

## Supplementary Online Content

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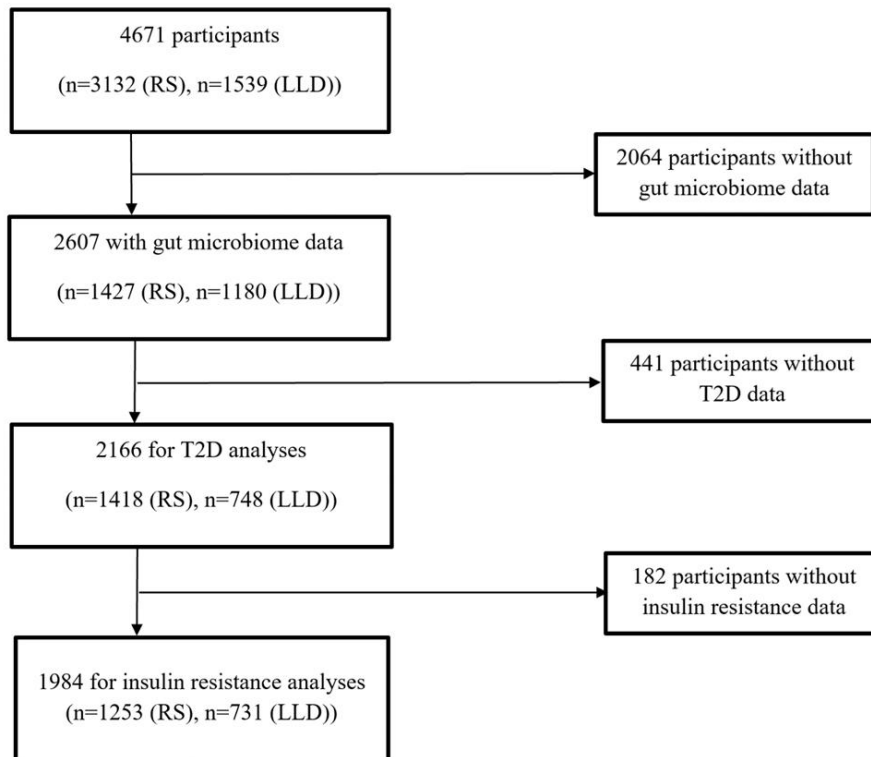
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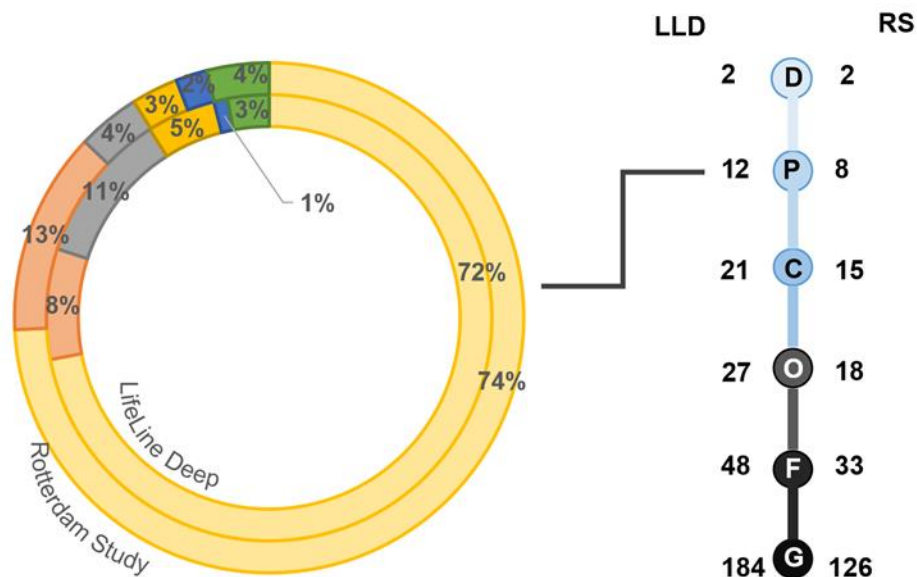
This supplementary material has been provided by the authors to give readers additional information about their work.

**eFigure 1.** Participant Selection

**eFigure 2.** Taxa in the Rotterdam Study and the Lifelines-Deep Study

### Five Major Phyla

- Firmicutes
- Bacteroidetes
- Actinobacteria
- Proteobacteria
- Verrucomicrobia
- Other



RS, Rotterdam Study; LLD, Lifelines Deep Study

D, domain; P, Phylum; C, Class; O, order; F, Family, G, Genus

**eTable 1.** Characteristics of Included and Excluded Participants

| <b>The Rotterdam Study</b>      | <b>Included participants</b> | <b>Excluded participants</b> |
|---------------------------------|------------------------------|------------------------------|
|                                 | n=1,41                       | n= 1,714                     |
| <b>Age (years)</b>              | 62.4 (5.9)                   | 61.7 (5.8)                   |
| <b>Sex (%)</b>                  |                              |                              |
| -Female                         | 815 (57.5%)                  | 972 (56.7%)                  |
| -Male                           | 603 (42.5%)                  | 742 (43.3%)                  |
| <b>Smoking (%)</b>              |                              |                              |
| -Current                        | 193 (13.6%)                  | 499 (29.1%)                  |
| -Non-smoker                     |                              |                              |
| Ever, quit                      | 706 (49.8%)                  | 715 (41.7%)                  |
| Never                           | 519 (36.6%)                  | 487 (28.4%)                  |
| <b>BMI (kg/m<sup>2</sup>)</b>   | 27.5 (4.5)                   | 27.8 (4.7)                   |
| <b>The Lifelines-Deep Study</b> | n=748                        | n=791                        |
| <b>Age (years)</b>              | 44.7 (13.4)                  | 45.17 (14.8)                 |
| <b>Sex (%)</b>                  |                              |                              |
| -Female                         | 431(57.6%)                   | 456 (57.7%)                  |
| -Male                           | 317 (42.4%)                  | 335 (42.3%)                  |
| <b>Smoking (%)</b>              |                              |                              |
| -Current                        | 155 (20.7%)                  | 371(46.94%)                  |
| -Non-smoker                     | 593 (79.3%)                  | 420(53.06%)                  |
| Ever, quit                      |                              |                              |
| Never                           |                              |                              |
| <b>BMI (kg/m<sup>2</sup>)</b>   | 25.2 (4.1)                   | 25.45 (4.2)                  |

Variables expressed as mean (SD), median (25th percentile–75th percentile), or percentage.

**eTable 2.** Associations of Taxa and Insulin Resistance

Effect estimates in RS and LLD were calculated using linear regression; pooled estimates were calculated based on a mixed-effect meta-analysis. Model 1: Adjusted for age, sex, Time in mail (RS), and Batch (RS).

Abbreviation, RS, Rotterdam Study, LLD, Lifelines-Deep Study. P<0.0005 indicates statistical significance

| Overlapping taxa in RS and LLD | Clade  | Phenotype | Beta_RS | Se_RS | Beta_LLD | Se_LLD | Beta_Meta | Lower95%CI_Meta | Upper95%CI_Meta | p_Meta | I <sup>2</sup> |
|--------------------------------|--------|-----------|---------|-------|----------|--------|-----------|-----------------|-----------------|--------|----------------|
| Bacteria.id.3                  | domain | Homa-IR   | 0.03    | 0.03  | 0.13     | 0.04   | 0.06      | 0.03            | 0.10            | 0.00   | 0.55           |
| Actinobacteria.id.400          | phylum | Homa-IR   | 0.03    | 0.03  | -0.01    | 0.04   | 0.02      | -0.03           | 0.06            | 0.48   | 0.07           |
| Bacteroidetes.id.905           | phylum | Homa-IR   | -0.07   | 0.03  | -0.04    | 0.04   | -0.05     | -0.10           | -0.01           | 0.01   | 0.00           |
| Cyanobacteria.id.1500          | phylum | Homa-IR   | -0.12   | 0.03  | -0.03    | 0.04   | -0.09     | -0.13           | -0.04           | 0.00   | 0.78           |
| Firmicutes.id.1672             | phylum | Homa-IR   | 0.01    | 0.03  | 0.09     | 0.04   | 0.04      | 0.00            | 0.09            | 0.04   | 0.70           |
| Proteobacteria.id.2375         | phylum | Homa-IR   | -0.04   | 0.03  | -0.02    | 0.04   | -0.03     | -0.08           | 0.01            | 0.13   | 0.00           |
| Tenericutes.id.3919            | phylum | Homa-IR   | -0.14   | 0.03  | -0.10    | 0.04   | -0.13     | -0.17           | -0.08           | 0.00   | 0.00           |
| Verrucomicrobia.id.3982        | phylum | Homa-IR   | -0.04   | 0.03  | -0.05    | 0.04   | -0.04     | -0.09           | 0.00            | 0.05   | 0.00           |
| Actinobacteria.id.419          | class  | Homa-IR   | 0.04    | 0.03  | -0.01    | 0.04   | 0.02      | -0.02           | 0.07            | 0.28   | 0.06           |
| Alphaproteobacteria.id.2379    | class  | Homa-IR   | -0.10   | 0.03  | -0.04    | 0.04   | -0.07     | -0.12           | -0.03           | 0.00   | 0.39           |
| Bacilli.id.1673                | class  | Homa-IR   | 0.12    | 0.03  | 0.09     | 0.03   | 0.11      | 0.06            | 0.15            | 0.00   | 0.00           |
| Bacteroidia.id.912             | class  | Homa-IR   | -0.07   | 0.03  | -0.04    | 0.04   | -0.05     | -0.10           | -0.01           | 0.01   | 0.00           |
| Betaproteobacteria.id.2867     | class  | Homa-IR   | -0.01   | 0.03  | 0.00     | 0.04   | -0.01     | -0.05           | 0.04            | 0.78   | 0.00           |
| Clostridia.id.1859             | class  | Homa-IR   | -0.04   | 0.03  | 0.04     | 0.04   | -0.01     | -0.05           | 0.03            | 0.68   | 0.71           |
| Coriobacteriia.id.809          | class  | Homa-IR   | -0.02   | 0.03  | -0.02    | 0.04   | -0.02     | -0.07           | 0.02            | 0.29   | 0.00           |
| Deltaproteobacteria.id.3087    | class  | Homa-IR   | -0.08   | 0.03  | -0.03    | 0.04   | -0.06     | -0.10           | -0.01           | 0.01   | 0.15           |
| Erysipelotrichia.id.2147       | class  | Homa-IR   | 0.05    | 0.03  | 0.05     | 0.04   | 0.05      | 0.01            | 0.10            | 0.02   | 0.00           |
| Gammaproteobacteria.id.3303    | class  | Homa-IR   | -0.04   | 0.03  | -0.01    | 0.04   | -0.03     | -0.07           | 0.01            | 0.17   | 0.00           |
| Melainabacteria.id.1589        | class  | Homa-IR   | -0.12   | 0.03  | -0.04    | 0.04   | -0.08     | -0.13           | -0.04           | 0.00   | 0.68           |
| Mollicutes.id.3920             | class  | Homa-IR   | -0.14   | 0.03  | -0.10    | 0.04   | -0.13     | -0.17           | -0.08           | 0.00   | 0.00           |
| Negativicutes.id.2164          | class  | Homa-IR   | 0.02    | 0.03  | -0.01    | 0.04   | 0.00      | -0.04           | 0.05            | 0.85   | 0.00           |
| Verrucomicrobiae.id.4029       | class  | Homa-IR   | -0.03   | 0.03  | -0.05    | 0.04   | -0.04     | -0.08           | 0.00            | 0.07   | 0.00           |
| Aeromonadales.id.3316          | order  | Homa-IR   | -0.03   | 0.03  | 0.04     | 0.04   | 0.00      | -0.04           | 0.04            | 0.95   | 0.55           |
| Bacteroidales.id.913           | order  | Homa-IR   | -0.07   | 0.03  | -0.04    | 0.04   | -0.05     | -0.10           | -0.01           | 0.01   | 0.00           |
| Bifidobacteriales.id.432       | order  | Homa-IR   | 0.03    | 0.03  | -0.01    | 0.04   | 0.02      | -0.03           | 0.06            | 0.43   | 0.00           |
| Burkholderiales.id.2874        | order  | Homa-IR   | -0.01   | 0.03  | 0.00     | 0.04   | -0.01     | -0.05           | 0.04            | 0.78   | 0.00           |
| Clostridiales.id.1863          | order  | Homa-IR   | -0.04   | 0.03  | 0.04     | 0.04   | -0.01     | -0.05           | 0.03            | 0.69   | 0.71           |

