                   | -0.3444131             | -0.0914384             | 0.0007333      | 0.0045218            |
| k_bacteria.p_firmicutes.c_bacilli.o_bacillales   | -0.1731560                   | -0.2757578             | -0.0705541             | 0.0009405      | 0.0049715            |
| k_bacteria.p_verrucomicrobia.c_verrucomicrobiae.o_verrucomicrobiales                                     | 0.1902859                    | 0.0337055              | 0.3468662              | 0.0172252      | 0.0637414            |
| k_bacteria.p_bacteroidetes.c_bacteroidia.o_bacteroidales   | 0.2299773                    | 0.0174714              | 0.4424833              | 0.0339130      | 0.0965217            |
| k_bacteria.p_firmicutes.c_erysipelotrichi.o_erysipelotrichales   | 0.1976105                    | 0.0098243              | 0.3853966              | 0.0391599      | 0.0965944            |
| <b>Family</b>  |                              |                        |                        |                |                      |
| k_bacteria.p_actinobacteria.c_coriobacteriia.o_coriobacteriales.f_coriobacteriaceae                      | 0.3158688                    | 0.2090123              | 0.4227252              | 0.0000000      | 0.0000001            |
| k_bacteria.p_proteobacteria.c_gammaproteobacteria.o_pasteurellales.f_pasteurellaceae                     | -0.2179258                   | -0.3444131             | -0.0914384             | 0.0007333      | 0.0069659            |
| k_bacteria.p_firmicutes.c_bacilli.o_bacillales.f_staphylococcaceae                                       | -0.1841218                   | -0.3014937             | -0.0667498             | 0.0021078      | 0.0160195            |
| k_bacteria.p_firmicutes.c_clostridia.o_clostridiales.f_peptostreptococcaceae                             | 0.1890903                    | 0.0485738              | 0.3296068              | 0.0083523      | 0.0577070            |
| k_bacteria.p_verrucomicrobia.c_verrucomicrobiae.o_verrucomicrobiales.f_verrucomicrobiaceae               | 0.1902859                    | 0.0337055              | 0.3468662              | 0.0172252      | 0.0872855            |
| k_bacteria.p_firmicutes.c_clostridia.o_clostridiales.f_ruminococcaceae                                   | 0.2044635                    | 0.0329990              | 0.3759280              | 0.0194305      | 0.0922951            |
| k_bacteria.p_firmicutes.c_clostridia.o_clostridiales.f_clostridiaceae                                    | 0.1418926                    | 0.0111478              | 0.2726374              | 0.0334136      | 0.1233860            |
| k_bacteria.p_firmicutes.c_clostridia.o_clostridiales.f_lachnospiraceae                                   | 0.3387166                    | 0.0254162              | 0.6520170              | 0.0340935      | 0.1233860            |
| k_bacteria.p_firmicutes.c_erysipelotrichi.o_erysipelotrichales.f_erysipelotrichaceae                     | 0.1976105                    | 0.0098243              | 0.3853966              | 0.0391599      | 0.1240064            |
| <b>Genus</b>   |                              |                        |                        |                |                      |
| k_bacteria.p_firmicutes.c_clostridia.o_clostridiales.f_lachnospiraceae.g_coprococcus                     | 0.3299376                    | 0.3175133              | 0.3423619              | 0.0000000      | 0.0000000            |
| k_bacteria.p_firmicutes.c_clostridia.o_clostridiales.f_lachnospiraceae.g_blautia                         | 0.3815612                    | 0.2505508              | 0.5125716              | 0.0000000      | 0.0000002            |
| k_bacteria.p_firmicutes.c_erysipelotrichi.o_erysipelotrichales.f_erysipelotrichaceae.g_eubacterium       | 0.3803923                    | 0.2260221              | 0.5347626              | 0.0000014      | 0.0000255            |
| k_bacteria.p_firmicutes.c_clostridia.o_clostridiales.f_lachnospiraceae.g                                 | 0.3369517                    | 0.1837122              | 0.4901911              | 0.0000163      | 0.0002707            |
| k_bacteria.p_proteobacteria.c_gammaproteobacteria.o_pasteurellales.f_pasteurellaceae.g_haemophilus       | -0.2280437                   | -0.3559103             | -0.1001770             | 0.0004732      | 0.0064094            |
| k_bacteria.p_firmicutes.c_bacilli.o_bacillales.f_staphylococcaceae.g_staphylococcus                      | -0.1829793                   | -0.2994629             | -0.0664956             | 0.0020782      | 0.0196292            |
| k_bacteria.p_verrucomicrobia.c_verrucomicrobiae.o_verrucomicrobiales.f_verrucomicrobiaceae.g_akkermansia | 0.1907668                    | 0.0341859              | 0.3473478              | 0.0169460      | 0.1166765            |
| k_bacteria.p_firmicutes.c_clostridia.o_clostridiales.f_peptostreptococcaceae.g                           | 0.2910458                    | 0.0146875              | 0.5674042              | 0.0390054      | 0.1823383            |

Five studies included are Bangladesh, Canada, USA (California-Massachusetts –Missouri), USA (North Carolina).

In each study, to test for trend across breastfeeding categories, breastfeeding was coded as a continuous variable in the model (exclusive breastfeeding (EBF)=1, non-EBF=2 and non-BF=3).

Only those with pooled p-values <0.05 are shown. OR: odds ratio; FDR: false discovery rate.

**Supplementary table 4. Sensitivity analysis (meta-analysis of six studies without data from North Carolina study): gut bacterial taxa with differential relative abundances between non-exclusively breastfed vs. exclusively breastfed infants ≤6 months of age.**

| Bacterial taxa  | Pooled estimate<br>(log(OR)) | 95% lower limit | 95% upper limit | Pooled p-value | FDR adjusted pooled p-value |
|---|------------------------------|-----------------|-----------------|----------------|-----------------------------|
| <b>Phylum</b>   |                              |                 |                 |                |                             |
| k_bacteria.p_firmicutes   | 0.2469023                    | 0.1112786       | 0.3825259       | 0.0003596      | 0.0025170                   |
| k_bacteria.p_bacteroidetes  | 0.1932696                    | 0.0435804       | 0.3429588       | 0.0113872      | 0.0398552                   |
| <b>Order</b>  |                              |                 |                 |                |                             |
| k_bacteria.p_firmicutes.c_clostridia.o_clostridiales  | 0.2819748                    | 0.1076835       | 0.4562662       | 0.0015197      | 0.0233017                   |
| k_bacteria.p_bacteroidetes.c_bacteroidia.o_bacteroidales  | 0.1953538                    | 0.0454767       | 0.3452308       | 0.0106289      | 0.0873019                   |
| k_bacteria.p_firmicutes.c_erysipelotrichi.o_erysipelotrichales                                      | 0.1990864                    | 0.0209516       | 0.3772211       | 0.0284888      | 0.1638107                   |
| <b>Family</b>   |                              |                 |                 |                |                             |
| k_bacteria.p_bacteroidetes.c_bacteroidia.o_bacteroidales.f_bacteroidaceae                           | 0.1947860                    | 0.0349794       | 0.3545925       | 0.0168956      | 0.2092121                   |
| k_bacteria.p_firmicutes.c_clostridia.o_clostridiales.f_veillonellaceae                              | 0.2232183                    | 0.0388955       | 0.4075410       | 0.0176179      | 0.2092121                   |
| k_bacteria.p_firmicutes.c_erysipelotrichi.o_erysipelotrichales.f_erysipelotrichaceae                | 0.1990864                    | 0.0209516       | 0.3772211       | 0.0284888      | 0.2460398                   |
| <b>Genus</b>  |                              |                 |                 |                |                             |
| k_bacteria.p_firmicutes.c_erysipelotrichi.o_erysipelotrichales.f_erysipelotrichaceae.g_eubacterium. | 0.3970460                    | 0.1469758       | 0.6471162       | 0.0018588      | 0.0887585                   |
| k_bacteria.p_firmicutes.c_clostridia.o_clostridiales.f_veillonellaceae.g_megasphaera                | 0.4000827                    | 0.1225438       | 0.6776217       | 0.0047227      | 0.1804084                   |
| k_bacteria.p_firmicutes.c_clostridia.o_clostridiales.f_clostridiaceae.g                             | 0.2425407                    | 0.0576242       | 0.4274571       | 0.0101483      | 0.2416618                   |
| k_bacteria.p_bacteroidetes.c_bacteroidia.o_bacteroidales.f_bacteroidaceae.g_bacteroides             | 0.1947860                    | 0.0349794       | 0.3545925       | 0.0168956      | 0.2804176                   |
| k_bacteria.p_firmicutes.c_clostridia.o_clostridiales.f_lachnospiraceae.g_clostridium                | 0.3454360                    | 0.0502793       | 0.6405927       | 0.0217997      | 0.3202883                   |

Only those with pooled p-values <0.05 are shown. OR: odds ratio; FDR: false discovery rate.

**Supplementary table 5. Sensitivity analysis (meta-analysis of six studies without data from Haiti study): gut bacterial taxa with differential relative abundances between non-exclusively breastfed vs. exclusively breastfed infants ≤6 months of age.**

| Bacterial taxa  | Pooled estimate<br>(log(OR)) | 95% Pooled lower limit | 95% Pooled upper limit | Pooled p-value | FDR adjusted p-value |
|---|------------------------------|------------------------|------------------------|----------------|----------------------|
| <b>Phylum</b>   |                              |                        |                        |                |                      |
| k_bacteria.p_firmicutes   | 0.2585644                    | 0.1214765              | 0.3956523              | 0.0002184      | 0.0013104            |
| k_bacteria.p_bacteroidetes  | 0.2137713                    | 0.0628560              | 0.3646866              | 0.0054984      | 0.0164951            |
| <b>Order</b>  |                              |                        |                        |                |                      |
| k_bacteria.p_firmicutes.c_clostridia.o_clostridiales  | 0.3197985                    | 0.1809883              | 0.4586087              | 0.0000063      | 0.0001200            |
| k_bacteria.p_bacteroidetes.c_bacteroidia.o_bacteroidales  | 0.2201357                    | 0.0691242              | 0.3711471              | 0.0042750      | 0.0324902            |
| k_bacteria.p_firmicutes.c_erysipelotrichi.o_erysipelotrichales                                      | 0.1839766                    | 0.0046213              | 0.3633320              | 0.0443820      | 0.2108145            |
| <b>Family</b>   |                              |                        |                        |                |                      |
| k_bacteria.p_bacteroidetes.c_bacteroidia.o_bacteroidales.f_bacteroidaceae                           | 0.2061111                    | 0.0448325              | 0.3673898              | 0.0122521      | 0.1347734            |
| k_bacteria.p_firmicutes.c_clostridia.o_clostridiales.f_veillonellaceae                              | 0.2060989                    | 0.0161050              | 0.3960927              | 0.0334947      | 0.2946724            |
| k_bacteria.p_firmicutes.c_erysipelotrichi.o_erysipelotrichales.f_erysipelotrichaceae                | 0.1839766                    | 0.0046213              | 0.3633320              | 0.0443820      | 0.2946724            |
| k_bacteria.p_firmicutes.c_clostridia.o_clostridiales.f_clostridiaceae                               | 0.1733438                    | 0.0031382              | 0.3435495              | 0.0459230      | 0.2946724            |
| <b>Genus</b>  |                              |                        |                        |                |                      |
| k_bacteria.p_firmicutes.c_clostridia.o_clostridiales.f_veillonellaceae.g_megasphaera                | 0.4521725                    | 0.1543202              | 0.7500249              | 0.0029257      | 0.1062738            |
| k_bacteria.p_firmicutes.c_erysipelotrichi.o_erysipelotrichales.f_erysipelotrichaceae.g_eubacterium. | 0.3594531                    | 0.1051810              | 0.6137251              | 0.0055934      | 0.1062738            |
| k_bacteria.p_bacteroidetes.c_bacteroidia.o_bacteroidales.f_bacteroidaceae.g_bacteroides             | 0.2061111                    | 0.0448325              | 0.3673898              | 0.0122521      | 0.1862323            |
| k_bacteria.p_firmicutes.c_clostridia.o_clostridiales.f_lachnospiraceae.g_clostridium                | 0.3557799                    | 0.0575687              | 0.6539911              | 0.0193702      | 0.2676612            |
| k_bacteria.p_firmicutes.c_clostridia.o_clostridiales.f_lachnospiraceae.g_coprococcus                | 0.5201042                    | 0.0494691              | 0.9907393              | 0.0303128      | 0.3839625            |
| k_bacteria.p_firmicutes.c_clostridia.o_clostridiales.f_clostridiaceae.g                             | 0.5344090                    | 0.0275369              | 1.0412811              | 0.0387867      | 0.3877940            |

Only those with pooled p-values <0.05 are shown. OR: odds ratio; FDR: false discovery rate.

**Supplementary table 6. Sensitivity analysis (meta-analysis of six studies without data from VDAART trial (USA(California- Massachusetts-Missouri)) study): gut bacterial taxa with differential relative abundances between non-exclusively breastfed vs. exclusively breastfed infants ≤6 months of age.**

| Bacterial taxa   | Pooled estimate<br>(log(OR)) | 95% lower limit | 95% upper limit | Pooled p-value | FDR<br>adjusted<br>pooled p-value |
|--|------------------------------|-----------------|-----------------|----------------|-----------------------------------|
| <b>Phylum</b>  |                              |                 |                 |                |                                   |
| k_bacteria.p_bacteroidetes   | 0.2312551                    | 0.0724455       | 0.3900646       | 0.0043165      | 0.0250675                         |
| k_bacteria.p_firmicutes  | 0.2006141                    | 0.0544015       | 0.3468267       | 0.0071621      | 0.0250675                         |
| <b>Order</b>   |                              |                 |                 |                |                                   |
| k_bacteria.p_bacteroidetes.c_bacteroidia.o_bacteroidales   | 0.2337644                    | 0.0747312       | 0.3927975       | 0.0039645      | 0.0549097                         |
| k_bacteria.p_firmicutes.c_clostridia.o_clostridiales   | 0.2968923                    | 0.0814516       | 0.5123329       | 0.0069138      | 0.0549097                         |
| k_bacteria.p_actinobacteria.c_actinobacteria.o_actinomycetales                                     | -0.1557879                   | -0.2820518      | -0.0295239      | 0.0155951      | 0.1024820                         |
| k_bacteria.p_firmicutes.c_erysipelotrichi.o_erysipelotrichales                                     | 0.2117009                    | 0.0169663       | 0.4064356       | 0.0331117      | 0.1692374                         |
| k_bacteria.p_firmicutes.c_bacilli.o_bacillales   | -0.2108602                   | -0.4147961      | -0.0069242      | 0.0427125      | 0.1964774                         |
| <b>Family</b>  |                              |                 |                 |                |                                   |
| k_bacteria.p_firmicutes.c_clostridia.o_clostridiales.f_veillonellaceae                             | 0.2996094                    | 0.1543601       | 0.4448586       | 0.0000528      | 0.0050161                         |
| k_bacteria.p_bacteroidetes.c_bacteroidia.o_bacteroidales.f_bacteroidaceae                          | 0.2375149                    | 0.0668422       | 0.4081877       | 0.0063804      | 0.0850503                         |
| k_bacteria.p_firmicutes.c_erysipelotrichi.o_erysipelotrichales.f_erysipelotrichaceae               | 0.2117009                    | 0.0169663       | 0.4064356       | 0.0331117      | 0.2621341                         |
| <b>Genus</b>   |                              |                 |                 |                |                                   |
| k_bacteria.p_firmicutes.c_clostridia.o_clostridiales.f_veillonellaceae.g_acidaminococcus           | 2.0640609                    | 0.9347797       | 3.1933421       | 0.0003405      | 0.0306461                         |
| k_bacteria.p_firmicutes.c_erysipelotrichi.o_erysipelotrichales.f_erysipelotrichaceae.g_eubacterium | 0.4120255                    | 0.1449526       | 0.6790984       | 0.0024968      | 0.1074319                         |
| k_bacteria.p_firmicutes.c_clostridia.o_clostridiales.f_veillonellaceae.g_megasphaera               | 0.4531996                    | 0.1359269       | 0.7704723       | 0.0051157      | 0.1074319                         |
| k_bacteria.p_bacteroidetes.c_bacteroidia.o_bacteroidales.f_bacteroidaceae.g_bacteroides            | 0.2375149                    | 0.0668422       | 0.4081877       | 0.0063804      | 0.1074319                         |
| k_bacteria.p_firmicutes.c_clostridia.o_clostridiales.f_veillonellaceae.g_veillonella               | 0.2611018                    | 0.0483038       | 0.4738997       | 0.0161785      | 0.2080092                         |
| k_bacteria.p_firmicutes.c_clostridia.o_clostridiales.f_lachnospiraceae.g_clostridium               | 0.3454360                    | 0.0502793       | 0.6405927       | 0.0217997      | 0.2615967                         |
| k_bacteria.p_firmicutes.c_clostridia.o_clostridiales.f_lachnospiraceae.g_coprococcus               | 0.5470330                    | 0.0429329       | 1.0511331       | 0.0334293      | 0.3166986                         |

Only those with pooled p-values <0.05 are shown. OR: odds ratio; FDR: false discovery rate.