|                            |       |         |       |      |       |      |       |       |       |      |      |
|----------------------------|-------|---------|-------|------|-------|------|-------|-------|-------|------|------|
| Coriobacteriales.id.810    | order | Homa-IR | -0.02 | 0.03 | -0.02 | 0.04 | -0.02 | -0.07 | 0.02  | 0.29 | 0.00 |
| Desulfovibrionales.id.3156 | order | Homa-IR | -0.08 | 0.03 | -0.03 | 0.04 | -0.06 | -0.10 | -0.01 | 0.01 | 0.16 |

|                                      |        |         |       |      |       |      |       |       |       |      |      |
|--------------------------------------|--------|---------|-------|------|-------|------|-------|-------|-------|------|------|
| Enterobacteriales.id.3468            | order  | Homa-IR | -0.03 | 0.03 | 0.00  | 0.04 | -0.02 | -0.06 | 0.02  | 0.36 | 0.00 |
| Erysipelotrichales.id.2148           | order  | Homa-IR | 0.05  | 0.03 | 0.05  | 0.04 | 0.05  | 0.01  | 0.10  | 0.02 | 0.00 |
| Gastranaerophilales.id.1591          | order  | Homa-IR | -0.11 | 0.03 | -0.04 | 0.04 | -0.08 | -0.13 | -0.04 | 0.00 | 0.67 |
| Lactobacillales.id.1800              | order  | Homa-IR | 0.12  | 0.03 | 0.09  | 0.03 | 0.11  | 0.06  | 0.15  | 0.00 | 0.00 |
| MollicutesRF9.id.11579               | order  | Homa-IR | -0.12 | 0.03 | -0.10 | 0.04 | -0.11 | -0.15 | -0.07 | 0.00 | 0.00 |
| Pasteurellales.id.3688               | order  | Homa-IR | 0.00  | 0.03 | -0.06 | 0.04 | -0.02 | -0.07 | 0.02  | 0.28 | 0.55 |
| Rhodospirillales.id.2667             | order  | Homa-IR | -0.10 | 0.03 | -0.04 | 0.04 | -0.07 | -0.12 | -0.03 | 0.00 | 0.44 |
| Selenomonadales.id.2165              | order  | Homa-IR | 0.02  | 0.03 | -0.01 | 0.04 | 0.00  | -0.04 | 0.05  | 0.85 | 0.00 |
| Verrucomicrobiales.id.4030           | order  | Homa-IR | -0.03 | 0.03 | -0.05 | 0.04 | -0.04 | -0.08 | 0.00  | 0.07 | 0.00 |
| Acidaminococcaceae.id.2166           | family | Homa-IR | -0.05 | 0.03 | -0.03 | 0.04 | -0.04 | -0.09 | 0.00  | 0.05 | 0.00 |
| Alcaligenaceae.id.2875               | family | Homa-IR | 0.00  | 0.03 | 0.02  | 0.04 | 0.01  | -0.03 | 0.05  | 0.68 | 0.00 |
| Bacteroidaceae.id.917                | family | Homa-IR | -0.03 | 0.03 | -0.02 | 0.04 | -0.03 | -0.07 | 0.02  | 0.24 | 0.00 |
| Bifidobacteriaceae.id.433            | family | Homa-IR | 0.03  | 0.03 | -0.01 | 0.04 | 0.02  | -0.03 | 0.06  | 0.43 | 0.00 |
| Christensenellaceae.id.1866          | family | Homa-IR | -0.15 | 0.03 | -0.14 | 0.04 | -0.15 | -0.19 | -0.10 | 0.00 | 0.00 |
| Clostridiaceae1.id.1869              | family | Homa-IR | -0.03 | 0.03 | -0.06 | 0.04 | -0.04 | -0.09 | 0.00  | 0.06 | 0.00 |
| ClostridialesvadinBB60group.id.11286 | family | Homa-IR | -0.15 | 0.03 | -0.08 | 0.03 | -0.12 | -0.17 | -0.08 | 0.00 | 0.61 |
| Coriobacteriaceae.id.811             | family | Homa-IR | -0.02 | 0.03 | -0.02 | 0.04 | -0.02 | -0.07 | 0.02  | 0.29 | 0.00 |
| Desulfovibrionaceae.id.3169          | family | Homa-IR | -0.08 | 0.03 | -0.03 | 0.04 | -0.06 | -0.10 | -0.01 | 0.01 | 0.14 |
| Enterobacteriaceae.id.3469           | family | Homa-IR | -0.03 | 0.03 | 0.00  | 0.04 | -0.02 | -0.06 | 0.02  | 0.36 | 0.00 |
| Enterococcaceae.id.1828              | family | Homa-IR | 0.06  | 0.03 | 0.02  | 0.04 | 0.05  | 0.00  | 0.09  | 0.03 | 0.07 |
| Erysipelotrichaceae.id.2149          | family | Homa-IR | 0.05  | 0.03 | 0.05  | 0.04 | 0.05  | 0.01  | 0.10  | 0.02 | 0.00 |
| FamilyXIII.id.1957                   | family | Homa-IR | -0.10 | 0.03 | -0.02 | 0.04 | -0.07 | -0.12 | -0.03 | 0.00 | 0.70 |
| Lachnospiraceae.id.1987              | family | Homa-IR | 0.06  | 0.03 | 0.08  | 0.04 | 0.07  | 0.02  | 0.11  | 0.00 | 0.00 |
| Lactobacillaceae.id.1836             | family | Homa-IR | 0.06  | 0.03 | 0.04  | 0.04 | 0.06  | 0.01  | 0.10  | 0.01 | 0.00 |
| Pasteurellaceae.id.3689              | family | Homa-IR | 0.00  | 0.03 | -0.06 | 0.04 | -0.02 | -0.07 | 0.02  | 0.28 | 0.55 |
| Peptococcaceae.id.2024               | family | Homa-IR | -0.06 | 0.03 | 0.01  | 0.04 | -0.03 | -0.07 | 0.01  | 0.16 | 0.63 |
| Peptostreptococcaceae.id.2042        | family | Homa-IR | -0.03 | 0.03 | 0.02  | 0.04 | -0.01 | -0.05 | 0.03  | 0.67 | 0.00 |
| Porphyromonadaceae.id.943            | family | Homa-IR | -0.09 | 0.03 | -0.08 | 0.04 | -0.09 | -0.13 | -0.04 | 0.00 | 0.00 |
| Prevotellaceae.id.960                | family | Homa-IR | -0.02 | 0.03 | 0.03  | 0.04 | 0.00  | -0.05 | 0.04  | 0.89 | 0.18 |
| Rhodospirillaceae.id.2717            | family | Homa-IR | -0.10 | 0.03 | -0.04 | 0.04 | -0.07 | -0.12 | -0.03 | 0.00 | 0.45 |
| Rikenellaceae.id.967                 | family | Homa-IR | -0.13 | 0.03 | -0.11 | 0.03 | -0.12 | -0.16 | -0.08 | 0.00 | 0.00 |
| Ruminococcaceae.id.2050              | family | Homa-IR | -0.12 | 0.03 | 0.00  | 0.04 | -0.07 | -0.12 | -0.03 | 0.00 | 0.85 |

|                             |        |         |       |      |      |      |      |       |      |      |      |
|-----------------------------|--------|---------|-------|------|------|------|------|-------|------|------|------|
| Streptococcaceae.id.1850    | family | Homa-IR | 0.11  | 0.03 | 0.09 | 0.03 | 0.10 | 0.06  | 0.15 | 0.00 | 0.00 |
| Succinivibrionaceae.id.3326 | family | Homa-IR | -0.03 | 0.03 | 0.04 | 0.04 | 0.00 | -0.04 | 0.04 | 0.93 | 0.56 |



|                                            |        |         |       |      |       |      |       |       |       |      |      |
|--------------------------------------------|--------|---------|-------|------|-------|------|-------|-------|-------|------|------|
| Veillonellaceae.id.2172                    | family | Homa-IR | 0.08  | 0.03 | -0.01 | 0.04 | 0.04  | 0.00  | 0.09  | 0.04 | 0.71 |
| Verrucomicrobiaceae.id.4036                | family | Homa-IR | -0.03 | 0.03 | -0.05 | 0.04 | -0.04 | -0.08 | 0.00  | 0.07 | 0.00 |
| unknownfamily.id.1000001214                | family | Homa-IR | -0.11 | 0.03 | -0.04 | 0.04 | -0.08 | -0.13 | -0.04 | 0.00 | 0.67 |
| unknownfamily.id.1000005471                | family | Homa-IR | -0.12 | 0.03 | -0.10 | 0.04 | -0.11 | -0.15 | -0.07 | 0.00 | 0.00 |
| unknownfamily.id.987                       | family | Homa-IR | -0.01 | 0.03 | -0.05 | 0.04 | -0.03 | -0.07 | 0.02  | 0.23 | 0.00 |
| Bacteroidespectinophilusgroup.id.14371     | genus  | Homa-IR | -0.07 | 0.03 | -0.03 | 0.04 | -0.05 | -0.10 | -0.01 | 0.02 | 0.00 |
| Eubacteriumcoprostanoligenesgroup.id.11375 | genus  | Homa-IR | -0.03 | 0.03 | 0.02  | 0.04 | -0.01 | -0.05 | 0.03  | 0.66 | 0.08 |
| Eubacteriumeligensgroup.id.14372           | genus  | Homa-IR | -0.11 | 0.03 | -0.03 | 0.04 | -0.08 | -0.12 | -0.04 | 0.00 | 0.66 |
| Eubacteriumhalliigroup.id.11338            | genus  | Homa-IR | 0.08  | 0.03 | 0.03  | 0.04 | 0.06  | 0.02  | 0.10  | 0.01 | 0.29 |
| Eubacteriumrectalegroup.id.14374           | genus  | Homa-IR | 0.07  | 0.03 | 0.07  | 0.04 | 0.07  | 0.03  | 0.11  | 0.00 | 0.00 |
| Eubacteriumruminantiumgroup.id.11340       | genus  | Homa-IR | -0.06 | 0.03 | -0.05 | 0.04 | -0.06 | -0.10 | -0.02 | 0.01 | 0.00 |
| Eubacteriumventriosumgroup.id.11341        | genus  | Homa-IR | 0.02  | 0.03 | 0.07  | 0.04 | 0.04  | 0.00  | 0.08  | 0.08 | 0.27 |
| Eubacteriumxylanophilumgroup.id.14375      | genus  | Homa-IR | -0.12 | 0.03 | -0.04 | 0.04 | -0.09 | -0.13 | -0.05 | 0.00 | 0.72 |
| Ruminococcusgavreuiiigroup.id.11342        | genus  | Homa-IR | 0.02  | 0.03 | 0.10  | 0.03 | 0.05  | 0.00  | 0.09  | 0.03 | 0.68 |
| Ruminococcusgnavusgroup.id.14376           | genus  | Homa-IR | 0.04  | 0.03 | 0.11  | 0.03 | 0.07  | 0.03  | 0.11  | 0.00 | 0.49 |
| Ruminococcusostorquesgroup.id.14377        | genus  | Homa-IR | 0.06  | 0.03 | 0.02  | 0.04 | 0.05  | 0.00  | 0.09  | 0.04 | 0.00 |
| Acidaminococcus.id.2167                    | genus  | Homa-IR | 0.07  | 0.03 | 0.06  | 0.03 | 0.07  | 0.02  | 0.11  | 0.00 | 0.00 |
| Adlercreutzia.id.812                       | genus  | Homa-IR | 0.05  | 0.03 | 0.04  | 0.04 | 0.04  | 0.00  | 0.09  | 0.05 | 0.00 |
| Akkermansia.id.4037                        | genus  | Homa-IR | -0.03 | 0.03 | -0.05 | 0.04 | -0.04 | -0.08 | 0.00  | 0.07 | 0.00 |
| Alistipes.id.968                           | genus  | Homa-IR | -0.13 | 0.03 | -0.10 | 0.03 | -0.12 | -0.16 | -0.07 | 0.00 | 0.00 |
| Alloprevotella.id.961                      | genus  | Homa-IR | -0.03 | 0.03 | 0.03  | 0.04 | 0.00  | -0.05 | 0.04  | 0.83 | 0.49 |
| Anaerostipes.id.1991                       | genus  | Homa-IR | 0.00  | 0.03 | 0.03  | 0.04 | 0.01  | -0.03 | 0.06  | 0.54 | 0.00 |
| Anaerotruncus.id.2054                      | genus  | Homa-IR | -0.13 | 0.03 | -0.05 | 0.04 | -0.10 | -0.14 | -0.05 | 0.00 | 0.60 |
| Bacteroides.id.918                         | genus  | Homa-IR | -0.03 | 0.03 | -0.02 | 0.04 | -0.03 | -0.07 | 0.02  | 0.24 | 0.00 |
| Barnesiella.id.944                         | genus  | Homa-IR | -0.08 | 0.03 | -0.03 | 0.04 | -0.06 | -0.10 | -0.02 | 0.01 | 0.00 |
| Bifidobacterium.id.436                     | genus  | Homa-IR | 0.03  | 0.03 | 0.00  | 0.04 | 0.02  | -0.02 | 0.06  | 0.37 | 0.00 |
| Blautia.id.1992                            | genus  | Homa-IR | 0.06  | 0.03 | 0.06  | 0.04 | 0.06  | 0.02  | 0.11  | 0.00 | 0.00 |
| Butyrivibrio.id.2055                       | genus  | Homa-IR | 0.03  | 0.03 | -0.01 | 0.04 | 0.01  | -0.03 | 0.05  | 0.61 | 0.00 |
| Butyrivibrio.id.945                        | genus  | Homa-IR | -0.07 | 0.03 | -0.06 | 0.04 | -0.07 | -0.11 | -0.02 | 0.00 | 0.00 |
| Butyrivibrio.id.1993                       | genus  | Homa-IR | -0.09 | 0.03 | -0.03 | 0.04 | -0.07 | -0.11 | -0.02 | 0.00 | 0.37 |
| Catenibacterium.id.2153                    | genus  | Homa-IR | 0.05  | 0.03 | 0.01  | 0.04 | 0.03  | -0.01 | 0.07  | 0.15 | 0.00 |
| ChristensenellaceaeR7group.id.11283        | genus  | Homa-IR | -0.14 | 0.03 | -0.13 | 0.04 | -0.14 | -0.18 | -0.09 | 0.00 | 0.00 |

|                                     |       |         |       |      |       |      |       |       |      |      |      |
|-------------------------------------|-------|---------|-------|------|-------|------|-------|-------|------|------|------|
| Clostridium sensu stricto 1.id.1873 | genus | Homa-IR | -0.03 | 0.03 | -0.06 | 0.04 | -0.04 | -0.09 | 0.00 | 0.05 | 0.00 |
| Collinsella.id.815                  | genus | Homa-IR | 0.04  | 0.03 | -0.01 | 0.04 | 0.02  | -0.02 | 0.07 | 0.32 | 0.12 |

|                                      |       |         |       |      |       |      |       |       |       |      |      |
|--------------------------------------|-------|---------|-------|------|-------|------|-------|-------|-------|------|------|
| Coprococcus1.id.11301                | genus | Homa-IR | -0.08 | 0.03 | -0.05 | 0.04 | -0.07 | -0.11 | -0.03 | 0.00 | 0.00 |
| Coprococcus2.id.11302                | genus | Homa-IR | -0.08 | 0.03 | -0.04 | 0.04 | -0.07 | -0.11 | -0.02 | 0.00 | 0.00 |
| Coprococcus3.id.11303                | genus | Homa-IR | 0.02  | 0.03 | 0.02  | 0.04 | 0.02  | -0.02 | 0.06  | 0.38 | 0.00 |
| Desulfovibrio.id.3173                | genus | Homa-IR | -0.08 | 0.03 | -0.03 | 0.04 | -0.06 | -0.10 | -0.02 | 0.01 | 0.33 |
| Dialister.id.2183                    | genus | Homa-IR | 0.06  | 0.03 | -0.02 | 0.04 | 0.03  | -0.02 | 0.07  | 0.22 | 0.63 |
| Dorea.id.1997                        | genus | Homa-IR | 0.04  | 0.03 | -0.02 | 0.04 | 0.02  | -0.03 | 0.06  | 0.49 | 0.45 |
| Eggerthella.id.819                   | genus | Homa-IR | 0.00  | 0.03 | 0.09  | 0.03 | 0.04  | -0.01 | 0.08  | 0.09 | 0.74 |
| Eisenbergiella.id.11304              | genus | Homa-IR | -0.04 | 0.03 | 0.01  | 0.04 | -0.02 | -0.07 | 0.02  | 0.28 | 0.25 |
| Enterococcus.id.1831                 | genus | Homa-IR | 0.06  | 0.03 | 0.03  | 0.04 | 0.05  | 0.01  | 0.09  | 0.03 | 0.00 |
| Enterorhabdus.id.820                 | genus | Homa-IR | -0.08 | 0.03 | -0.06 | 0.04 | -0.07 | -0.11 | -0.03 | 0.00 | 0.00 |
| Erysipelatoclostridium.id.11381      | genus | Homa-IR | -0.01 | 0.03 | 0.05  | 0.04 | 0.01  | -0.03 | 0.05  | 0.62 | 0.40 |
| ErysipelotrichaceaeUCG003.id.11384   | genus | Homa-IR | 0.00  | 0.03 | 0.02  | 0.04 | 0.01  | -0.03 | 0.06  | 0.57 | 0.00 |
| Faecalibacterium.id.2057             | genus | Homa-IR | -0.03 | 0.03 | 0.04  | 0.04 | 0.00  | -0.05 | 0.04  | 0.88 | 0.61 |
| FamilyXIIAD3011group.id.11293        | genus | Homa-IR | -0.12 | 0.03 | -0.11 | 0.03 | -0.12 | -0.16 | -0.07 | 0.00 | 0.00 |
| FamilyXIIUCG001.id.11294             | genus | Homa-IR | -0.04 | 0.03 | -0.04 | 0.04 | -0.04 | -0.09 | 0.00  | 0.05 | 0.00 |
| Fusicatenibacter.id.11305            | genus | Homa-IR | 0.05  | 0.03 | 0.05  | 0.04 | 0.05  | 0.01  | 0.09  | 0.02 | 0.00 |
| Haemophilus.id.3698                  | genus | Homa-IR | 0.00  | 0.03 | -0.06 | 0.04 | -0.02 | -0.06 | 0.02  | 0.32 | 0.43 |
| Holdemanella.id.11393                | genus | Homa-IR | 0.04  | 0.03 | 0.06  | 0.04 | 0.05  | 0.01  | 0.09  | 0.03 | 0.00 |
| Intestinibacter.id.11345             | genus | Homa-IR | 0.00  | 0.03 | 0.03  | 0.04 | 0.01  | -0.03 | 0.05  | 0.61 | 0.00 |
| Intestinimonas.id.2062               | genus | Homa-IR | -0.08 | 0.03 | -0.05 | 0.04 | -0.07 | -0.11 | -0.03 | 0.00 | 0.00 |
| Lachnoclostridium.id.11308           | genus | Homa-IR | 0.01  | 0.03 | 0.09  | 0.04 | 0.04  | 0.00  | 0.09  | 0.05 | 0.67 |
| Lachnospira.id.2004                  | genus | Homa-IR | -0.02 | 0.03 | 0.02  | 0.04 | 0.00  | -0.05 | 0.04  | 0.91 | 0.00 |
| LachnospiraceaeFCS020group.id.11314  | genus | Homa-IR | -0.03 | 0.03 | -0.08 | 0.03 | -0.05 | -0.09 | -0.01 | 0.02 | 0.35 |
| LachnospiraceaeND3007group.id.11317  | genus | Homa-IR | -0.05 | 0.03 | -0.01 | 0.04 | -0.04 | -0.08 | 0.01  | 0.08 | 0.00 |
| LachnospiraceaeNK4A136group.id.11319 | genus | Homa-IR | -0.07 | 0.03 | 0.01  | 0.04 | -0.04 | -0.08 | 0.00  | 0.08 | 0.69 |
| LachnospiraceaeUCG001.id.11321       | genus | Homa-IR | -0.02 | 0.03 | 0.01  | 0.04 | -0.01 | -0.05 | 0.03  | 0.70 | 0.00 |
| LachnospiraceaeUCG004.id.11324       | genus | Homa-IR | -0.04 | 0.03 | -0.04 | 0.04 | -0.04 | -0.09 | 0.00  | 0.04 | 0.00 |
| LachnospiraceaeUCG010.id.11330       | genus | Homa-IR | -0.02 | 0.03 | -0.06 | 0.03 | -0.04 | -0.08 | 0.01  | 0.09 | 0.00 |
| Lactobacillus.id.1837                | genus | Homa-IR | 0.07  | 0.03 | 0.05  | 0.04 | 0.06  | 0.02  | 0.11  | 0.00 | 0.00 |
| Marvinbryantia.id.2005               | genus | Homa-IR | -0.12 | 0.03 | -0.08 | 0.04 | -0.11 | -0.15 | -0.06 | 0.00 | 0.00 |
| Megamonas.id.2184                    | genus | Homa-IR | 0.03  | 0.03 | -0.01 | 0.04 | 0.02  | -0.03 | 0.06  | 0.45 | 0.00 |
| Megasphaera.id.2185                  | genus | Homa-IR | 0.01  | 0.03 | 0.06  | 0.03 | 0.03  | -0.01 | 0.07  | 0.15 | 0.14 |