**Supplementary table 7. Meta-analysis stratified by mode of delivery: gut bacterial taxa with differential relative abundances between non-exclusively breastfed vs. exclusively breastfed infants ≤6 months of age.**

|  | Pooled estimate (log(OR)) | 95% Pooled lower limit | 95% Pooled upper limit | Pooled p-value | FDR adjusted pooled p-value |
|--|---------------------------|------------------------|------------------------|----------------|-----------------------------|
| <b>Vaginally born infants</b>  |                           |                        |                        |                |                             |
| Phylum   |                           |                        |                        |                |                             |
| k_bacteria.p_proteobacteria  | -0.3069577                | -0.5063356             | -0.1075798             | 0.0025486      | 0.0178399                   |
| Order  |                           |                        |                        |                |                             |
| k_bacteria.p_proteobacteria.c_gammaproteobacteria.o_enterobacteriales                                  | -0.2990541                | -0.5096705             | -0.0884377             | 0.0053867      | 0.1158139                   |
| k_bacteria.p_firmicutes.c_erysipelotrichi.o_erysipelotrichales   | 0.2827724                 | 0.0412747              | 0.5242700              | 0.0217363      | 0.2336654                   |
| Family   |                           |                        |                        |                |                             |
| k_bacteria.p_firmicutes.c_bacilli.o_bacillales.f_staphylococcaceae                                     | -0.3327091                | -0.5628181             | -0.1026001             | 0.0045989      | 0.1157163                   |
| k_bacteria.p_proteobacteria.c_gammaproteobacteria.o_enterobacteriales.f_enterobacteriaceae             | -0.2990541                | -0.5096705             | -0.0884377             | 0.0053867      | 0.1157163                   |
| k_bacteria.p_bacteroidetes.c_bacteroidia.o_bacteroidales.f_bacteroidaceae                              | 0.3016820                 | 0.0849923              | 0.5183717              | 0.0063580      | 0.1157163                   |
| k_bacteria.p_firmicutes.c_clostridia.o_clostridiales.f_eubacteriaceae                                  | 0.8045605                 | 0.1891515              | 1.4199695              | 0.0103958      | 0.1576704                   |
| k_bacteria.p_firmicutes.c_erysipelotrichi.o_erysipelotrichales.f_erysipelotrichaceae                   | 0.2827724                 | 0.0412747              | 0.5242700              | 0.0217363      | 0.2197783                   |
| Genus  |                           |                        |                        |                |                             |
| k_bacteria.p_firmicutes.c_clostridia.o_clostridiales.f_veillonellaceae.g_acidaminococcus               | 3.3685160                 | 2.5257196              | 4.2113123              | 0.0000000      | 0.0000000                   |
| k_bacteria.p_firmicutes.c_bacilli.o_bacillales.f_staphylococcaceae.g_staphylococcus                    | -0.3330596                | -0.5631799             | -0.1029393             | 0.0045581      | 0.1176238                   |
| k_bacteria.p_firmicutes.c_clostridia.o_clostridiales.f_eubacteriaceae.g_pseudoramibacter_eubacterium   | 0.8762232                 | 0.2572683              | 1.4951780              | 0.0055266      | 0.1176238                   |
| k_bacteria.p_firmicutes.c_clostridia.o_clostridiales.f_lachnospiraceae.g_                              | 0.3180415                 | 0.0899972              | 0.5460858              | 0.0062673      | 0.1176238                   |
| k_bacteria.p_bacteroidetes.c_bacteroidia.o_bacteroidales.f_bacteroidaceae.g_bacteroides                | 0.3016820                 | 0.0849923              | 0.5183717              | 0.0063580      | 0.1176238                   |
| k_bacteria.p_firmicutes.c_erysipelotrichi.o_erysipelotrichales.f_erysipelotrichaceae.g_eubacterium.    | 0.5384916                 | 0.1412408              | 0.9357425              | 0.0078881      | 0.1326643                   |
| k_bacteria.p_proteobacteria.c_gammaproteobacteria.o_enterobacteriales.f_enterobacteriaceae.g_          | -0.2862286                | -0.5112532             | -0.0612040             | 0.0126651      | 0.1802335                   |
| k_bacteria.p_firmicutes.c_clostridia.o_clostridiales.f_clostridiaceae.g_                               | 0.3027671                 | 0.0599398              | 0.5455944              | 0.0145349      | 0.1920686                   |
| k_bacteria.p_proteobacteria.c_gammaproteobacteria.o_pasteurellales.f_pasteurellaceae.g_aggregatibacter | 0.5722694                 | 0.0867128              | 1.0578260              | 0.0208891      | 0.2234010                   |
| k_bacteria.p_firmicutes.c_bacilli.o_lactobacillales.f_streptococcaceae.g_lactococcus                   | 0.5835624                 | 0.0588868              | 1.1082381              | 0.0292619      | 0.2849187                   |
| k_bacteria.p_firmicutes.c_clostridia.o_clostridiales.f_lachnospiraceae.g_blautia                       | 0.3639237                 | 0.0015626              | 0.7262849              | 0.0490202      | 0.4534368                   |
| <b>C-section born infants</b>  |                           |                        |                        |                |                             |
| Phylum   |                           |                        |                        |                |                             |
| k_bacteria.p_proteobacteria  | -0.719666                 | -1.054589              | -0.3847433             | 2.54e-05       | 0.0001522                   |
| Order  |                           |                        |                        |                |                             |
| k_bacteria.p_proteobacteria.c_gammaproteobacteria.o_enterobacteriales                                  | -0.5794373                | -1.034968              | -0.1239071             | 0.0126638      | 0.1561867                   |
| Family   |                           |                        |                        |                |                             |
| k_bacteria.p_proteobacteria.c_gammaproteobacteria.o_enterobacteriales.f_enterobacteriaceae             | -0.5794373                | -1.034968              | -0.1239071             | 0.0126638      | 0.2596077                   |
| Genus  |                           |                        |                        |                |                             |
| k_bacteria.p_proteobacteria.c_gammaproteobacteria.o_enterobacteriales.f_enterobacteriaceae.g_proteus   | -0.2578897                | -0.2595351             | -0.2562442             | 0.0000000      | 0.0000000                   |
| k_bacteria.p_firmicutes.c_clostridia.o_clostridiales.f_ruminococcaceae.g_anerotruncus                  | -2.9244379                | -4.3083283             | -1.5405475             | 0.0000345      | 0.0018723                   |
| k_bacteria.p_firmicutes.c_clostridia.o_clostridiales.f_veillonellaceae.g_phascolarctobacterium         | -1.8840686                | -3.5632478             | -0.2048894             | 0.0278698      | 0.6489685                   |
| k_bacteria.p_proteobacteria.c_gammaproteobacteria.o_enterobacteriales.f_enterobacteriaceae.g_          | -0.5225859                | -1.0338148             | -0.0113570             | 0.0451232      | 0.9153914                   |

Four studies included are Canada, Haiti, USA (California-Florida), USA (California-Massachusetts -Missouri).

Only those with pooled p-values <0.05 are shown. OR: odds ratio; FDR: false discovery rate.

**Supplementary table 8. Meta-analysis of all seven included studies: gut bacterial KEGG (Kyoto Encyclopedia of Genes and Genomes) pathways with differential relative abundances between non-exclusively breastfed vs. exclusively breastfed infants ≤6 months of age.**

| KEGG pathway   | Pooled estimate<br>(log(OR)) | 95% Pooled<br>lower limit | 95% Pooled<br>upper limit | Pooled p-<br>value | FDR adjusted<br>pooled p-value |
|--|------------------------------|---------------------------|---------------------------|--------------------|--------------------------------|
| <b>Level 2 KEGG pathway</b>  |                              |                           |                           |                    |                                |
| Environmental.Information.Processing.Signaling.Molecules.and.Interaction                   | -0.0478456                   | -0.0816924                | -0.0139989                | 0.0055954          | 0.1412268                      |
| Genetic.Information.Processing.Transcription   | 0.0159685                    | 0.0042371                 | 0.0276999                 | 0.0076339          | 0.1412268                      |
| Metabolism.Carbohydrate.Metabolism   | 0.0139464                    | 0.0014303                 | 0.0264625                 | 0.0289665          | 0.3572540                      |
| <b>Level 3 KEGG pathway</b>  |                              |                           |                           |                    |                                |
| Metabolism.Carbohydrate.Metabolism.Fructose.and.mannose.metabolism                         | 0.0780373                    | 0.0480195                 | 0.1080552                 | 0.0000003          | 0.0000776                      |
| Cellular.Processes.Transport.and.Catabolism.Peroxisome                                     | -0.0635099                   | -0.0926066                | -0.0344132                | 0.0000189          | 0.0021023                      |
| Metabolism.Lipid.Metabolism.Fatty.acid.metabolism  | -0.0890548                   | -0.1367181                | -0.0413915                | 0.0002502          | 0.0186004                      |
| Metabolism.Carbohydrate.Metabolism.Pentose.and.glucuronate.interconversions                | 0.0635666                    | 0.0267088                 | 0.1004244                 | 0.0007242          | 0.0376660                      |
| Metabolism.Lipid.Metabolism.Fatty.acid.biosynthesis  | 0.0432479                    | 0.0178524                 | 0.0686434                 | 0.0008445          | 0.0376660                      |
| Metabolism.Metabolism.of.Cofactors.and.Vitamins.Vitamin.B6.metabolism                      | -0.0294861                   | -0.0471238                | -0.0118484                | 0.0010506          | 0.0390489                      |
| Metabolism.Metabolism.of.Terpenoids.and.Polyketides.Biosynthesis.of.ansamycins             | 0.0780705                    | 0.0302201                 | 0.1259209                 | 0.0013849          | 0.0441177                      |
| Metabolism.Carbohydrate.Metabolism.Pentose.phosphate.pathway                               | 0.0366342                    | 0.0132619                 | 0.0600064                 | 0.0021256          | 0.0592523                      |
| Genetic.Information.Processing.Translation.Ribosome.biogenesis.in.eukaryotes               | -0.0704462                   | -0.1184532                | -0.0224392                | 0.0040265          | 0.0997667                      |
| Organismal.Systems.Endocrine.System.Adipocytokine.signaling.pathway                        | -0.1169978                   | -0.1983953                | -0.0356003                | 0.0048447          | 0.1080375                      |
| Genetic.Information.Processing.Replication.and.Repair.Base.excision.repair                 | 0.0146276                    | 0.0042334                 | 0.0250219                 | 0.0058118          | 0.1178214                      |
| Metabolism.Xenobiotics.Biodegradation.and.Metabolism.Xylene.degradation                    | -0.0445734                   | -0.0793754                | -0.0097713                | 0.0120642          | 0.2193890                      |
| Metabolism.Energy.Metabolism.Carbon.fixation.in.photosynthetic.organisms                   | 0.0319173                    | 0.0067487                 | 0.0570858                 | 0.0129367          | 0.2193890                      |
| Metabolism.Xenobiotics.Biodegradation.and.Metabolism.Drug.metabolism..other.enzymes        | 0.0324960                    | 0.0066382                 | 0.0583538                 | 0.0137733          | 0.2193890                      |
| Unclassified.Genetic.Information.Processing.Protein.folding.and.associated.processing      | -0.0115250                   | -0.0213113                | -0.0017387                | 0.0209884          | 0.3120277                      |
| Metabolism.Metabolism.of.Cofactors.and.Vitamins.Nicotinate.and.nicotinamide.metabolism     | -0.0318195                   | -0.0594972                | -0.0036917                | 0.0266094          | 0.3292788                      |
| Unclassified.Cellular.Processes.and.Signalng.Inorganic.ion.transport.and.metabolism        | -0.0739734                   | -0.1399827                | -0.0079640                | 0.0280609          | 0.3292788                      |
| Organismal.Systems.Endocrine.System.Insulin.signaling.pathway                              | 0.0591499                    | 0.0061849                 | 0.1121149                 | 0.0286089          | 0.3292788                      |
| Metabolism.Carbohydrate.Metabolism.Amino.sugar.and.nucleotide.sugar.metabolism             | 0.0288516                    | 0.0025510                 | 0.0551522                 | 0.0315495          | 0.3292788                      |
| Metabolism.Metabolism.of.Other.Amino.Acids.D.Alanine.metabolism                            | 0.0213783                    | 0.0018603                 | 0.0408964                 | 0.0318118          | 0.3292788                      |
| Metabolism.Xenobiotics.Biodegradation.and.Metabolism.Drug.metabolism..cytochrome.P450      | -0.1002695                   | -0.1922416                | -0.0082974                | 0.0326155          | 0.3292788                      |
| Metabolism.Xenobiotics.Biodegradation.and.Metabolism.Toluene.degradation                   | -0.0711149                   | -0.1367550                | -0.0054749                | 0.0337170          | 0.3292788                      |
| Metabolism.Lipid.Metabolism.Glycerolipid.metabolism  | 0.0348521                    | 0.0026390                 | 0.0670653                 | 0.0339615          | 0.3292788                      |
| Metabolism.Glycan.Biosynthesis.and.Metabolism.Glycosphingolipid.biosynthesis..globo.series | 0.0801427                    | 0.0014571                 | 0.1588283                 | 0.0459058          | 0.4265416                      |

Only those with pooled p-values <0.05 are shown. OR: odds ratio; FDR: false discovery rate.