|                     |       |         |       |      |       |      |       |       |       |      |      |
|---------------------|-------|---------|-------|------|-------|------|-------|-------|-------|------|------|
| Mitsuokella.id.2186 | genus | Homa-IR | 0.05  | 0.03 | 0.02  | 0.04 | 0.04  | 0.00  | 0.08  | 0.06 | 0.00 |
| Odoribacter.id.952  | genus | Homa-IR | -0.09 | 0.03 | -0.09 | 0.04 | -0.09 | -0.13 | -0.05 | 0.00 | 0.00 |

|                                      |       |         |       |      |       |      |       |       |       |      |      |
|--------------------------------------|-------|---------|-------|------|-------|------|-------|-------|-------|------|------|
| Olsenella.id.822                     | genus | Homa-IR | 0.02  | 0.03 | -0.05 | 0.04 | -0.01 | -0.05 | 0.03  | 0.66 | 0.56 |
| Oscillospira.id.2064                 | genus | Homa-IR | -0.09 | 0.03 | -0.05 | 0.04 | -0.07 | -0.12 | -0.03 | 0.00 | 0.00 |
| Parabacteroides.id.954               | genus | Homa-IR | -0.07 | 0.03 | -0.07 | 0.04 | -0.07 | -0.11 | -0.03 | 0.00 | 0.00 |
| Paraprevotella.id.962                | genus | Homa-IR | -0.04 | 0.03 | -0.05 | 0.04 | -0.04 | -0.09 | 0.00  | 0.05 | 0.00 |
| Parasutterella.id.2892               | genus | Homa-IR | 0.01  | 0.03 | 0.06  | 0.04 | 0.03  | -0.01 | 0.08  | 0.13 | 0.21 |
| Peptococcus.id.2037                  | genus | Homa-IR | -0.02 | 0.03 | 0.02  | 0.04 | 0.00  | -0.05 | 0.04  | 0.85 | 0.00 |
| Phascolarctobacterium.id.2168        | genus | Homa-IR | -0.06 | 0.03 | -0.04 | 0.04 | -0.06 | -0.10 | -0.01 | 0.01 | 0.00 |
| Prevotella2.id.11180                 | genus | Homa-IR | 0.01  | 0.03 | -0.02 | 0.04 | 0.00  | -0.05 | 0.04  | 0.90 | 0.00 |
| Prevotella7.id.11182                 | genus | Homa-IR | 0.01  | 0.03 | 0.03  | 0.04 | 0.02  | -0.02 | 0.06  | 0.39 | 0.00 |
| Prevotella9.id.11183                 | genus | Homa-IR | -0.02 | 0.03 | 0.02  | 0.04 | 0.00  | -0.04 | 0.04  | 0.94 | 0.00 |
| PrevotellaceaeNK3B31group.id.11185   | genus | Homa-IR | 0.00  | 0.03 | 0.02  | 0.04 | 0.01  | -0.04 | 0.05  | 0.78 | 0.00 |
| PrevotellaceaeUCG001.id.11186        | genus | Homa-IR | -0.06 | 0.03 | 0.03  | 0.04 | -0.03 | -0.07 | 0.02  | 0.22 | 0.76 |
| RikenellaceaeRC9gutgroup.id.11191    | genus | Homa-IR | -0.01 | 0.03 | -0.05 | 0.04 | -0.03 | -0.07 | 0.02  | 0.22 | 0.00 |
| Romboutsia.id.11347                  | genus | Homa-IR | -0.03 | 0.03 | 0.01  | 0.04 | -0.01 | -0.06 | 0.03  | 0.53 | 0.06 |
| Roseburia.id.2012                    | genus | Homa-IR | 0.02  | 0.03 | 0.04  | 0.04 | 0.03  | -0.02 | 0.07  | 0.23 | 0.00 |
| Ruminiclostridium5.id.11355          | genus | Homa-IR | -0.09 | 0.03 | 0.01  | 0.04 | -0.05 | -0.09 | -0.01 | 0.02 | 0.79 |
| Ruminiclostridium6.id.11356          | genus | Homa-IR | -0.15 | 0.03 | -0.03 | 0.04 | -0.10 | -0.15 | -0.06 | 0.00 | 0.87 |
| Ruminiclostridium9.id.11357          | genus | Homa-IR | -0.09 | 0.03 | -0.14 | 0.03 | -0.11 | -0.15 | -0.06 | 0.00 | 0.29 |
| RuminococcaceaeNK4A214group.id.11358 | genus | Homa-IR | -0.16 | 0.03 | -0.15 | 0.03 | -0.15 | -0.20 | -0.11 | 0.00 | 0.00 |
| RuminococcaceaeUCG002.id.11360       | genus | Homa-IR | -0.12 | 0.03 | -0.13 | 0.03 | -0.12 | -0.17 | -0.08 | 0.00 | 0.00 |
| RuminococcaceaeUCG003.id.11361       | genus | Homa-IR | -0.06 | 0.03 | -0.12 | 0.03 | -0.09 | -0.13 | -0.04 | 0.00 | 0.39 |
| RuminococcaceaeUCG004.id.11362       | genus | Homa-IR | 0.00  | 0.03 | -0.01 | 0.04 | -0.01 | -0.05 | 0.04  | 0.78 | 0.00 |
| RuminococcaceaeUCG005.id.11363       | genus | Homa-IR | -0.16 | 0.03 | -0.11 | 0.04 | -0.14 | -0.18 | -0.10 | 0.00 | 0.32 |
| RuminococcaceaeUCG008.id.11365       | genus | Homa-IR | -0.12 | 0.03 | -0.07 | 0.04 | -0.10 | -0.14 | -0.06 | 0.00 | 0.33 |
| RuminococcaceaeUCG010.id.11367       | genus | Homa-IR | -0.17 | 0.03 | -0.14 | 0.03 | -0.16 | -0.20 | -0.12 | 0.00 | 0.00 |
| RuminococcaceaeUCG013.id.11370       | genus | Homa-IR | 0.00  | 0.03 | 0.08  | 0.04 | 0.03  | -0.01 | 0.08  | 0.14 | 0.67 |
| RuminococcaceaeUCG014.id.11371       | genus | Homa-IR | -0.13 | 0.03 | -0.10 | 0.04 | -0.12 | -0.16 | -0.08 | 0.00 | 0.00 |
| Ruminococcus1.id.11373               | genus | Homa-IR | -0.09 | 0.03 | 0.05  | 0.04 | -0.03 | -0.07 | 0.01  | 0.15 | 0.90 |
| Ruminococcus2.id.11374               | genus | Homa-IR | 0.02  | 0.03 | 0.05  | 0.04 | 0.03  | -0.01 | 0.07  | 0.15 | 0.00 |
| Sellimonas.id.14369                  | genus | Homa-IR | 0.04  | 0.03 | 0.06  | 0.04 | 0.05  | 0.00  | 0.09  | 0.03 | 0.00 |
| Senegalimassilia.id.11160            | genus | Homa-IR | -0.01 | 0.03 | -0.07 | 0.03 | -0.03 | -0.07 | 0.01  | 0.16 | 0.39 |
| Slackia.id.825                       | genus | Homa-IR | 0.05  | 0.03 | -0.07 | 0.04 | 0.00  | -0.04 | 0.05  | 0.83 | 0.85 |

|                         |       |         |       |      |      |      |      |       |      |      |      |
|-------------------------|-------|---------|-------|------|------|------|------|-------|------|------|------|
| Streptococcus.id.1853   | genus | Homa-IR | 0.12  | 0.03 | 0.09 | 0.03 | 0.11 | 0.06  | 0.15 | 0.00 | 0.00 |
| Subdoligranulum.id.2070 | genus | Homa-IR | -0.01 | 0.03 | 0.02 | 0.04 | 0.00 | -0.04 | 0.04 | 0.98 | 0.00 |

|                            |       |         |       |      |       |      |       |       |       |      |      |
|----------------------------|-------|---------|-------|------|-------|------|-------|-------|-------|------|------|
| Succiniclasicum.id.2169    | genus | Homa-IR | -0.01 | 0.03 | -0.01 | 0.04 | -0.01 | -0.05 | 0.04  | 0.75 | 0.00 |
| Sutterella.id.2896         | genus | Homa-IR | -0.02 | 0.03 | -0.05 | 0.04 | -0.03 | -0.08 | 0.01  | 0.15 | 0.00 |
| Terrisporobacter.id.11348  | genus | Homa-IR | -0.04 | 0.03 | -0.03 | 0.04 | -0.04 | -0.08 | 0.01  | 0.11 | 0.00 |
| Turicibacter.id.2162       | genus | Homa-IR | -0.04 | 0.03 | -0.06 | 0.04 | -0.05 | -0.09 | 0.00  | 0.03 | 0.00 |
| Tyzzereila3.id.11335       | genus | Homa-IR | 0.06  | 0.03 | 0.02  | 0.04 | 0.04  | 0.00  | 0.09  | 0.04 | 0.00 |
| Veillonella.id.2198        | genus | Homa-IR | 0.03  | 0.03 | -0.03 | 0.04 | 0.01  | -0.04 | 0.05  | 0.77 | 0.47 |
| unknowngenus.id.1000000073 | genus | Homa-IR | -0.15 | 0.03 | -0.08 | 0.03 | -0.12 | -0.17 | -0.08 | 0.00 | 0.61 |
| unknowngenus.id.1000001215 | genus | Homa-IR | -0.11 | 0.03 | -0.04 | 0.04 | -0.08 | -0.13 | -0.04 | 0.00 | 0.67 |
| unknowngenus.id.1000005472 | genus | Homa-IR | -0.12 | 0.03 | -0.10 | 0.04 | -0.11 | -0.15 | -0.07 | 0.00 | 0.00 |
| unknowngenus.id.1000005479 | genus | Homa-IR | -0.08 | 0.03 | -0.04 | 0.04 | -0.06 | -0.11 | -0.02 | 0.00 | 0.00 |
| unknowngenus.id.1000013899 | genus | Homa-IR | -0.01 | 0.03 | -0.05 | 0.04 | -0.03 | -0.07 | 0.02  | 0.23 | 0.00 |
| unknowngenus.id.2071       | genus | Homa-IR | -0.15 | 0.03 | -0.05 | 0.04 | -0.11 | -0.16 | -0.07 | 0.00 | 0.81 |
| unknowngenus.id.2755       | genus | Homa-IR | -0.10 | 0.03 | -0.03 | 0.04 | -0.07 | -0.11 | -0.03 | 0.00 | 0.46 |
| unknowngenus.id.826        | genus | Homa-IR | -0.07 | 0.03 | -0.02 | 0.04 | -0.05 | -0.09 | -0.01 | 0.02 | 0.29 |
| unknowngenus.id.964        | genus | Homa-IR | 0.03  | 0.03 | 0.01  | 0.04 | 0.02  | -0.02 | 0.07  | 0.30 | 0.00 |

| Taxa in RS only                            | Clade  | Phenotype | Beta_RS | Se_RS |
|--------------------------------------------|--------|-----------|---------|-------|
| BacteroidalesS247group.id.11173            | family | Homa-IR   | -0.08   | 0.03  |
| Veillonellaceae.id.2172                    | family | Homa-IR   | 0.08    | 0.03  |
| Bacteroidespectinophilusgroup.id.14371     | genus  | Homa-IR   | -0.07   | 0.03  |
| Enterobacter.id.3502                       | genus  | Homa-IR   | 0.08    | 0.03  |
| EscherichiaShigella.id.3504                | genus  | Homa-IR   | -0.04   | 0.03  |
| Eubacteriumcoprostanoligenesgroup.id.11375 | genus  | Homa-IR   | -0.03   | 0.03  |
| Eubacteriumeligensgroup.id.14372           | genus  | Homa-IR   | -0.11   | 0.03  |
| Eubacteriumhalliigroup.id.11338            | genus  | Homa-IR   | 0.08    | 0.03  |
| Eubacteriumoxidoreducensgroup.id.11339     | genus  | Homa-IR   | -0.17   | 0.03  |
| Eubacteriumxylanophilumgroup.id.14375      | genus  | Homa-IR   | -0.12   | 0.03  |
| Hungatella.id.11306                        | genus  | Homa-IR   | -0.04   | 0.03  |
| Klebsiella.id.3507                         | genus  | Homa-IR   | 0.05    | 0.03  |
| LachnospiraceaeNC2004group.id.11316        | genus  | Homa-IR   | -0.12   | 0.03  |

|                                |       |         |       |      |
|--------------------------------|-------|---------|-------|------|
| LachnospiraceaeUCG008.id.11328 | genus | Homa-IR | -0.06 | 0.03 |
| unknowngenus.id.1868           | genus | Homa-IR | -0.13 | 0.03 |



| Taxa in LLD only                  | Clade  | Phenotype | Beta_LLD | Se_LLD |
|-----------------------------------|--------|-----------|----------|--------|
| Archaea.id.2                      | domain | Homa-IR   | -0.13    | 0.04   |
| Euryarchaeota.id.55               | phylum | Homa-IR   | -0.13    | 0.04   |
| Lentisphaerae.id.2238             | phylum | Homa-IR   | -0.05    | 0.04   |
| Actinomycetales.id.420            | order  | Homa-IR   | 0.04     | 0.04   |
| Mycoplasmatales.id.3946           | order  | Homa-IR   | -0.03    | 0.04   |
| NB1.n.id.3953                     | order  | Homa-IR   | -0.05    | 0.04   |
| Pseudomonadales.id.3709           | order  | Homa-IR   | -0.02    | 0.04   |
| Spirochaetales.id.3870            | order  | Homa-IR   | -0.02    | 0.04   |
| Synergistales.id.3900             | order  | Homa-IR   | -0.05    | 0.04   |
| Thermoplasmatales.id.220          | order  | Homa-IR   | -0.03    | 0.04   |
| unknownorder.id.1000000003        | order  | Homa-IR   | 0.01     | 0.04   |
| Verrucomicrobiales.id.4030        | order  | Homa-IR   | -0.05    | 0.04   |
| Victivallales.id.2254             | order  | Homa-IR   | -0.05    | 0.04   |
| Xanthomonadales.id.3786           | order  | Homa-IR   | -0.02    | 0.04   |
| Spirochaetes.id.3856              | class  | Homa-IR   | -0.02    | 0.04   |
| Synergistia.id.3899               | class  | Homa-IR   | -0.05    | 0.04   |
| Thermoplasmata.id.210             | class  | Homa-IR   | -0.03    | 0.04   |
| Actinomycetaceae.id.421           | family | Homa-IR   | 0.04     | 0.04   |
| BacteroidalesS24.7group.id.11173  | family | Homa-IR   | -0.04    | 0.04   |
| Christensenellaceae.id.1866       | family | Homa-IR   | -0.14    | 0.04   |
| FamilyXI.id.1936                  | family | Homa-IR   | 0.00     | 0.04   |
| unknownfamily.id.1000000004       | family | Homa-IR   | 0.01     | 0.04   |
| unknownfamily.id.1000006161       | family | Homa-IR   | -0.05    | 0.04   |
| unknownfamily.id.1855             | family | Homa-IR   | -0.01    | 0.04   |
| vadinBE97.id.14446                | family | Homa-IR   | -0.03    | 0.04   |
| Veillonellaceae.id.2172           | family | Homa-IR   | -0.01    | 0.04   |
| Xanthomonadaceae.id.3799          | family | Homa-IR   | -0.02    | 0.04   |
| Clostridiuminnocuumgroup.id.14397 | genus  | Homa-IR   | 0.04     | 0.04   |
| Eubacteriumbrachygroup.id.11296   | genus  | Homa-IR   | 0.07     | 0.04   |
| Abiotrophia.id.1803               | genus  | Homa-IR   | 0.01     | 0.04   |
| Actinomyces.id.423                | genus  | Homa-IR   | 0.06     | 0.04   |

|                       |       |         |       |      |
|-----------------------|-------|---------|-------|------|
| Actinotignum.id.11137 | genus | Homa-IR | -0.04 | 0.04 |
| Allisonella.id.2174   | genus | Homa-IR | 0.10  | 0.03 |

|                                     |       |         |       |      |
|-------------------------------------|-------|---------|-------|------|
| Arcanobacterium.id.424              | genus | Homa-IR | 0.00  | 0.04 |
| Asaccharobacter.id.813              | genus | Homa-IR | 0.03  | 0.04 |
| Bilophila.id.3170                   | genus | Homa-IR | -0.02 | 0.04 |
| CandidatusMethanogranum.id.11110    | genus | Homa-IR | -0.01 | 0.04 |
| Catenisphaera.id.14395              | genus | Homa-IR | 0.00  | 0.04 |
| Cellulosilyticum.id.1995            | genus | Homa-IR | -0.06 | 0.04 |
| Cetobacterium.id.2209               | genus | Homa-IR | 0.06  | 0.04 |
| Cloacibacillus.id.3908              | genus | Homa-IR | -0.03 | 0.04 |
| Coprobacillus.id.2154               | genus | Homa-IR | 0.03  | 0.04 |
| CoriobacteriaceaeUCG.002.id.11158   | genus | Homa-IR | -0.05 | 0.04 |
| CoriobacteriaceaeUCG.003.id.11159   | genus | Homa-IR | 0.05  | 0.04 |
| Denitrobacterium.id.818             | genus | Homa-IR | -0.02 | 0.04 |
| dgA.11gutgroup.id.978               | genus | Homa-IR | 0.03  | 0.04 |
| Dielma.id.11380                     | genus | Homa-IR | -0.01 | 0.04 |
| Epulopiscium.id.1998                | genus | Homa-IR | 0.04  | 0.04 |
| ErysipelotrichaceaeUCG006.id.11386  | genus | Homa-IR | 0.01  | 0.04 |
| ErysipelotrichaceaeUCG009.id.11389  | genus | Homa-IR | 0.05  | 0.04 |
| Escherichia.Shigella.id.3504        | genus | Homa-IR | 0.00  | 0.04 |
| Eubacterium.id.1932                 | genus | Homa-IR | 0.06  | 0.04 |
| Faecalicoccus.id.11391              | genus | Homa-IR | -0.01 | 0.04 |
| Faecalitalea.id.11392               | genus | Homa-IR | 0.05  | 0.04 |
| Flavonifractor.id.2059              | genus | Homa-IR | 0.01  | 0.04 |
| Gardnerella.id.437                  | genus | Homa-IR | 0.01  | 0.04 |
| Gordonibacter.id.821                | genus | Homa-IR | 0.01  | 0.04 |
| Hafnia.Obesumbacterium.id.14636     | genus | Homa-IR | 0.01  | 0.04 |
| Howardella.id.2000                  | genus | Homa-IR | 0.00  | 0.04 |
| LachnospiraceaeNK3A20group.id.11318 | genus | Homa-IR | 0.01  | 0.04 |
| Lactococcus.id.1851                 | genus | Homa-IR | -0.03 | 0.04 |
| Lautropia.id.2905                   | genus | Homa-IR | 0.01  | 0.04 |
| Leuconostoc.id.1841                 | genus | Homa-IR | 0.01  | 0.04 |
| Methanobrevibacter.id.123           | genus | Homa-IR | -0.12 | 0.04 |
| Methanosphaera.id.124               | genus | Homa-IR | -0.07 | 0.04 |

|                       |       |         |      |      |
|-----------------------|-------|---------|------|------|
| Mogibacterium.id.1960 | genus | Homa-IR | 0.00 | 0.04 |
| Morganella.id.3512    | genus | Homa-IR | 0.04 | 0.04 |

|                                      |       |         |       |      |
|--------------------------------------|-------|---------|-------|------|
| Porphyromonas.id.956                 | genus | Homa-IR | -0.01 | 0.04 |
| Prevotella1.id.11179                 | genus | Homa-IR | 0.02  | 0.04 |
| PrevotellaceaeUCG003.id.11187        | genus | Homa-IR | 0.07  | 0.03 |
| PrevotellaceaeUCG004.id.11188        | genus | Homa-IR | -0.06 | 0.04 |
| Pseudomonas.id.3723                  | genus | Homa-IR | -0.02 | 0.04 |
| Rikenella.id.973                     | genus | Homa-IR | 0.01  | 0.04 |
| RuminococcaceaeNK4A214group.id.11358 | genus | Homa-IR | -0.15 | 0.03 |
| RuminococcaceaeUCG005.id.11363       | genus | Homa-IR | -0.11 | 0.04 |
| RuminococcaceaeUCG008.id.11365       | genus | Homa-IR | -0.07 | 0.04 |
| RuminococcaceaeUCG010.id.11367       | genus | Homa-IR | -0.14 | 0.03 |
| Sarcina.id.1896                      | genus | Homa-IR | 0.06  | 0.04 |
| Solobacterium.id.2161                | genus | Homa-IR | 0.05  | 0.04 |
| Staphylococcus.id.1780               | genus | Homa-IR | 0.04  | 0.04 |
| Stenotrophomonas.id.3818             | genus | Homa-IR | -0.02 | 0.04 |
| Succinivibrio.id.3331                | genus | Homa-IR | 0.04  | 0.04 |
| Synergistes.id.3913                  | genus | Homa-IR | -0.03 | 0.04 |
| Syntrophococcus.id.2016              | genus | Homa-IR | 0.00  | 0.04 |
| Treponema2.id.11577                  | genus | Homa-IR | -0.02 | 0.04 |
| Tyzzerella4.id.11336                 | genus | Homa-IR | 0.04  | 0.04 |
| unknowngenus.id.1000000005           | genus | Homa-IR | 0.01  | 0.04 |
| unknowngenus.id.1000027565           | genus | Homa-IR | -0.03 | 0.04 |
| unknowngenus.id.1000043796           | genus | Homa-IR | -0.01 | 0.04 |
| unknowngenus.id.1854                 | genus | Homa-IR | -0.02 | 0.04 |
| unknowngenus.id.2163                 | genus | Homa-IR | -0.05 | 0.04 |
| unknowngenus.id.3332                 | genus | Homa-IR | 0.05  | 0.04 |
| unknowngenus.id.441                  | genus | Homa-IR | -0.08 | 0.04 |
| Ureaplasma.id.3951                   | genus | Homa-IR | -0.03 | 0.04 |
| Varibaculum.id.427                   | genus | Homa-IR | 0.00  | 0.04 |
| Veillonella.id.2198                  | genus | Homa-IR | -0.03 | 0.04 |
| Weissella.id.1843                    | genus | Homa-IR | 0.00  | 0.04 |