**Supplementary table 9. Sensitivity analysis (meta-analysis of included studies without data from either North Carolina, Haiti or VDAART trial (USA(CA-MA-MO)) study): gut bacterial KEGG (Kyoto Encyclopedia of Genes and Genomes) pathways at level 3 with differential relative abundances between non-exclusively breastfed vs. exclusively breastfed infants ≤6 months of age.**

**Level 3 KEGG pathways**

|   | Pooled estimate<br>(log(OR)) | 95% lower limit | 95% upper limit | Pooled p-value | FDR adjusted pooled p-value |
|---|------------------------------|-----------------|-----------------|----------------|-----------------------------|
| <b>Meta-analysis without North Carolina data</b>  |                              |                 |                 |                |                             |
| Metabolism..Carbohydrate.Metabolism..Fructose.and.mannose.metabolism                                | 0.0748047                    | 0.0447254       | 0.1048841       | 0.0000011      | 0.0002468                   |
| Cellular.Processes..Transport.and.Catabolism..Peroxisome  | -0.0634911                   | -0.0928925      | -0.0340896      | 0.0000231      | 0.0026121                   |
| Metabolism..Lipid.Metabolism..Fatty.acid.metabolism   | -0.0862183                   | -0.1365700      | -0.0358667      | 0.0007905      | 0.0595520                   |
| Genetic.Information.Processing..Replication.and.Repair..Base.excision.repair                        | 0.0170264                    | 0.0062925       | 0.0277602       | 0.0018775      | 0.0874960                   |
| Metabolism..Carbohydrate.Metabolism..Pentose.and.glucuronate.interconversions                       | 0.0618250                    | 0.0223944       | 0.1012557       | 0.0021184      | 0.0874960                   |
| Metabolism..Metabolism.of.Terpenoids.and.Polyketides..Biosynthesis.of.ansamycins                    | 0.0758176                    | 0.0270245       | 0.1246108       | 0.0023229      | 0.0874960                   |
| Metabolism..Metabolism.of.Cofactors.and.Vitamins..Vitamin.B6.metabolism                             | -0.0286169                   | -0.0474861      | -0.0097477      | 0.0029542      | 0.0953784                   |
| Metabolism..Lipid.Metabolism..Fatty.acid.biosynthesis   | 0.0415976                    | 0.0133905       | 0.0698047       | 0.0038475      | 0.1004504                   |
| Genetic.Information.Processing..Translation..Ribosome.biogenesis.in.eukaryotes                      | -0.0707846                   | -0.1189877      | -0.0225816      | 0.0040002      | 0.1004504                   |
| Metabolism..Carbohydrate.Metabolism..Pentose.phosphate.pathway                                      | 0.039486                     | 0.0098585       | 0.0580387       | 0.0057441      | 0.1298157                   |
| Metabolism..Metabolism.of.Other.Amino.Acids..D.Alanine.metabolism                                   | 0.0230465                    | 0.0032242       | 0.0428689       | 0.0226811      | 0.4659945                   |
| Unclassified..Genetic.Information.Processing..Protein.folding.and.associated.processing             | -0.0110941                   | -0.0209256      | -0.0012625      | 0.0269906      | 0.5077651                   |
| Metabolism..Xenobiotics.Biodegradation.and.Metabolism..Drug.metabolism...other.enzymes              | 0.0306056                    | 0.0026166       | 0.0585946       | 0.0320978      | 0.5077651                   |
| Organismal.Systems..Endocrine.System..Adipocytokine.signaling.pathway                               | -0.1040949                   | -0.208994       | -0.0072905      | 0.0350680      | 0.5077651                   |
| Metabolism..Energy.Metabolism..Carbon.fixation.in.photosynthetic.organisms                          | 0.0263807                    | 0.0017639       | 0.0509975       | 0.0356934      | 0.5077651                   |
| Metabolism..Xenobiotics.Biodegradation.and.Metabolism..Drug.metabolism...cytochrome.P450            | -0.0998941                   | -0.1932373      | -0.0065509      | 0.0359480      | 0.5077651                   |
| Human.Diseases..Infectious.Diseases..Epithelial.cell.signalizing.in.Helicobacter.pylori.infection   | 0.0476778                    | 0.0018550       | 0.0935006       | 0.0414192      | 0.5377872                   |
| Metabolism..Metabolism.of.Cofactors.and.Vitamins..Nicotinate.and.nicotinamide.metabolism            | -0.0310355                   | -0.0613386      | -0.0007324      | 0.0447142      | 0.5377872                   |
| Metabolism..Carbohydrate.Metabolism..Amino.sugar.and.nucleotide.sugar.metabolism                    | 0.0289152                    | 0.0001557       | 0.0576747       | 0.0487726      | 0.5377872                   |
| <b>Meta-analysis without Haiti data</b>   |                              |                 |                 |                |                             |
| Metabolism..Carbohydrate.Metabolism..Fructose.and.mannose.metabolism                                | 0.0806811                    | 0.0487659       | 0.1125964       | 0.0000007      | 0.0001622                   |
| Cellular.Processes..Transport.and.Catabolism..Peroxisome  | -0.0650783                   | -0.0945174      | -0.0356393      | 0.0000147      | 0.0016496                   |
| Metabolism..Lipid.Metabolism..Fatty.acid.metabolism   | -0.0946530                   | -0.1399040      | -0.0494021      | 0.0000414      | 0.0030885                   |
| Metabolism..Carbohydrate.Metabolism..Pentose.and.glucuronate.interconversions                       | 0.0606993                    | 0.0303662       | 0.1018323       | 0.0002883      | 0.0161472                   |
| Metabolism..Metabolism.of.Terpenoids.and.Polyketides..Biosynthesis.of.ansamycins                    | 0.0880979                    | 0.0392229       | 0.1369729       | 0.0004111      | 0.0184164                   |
| Metabolism..Carbohydrate.Metabolism..Pentose.phosphate.pathway                                      | 0.0397027                    | 0.0162125       | 0.0631929       | 0.0009240      | 0.0301535                   |
| Organismal.Systems..Environmental.Adaptation..Plant.pathogen.interaction                            | 0.0459717                    | 0.0187273       | 0.0732161       | 0.0009423      | 0.0301535                   |
| Metabolism..Lipid.Metabolism..Fatty.acid.biosynthesis   | 0.0443805                    | 0.0163880       | 0.0723729       | 0.0018873      | 0.0528452                   |
| Organismal.Systems..Endocrine.System..Adipocytokine.signaling.pathway                               | -0.1279232                   | -0.2107885      | -0.0450579      | 0.0024806      | 0.0617403                   |
| Genetic.Information.Processing..Translation..Ribosome.biogenesis.in.eukaryotes                      | -0.0721010                   | -0.1203080      | -0.0238213      | 0.0034224      | 0.0766609                   |
| Metabolism..Metabolism.of.Cofactors.and.Vitamins..Vitamin.B6.metabolism                             | -0.0291619                   | -0.0489563      | -0.0093676      | 0.0038831      | 0.0790743                   |
| Metabolism..Metabolism.of.Cofactors.and.Vitamins..Porphyrin.and.chlorophyll.metabolism              | 0.0626417                    | 0.0187615       | 0.1065219       | 0.0051425      | 0.0959931                   |
| Metabolism..Energy.Metabolism..Carbon.fixation.in.photosynthetic.organisms                          | 0.0364030                    | 0.0106170       | 0.0621889       | 0.0056584      | 0.0974979                   |
| Metabolism..Xenobiotics.Biodegradation.and.Metabolism..Drug.metabolism...other.enzymes              | 0.0353067                    | 0.0094477       | 0.0611657       | 0.0074497      | 0.1191955                   |
| Genetic.Information.Processing..Replication.and.Repair..Base.excision.repair                        | 0.0148692                    | 0.0035677       | 0.0261706       | 0.0099175      | 0.1481015                   |
| Metabolism..Metabolism.of.Cofactors.and.Vitamins..Biotin.metabolism                                 | 0.0443338                    | 0.0089842       | 0.0796835       | 0.0139677      | 0.1955472                   |
| Unclassified..Cellular.Processes.and.Signaling..Inorganic.ion.transport.and.metabolism              | -0.0854735                   | -0.1567790      | -0.0141680      | 0.0188039      | 0.2441364                   |
| Metabolism..Lipid.Metabolism..Glycerolipid.metabolism   | 0.0381790                    | 0.0061125       | 0.0702456       | 0.0196181      | 0.2441364                   |
| Metabolism..Xenobiotics.Biodegradation.and.Metabolism..Toluene.degradation                          | -0.0789239                   | -0.1468262      | -0.0110215      | 0.0227210      | 0.2625265                   |
| Metabolism..Xenobiotics.Biodegradation.and.Metabolism..Drug.metabolism...cytochrome.P450            | -0.1077738                   | -0.2009843      | -0.0145632      | 0.0234399      | 0.2625265                   |
| Organismal.Systems..Endocrine.System..Insulin.signaling.pathway                                     | 0.0604418                    | 0.0064843       | 0.1143993       | 0.0281278      | 0.2934589                   |
| Unclassified..Genetic.Information.Processing..Protein.folding.and.associated.processing             | -0.0110271                   | -0.0209143      | -0.0011398      | 0.0288219      | 0.2934589                   |
| Metabolism..Metabolism.of.Other.Amino.Acids..D.Alanine.metabolism                                   | 0.0214157                    | 0.0017453       | 0.0410862       | 0.0328537      | 0.3199669                   |
| Metabolism..Amino.Acid.Metabolism..Glycine..serine.and.threonine.metabolism                         | -0.0151926                   | -0.0293685      | -0.0010168      | 0.0356812      | 0.3248701                   |
| Metabolism..Metabolism.of.Cofactors.and.Vitamins..Nicotinate.and.nicotinamide.metabolism            | -0.0326563                   | -0.0633275      | -0.0019850      | 0.0369051      | 0.3248701                   |
| Metabolism..Xenobiotics.Biodegradation.and.Metabolism..Metabolism.of.xenobiotics.by.cytochrome.P450 | -0.0993704                   | -0.1935887      | -0.0051520      | 0.0387213      | 0.3248701                   |
| Genetic.Information.Processing..Translation..RNA.transport  | 0.0621342                    | 0.0030895       | 0.1211788       | 0.0391584      | 0.3248701                   |
| Metabolism..Metabolism.of.Terpenoids.and.Polyketides..Tetracycline biosynthesis                     | 0.0562197                    | 0.0010072       | 0.1114323       | 0.0459647      | 0.3514947                   |
| Genetic.Information.Processing..Folding..Sorting..Degradation..Proteasome                           | -0.0963819                   | -0.1913081      | -0.0014557      | 0.0465887      | 0.3514947                   |
| Human.Diseases..Infectious.Diseases..Epithelial.cell.signalizing.in.Helicobacter.pylori.infection   | 0.0458477                    | 0.0005050       | 0.0911903       | 0.0475022      | 0.3514947                   |
| Metabolism..Carbohydrate.Metabolism..Amino.sugar.and.nucleotide.sugar.metabolism                    | 0.0282869                    | 0.0001683       | 0.0564055       | 0.0486444      | 0.3514947                   |
| <b>Meta-analysis without VDAART trial (USA (CA-MA-MO)) data</b>                                     |                              |                 |                 |                |                             |
| Metabolism..Carbohydrate.Metabolism..Fructose.and.mannose.metabolism                                | 0.0695846                    | 0.0419821       | 0.0971870       | 0.0000008      | 0.0001757                   |
| Cellular.Processes..Transport.and.Catabolism..Peroxisome  | -0.0593738                   | -0.0905051      | -0.0282425      | 0.0001854      | 0.0209558                   |
| Metabolism..Xenobiotics.Biodegradation.and.Metabolism..Xylene.degradation                           | -0.0564881                   | -0.0932235      | -0.0197527      | 0.0025797      | 0.1577341                   |
| Metabolism..Lipid.Metabolism..Fatty.acid.metabolism   | -0.0893386                   | -0.1479559      | -0.0307213      | 0.0028156      | 0.1577341                   |
| Genetic.Information.Processing..Folding..Sorting.and.Degradation..Chaperones.and.folding.catalysts  | 0.0242035                    | 0.0078934       | 0.0405136       | 0.0036316      | 0.1577341                   |
| Genetic.Information.Processing..Translation..Ribosome.biogenesis.in.eukaryotes                      | -0.0711084                   | -0.1199190      | -0.0222978      | 0.0042993      | 0.1577341                   |
| Metabolism..Carbohydrate.Metabolism..Pentose.and.glucuronate.interconversions                       | 0.0503206                    | 0.0150873       | 0.0855539       | 0.0051223      | 0.1577341                   |
| Metabolism..Lipid.Metabolism..Fatty.acid.biosynthesis   | 0.0451811                    | 0.0132272       | 0.0771349       | 0.0055835      | 0.1577341                   |
| Metabolism..Metabolism.of.Terpenoids.and.Polyketides..Biosynthesis.of.ansamycins                    | 0.0717378                    | 0.0179408       | 0.1255348       | 0.0089596      | 0.2249850                   |
| Metabolism..Metabolism.of.Cofactors.and.Vitamins..Vitamin.B6.metabolism                             | -0.0243667                   | -0.0430052      | -0.0057281      | 0.0103977      | 0.2302045                   |
| Metabolism..Metabolism.of.Cofactors.and.Vitamins..Biotin.metabolism                                 | 0.0480086                    | 0.0106359       | 0.0853814       | 0.0118107      | 0.2302045                   |
| Metabolism..Carbohydrate.Metabolism..Pentose.phosphate.pathway                                      | 0.0334309                    | 0.0072805       | 0.0595814       | 0.0122232      | 0.2302045                   |
| Metabolism..Xenobiotics.Biodegradation.and.Metabolism..Drug.metabolism...other.enzymes              | 0.0381120                    | 0.0067842       | 0.0694399       | 0.0171069      | 0.2973962                   |
| Metabolism..Xenobiotics.Biodegradation.and.Metabolism..Chloroalkane.and.chloroalkane.degradation    | -0.04040491                  | -0.0807769      | -0.0073214      | 0.0187396      | 0.3025111                   |
| Genetic.Information.Processing..Replication.and.Repair..Base.excision.repair                        | 0.0136657                    | 0.0020258       | 0.0253056       | 0.0213877      | 0.3222407                   |
| Metabolism..Xenobiotics.Biodegradation.and.Metabolism..Drug.metabolism..cytochrome.P450             | -0.1047320                   | -0.2000359      | -0.0094280      | 0.0312515      | 0.4116602                   |

| Level 3 KEGG pathways   | Pooled estimate<br>(log(OR)) | 95% Pooled lower limit | 95% Pooled upper limit | Pooled p-value | adjusted pooled p-value | FDR |
|---|------------------------------|------------------------|------------------------|----------------|-------------------------|-----|
| Environmental.Information.Processing..Signal.Transduction..Phosphatidylinositol.signalng.system | 0.0181668                    | 0.0016186              | 0.0347150              | 0.0314231      | 0.4116602               |     |
| Metabolism..Energy.Metabolism..Carbon.fixation.in.photosynthetic.organisms                      | 0.0344968                    | 0.0028235              | 0.0661702              | 0.0327871      | 0.4116602               |     |
| Metabolism..Metabolism.of.Other.Amino.Acids..D.Alanine.metabolism                               | 0.0224208                    | 0.0014253              | 0.0434164              | 0.0363479      | 0.4323489               |     |
| Genetic.Information.Processing..Folding.Sorting.and.Degradation..Proteasome                     | -0.1014237                   | -0.1995265             | -0.0033209             | 0.0427329      | 0.4828817               |     |

Only those with pooled p-values <0.05 are shown. OR: odds ratio; FDR: false discovery rate.

**Supplementary table 10. Meta-analysis stratified by mode of delivery: gut bacterial KEGG (Kyoto Encyclopedia of Genes and Genomes) pathways with differential relative abundances between non-exclusively breastfed vs. exclusively breastfed infants ≤6 months of age.**

|  | Pooled estimate (log(OR)) | 95% Pooled lower limit | 95% Pooled upper limit | Pooled p-value | FDR adjusted pooled p-value |
|--|---------------------------|------------------------|------------------------|----------------|-----------------------------|
| <b>Vaginal birth infants</b>   |                           |                        |                        |                |                             |
| <b>Level 2 KEGG pathways</b>   |                           |                        |                        |                |                             |
| Human.Diseases..Infectious.Diseases  | -0.0484981                | -0.0757982             | -0.0211980             | 0.0004980      | 0.0189234                   |
| Human.Diseases..Neurodegenerative.Diseases   | -0.0840083                | -0.1400809             | -0.0279357             | 0.0033201      | 0.0630826                   |
| Unclassified..Genetic.Information.Processing   | -0.0202899                | -0.0366680             | -0.0039118             | 0.0151785      | 0.1607306                   |
| Environmental.Information.Processing..Signal.Transduction                                    | -0.0553524                | -0.1007744             | -0.0099304             | 0.0169190      | 0.1607306                   |
| Metabolism..Metabolism.of.Other.Amino.Acids  | -0.0167393                | -0.0316685             | -0.0018101             | 0.0279775      | 0.2126291                   |
| <b>Level 3 KEGG pathways</b>   |                           |                        |                        |                |                             |
| Metabolism..Carbohydrate.Metabolism..Pentose.phosphate.pathway                               | 0.0461974                 | 0.0280921              | 0.0643027              | 0.0000006      | 0.0001306                   |
| Metabolism..Carbohydrate.Metabolism..Propanoate.metabolism                                   | -0.0570404                | -0.0834447             | -0.0306362             | 0.0000230      | 0.0026279                   |
| Metabolism..Lipid.Metabolism..Fatty.acid.metabolism  | -0.0993213                | -0.1551250             | -0.0435176             | 0.0004859      | 0.0370903                   |
| Metabolism..Carbohydrate.Metabolism..Fructose.and.mannose.metabolism                         | 0.0720518                 | 0.0290068              | 0.1150969              | 0.0010354      | 0.0592770                   |
| Unclassified..Cellular.Processes.and.Signaling..Sporulation                                  | 0.2691131                 | 0.0965881              | 0.4416381              | 0.0022338      | 0.0994375                   |
| Metabolism..Carbohydrate.Metabolism..Amino.sugar.and.nucleotide.sugar.metabolism             | 0.0398818                 | 0.0139199              | 0.0658437              | 0.0026054      | 0.0994375                   |
| Metabolism..Enzyme.Families..Peptidases  | 0.0213727                 | 0.0071530              | 0.0355924              | 0.0032202      | 0.1053451                   |
| Metabolism..Metabolism.of.Cofactors.and.Vitamins..Pantothenate.and.CoA.biosynthesis          | 0.0229267                 | 0.0060172              | 0.0398362              | 0.0078743      | 0.2154792                   |
| Metabolism..Energy.Metabolism..Carbon.fixation.in.photosynthetic.organisms                   | 0.0343939                 | 0.0084757              | 0.0603121              | 0.0092979      | 0.2154792                   |
| Metabolism..Carbohydrate.Metabolism..Butanoate.metabolism                                    | -0.0390622                | -0.0690281             | -0.0090962             | 0.0106214      | 0.2154792                   |
| Metabolism..Metabolism.of.Other.Amino.Acids..Glutathione.metabolism                          | -0.0759232                | -0.1345127             | -0.0173336             | 0.0110911      | 0.2154792                   |
| Metabolism..Amino.Acid.Metabolism..Tryptophan.metabolism                                     | -0.1037075                | -0.1842150             | -0.0232001             | 0.0115773      | 0.2154792                   |
| Metabolism..Amino.Acid.Metabolism..Lysine.degradation  | -0.0938693                | -0.1679263             | -0.0198124             | 0.0129803      | 0.2154792                   |
| Environmental.Information.Processing..Membrane.Transport..Bacterial.secretion.system         | -0.0478536                | -0.0856872             | -0.0100200             | 0.0131734      | 0.2154792                   |
| Unclassified..Genetic.Information.Processing..Replication..recombination.and.repair.proteins | -0.0443230                | -0.0798220             | -0.0088241             | 0.0143987      | 0.2198206                   |
| Environmental.Information.Processing..Signal.Transduction..Two.component.system              | -0.0610081                | -0.1125477             | -0.0094685             | 0.0203390      | 0.2911026                   |
| Metabolism..Carbohydrate.Metabolism..Pentose.and.glucuronate.interconversions                | 0.0597831                 | 0.0075434              | 0.1120228              | 0.0248979      | 0.3300089                   |
| Metabolism..Lipid.Metabolism..Sphingolipid.metabolism  | 0.0973295                 | 0.0116751              | 0.1829839              | 0.0259396      | 0.3300089                   |
| Metabolism..Metabolism.of.Terpenoids.and.Polyketides..Limonene.and.pinene.degradation        | -0.0813978                | -0.1571928             | -0.0056027             | 0.0353049      | 0.4255172                   |
| Metabolism..Amino.Acid.Metabolism..Valine..leucine.and.isoleucine.degradation                | -0.0895058                | -0.1746557             | -0.0043559             | 0.0393768      | 0.4326503                   |
| Metabolism..Energy.Metabolism..Methane.metabolism  | 0.0355941                 | 0.0015675              | 0.0696207              | 0.0403400      | 0.4326503                   |

|  |            |            |            |           |           |
|--|------------|------------|------------|-----------|-----------|
| Metabolism..Metabolism.of.Cofactors.and.Vitamins..Vitamin.B6.metabolism                | -0.0328569 | -0.0646435 | -0.0010703 | 0.0427691 | 0.4326503 |
| Organismal.Systems..Endocrine.System..Insulin.signalng.pathway                         | 0.0703689  | 0.0014731  | 0.1392648  | 0.0452986 | 0.4326503 |
| Environmental.Information.Processing..Membrane.Transport..Secretion.system             | -0.0508999 | -0.1009642 | -0.0008357 | 0.0462966 | 0.4326503 |
| Metabolism..Metabolism.of.Terpenoids.and.Polyketides..Biosynthesis.of.ansamycins       | 0.0805279  | 0.0009840  | 0.1600719  | 0.0472326 | 0.4326503 |
| <b>C-section born infants</b>  |            |            |            |           |           |
| <b>Level 2 KEGG pathways</b>   |            |            |            |           |           |
| Human.Diseases..Infectious.Diseases  | -0.1126764 | -0.1634341 | -0.0619188 | 0.0000136 | 0.0005152 |
| Environmental.Information.Processing..Signal.Transduction                              | -0.1416460 | -0.2147171 | -0.0685750 | 0.0001451 | 0.0027566 |
| Unclassified..Poorly.Characterized   | -0.1803121 | -0.3159502 | -0.0446739 | 0.0091740 | 0.0868309 |
| Metabolism..Energy.Metabolism  | 0.0374528  | 0.0085859  | 0.0663197  | 0.0109930 | 0.0868309 |
| Human.Diseases..Neurodegenerative.Diseases   | -0.1436055 | -0.2548806 | -0.0323303 | 0.0114251 | 0.0868309 |
| Genetic.Information.Processing..Replication.and.Repair                                 | 0.1053877  | 0.0127404  | 0.1980350  | 0.0257815 | 0.1311394 |
| Metabolism..Nucleotide.Metabolism  | 0.1138804  | 0.0137370  | 0.2140238  | 0.0258259 | 0.1311394 |
| Metabolism..Amino.Acid.Metabolism  | 0.0256341  | 0.0025291  | 0.0487391  | 0.0296674 | 0.1311394 |
| Unclassified..Cellular.Processes.and.Signaling   | -0.1513433 | -0.2908525 | -0.0118341 | 0.0334848 | 0.1311394 |
| Metabolism..Carbohydrate.Metabolism  | 0.0257629  | 0.0018779  | 0.0496480  | 0.0345104 | 0.1311394 |
| <b>Level 3 KEGG pathways</b>   |            |            |            |           |           |
| Metabolism..Amino.Acid.Metabolism..Lysine.degradation                                  | -0.2410428 | -0.3566318 | -0.1254538 | 0.0000437 | 0.0052013 |
| Environmental.Information.Processing..Membrane.Transport..Secretion.system             | -0.1668053 | -0.2469752 | -0.0866354 | 0.0000454 | 0.0052013 |
| Cellular.Processes..Cell.Motility..Cytoskeleton.proteins                               | 0.1946407  | 0.0962873  | 0.2929941  | 0.0001050 | 0.0080144 |
| Environmental.Information.Processing..Signal.Transduction..Two.component.system        | -0.1563058 | -0.2381040 | -0.0745076 | 0.0001802 | 0.0103178 |
| Metabolism..Amino.Acid.Metabolism..Lysine.biosynthesis                                 | 0.0932496  | 0.0420471  | 0.1444521  | 0.0003577 | 0.0147737 |
| Metabolism..Amino.Acid.Metabolism..Tryptophan.metabolism                               | -0.2173867 | -0.3374491 | -0.0973242 | 0.0003871 | 0.0147737 |
| Metabolism..Metabolism.of.Cofactors.and.Vitamins..Thiamine.metabolism                  | 0.0778945  | 0.0333146  | 0.1224745  | 0.0006156 | 0.0201389 |
| Metabolism..Lipid.Metabolism..Biosynthesis.of.unsaturated.fatty.acids                  | -0.1598449 | -0.2539276 | -0.0657621 | 0.0008686 | 0.0248649 |
| Metabolism..Xenobiotics.Biodegradation.and.Metabolism..Drug.metabolism..other.enzymes  | 0.0699567  | 0.0283025  | 0.1116109  | 0.0009959 | 0.0253399 |
| Metabolism..Lipid.Metabolism..Fatty.acid.metabolism                                    | -0.1490154 | -0.2389524 | -0.0590784 | 0.0011645 | 0.0266667 |
| Genetic.Information.Processing..Folding..Sorting.and.Degradation..Sulfur.relay.system  | -0.1371891 | -0.2221315 | -0.0522467 | 0.0015481 | 0.0299670 |
| Metabolism..Carbohydrate.Metabolism..Galactose.metabolism                              | 0.1151450  | 0.0437581  | 0.1865320  | 0.0015703 | 0.0299670 |
| Genetic.Information.Processing..Replication.and.Repair..Mismatch.repair                | 0.0832394  | 0.0305117  | 0.1359671  | 0.0019739 | 0.0347716 |
| Metabolism..Enzyme.Families..Peptidases  | 0.0367908  | 0.0132236  | 0.0603581  | 0.0022156 | 0.0362412 |
| Unclassified..Cellular.Processes.and.Signaling..Inorganic.ion.transport.and.metabolism | -0.2280142 | -0.3757408 | -0.0802875 | 0.0024849 | 0.0378887 |
| Metabolism..Biosynthesis.of.Other.Secondary.Metabolites..Phenylpropanoid.biosynthesis  | 0.1624628  | 0.0559814  | 0.2689443  | 0.0027862 | 0.0378887 |
| Genetic.Information.Processing..Replication.and.Repair..Nucleotide.excision.repair     | 0.1893190  | 0.0650986  | 0.3135395  | 0.0028164 | 0.0378887 |
| Metabolism..Carbohydrate.Metabolism..Amino.sugar.and.nucleotide.sugar.metabolism       | 0.0854708  | 0.0287632  | 0.1421784  | 0.0031359 | 0.0378887 |
| Genetic.Information.Processing..Replication.and.Repair..DNA.replication.proteins       | 0.0714555  | 0.0240344  | 0.1188765  | 0.0031436 | 0.0378887 |
| Unclassified..Cellular.Processes.and.Signaling..Sporulation                            | 0.4258710  | 0.1299770  | 0.7217649  | 0.0047887 | 0.0548305 |
| Unclassified..Cellular.Processes.and.Signaling..Other.ion.coupled.transporters         | -0.1077009 | -0.1836842 | -0.0317177 | 0.0054676 | 0.0596224 |
| Metabolism..Amino.Acid.Metabolism..Valine..leucine.and.isoleucine.degradation          | -0.1456712 | -0.2508764 | -0.0404661 | 0.0066508 | 0.0666673 |

|   |            |            |            |           |           |
|---|------------|------------|------------|-----------|-----------|
| Metabolism..Metabolism.of.Other.Amino.Acids..Glutathione.metabolism   | -0.1200119 | -0.2068134 | -0.0332105 | 0.0067313 | 0.0666673 |
| Metabolism..Energy.Metabolism..Carbon.fixation.in.photosynthetic.organisms                                    | 0.0526806  | 0.0144032  | 0.0909581  | 0.0069870 | 0.0666673 |
| Unclassified..Metabolism..Metabolism.of.cofactors.and.vitamins  | -0.1333637 | -0.2310416 | -0.0356858 | 0.0074502 | 0.0682438 |
| Human.Diseases..Infectious.Diseases..Vibrio.cholerae.pathogenic.cycle   | -0.1267418 | -0.2201966 | -0.0332870 | 0.0078590 | 0.0692195 |
| Metabolism..Nucleotide.Metabolism..Pyrimidine.metabolism  | 0.1104510  | 0.0262793  | 0.1946228  | 0.0101147 | 0.0815516 |
| Metabolism..Amino.Acid.Metabolism..Phenylalanine..tyrosine.and.tryptophan.biosynthesis                        | 0.0758791  | 0.0174605  | 0.1342977  | 0.0109036 | 0.0815516 |
| Unclassified..Poorly.Characterized..Function.unknown  | -0.1569012 | -0.2778123 | -0.0359902 | 0.0109791 | 0.0815516 |
| Unclassified..Metabolism..Biosynthesis.and.biodegradation.of.secondary.metabolites                            | -0.2158734 | -0.3825210 | -0.0492257 | 0.0111197 | 0.0815516 |
| Metabolism..Enzyme.Families..Protein.kinases  | -0.1293255 | -0.2293288 | -0.0293222 | 0.0112560 | 0.0815516 |
| Metabolism..Metabolism.of.Cofactors.and.Vitamins..One.carbon.pool.by.folate                                   | 0.1439633  | 0.0324506  | 0.2554761  | 0.0113959 | 0.0815516 |
| Metabolism..Energy.Metabolism..Methane.metabolism   | 0.0633891  | 0.0140256  | 0.1127526  | 0.0118410 | 0.0821696 |
| Cellular.Processes..Cell.Growth.and.Death..Cell.cycle..Caulobacter  | 0.2069000  | 0.0422384  | 0.3715616  | 0.0137885 | 0.0928694 |
| Genetic.Information.Processing..Replication.and.Repair..DNA.replication                                       | 0.0956593  | 0.0189480  | 0.1723706  | 0.0145221 | 0.0950160 |
| Metabolism..Metabolism.of.Cofactors.and.Vitamins..Ubiquinone.and.other.terpenoid.quinone.biosynthesis         | -0.1294977 | -0.2356083 | -0.0233871 | 0.0167593 | 0.1066077 |
| Human.Diseases..Infectious.Diseases..Pertussis  | -0.3459067 | -0.6327068 | -0.0591067 | 0.0180840 | 0.1119254 |
| Metabolism..Carbohydrate.Metabolism..Starch.and.sucrose.metabolism  | 0.0968519  | 0.0152222  | 0.1784815  | 0.0200476 | 0.1186550 |
| Metabolism..Xenobiotics.Biodegradation.and.Metabolism..Polycyclic.aromatic.hydrocarbon.degradation            | 0.1728426  | 0.0268082  | 0.3188769  | 0.0203536 | 0.1186550 |
| Metabolism..Metabolism.of.Cofactors.and.Vitamins..Pantothenate.and.CoA.biosynthesis                           | 0.0398297  | 0.0060784  | 0.0735810  | 0.0207258 | 0.1186550 |
| Unclassified..Cellular.Processes.and.Signaling..Electron.transfer.carriers                                    | -0.3152297 | -0.5838763 | -0.0465831 | 0.0214584 | 0.1198530 |
| Cellular.Processes..Cell.Motility..Bacterial.motility.proteins  | -0.1964298 | -0.3666517 | -0.0262078 | 0.0237144 | 0.1292999 |
| Metabolism..Amino.Acid.Metabolism..Amino.acid.related.enzymes   | 0.1029036  | 0.0128789  | 0.1929283  | 0.0250679 | 0.1335010 |
| Metabolism..Glycan.Biosynthesis.and.Metabolism..Peptidoglycan.biosynthesis                                    | 0.1655029  | 0.0200473  | 0.3109585  | 0.0257412 | 0.1337390 |
| Metabolism..Glycan.Biosynthesis.and.Metabolism..Lipopolysaccharide.biosynthesis.proteins                      | -0.4913860 | -0.9248161 | -0.0579560 | 0.0262806 | 0.1337390 |
| Unclassified..Cellular.Processes.and.Signaling..Membrane.and.intracellular.structural.molecules               | -0.3249676 | -0.6132583 | -0.0366768 | 0.0271528 | 0.1338000 |
| Metabolism..Energy.Metabolism..Photosynthesis   | 0.3092523  | 0.0343539  | 0.5841507  | 0.0274611 | 0.1338000 |
| Metabolism..Energy.Metabolism..Photosynthesis.proteins  | 0.2924081  | 0.0244100  | 0.5604062  | 0.0324776 | 0.1419698 |
| Genetic.Information.Processing..Replication.and.Repair..Homologous.recombination                              | 0.1521295  | 0.0125825  | 0.2916766  | 0.0326234 | 0.1419698 |
| Genetic.Information.Processing..Folding..Sorting.and.Degradation..Protein.export                              | 0.2001823  | 0.0165063  | 0.3838583  | 0.0326714 | 0.1419698 |
| Metabolism..Lipid.Metabolism..Sphingolipid.metabolism   | 0.3160602  | 0.0252501  | 0.6068702  | 0.0331600 | 0.1419698 |
| Genetic.Information.Processing..Translation..Translation.factors  | 0.1979245  | 0.0151195  | 0.3807294  | 0.0338319 | 0.1419698 |
| Genetic.Information.Processing..Replication.and.Repair..DNA.repair.and.recombination.proteins                 | 0.1416179  | 0.0105526  | 0.2726833  | 0.0341947 | 0.1419698 |
| Metabolism..Metabolism.of.Terpenoids.and.Polyketides..Prenyltransferases                                      | 0.0689059  | 0.0050264  | 0.1327855  | 0.0344996 | 0.1419698 |
| Unclassified..Poorly.Characterized..General.function.prediction.only  | -0.1479579 | -0.2851369 | -0.0107788 | 0.0345180 | 0.1419698 |
| Unclassified..Cellular.Processes.and.Signaling..Signal.transduction.mechanisms                                | -0.1179107 | -0.2273522 | -0.0084693 | 0.0347175 | 0.1419698 |
| Metabolism..Metabolism.of.Other.Amino.Acids..beta.Alanine.metabolism  | -0.1460591 | -0.2860661 | -0.0060521 | 0.0408857 | 0.1642602 |
| Metabolism..Metabolism.of.Terpenoids.and.Polyketides..Limonene.and.pinene.degradation                         | -0.1832241 | -0.3596813 | -0.0067669 | 0.0418382 | 0.1651887 |
| Metabolism..Metabolism.of.Terpenoids.and.Polyketides..Biosynthesis.of.siderophore.group.nonribosomal.peptides | -0.2787206 | -0.5495580 | -0.0078831 | 0.0436943 | 0.1690090 |
| Genetic.Information.Processing..Translation..Ribosome   | 0.2622067  | 0.0067069  | 0.5177065  | 0.0442818 | 0.1690090 |