**Supplementary Table 2 - Associations of taxa and insulin resistance**

Effect estimates in RS and LLD were calculated using linear regression; pooled estimates were calculated based on a mixed-effect meta-analysis. Model 2: Adjusted for age, sex, Time in mail (RS), Batch (RS), smoking, education level (RS), physical activity, alcohol intake, and total energy intake. Abbreviation, RS, Rotterdam Study, LLD, Lifelines-Deep Study. P<0.0005 indicates statistical significance

| Overlapping taxa in RS and LLD | Clade | Phenotype | Beta_RS | Se_RS | Beta_LLD | Se_LLD | Beta_Meta | Lower95%CI_Meta | Upper95%CI_Meta | p_Meta | I <sup>2</sup> |
|--------------------------------|-------|-----------|---------|-------|----------|--------|-----------|-----------------|-----------------|--------|----------------|
| Bacteria.id.3                  | domai | Homa-     | 0.0     | 0.0   | 0.1      | 0.03   | 0.05      | 0.02            | 0.09            | 0.0    | 0.             |
| Actinobacteria.id.400          | phylu | Homa-     | 0.0     | 0.0   | -        | 0.03   | 0.00      | -0.04           | 0.05            | 0.8    | 0.             |
| Bacteroidetes.id.905           | phylu | Homa-     | -       | 0.0   | -        | 0.03   | -0.05     | -0.10           | -0.01           | 0.0    | 0.             |
| Cyanobacteria.id.1500          | phylu | Homa-     | -       | 0.0   | -        | 0.03   | -0.08     | -0.13           | -0.04           | 0.0    | 0.             |
| Firmicutes.id.1672             | phylu | Homa-     | 0.0     | 0.0   | 0.1      | 0.03   | 0.05      | 0.01            | 0.10            | 0.0    | 0.             |
| Proteobacteria.id.2375         | phylu | Homa-     | -       | 0.0   | -        | 0.03   | -0.03     | -0.08           | 0.02            | 0.2    | 0.             |
| Tenericutes.id.3919            | phylu | Homa-     | -       | 0.0   | -        | 0.03   | -0.12     | -0.17           | -0.08           | 0.0    | 0.             |
| Verrucomicrobia.id.3982        | phylu | Homa-     | -       | 0.0   | -        | 0.03   | -0.03     | -0.08           | 0.01            | 0.1    | 0.             |
| Actinobacteria.id.419          | class | Homa-     | 0.0     | 0.0   | -        | 0.04   | 0.01      | -0.04           | 0.05            | 0.7    | 0.             |
| Alphaproteobacteria.id.2379    | class | Homa-     | -       | 0.0   | -        | 0.03   | -0.08     | -0.13           | -0.04           | 0.0    | 0.             |
| Bacilli.id.1673                | class | Homa-     | 0.0     | 0.0   | 0.0      | 0.03   | 0.08      | 0.03            | 0.12            | 0.0    | 0.             |
| Bacteroidia.id.912             | class | Homa-     | -       | 0.0   | -        | 0.03   | -0.05     | -0.10           | -0.01           | 0.0    | 0.             |
| Betaproteobacteria.id.2867     | class | Homa-     | -       | 0.0   | 0.0      | 0.03   | -0.01     | -0.05           | 0.04            | 0.7    | 0.             |
| Clostridia.id.1859             | class | Homa-     | -       | 0.0   | 0.0      | 0.03   | 0.00      | -0.04           | 0.05            | 0.9    | 0.             |
| Coriobacteriia.id.809          | class | Homa-     | -       | 0.0   | -        | 0.03   | -0.01     | -0.06           | 0.03            | 0.6    | 0.             |
| Deltaproteobacteria.id.3087    | class | Homa-     | -       | 0.0   | -        | 0.03   | -0.04     | -0.09           | 0.00            | 0.0    | 0.             |
| Erysipelotrichia.id.2147       | class | Homa-     | 0.0     | 0.0   | 0.0      | 0.03   | 0.07      | 0.03            | 0.12            | 0.0    | 0.             |
| Gammaproteobacteria.id.3303    | class | Homa-     | -       | 0.0   | 0.0      | 0.03   | -0.03     | -0.07           | 0.02            | 0.2    | 0.             |
| Melainabacteria.id.1589        | class | Homa-     | -       | 0.0   | -        | 0.03   | -0.08     | -0.13           | -0.04           | 0.0    | 0.             |
| Mollicutes.id.3920             | class | Homa-     | -       | 0.0   | -        | 0.03   | -0.12     | -0.17           | -0.08           | 0.0    | 0.             |
| Negativicutes.id.2164          | class | Homa-     | 0.0     | 0.0   | -        | 0.03   | -0.01     | -0.05           | 0.04            | 0.8    | 0.             |
| Verrucomicrobiae.id.4029       | class | Homa-     | -       | 0.0   | -        | 0.03   | -0.03     | -0.08           | 0.01            | 0.1    | 0.             |
| Aeromonadales.id.3316          | orde  | Homa-     | -       | 0.0   | 0.0      | 0.03   | 0.01      | -0.04           | 0.05            | 0.7    | 0.             |
| Bacteroidales.id.913           | orde  | Homa-     | -       | 0.0   | -        | 0.03   | -0.05     | -0.10           | -0.01           | 0.0    | 0.             |
| Bifidobacteriales.id.432       | orde  | Homa-     | 0.0     | 0.0   | -        | 0.04   | 0.00      | -0.05           | 0.05            | 0.9    | 0.             |
| Burkholderiales.id.2874        | orde  | Homa-     | -       | 0.0   | 0.0      | 0.03   | -0.01     | -0.05           | 0.04            | 0.7    | 0.             |
| Clostridiales.id.1863          | orde  | Homa-     | -       | 0.0   | 0.0      | 0.03   | 0.00      | -0.04           | 0.05            | 0.9    | 0.             |
| Coriobacteriales.id.810        | orde  | Homa-     | -       | 0.0   | -        | 0.03   | -0.01     | -0.06           | 0.03            | 0.6    | 0.             |
| Desulfovibrionales.id.3156     | orde  | Homa-     | -       | 0.0   | -        | 0.03   | -0.04     | -0.09           | 0.00            | 0.0    | 0.             |
| Enterobacteriales.id.3468      | orde  | Homa-     | -       | 0.0   | 0.0      | 0.03   | -0.01     | -0.06           | 0.03            | 0.5    | 0.             |
| Erysipelotrichales.id.2148     | orde  | Homa-     | 0.0     | 0.0   | 0.0      | 0.03   | 0.07      | 0.03            | 0.12            | 0.0    | 0.             |
| Gastranaerophilales.id.1591    | orde  | Homa-     | -       | 0.0   | -        | 0.03   | -0.08     | -0.13           | -0.04           | 0.0    | 0.             |
| Lactobacillales.id.1800        | orde  | Homa-     | 0.0     | 0.0   | 0.0      | 0.03   | 0.08      | 0.03            | 0.12            | 0.0    | 0.             |
| MollicutesRF9.id.11579         | orde  | Homa-     | -       | 0.0   | -        | 0.03   | -0.11     | -0.15           | -0.06           | 0.0    | 0.             |
| Pasteurellales.id.3688         | orde  | Homa-     | -       | 0.0   | -        | 0.03   | -0.03     | -0.08           | 0.01            | 0.1    | 0.             |
| Rhodospirillales.id.2667       | orde  | Homa-     | -       | 0.0   | -        | 0.03   | -0.08     | -0.13           | -0.04           | 0.0    | 0.             |
| Selenomonadales.id.2165        | orde  | Homa-     | 0.0     | 0.0   | -        | 0.03   | -0.01     | -0.05           | 0.04            | 0.8    | 0.             |
| Verrucomicrobiales.id.4030     | orde  | Homa-     | -       | 0.0   | -        | 0.03   | -0.03     | -0.08           | 0.01            | 0.1    | 0.             |
| Acidaminococcaceae.id.2166     | famil | Homa-     | -       | -     | 0.0      | -      | -0.09     | 0.04            | -0.04           | -      | 0.             |

|                           |       |       |     |     |     |      |       |       |      |     |    |
|---------------------------|-------|-------|-----|-----|-----|------|-------|-------|------|-----|----|
| Alcaligenaceae.id.2875    | famil | Homa- | 0.0 | 0.0 | 0.0 | 0.03 | 0.01  | -0.04 | 0.06 | 0.7 | 0. |
| Bacteroidaceae.id.917     | famil | Homa- | -   | 0.0 | -   | 0.03 | -0.05 | -0.09 | 0.00 | 0.0 | 0. |
| Bifidobacteriaceae.id.433 | famil | Homa- | 0.0 | 0.0 | -   | 0.04 | 0.00  | -0.05 | 0.05 | 0.9 | 0. |
|                           |       |       | 1   | 2   | 0.0 |      |       |       |      | 5   | 0. |