|  |            |            |            |           |           |
|--|------------|------------|------------|-----------|-----------|
| Metabolism..Xenobiotics.Biodegradation.and.Metabolism..Toluene.degradation   | -0.0942549 | -0.1867207 | -0.0017891 | 0.0457289 | 0.1716708 |
| Genetic.Information.Processing..Replication.and.Repair..Chromosome           | 0.0281142  | 0.0004085  | 0.0558200  | 0.0467165 | 0.1725498 |
| Metabolism..Carbohydrate.Metabolism..Glyoxylate.and.dicarboxylate.metabolism | -0.0952237 | -0.1898776 | -0.0005698 | 0.0486368 | 0.1767908 |

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Four studies included are Canada, Haïti, USA (California-Florida), USA (California-Massachusetts –Missouri).

Only those with pooled p-values <0.05 are shown. OR: odds ratio; FDR: false discovery rate.

**Supplementary table 11. Gut bacterial taxa with differential relative abundances from 6 months to 2 years of age between infants with duration of exclusive breastfeeding >2 months vs. <=2 months from birth.**

| Bacterial taxa  | Estimate<br>(log(OR)) | 95% Lower<br>limit | 95% Upper<br>limit | p-value   | FDR adjusted p-<br>value |
|---|-----------------------|--------------------|--------------------|-----------|--------------------------|
| Phylum  |                       |                    |                    |           |                          |
| k_bacteria.p_firmicutes   | -0.2451898            | -0.3692779         | -0.1211016         | 0.0001188 | 0.0004750                |
| k_bacteria.p_actinobacteria   | 0.2267863             | 0.0877156          | 0.3658570          | 0.0014620 | 0.0029239                |
| Order   |                       |                    |                    |           |                          |
| k_bacteria.p_actinobacteria.c_coriobacteria.o_coriobacteriales  | -0.2485089            | -0.3764097         | -0.1206081         | 0.0001536 | 0.0007304                |
| k_bacteria.p_firmicutes.c_bacilli.o_lactobacillales   | -0.2705907            | -0.4127786         | -0.1284028         | 0.0002087 | 0.0007304                |
| k_bacteria.p_actinobacteria.c_actinobacteria.o_bifidobacteriales  | 0.2543014             | 0.1147125          | 0.3938904          | 0.0003831 | 0.0008938                |
| k_bacteria.p_firmicutes.c_erysipelotrichi.o_erysipelotrichales  | -0.1523709            | -0.3009192         | -0.0038227         | 0.0448092 | 0.0784160                |
| Family  |                       |                    |                    |           |                          |
| k_bacteria.p_firmicutes.c_bacilli.o_lactobacillales.f_lactobacillaceae                                  | -0.3106381            | -0.4591458         | -0.1621304         | 0.0000467 | 0.0006074                |
| k_bacteria.p_actinobacteria.c_coriobacteria.o_coriobacteriales.f_coriobacteriaceae                      | -0.2485089            | -0.3764097         | -0.1206081         | 0.0001536 | 0.0009984                |
| k_bacteria.p_actinobacteria.c_actinobacteria.o_bifidobacteriales.f_bifidobacteriaceae                   | 0.2543014             | 0.1147125          | 0.3938904          | 0.0003831 | 0.0016600                |
| k_bacteria.p_bacteroidetes.c_bacteroidia.o_bacteroidales.f_prevotellaceae                               | -0.2684295            | -0.4252954         | -0.1115636         | 0.0008441 | 0.0027434                |
| k_bacteria.p_firmicutes.c_clostridia.o_clostridiales.f_clostridiaceae                                   | -0.2173273            | -0.3739319         | -0.0607226         | 0.0067053 | 0.0174337                |
| k_bacteria.p_firmicutes.c_bacilli.o_lactobacillales.f_enterococcaceae                                   | 0.1916596             | 0.0314478          | 0.3518714          | 0.0193459 | 0.0419160                |
| k_bacteria.p_firmicutes.c_erysipelotrichi.o_erysipelotrichales.f_erysipelotrichaceae                    | -0.1523709            | -0.3009192         | -0.0038227         | 0.0448092 | 0.0789058                |
| k_bacteria.p_firmicutes.c_clostridia.o_clostridiales.f_lachnospiraceae                                  | -0.1427715            | -0.2843695         | -0.0011734         | 0.0485574 | 0.0789058                |
| Genus   |                       |                    |                    |           |                          |
| k_bacteria.p_firmicutes.c_bacilli.o_lactobacillales.f_lactobacillaceae.g_lactobacillus                  | -0.3315173            | -0.4796795         | -0.1833552         | 0.0000135 | 0.0002844                |
| k_bacteria.p_firmicutes.c_clostridia.o_clostridiales.f.g_   | -0.3365252            | -0.4939403         | -0.1791101         | 0.0000318 | 0.0003341                |
| k_bacteria.p_actinobacteria.c_actinobacteria.o_bifidobacteriales.f_bifidobacteriaceae.g_bifidobacterium | 0.2542917             | 0.1147032          | 0.3938803          | 0.0003833 | 0.0026828                |
| k_bacteria.p_firmicutes.c_clostridia.o_clostridiales.f_lachnospiraceae.g_ruminococcus                   | -0.2516784            | -0.3970545         | -0.1063022         | 0.0007339 | 0.0035457                |
| k_bacteria.p_bacteroidetes.c_bacteroidia.o_bacteroidales.f_prevotellaceae.g_prevotella                  | -0.2684274            | -0.4252933         | -0.1115615         | 0.0008442 | 0.0035457                |
| k_bacteria.p_actinobacteria.c_coriobacteria.o_coriobacteriales.f_coriobacteriaceae.g_                   | -0.2173260            | -0.3585566         | -0.0760954         | 0.0026637 | 0.0093228                |
| k_bacteria.p_firmicutes.c_clostridia.o_clostridiales.f_clostridiaceae.g_                                | -0.2429816            | -0.4091452         | -0.0768181         | 0.0042923 | 0.0128768                |
| k_bacteria.p_firmicutes.c_clostridia.o_clostridiales.f_lachnospiraceae.g_blautia                        | -0.2191360            | -0.3742548         | -0.0640173         | 0.0057874 | 0.0151919                |
| k_bacteria.p_actinobacteria.c_coriobacteria.o_coriobacteriales.f_coriobacteriaceae.g_collinsella        | -0.1709286            | -0.3046898         | -0.0371675         | 0.0125085 | 0.0291864                |
| k_bacteria.p_firmicutes.c_erysipelotrichi.o_erysipelotrichales.f_erysipelotrichaceae.g_catenebacterium  | -0.2297013            | -0.4169284         | -0.0424743         | 0.0164716 | 0.0345904                |
| k_bacteria.p_firmicutes.c_clostridia.o_clostridiales.f_lachnospiraceae.g_                               | -0.1613206            | -0.3028823         | -0.0197590         | 0.0258594 | 0.0493679                |
| k_bacteria.p_firmicutes.c_bacilli.o_lactobacillales.f_enterococcaceae.g_enterococcus                    | 0.1801273             | 0.0167905          | 0.3434641          | 0.0310272 | 0.0542975                |

Data from Bangladesh study only.

Only those with p-values <0.05 are shown. OR: odds ratio; FDR: false discovery rate.

**Supplementary table 12. Breastfeeding is associated with reduced differences in gut bacterial taxa relative abundances between those who had vs did not have diarrhea at the time of stool sample collection in infants from 6 months to 2 years of age.**

|   | Estimate (log(OR)) | 95% Lower limit | 95% Upper limit | p-value   | FDR adjusted p-value |
|---|--------------------|-----------------|-----------------|-----------|----------------------|
| <b>Stratified by duration of exclusive breastfeeding (EBF)</b>                              |                    |                 |                 |           |                      |
| <i>In infants with duration of EBF &lt;=2 months (diarrhea vs. no diarrhea comparison)</i>  |                    |                 |                 |           |                      |
| k_bacteria.p_actinobacteria.c_actinobacteria.o_bifidobacteriales.f_bifidobacteriaceae       | -0.7714898         | -1.1622815      | -0.3806981      | 0.0001287 | 0.0016732            |
| k_bacteria.p_actinobacteria.c_coriobacteriia.o_coriobacteriales.f_coriobacteriaceae         | -0.6912195         | -1.0754847      | -0.3069543      | 0.0004749 | 0.0030865            |
| k_bacteria.p_firmicutes.c_bacilli.o_lactobacillales.f_streptococcaceae                      | 0.5260925          | 0.1662351       | 0.8859498       | 0.0043999 | 0.0190660            |
| <i>In infants with duration of EBF &gt;2 months (diarrhea vs. no diarrhea comparison)</i>   |                    |                 |                 |           |                      |
| No bacterial family with change in relative abundance p-value <0.05                         |                    |                 |                 |           |                      |
| <b>Stratified by breastfeeding status at the time of diarrhea</b>                           |                    |                 |                 |           |                      |
| <i>In infants without breastfeeding when diarrhea (diarrhea vs. no diarrhea comparison)</i> |                    |                 |                 |           |                      |
| k_bacteria.p_firmicutes.c_bacilli.o_lactobacillales.f_streptococcaceae                      | 2.090855           | 0.8665651       | 3.3151455       | 0.0017567 | 0.0228374            |
| k_bacteria.p_actinobacteria.c_actinobacteria.o_bifidobacteriales.f_bifidobacteriaceae       | -1.840426          | -3.3404553      | -0.3403967      | 0.0207821 | 0.1350835            |
| <i>In infants with breastfeeding when diarrhea (diarrhea vs. no diarrhea comparison)</i>    |                    |                 |                 |           |                      |
| k_bacteria.p_actinobacteria.c_coriobacteriia.o_coriobacteriales.f_coriobacteriaceae         | -0.3440389         | -0.6305337      | -0.0575442      | 0.0189040 | 0.2457518            |
| k_bacteria.p_actinobacteria.c_actinobacteria.o_bifidobacteriales.f_bifidobacteriaceae       | -0.2512789         | -0.5485430      | 0.0459851       | 0.0980727 | 0.4727405            |

Data from Bangladesh study only.

Only taxa with p-value <0.05 are shown. OR: odds ratio; FDR: false discovery rate.

**Supplementary figure 1. Sensitivity analysis: meta-analysis of microbial alpha diversity (Shannon index) difference between non-exclusively breastfed vs. exclusively breastfed infants of included studies without estimates from either North Carolina, Haiti or VDAART trial (USA(CA-MA-MO)) study.**

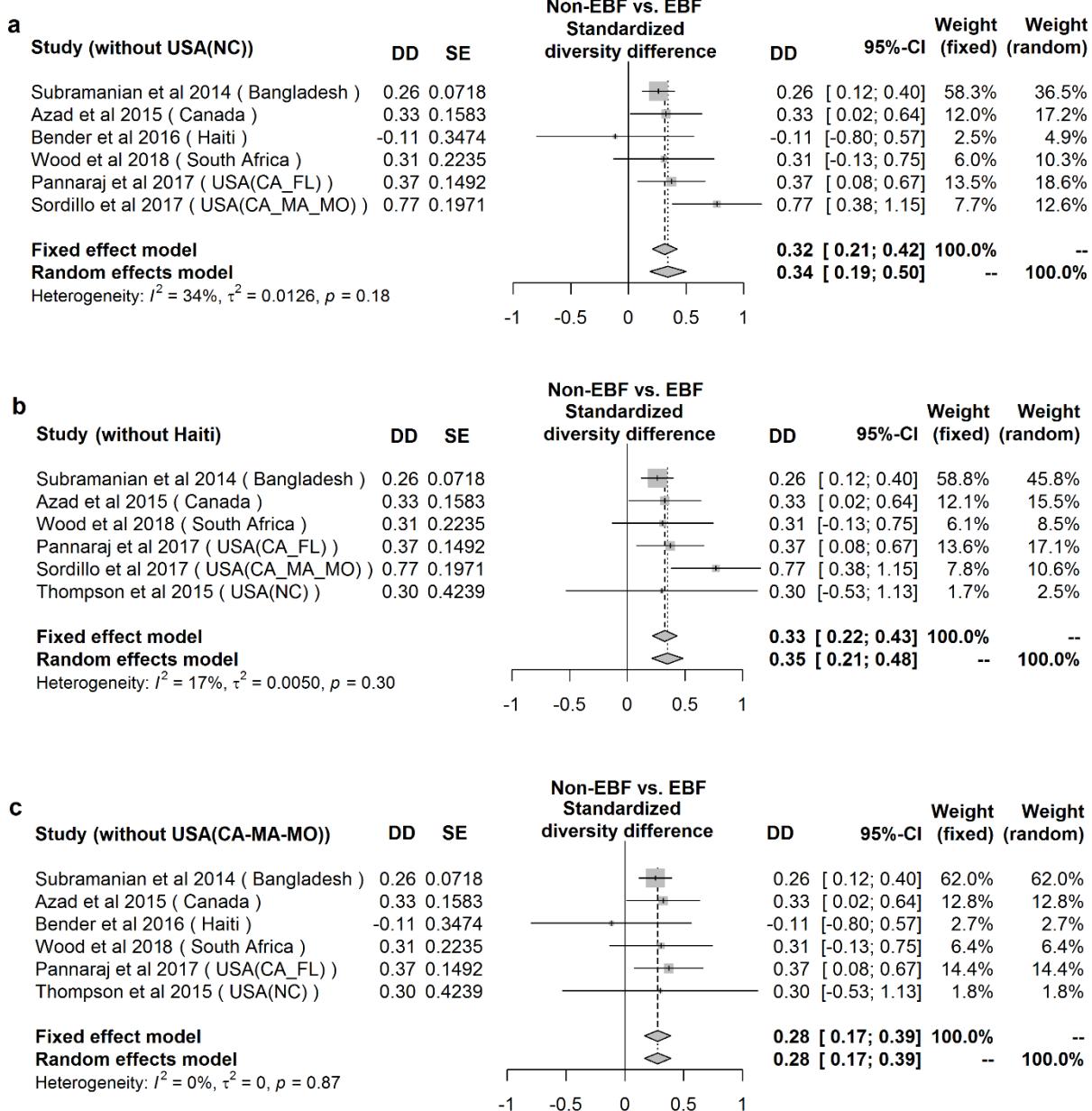
**a:** Meta-analysis without estimates from USA (North Carolina) study.

**b:** Meta-analysis without estimates from Haiti study.

**c:** Meta-analysis without estimates from VDAART trial (USA(California-Massachusetts-Missouri)) study.

The figures show the difference in gut microbial alpha diversity (standardized Shannon index) between non-exclusively breastfed (non-EBF) vs. EBF infants  $\leq$  6 months of age from each study and the pooled effect across studies. Estimates for diversity difference and corresponding standard errors from each study were from linear mixed effect models (for longitudinal data) or linear models (for non-longitudinal data) and were adjusted for age of infants at sample collection.

EBF: exclusive breastfeeding; non-EBF: non-exclusive breastfeeding; USA: United States of America; CA: California; FL: Florida; MA: Massachusetts; MO: Missouri; NC: North Carolina; DD: Diversity difference; SE: Standard error.



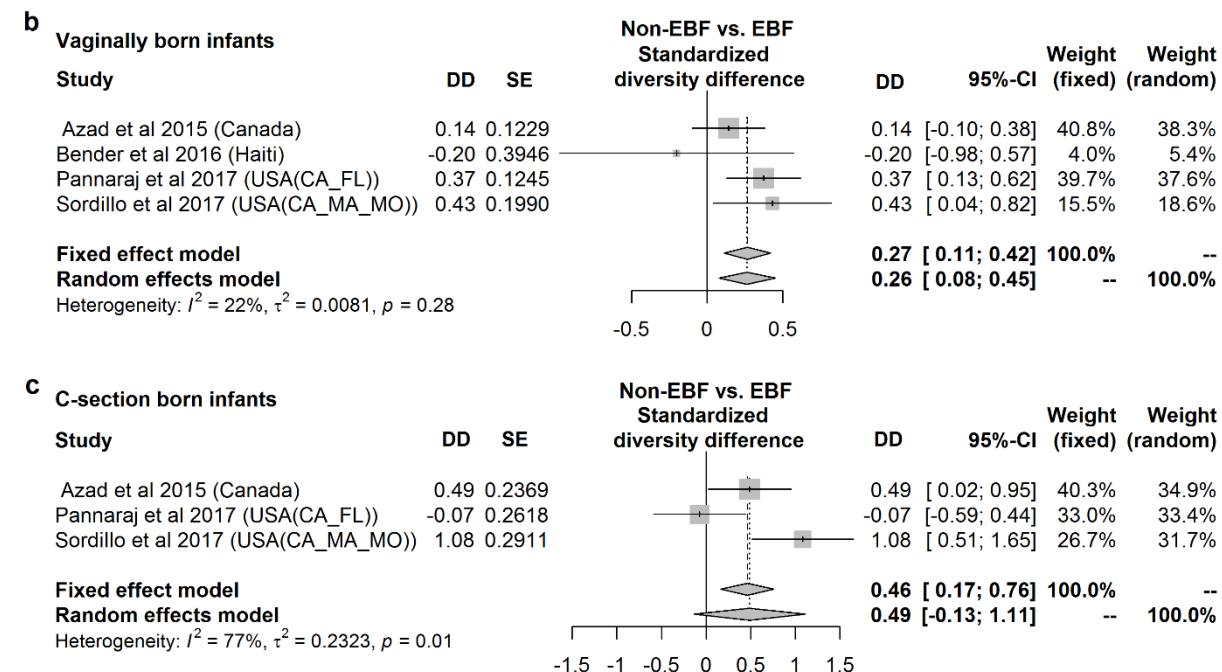
**Supplementary figure 2. Meta-analysis stratified by mode of delivery: differences in microbial alpha diversity (Shannon index) between non-exclusively breastfed vs. exclusively breastfed infants  $\leq$  6 months of age.**

a. Meta-analysis of vaginally delivered infants.

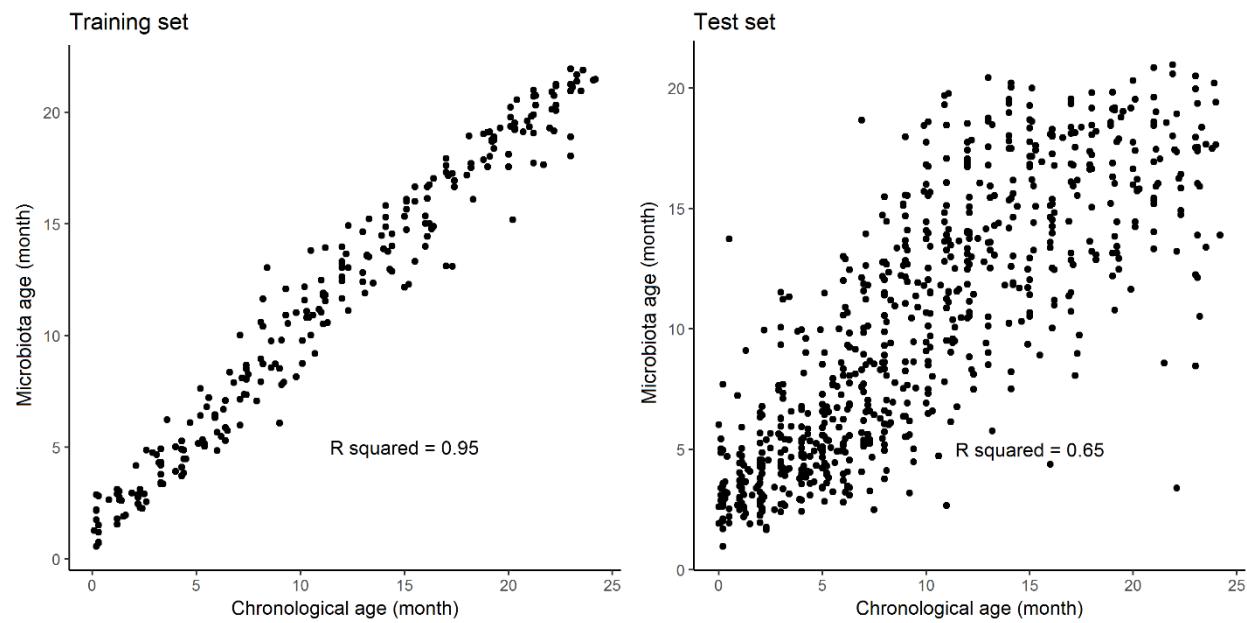
b. Meta-analysis of cesarean delivered infants.

The figures show the difference in gut alpha diversity (standardized Shannon index) between non-exclusively breastfed (non-EBF) vs. EBF infants  $\leq$  6 months of age from each study and the pooled effect across studies. Estimates for diversity difference and corresponding standard errors from each study were from linear mixed effect models (for longitudinal data) or linear models (for non-longitudinal data) and were adjusted for age of infants at sample collection.

EBF: exclusive breastfeeding; non-EBF: non-exclusive breastfeeding; USA: United States of America; CA: California; FL: Florida; MA: Massachusetts; MO: Missouri; DD: Diversity difference; SE: Standard error.



**Supplementary figure 3. Performance of Random Forest model in prediction of gut microbiota age on the training and test set of Bangladesh data.**



**Supplementary figure 4. Sensitivity analysis: meta-analysis of microbiota age of included studies without estimates from either North Carolina, Haiti or VDAART trial (USA(CA-MA-MO) study.**

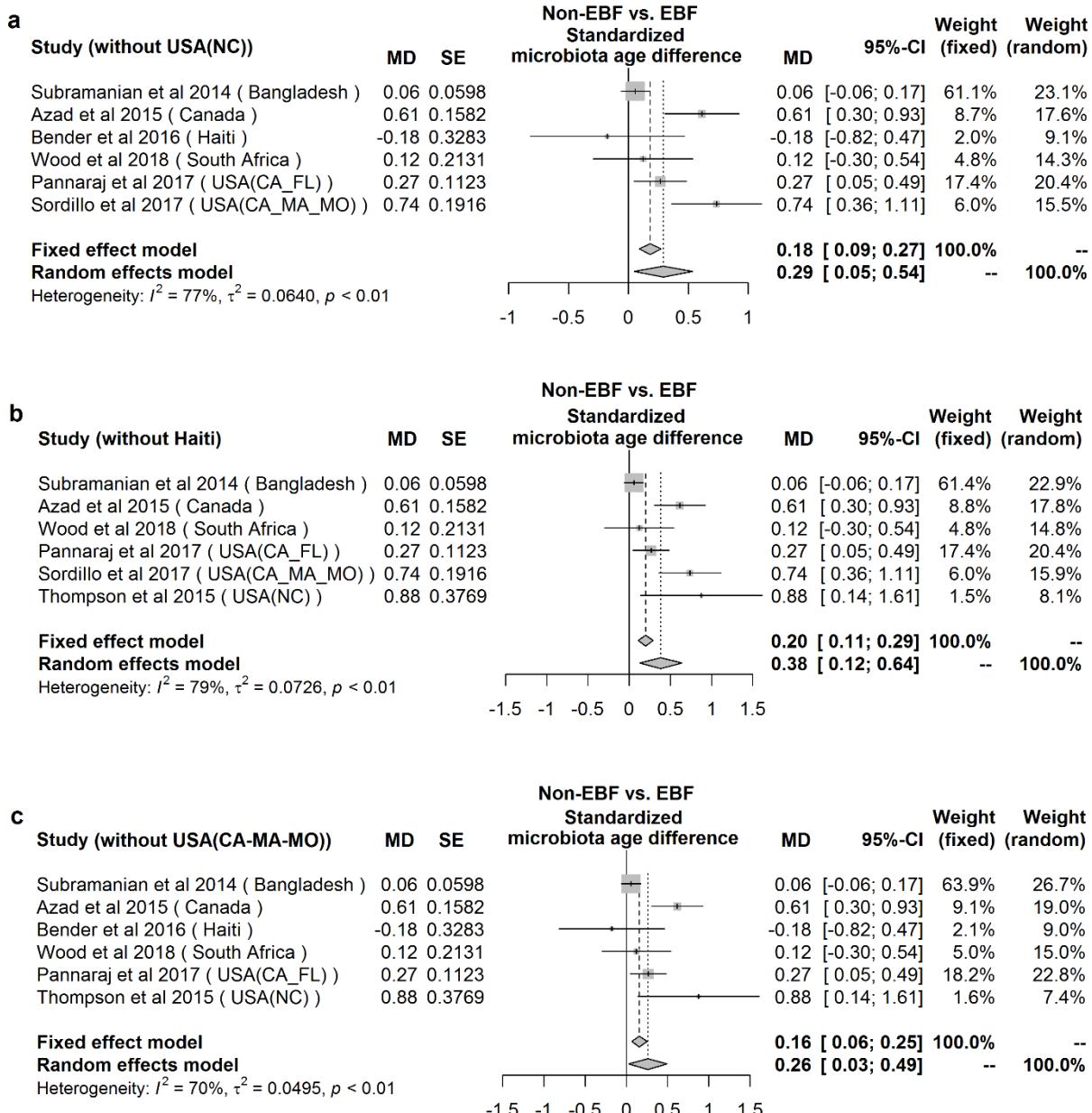
**a:** Meta-analysis without estimates from North Carolina study.

**b:** Meta-analysis without estimates from Haiti study.

**c:** Meta-analysis without estimates from VDAART trial (USA(California-Massachusetts-Missouri)) study.

The figures show the difference in gut (standardized) microbiota age between non-exclusively breastfed (non-EBF) vs. EBF infants  $\leq$  6 months of age from each study and the pooled effect across studies. Estimates for microbiota age difference and corresponding standard error from each study were from linear mixed effect models (for longitudinal data) or linear models (for non-longitudinal data) and were adjusted for age of infants at sample collection.

EBF: exclusive breastfeeding; non-EBF: non-exclusive breastfeeding; USA: United States of America; CA: California; FL: Florida; MA: Massachusetts; MO: Missouri; NC: North Carolina; MD: Microbiota age difference; SE: Standard error.

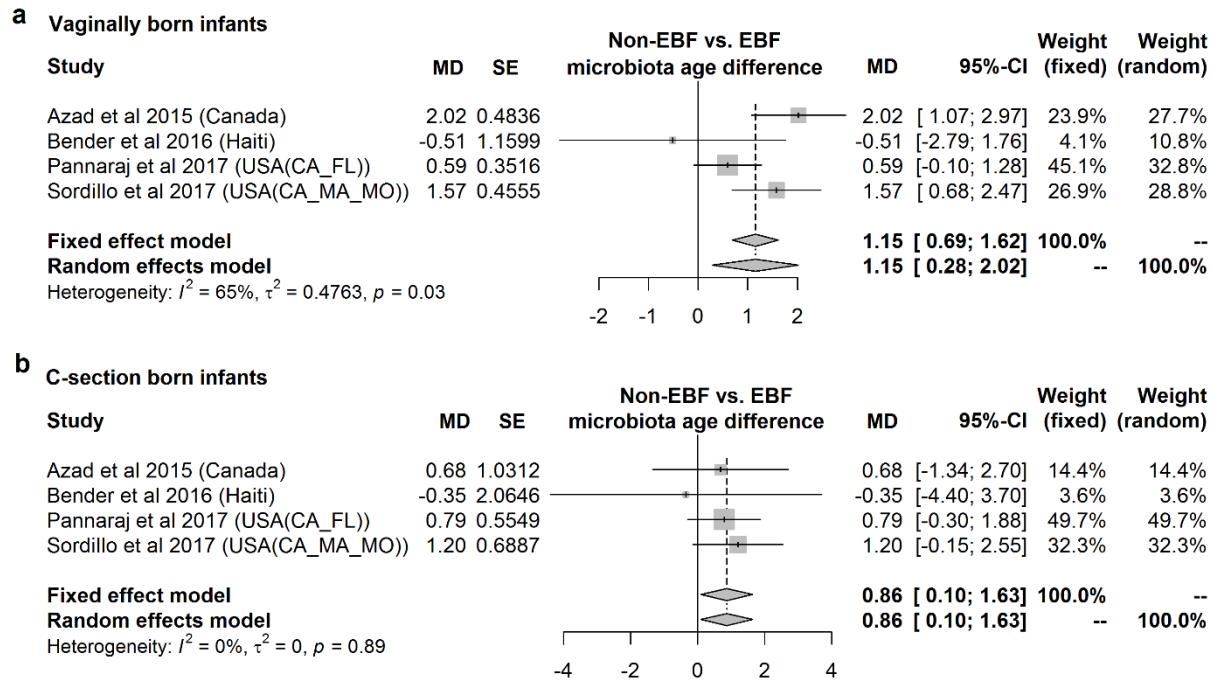


**Supplementary figure 5. Meta-analysis stratified by mode of delivery: differences in microbiota age between non-exclusively breastfed vs. exclusively breastfed infants  $\leq$  6 months of age.**

- a. Meta-analysis of vaginal born infants only.
- b. Meta-analysis of C-section born infants only.