|                                            |        |         |       |      |       |      |       |       |       |      |      |
|--------------------------------------------|--------|---------|-------|------|-------|------|-------|-------|-------|------|------|
| Christensenellaceae.id.1866                | family | Homa-IR | -0.17 | 0.03 | -0.14 | 0.03 | -0.16 | -0.21 | -0.11 | 0.00 | 0.00 |
| Clostridiaceae1.id.1869                    | family | Homa-IR | -0.04 | 0.03 | -0.04 | 0.04 | -0.04 | -0.09 | 0.01  | 0.09 | 0.00 |
| ClostridialesvadinBB60group.id.11286       | family | Homa-IR | -0.16 | 0.03 | -0.08 | 0.03 | -0.12 | -0.17 | -0.08 | 0.00 | 0.70 |
| Coriobacteriaceae.id.811                   | family | Homa-IR | -0.01 | 0.03 | -0.01 | 0.03 | -0.01 | -0.06 | 0.03  | 0.62 | 0.00 |
| Desulfovibrionaceae.id.3169                | family | Homa-IR | -0.07 | 0.03 | -0.02 | 0.03 | -0.04 | -0.09 | 0.00  | 0.05 | 0.00 |
| Enterobacteriaceae.id.3469                 | family | Homa-IR | -0.03 | 0.03 | 0.01  | 0.03 | -0.01 | -0.06 | 0.03  | 0.58 | 0.00 |
| Enterococcaceae.id.1828                    | family | Homa-IR | 0.08  | 0.03 | 0.02  | 0.03 | 0.05  | 0.01  | 0.10  | 0.02 | 0.52 |
| Erysipelotrichaceae.id.2149                | family | Homa-IR | 0.07  | 0.03 | 0.07  | 0.03 | 0.07  | 0.03  | 0.12  | 0.00 | 0.00 |
| FamilyXIII.id.1957                         | family | Homa-IR | -0.11 | 0.03 | -0.03 | 0.03 | -0.07 | -0.12 | -0.03 | 0.00 | 0.63 |
| Lachnospiraceae.id.1987                    | family | Homa-IR | 0.07  | 0.03 | 0.08  | 0.03 | 0.08  | 0.03  | 0.12  | 0.00 | 0.00 |
| Lactobacillaceae.id.1836                   | family | Homa-IR | 0.03  | 0.03 | 0.01  | 0.03 | 0.02  | -0.02 | 0.07  | 0.33 | 0.00 |
| Pasteurellaceae.id.3689                    | family | Homa-IR | -0.01 | 0.03 | -0.06 | 0.03 | -0.03 | -0.08 | 0.01  | 0.16 | 0.18 |
| Peptococcaceae.id.2024                     | family | Homa-IR | -0.05 | 0.03 | 0.03  | 0.03 | -0.01 | -0.06 | 0.03  | 0.55 | 0.71 |
| Peptostreptococcaceae.id.2042              | family | Homa-IR | -0.03 | 0.03 | 0.01  | 0.04 | -0.01 | -0.06 | 0.03  | 0.55 | 0.00 |
| Porphyromonadaceae.id.943                  | family | Homa-IR | -0.10 | 0.03 | -0.08 | 0.03 | -0.09 | -0.14 | -0.05 | 0.00 | 0.00 |
| Prevotellaceae.id.960                      | family | Homa-IR | 0.00  | 0.03 | 0.03  | 0.03 | 0.01  | -0.03 | 0.06  | 0.55 | 0.00 |
| Rhodospirillaceae.id.2717                  | family | Homa-IR | -0.13 | 0.03 | -0.03 | 0.03 | -0.08 | -0.13 | -0.04 | 0.00 | 0.79 |
| Rikenellaceae.id.967                       | family | Homa-IR | -0.13 | 0.03 | -0.10 | 0.03 | -0.12 | -0.16 | -0.07 | 0.00 | 0.00 |
| Ruminococcaceae.id.2050                    | family | Homa-IR | -0.12 | 0.03 | 0.02  | 0.03 | -0.06 | -0.10 | -0.01 | 0.01 | 0.89 |
| Streptococcaceae.id.1850                   | family | Homa-IR | 0.10  | 0.03 | 0.06  | 0.03 | 0.08  | 0.03  | 0.13  | 0.00 | 0.00 |
| Succinivibrionaceae.id.3326                | family | Homa-IR | -0.03 | 0.03 | 0.04  | 0.03 | 0.01  | -0.04 | 0.05  | 0.82 | 0.51 |
| Veillonellaceae.id.2172                    | family | Homa-IR | 0.08  | 0.03 | -0.02 | 0.03 | 0.04  | -0.01 | 0.08  | 0.11 | 0.79 |
| Verrucomicrobiaceae.id.4036                | family | Homa-IR | -0.13 | 0.03 | -0.03 | 0.03 | -0.08 | -0.13 | -0.04 | 0.00 | 0.77 |
| unknownfamily.id.1000001214                | family | Homa-IR | -0.12 | 0.03 | -0.10 | 0.03 | -0.11 | -0.15 | -0.06 | 0.00 | 0.00 |
| unknownfamily.id.1000005471                | family | Homa-IR | 0.01  | 0.03 | -0.04 | 0.03 | -0.01 | -0.06 | 0.03  | 0.58 | 0.37 |
| unknownfamily.id.987                       | family | Homa-IR | -0.01 | 0.03 | -0.06 | 0.03 | -0.03 | -0.08 | 0.01  | 0.16 | 0.00 |
| Bacteroidespectinophilusgroup.id.14371     | genus  | Homa-IR | -0.06 | 0.03 | -0.03 | 0.03 | -0.05 | -0.09 | 0.00  | 0.03 | 0.00 |
| Eubacteriumcoprostanoligenesgroup.id.11375 | genus  | Homa-IR | -0.03 | 0.03 | 0.01  | 0.03 | -0.01 | -0.06 | 0.04  | 0.68 | 0.00 |
| Eubacteriumeligenesgroup.id.14372          | genus  | Homa-IR | -0.13 | 0.03 | -0.02 | 0.03 | -0.08 | -0.13 | -0.04 | 0.00 | 0.81 |
| Eubacteriumhalliigroup.id.11338            | genus  | Homa-IR | 0.09  | 0.03 | 0.04  | 0.03 | 0.07  | 0.02  | 0.12  | 0.00 | 0.16 |
| Eubacteriumrectalegroup.id.14374           | genus  | Homa-IR | 0.08  | 0.03 | 0.06  | 0.03 | 0.07  | 0.02  | 0.12  | 0.00 | 0.00 |
| Eubacteriumruminantiumgroup.id.11340       | genus  | Homa-IR | -0.07 | 0.03 | -0.05 | 0.03 | -0.06 | -0.11 | -0.02 | 0.01 | 0.00 |
| Eubacteriumventriosumgroup.id.11341        | genus  | Homa-IR | 0.03  | 0.03 | 0.07  | 0.03 | 0.05  | 0.00  | 0.10  | 0.04 | 0.00 |
| Eubacteriumxylanophilumgroup.id.14375      | genus  | Homa-IR | -0.13 | 0.03 | -0.03 | 0.03 | -0.08 | -0.13 | -0.03 | 0.00 | 0.74 |
| Ruminococcusgavreuiigroup.id.11342         | genus  | Homa-IR | 0.02  | 0.03 | 0.10  | 0.03 | 0.05  | 0.01  | 0.10  | 0.02 | 0.65 |
| Ruminococcusgnavusgroup.id.14376           | genus  | Homa-IR | 0.05  | 0.03 | 0.09  | 0.03 | 0.07  | 0.02  | 0.11  | 0.00 | 0.00 |
| Ruminococcusstorquesgroup.id.14377         | genus  | Homa-IR | 0.07  | 0.03 | 0.03  | 0.03 | 0.05  | 0.01  | 0.10  | 0.03 | 0.10 |
| Acidaminococcus.id.2167                    | genus  | Homa-IR | 0.06  | 0.03 | 0.05  | 0.03 | 0.06  | 0.01  | 0.10  | 0.02 | 0.00 |
| Adlercreutzia.id.812                       | genus  | Homa-IR | 0.07  | 0.03 | 0.04  | 0.03 | 0.06  | 0.01  | 0.10  | 0.02 | 0.00 |
| Akkermansia.id.4037                        | genus  | Homa-IR | -0.01 | 0.03 | -0.06 | 0.03 | -0.03 | -0.08 | 0.01  | 0.16 | 0.00 |
| Alistipes.id.968                           | genus  | Homa-IR | -0.13 | 0.03 | -0.09 | 0.03 | -0.11 | -0.16 | -0.07 | 0.00 | 0.00 |
| Alloprevotella.id.961                      | genus  | Homa-IR | -0.03 | 0.03 | 0.04  | 0.03 | 0.00  | -0.04 | 0.05  | 0.87 | 0.43 |
| Anaerostipes.id.1991                       | genus  | Homa-IR | 0.02  | 0.03 | 0.03  | 0.03 | 0.03  | -0.02 | 0.08  | 0.21 | 0.00 |
| Anaerotruncus.id.2054                      | genus  | Homa-IR | -0.12 | 0.03 | -0.04 | 0.03 | -0.09 | -0.13 | -0.04 | 0.00 | 0.67 |



|                        |       |         |       |      |       |      |       |       |       |      |      |
|------------------------|-------|---------|-------|------|-------|------|-------|-------|-------|------|------|
| Bacteroides.id.918     | genus | Homa-IR | -0.06 | 0.03 | -0.04 | 0.03 | -0.05 | -0.09 | 0.00  | 0.05 | 0.00 |
| Barnesiella.id.944     | genus | Homa-IR | -0.08 | 0.03 | -0.04 | 0.03 | -0.06 | -0.11 | -0.01 | 0.01 | 0.06 |
| Bifidobacterium.id.436 | genus | Homa-IR | 0.01  | 0.03 | 0.00  | 0.04 | 0.00  | -0.04 | 0.05  | 0.85 | 0.00 |
| Blautia.id.1992        | genus | Homa-IR | 0.02  | 0.01 | 0.00  | 0.03 | 0.00  | -0.03 | 0.03  | 0.75 | 0.00 |
|                        |       |         |       |      |       |      |       |       |       |      |      |