The figures show the difference in gut microbiota age between non-exclusively breastfed (non-EBF) vs. EBF infants  $\leq$  6 months of age from each study and the pooled effect (meta-analysis) across four studies with available mode of delivery information. Estimates for microbiota age difference and corresponding standard error from each study were from linear mixed effect models (for longitudinal data) or linear models (for non-longitudinal data) and were adjusted for age of infants at sample collection.

EBF: exclusive breastfeeding; non-EBF: non-exclusive breastfeeding; USA: United States of America; CA: California; FL: Florida; MA: Massachusetts; MO: Missouri; MD: Microbiota age difference; SE: Standard error.



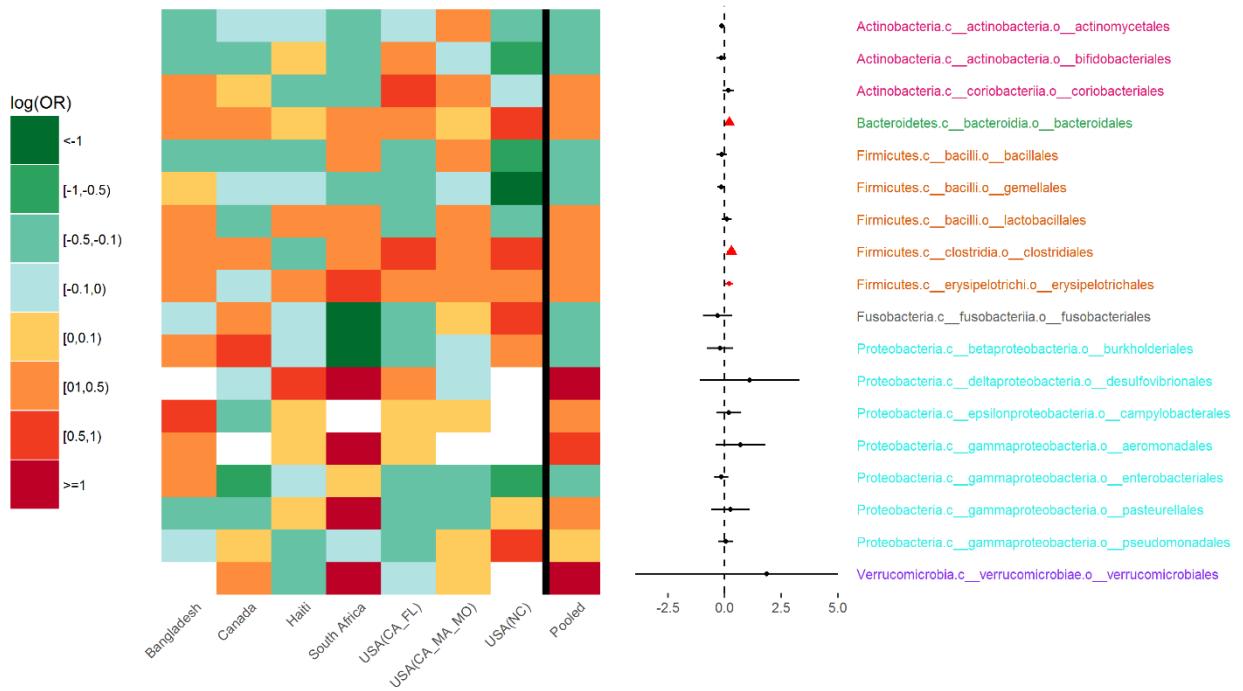
**Supplementary figure 6. Meta-analysis of seven included studies: the effects of non-exclusive vs. exclusive breastfeeding on relative abundance of gut bacterial taxa at order level in infants  $\leq$  6 months.**

Heatmap of log(odds ratio) (log(OR)) of relative abundance of all gut bacterial taxa at order level between non-exclusively breastfed (non-EBF) vs. exclusively breastfed (EBF) infants for each study and pooled estimates of all studies with 95% confidence intervals (forest plot). All log(OR) estimates of each order from each study were from Generalized Additive Models for Location Scale and Shape (GAMLSS) with beta zero inflated family (BEZI) and were adjusted for age of infants at sample collection. Pooled log(OR) estimates and 95% confidence intervals (forest plot) were from random effect meta-analysis models based on the adjusted log(OR) estimates and corresponding standard errors of all included studies.

Pooled log(OR) estimates with pooled p-values $<0.05$  are in red and those with false discovery rate (FDR) adjusted pooled p-values  $<0.1$  are in triangle shape.

Missing (unavailable) values are in white.

USA: United States of America; CA: California; FL: Florida; MA: Massachusetts; MO: Missouri; NC: North Carolina.



**Supplementary figure 7. Meta-analysis of seven included studies: the effects of non-exclusive vs. exclusive breastfeeding on relative abundance of gut bacterial taxa at genus level in infants  $\leq$  6 months.**

Heatmap of log(odds ratio) (log(OR)) of relative abundance of all gut bacterial taxa at genus level between non-exclusively breastfed (non-EBF) vs. exclusively breastfed (EBF) infants for each study and pooled estimates of all studies with 95% confidence intervals (forest plot). All log(OR) estimates of each genus from each study were from Generalized Additive Models for Location Scale and Shape (GAMLSS) with beta zero inflated family (BEZI) and were adjusted for age of infants at sample collection. Pooled log(OR) estimates and 95% confidence intervals (forest plot) were from random effect meta-analysis models based on the adjusted log(OR) estimates and corresponding standard errors of all included studies.

Pooled log(OR) estimates with pooled p-values $<0.05$  are in red and those with false discovery rate (FDR) adjusted pooled p-values  $<0.1$  are in triangle shape.

Missing (unavailable) values are in white. Taxa with unassigned name are numbered.

USA: United States of America; CA: California; FL: Florida; MA: Massachusetts; MO: Missouri; NC: North Carolina.



**Supplementary figure 8. Meta-analysis stratified by mode of delivery: the effects of non-exclusive vs. exclusive breastfeeding on relative abundance of gut bacterial taxa at phylum level in infants  $\leq$  6 months.**

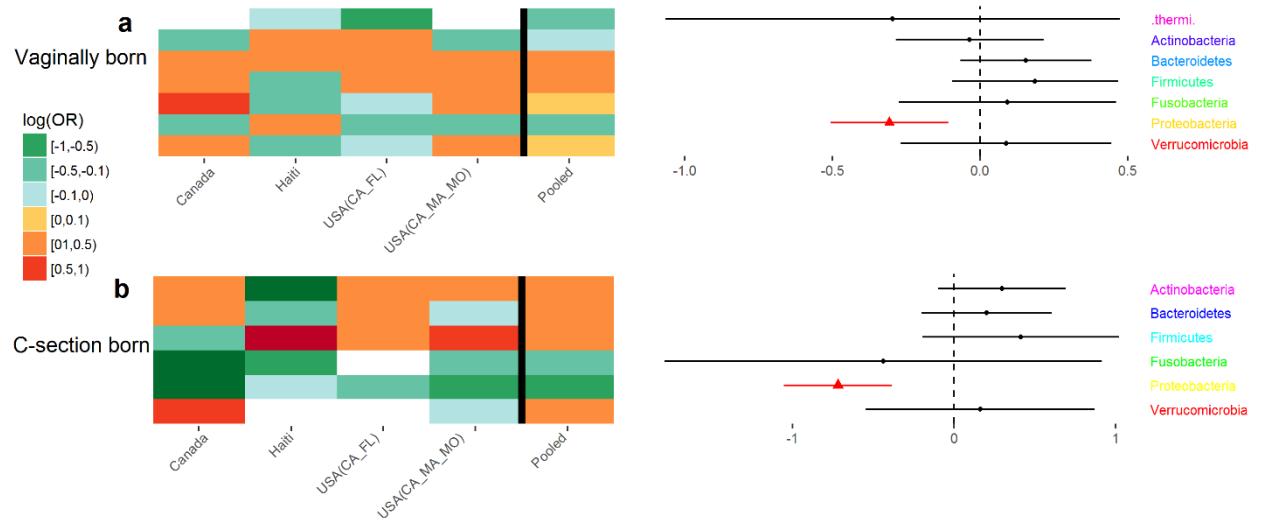
- a. Meta-analysis of vaginally born infants only. Heatmap of log(odds ratio) (log(OR)) of relative abundances of all gut bacterial phyla between non-exclusively breastfed (non-EBF) vs. exclusively breastfed (EBF) infants for each study and pooled estimates across four studies (with available mode of delivery information) and 95% confidence intervals (95% CI) (forest plot).
- b. Meta-analysis of C-section born infants only. Heatmap of log(OR) of relative abundances of all gut bacterial phyla between non-EBF vs. EBF infants for each study and pooled estimates across four studies (with available mode of delivery information) and 95% confidence intervals (95% CI) (forest plot).

All log(OR) estimates of each bacterial taxa from each study were from Generalized Additive Models for Location Scale and Shape (GAMLSS) with beta zero inflated family (BEZI) and were adjusted for age of infants at sample collection. Pooled log(OR) estimates and 95% CI (forest plot) were from random effect meta-analysis models based on the adjusted log(OR) estimates and corresponding standard errors of all included studies.

Pooled log(OR) estimates with pooled p-values  $<0.05$  are in red and those with false discovery rate (FDR) adjusted pooled p-values  $<0.1$  are in triangle shape.

Missing (unavailable) values are in white.

USA: United States of America; CA: California; FL: Florida; MA: Massachusetts; MO: Missouri.



**Supplementary figure 9. Meta-analysis stratified on vaginal delivered infants: the effects of non-exclusive vs. exclusive breastfeeding on relative abundance of gut bacterial taxa at family level in infants  $\leq$  6 months.**

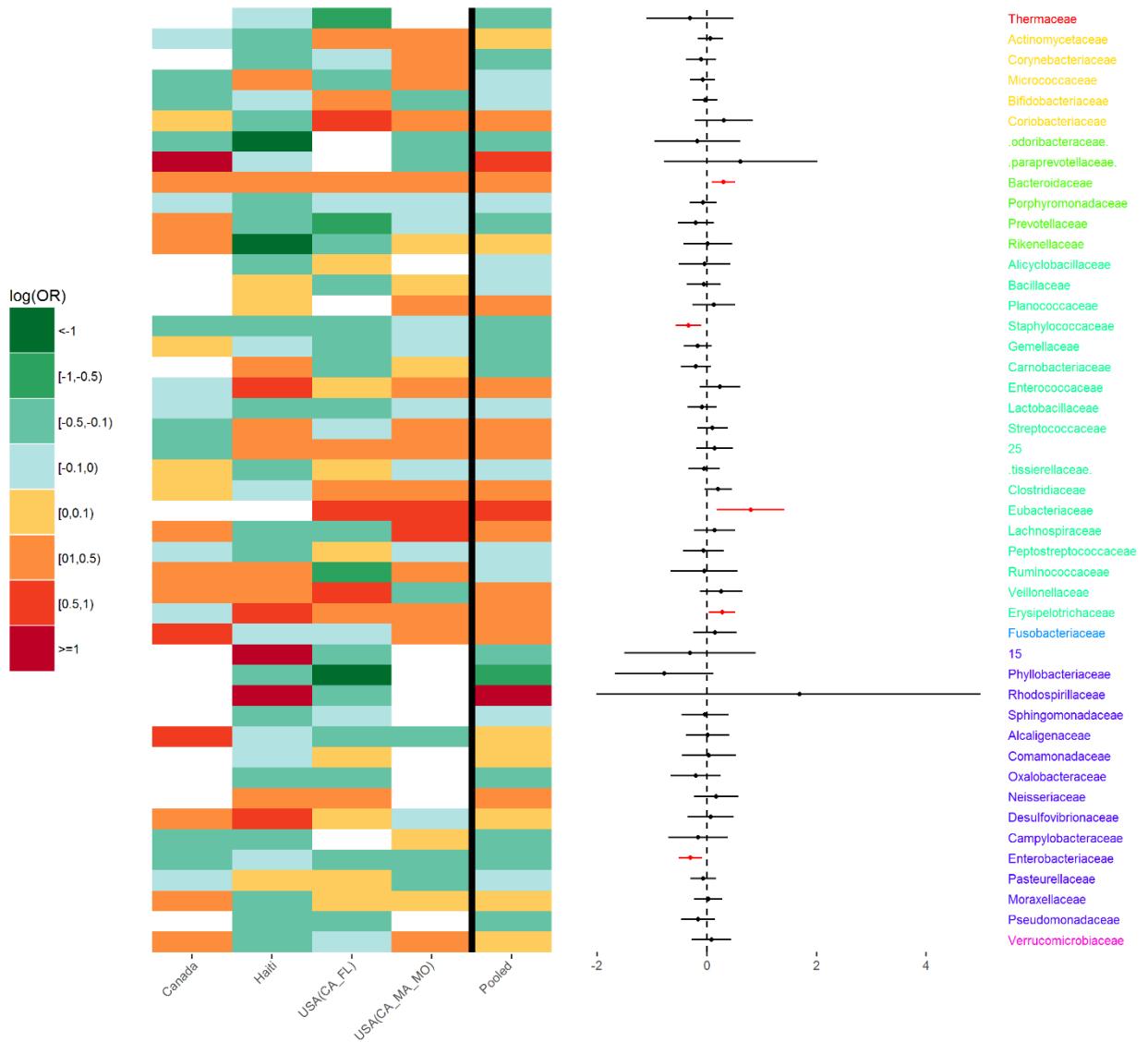
Heatmap of log(odds ratio) (log(OR)) of relative abundances of all gut bacterial families between non-exclusively breastfed (non-EBF) vs. exclusively breastfed (EBF) infants for each study and pooled estimates across four studies (with available mode of delivery information) and 95% confidence intervals (95% CI) (forest plot).

All log(OR) estimates of each bacterial taxa from each study were from Generalized Additive Models for Location Scale and Shape (GAMLSS) with beta zero inflated family (BEZI) and were adjusted for age of infants at sample collection. Pooled log(OR) estimates and 95% CI (forest plot) were from random effect meta-analysis models based on the adjusted log(OR) estimates and corresponding standard errors of all included studies.

Pooled log(OR) estimates with pooled p-values  $<0.05$  are in red and those with false discovery rate (FDR) adjusted pooled p-values  $<0.1$  are in triangle shape.

Missing (unavailable) values are in white. Taxa with unassigned name are numbered.

USA: United States of America; CA: California; FL: Florida; MA: Massachusetts; MO: Missouri.



**Supplementary figure 10. Meta-analysis stratified on C-section delivered infants: the effects of non-exclusive vs. exclusive breastfeeding on relative abundance of gut bacterial taxa at family level in infants  $\leq$  6 months.**

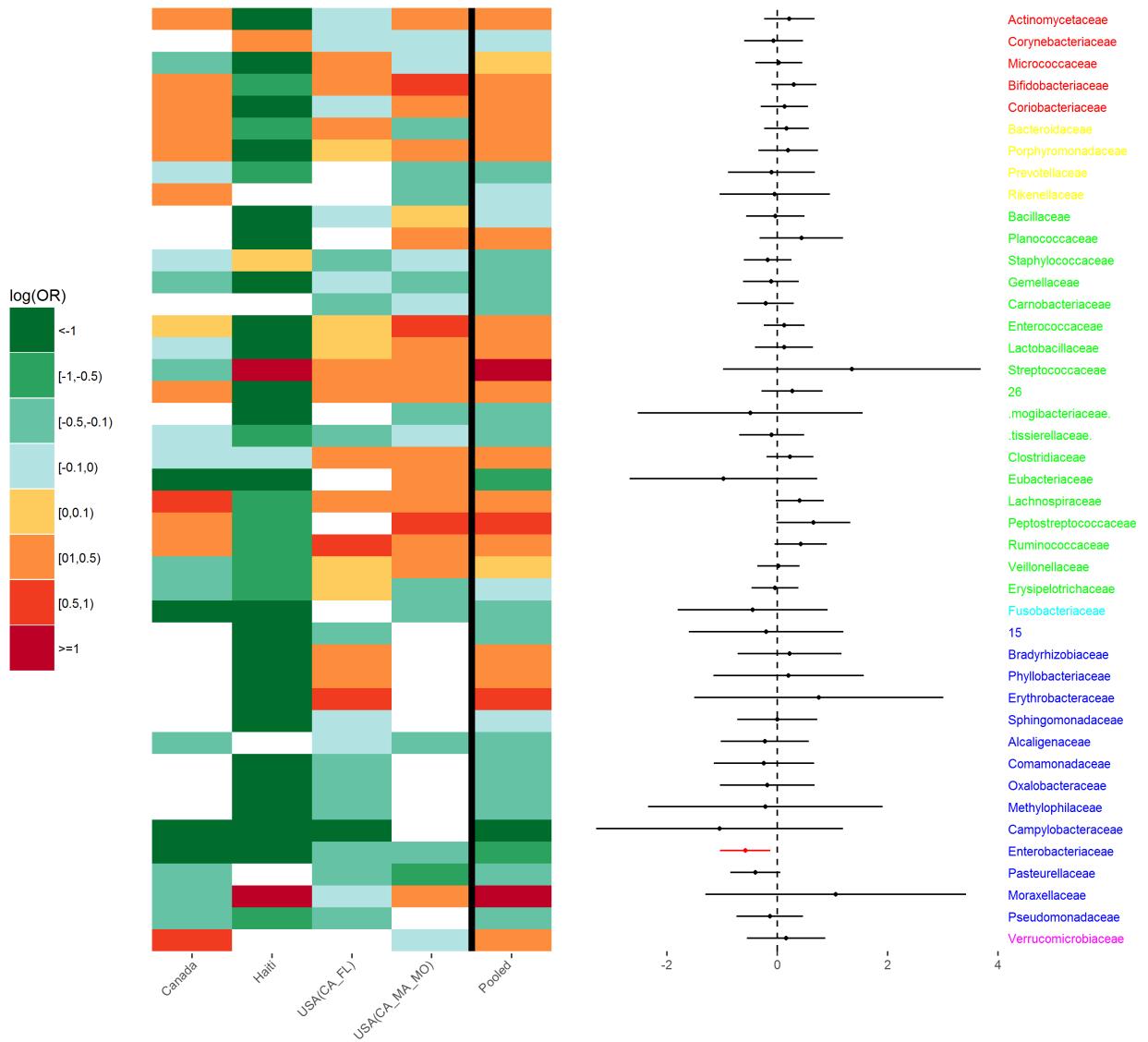
Heatmap of log(odds ratio) (log(OR)) of relative abundances of all gut bacterial families between non-exclusively breastfed (non-EBF) vs. exclusively breastfed (EBF) infants for each study and pooled estimates across four studies (with available mode of delivery information) and 95% confidence intervals (95% CI) (forest plot).

All log(OR) estimates of each bacterial taxa from each study were from Generalized Additive Models for Location Scale and Shape (GAMLSS) with beta zero inflated family (BEZI) and were adjusted for age of infants at sample collection. Pooled log(OR) estimates and 95% CI (forest plot) were from random effect meta-analysis models based on the adjusted log(OR) estimates and corresponding standard errors of all included studies.

Pooled log(OR) estimates with pooled p-values  $<0.05$  are in red and those with false discovery rate (FDR) adjusted pooled p-values  $<0.1$  are in triangle shape.

Missing (unavailable) values are in white. Taxa with unassigned name are numbered.

USA: United States of America; CA: California; FL: Florida; MA: Massachusetts; MO: Missouri.



**Supplementary figure 11. Meta-analysis stratified on vaginal delivered infants: the effects of non-exclusive vs. exclusive breastfeeding on relative abundance of gut bacterial taxa at genus level in infants  $\leq$  6 months.**

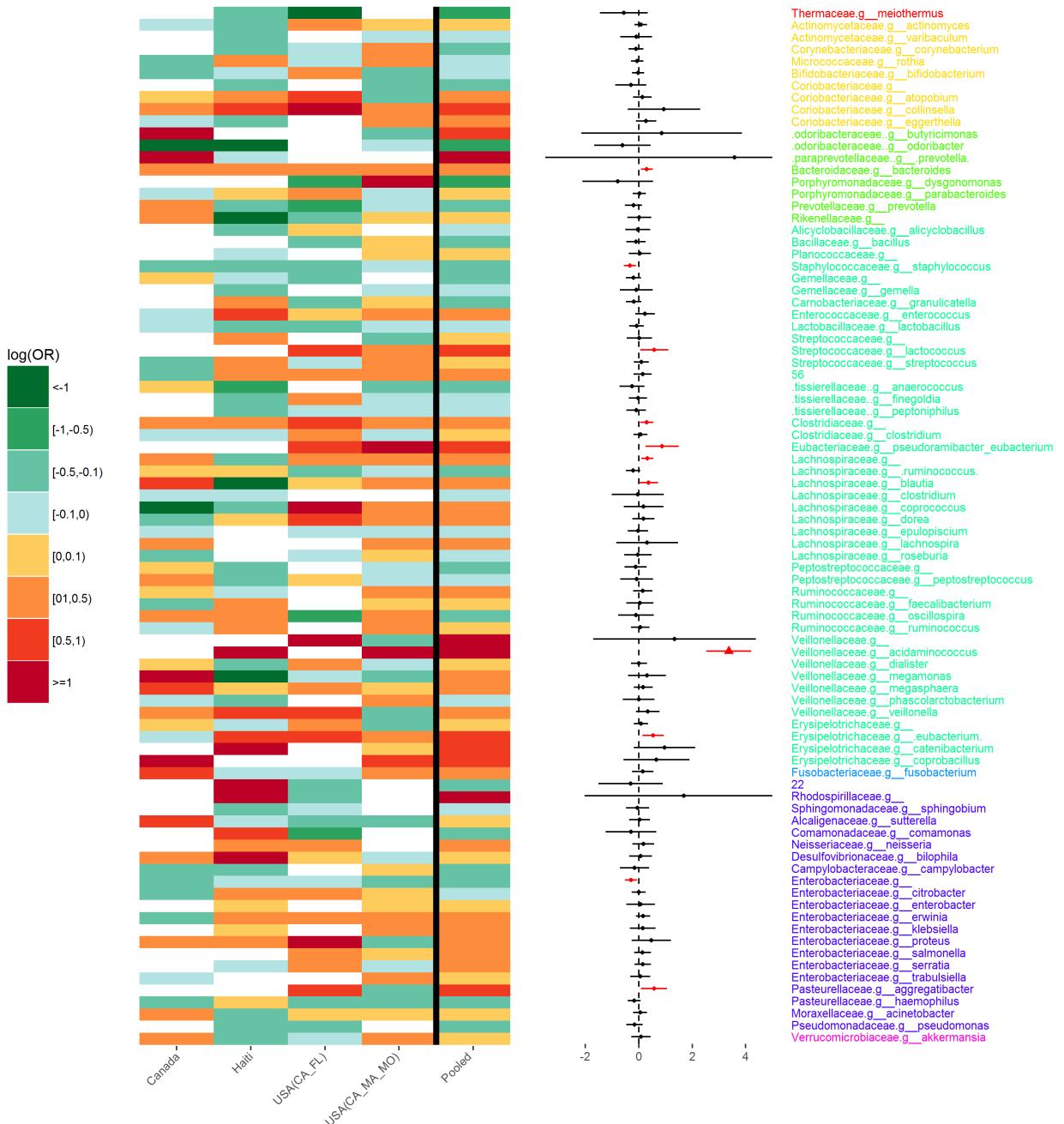
Heatmap of log(odds ratio) (log(OR)) of relative abundances of all gut bacterial genera between non-exclusively breastfed (non-EBF) vs. exclusively breastfed (EBF) infants for each study and pooled estimates across four studies (with available mode of delivery information) and 95% confidence intervals (95% CI) (forest plot).

All log(OR) estimates of each bacterial taxa from each study were from Generalized Additive Models for Location Scale and Shape (GAMLSS) with beta zero inflated family (BEZI) and were adjusted for age of infants at sample collection. Pooled log(OR) estimates and 95% CI (forest plot) were from random effect meta-analysis models based on the adjusted log(OR) estimates and corresponding standard errors of all included studies.

Pooled log(OR) estimates with pooled p-values  $<0.05$  are in red and those with false discovery rate (FDR) adjusted pooled p-values  $<0.1$  are in triangle shape.

Missing (unavailable) values are in white. Taxa with unassigned name are numbered.

USA: United States of America; CA: California; FL: Florida; MA: Massachusetts; MO: Missouri.



**Supplementary figure 12. Meta-analysis stratified on C-section delivered infants: the effects of non-exclusive vs. exclusive breastfeeding on relative abundance of gut bacterial taxa at genus level in infants  $\leq$  6 months.**

Heatmap of log(odds ratio) (log(OR)) of relative abundances of all gut bacterial genera between non-exclusively breastfed (non-EBF) vs. exclusively breastfed (EBF) infants for each study and pooled estimates across four studies (with available mode of delivery information) and 95% confidence intervals (95% CI) (forest plot).

All log(OR) estimates of each bacterial taxa from each study were from Generalized Additive Models for Location Scale and Shape (GAMLSS) with beta zero inflated family (BEZI) and were adjusted for age of infants at sample collection. Pooled log(OR) estimates and 95% CI (forest plot) were from random effect meta-analysis models based on the adjusted log(OR) estimates and corresponding standard errors of all included studies.

Pooled log(OR) estimates with pooled p-values  $<0.05$  are in red and those with false discovery rate (FDR) adjusted pooled p-values  $<0.1$  are in triangle shape.

Missing (unavailable) values are in white. Taxa with unassigned name are numbered.

USA: United States of America; CA: California; FL: Florida; MA: Massachusetts; MO: Missouri.

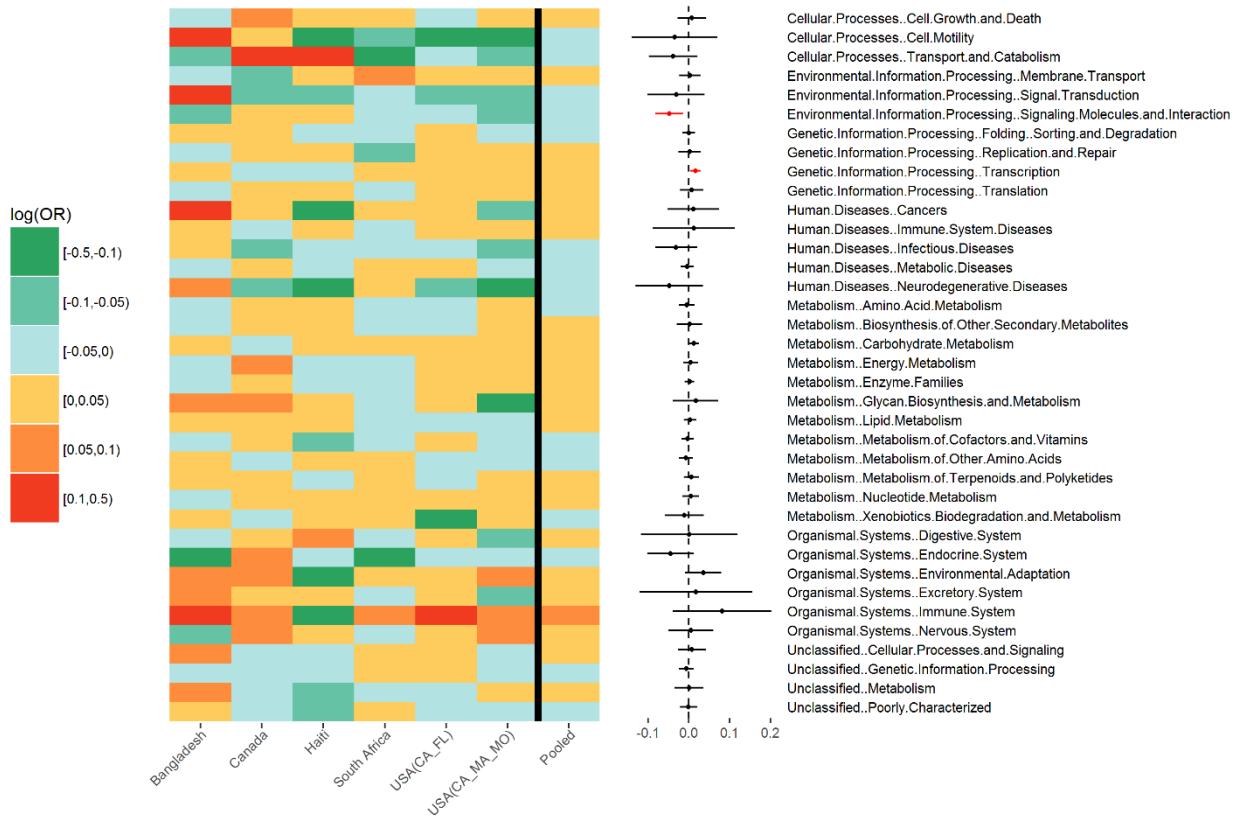


**Supplementary figure 13. Meta-analysis of seven included studies: the effects of non-exclusive vs. exclusive breastfeeding on relative abundances of gut microbial KEGG (Kyoto Encyclopedia of Genes and Genomes) pathways at level two in infants  $\leq$  6 months.**

Heatmap of log(odds ratio) (log(OR)) of relative abundances of all gut microbial KEGG pathways at level 2 between non-exclusively breastfed (non-EBF) vs. exclusively breastfed (EBF) infants for each study and pooled estimates of all studies with 95% confidence intervals (forest plot). All log(OR) estimates of each pathway from each study were from Generalized Additive Models for Location Scale and Shape (GAMLSS) with beta zero inflated family (BEZI) and were adjusted for age of infants at sample collection. Pooled log(OR) estimates and 95% confidence intervals (forest plot) were from random effect meta-analysis models based on the adjusted log(OR) estimates and corresponding standard errors of all included studies.

Pooled log(OR) estimates with pooled p-values $<0.05$  are in red and those with false discovery rate (FDR) adjusted pooled p-values  $<0.1$  are in triangle shape.

USA: United States of America; CA: California; FL: Florida; MA: Massachusetts; MO: Missouri; NC: North Carolina.



**Supplementary figure 14. Duration of exclusive breastfeeding mitigated the effects of diarrhea at the time of stool sample collection on gut microbiome diversity of infants from 6 months to 2 years of age.**

Alpha diversity indexes: Observed species, Phylogenetic diversity whole tree and Chao1 are shown.

Fitted lines and 95% confidence intervals (95% CI) were from Generalized Additive Mixed models (GAMM).