|                                      |       |         |       |      |       |      |       |       |       |      |      |
|--------------------------------------|-------|---------|-------|------|-------|------|-------|-------|-------|------|------|
| Butyricoccus.id.2055                 | genus | Homa-IR | 0.05  | 0.03 | 0.01  | 0.03 | 0.03  | -0.01 | 0.08  | 0.15 | 0.00 |
| Butyricimonas.id.945                 | genus | Homa-IR | -0.09 | 0.03 | -0.08 | 0.03 | -0.08 | -0.13 | -0.04 | 0.00 | 0.00 |
| Butyrivibrio.id.1993                 | genus | Homa-IR | -0.09 | 0.03 | -0.03 | 0.03 | -0.06 | -0.11 | -0.02 | 0.01 | 0.46 |
| Catenibacterium.id.2153              | genus | Homa-IR | 0.05  | 0.03 | 0.02  | 0.03 | 0.03  | -0.01 | 0.08  | 0.16 | 0.00 |
| ChristensenellaceaeR7group.id.11283  | genus | Homa-IR | -0.17 | 0.03 | -0.13 | 0.03 | -0.15 | -0.20 | -0.11 | 0.00 | 0.00 |
| Clostridiumsensustricto1.id.1873     | genus | Homa-IR | -0.04 | 0.03 | -0.05 | 0.04 | -0.04 | -0.09 | 0.01  | 0.08 | 0.00 |
| Collinsella.id.815                   | genus | Homa-IR | 0.05  | 0.03 | 0.00  | 0.03 | 0.02  | -0.02 | 0.07  | 0.34 | 0.07 |
| Coprococcus1.id.11301                | genus | Homa-IR | -0.08 | 0.03 | -0.04 | 0.03 | -0.06 | -0.11 | -0.02 | 0.01 | 0.00 |
| Coprococcus2.id.11302                | genus | Homa-IR | -0.08 | 0.03 | -0.03 | 0.03 | -0.06 | -0.10 | -0.01 | 0.01 | 0.00 |
| Coprococcus3.id.11303                | genus | Homa-IR | 0.04  | 0.03 | 0.03  | 0.03 | 0.04  | -0.01 | 0.08  | 0.11 | 0.00 |
| Desulfovibrio.id.3173                | genus | Homa-IR | -0.06 | 0.03 | -0.02 | 0.03 | -0.04 | -0.09 | 0.00  | 0.06 | 0.00 |
| Dialister.id.2183                    | genus | Homa-IR | 0.06  | 0.03 | -0.03 | 0.03 | 0.02  | -0.03 | 0.06  | 0.48 | 0.70 |
| Dorea.id.1997                        | genus | Homa-IR | 0.07  | 0.03 | 0.00  | 0.03 | 0.04  | -0.01 | 0.08  | 0.13 | 0.57 |
| Eggerthella.id.819                   | genus | Homa-IR | 0.00  | 0.03 | 0.07  | 0.03 | 0.03  | -0.01 | 0.08  | 0.17 | 0.63 |
| Eisenbergiella.id.11304              | genus | Homa-IR | -0.05 | 0.03 | 0.01  | 0.03 | -0.02 | -0.07 | 0.02  | 0.32 | 0.40 |
| Enterococcus.id.1831                 | genus | Homa-IR | 0.08  | 0.03 | 0.02  | 0.03 | 0.05  | 0.01  | 0.10  | 0.02 | 0.40 |
| Enterorhabdus.id.820                 | genus | Homa-IR | -0.07 | 0.03 | -0.05 | 0.03 | -0.06 | -0.11 | -0.01 | 0.01 | 0.00 |
| Erysipelatoclostridium.id.11381      | genus | Homa-IR | -0.02 | 0.03 | 0.05  | 0.03 | 0.01  | -0.03 | 0.06  | 0.55 | 0.54 |
| ErysipelotrichaceaeUCG003.id.11384   | genus | Homa-IR | 0.04  | 0.03 | 0.04  | 0.03 | 0.04  | -0.01 | 0.09  | 0.10 | 0.00 |
| Faecalibacterium.id.2057             | genus | Homa-IR | -0.02 | 0.03 | 0.07  | 0.03 | 0.02  | -0.03 | 0.06  | 0.47 | 0.72 |
| FamilyXIIAD3011group.id.11293        | genus | Homa-IR | -0.12 | 0.03 | -0.10 | 0.03 | -0.11 | -0.16 | -0.07 | 0.00 | 0.00 |
| FamilyXIIUCG001.id.11294             | genus | Homa-IR | -0.04 | 0.03 | -0.04 | 0.03 | -0.04 | -0.08 | 0.01  | 0.11 | 0.00 |
| Fusicatenibacter.id.11305            | genus | Homa-IR | 0.07  | 0.03 | 0.05  | 0.03 | 0.06  | 0.02  | 0.11  | 0.01 | 0.00 |
| Haemophilus.id.3698                  | genus | Homa-IR | -0.01 | 0.03 | -0.05 | 0.03 | -0.03 | -0.08 | 0.01  | 0.19 | 0.00 |
| Holdemanella.id.11393                | genus | Homa-IR | 0.07  | 0.03 | 0.07  | 0.03 | 0.07  | 0.02  | 0.11  | 0.00 | 0.00 |
| Intestinibacter.id.11345             | genus | Homa-IR | 0.00  | 0.03 | 0.03  | 0.04 | 0.02  | -0.03 | 0.06  | 0.51 | 0.00 |
| Intestinimonas.id.2062               | genus | Homa-IR | -0.10 | 0.03 | -0.03 | 0.03 | -0.07 | -0.12 | -0.03 | 0.00 | 0.52 |
| Lachnoclostridium.id.11308           | genus | Homa-IR | 0.03  | 0.03 | 0.07  | 0.03 | 0.05  | 0.00  | 0.09  | 0.05 | 0.00 |
| Lachnospira.id.2004                  | genus | Homa-IR | -0.01 | 0.03 | 0.03  | 0.03 | 0.01  | -0.04 | 0.06  | 0.69 | 0.00 |
| LachnospiraceaeFCS020group.id.11314  | genus | Homa-IR | -0.03 | 0.03 | -0.08 | 0.03 | -0.05 | -0.10 | -0.01 | 0.02 | 0.19 |
| LachnospiraceaeND3007group.id.11317  | genus | Homa-IR | -0.06 | 0.03 | 0.00  | 0.03 | -0.03 | -0.08 | 0.01  | 0.18 | 0.52 |
| LachnospiraceaeNK4A136group.id.11319 | genus | Homa-IR | -0.07 | 0.03 | 0.02  | 0.03 | -0.03 | -0.07 | 0.02  | 0.23 | 0.72 |
| LachnospiraceaeUCG001.id.11321       | genus | Homa-IR | 0.01  | 0.03 | 0.01  | 0.03 | 0.01  | -0.04 | 0.06  | 0.68 | 0.00 |
| LachnospiraceaeUCG004.id.11324       | genus | Homa-IR | -0.03 | 0.03 | -0.04 | 0.03 | -0.04 | -0.08 | 0.01  | 0.12 | 0.00 |
| LachnospiraceaeUCG010.id.11330       | genus | Homa-IR | -0.03 | 0.03 | -0.05 | 0.03 | -0.04 | -0.09 | 0.01  | 0.09 | 0.00 |
| Lactobacillus.id.1837                | genus | Homa-IR | 0.04  | 0.03 | 0.02  | 0.03 | 0.03  | -0.01 | 0.08  | 0.18 | 0.00 |
| Marvinbryantia.id.2005               | genus | Homa-IR | -0.12 | 0.03 | -0.08 | 0.03 | -0.10 | -0.15 | -0.06 | 0.00 | 0.00 |
| Megamonas.id.2184                    | genus | Homa-IR | 0.04  | 0.03 | 0.00  | 0.03 | 0.02  | -0.02 | 0.07  | 0.31 | 0.00 |
| Megasphaera.id.2185                  | genus | Homa-IR | 0.04  | 0.03 | 0.06  | 0.03 | 0.05  | 0.00  | 0.09  | 0.04 | 0.00 |
| Mitsuokella.id.2186                  | genus | Homa-IR | 0.08  | 0.03 | 0.01  | 0.03 | 0.05  | 0.00  | 0.09  | 0.04 | 0.58 |
| Odoribacter.id.952                   | genus | Homa-IR | -0.14 | 0.03 | -0.08 | 0.03 | -0.11 | -0.16 | -0.06 | 0.00 | 0.35 |
| Olsenella.id.822                     | genus | Homa-IR | 0.02  | 0.03 | -0.05 | 0.03 | -0.01 | -0.06 | 0.03  | 0.55 | 0.45 |
| Oscillospira.id.2064                 | genus | Homa-IR | -0.07 | 0.03 | -0.05 | 0.03 | -0.06 | -0.11 | -0.01 | 0.01 | 0.00 |
| Parabacteroides.id.954               | genus | Homa-IR | -0.07 | 0.03 | -0.07 | 0.03 | -0.07 | -0.12 | -0.02 | 0.00 | 0.00 |
| Paraprevotella.id.962                | genus | Homa-IR | -0.03 | 0.03 | -0.04 | 0.03 | -0.03 | -0.08 | 0.01  | 0.14 | 0.00 |

|                        |       |         |      |      |      |      |      |       |      |      |      |
|------------------------|-------|---------|------|------|------|------|------|-------|------|------|------|
| Parasutterella.id.2892 | genus | Homa-IR | 0.01 | 0.03 | 0.06 | 0.03 | 0.03 | -0.01 | 0.08 | 0.16 | 0.00 |
|------------------------|-------|---------|------|------|------|------|------|-------|------|------|------|

|                                      |       |         |       |      |       |      |       |       |       |      |      |
|--------------------------------------|-------|---------|-------|------|-------|------|-------|-------|-------|------|------|
| Peptococcus.id.2037                  | genus | Homa-IR | -0.01 | 0.03 | 0.04  | 0.03 | 0.01  | -0.04 | 0.06  | 0.65 | 0.18 |
| Phascolarctobacterium.id.2168        | genus | Homa-IR | -0.07 | 0.03 | -0.04 | 0.03 | -0.05 | -0.10 | -0.01 | 0.03 | 0.00 |
| Prevotella2.id.11180                 | genus | Homa-IR | 0.01  | 0.03 | -0.02 | 0.03 | -0.01 | -0.05 | 0.04  | 0.82 | 0.00 |
| Prevotella7.id.11182                 | genus | Homa-IR | 0.00  | 0.03 | 0.03  | 0.03 | 0.02  | -0.03 | 0.06  | 0.52 | 0.00 |
| Prevotella9.id.11183                 | genus | Homa-IR | 0.02  | 0.03 | 0.02  | 0.03 | 0.02  | -0.02 | 0.07  | 0.32 | 0.00 |
| PrevotellaceaeNK3B31group.id.11185   | genus | Homa-IR | 0.00  | 0.03 | 0.03  | 0.03 | 0.02  | -0.03 | 0.06  | 0.46 | 0.00 |
| PrevotellaceaeUCG001.id.11186        | genus | Homa-IR | -0.02 | 0.03 | 0.02  | 0.03 | 0.00  | -0.04 | 0.05  | 0.99 | 0.00 |
| RikenellaceaeRC9gutgroup.id.11191    | genus | Homa-IR | 0.00  | 0.03 | -0.04 | 0.03 | -0.02 | -0.07 | 0.03  | 0.40 | 0.00 |
| Romboutsia.id.11347                  | genus | Homa-IR | -0.05 | 0.03 | 0.00  | 0.03 | -0.03 | -0.07 | 0.02  | 0.26 | 0.00 |
| Roseburia.id.2012                    | genus | Homa-IR | 0.05  | 0.03 | 0.05  | 0.03 | 0.05  | 0.00  | 0.10  | 0.03 | 0.00 |
| Ruminiclostridium5.id.11355          | genus | Homa-IR | -0.10 | 0.03 | -0.01 | 0.03 | -0.06 | -0.10 | -0.01 | 0.02 | 0.71 |
| Ruminiclostridium6.id.11356          | genus | Homa-IR | -0.16 | 0.03 | -0.02 | 0.03 | -0.09 | -0.14 | -0.05 | 0.00 | 0.89 |
| Ruminiclostridium9.id.11357          | genus | Homa-IR | -0.09 | 0.03 | -0.14 | 0.03 | -0.11 | -0.16 | -0.06 | 0.00 | 0.04 |
| RuminococcaceaeNK4A214group.id.11358 | genus | Homa-IR | -0.18 | 0.03 | -0.15 | 0.03 | -0.16 | -0.21 | -0.12 | 0.00 | 0.00 |
| RuminococcaceaeUCG002.id.11360       | genus | Homa-IR | -0.13 | 0.03 | -0.13 | 0.03 | -0.13 | -0.17 | -0.08 | 0.00 | 0.00 |
| RuminococcaceaeUCG003.id.11361       | genus | Homa-IR | -0.08 | 0.03 | -0.10 | 0.03 | -0.09 | -0.14 | -0.04 | 0.00 | 0.00 |
| RuminococcaceaeUCG004.id.11362       | genus | Homa-IR | 0.01  | 0.03 | -0.01 | 0.03 | 0.00  | -0.04 | 0.05  | 0.93 | 0.00 |
| RuminococcaceaeUCG005.id.11363       | genus | Homa-IR | -0.20 | 0.03 | -0.11 | 0.03 | -0.16 | -0.20 | -0.11 | 0.00 | 0.74 |
| RuminococcaceaeUCG008.id.11365       | genus | Homa-IR | -0.13 | 0.03 | -0.06 | 0.03 | -0.10 | -0.14 | -0.05 | 0.00 | 0.64 |
| RuminococcaceaeUCG010.id.11367       | genus | Homa-IR | -0.19 | 0.03 | -0.13 | 0.03 | -0.17 | -0.21 | -0.12 | 0.00 | 0.47 |
| RuminococcaceaeUCG013.id.11370       | genus | Homa-IR | -0.01 | 0.03 | 0.08  | 0.03 | 0.04  | -0.01 | 0.08  | 0.13 | 0.70 |
| RuminococcaceaeUCG014.id.11371       | genus | Homa-IR | -0.14 | 0.03 | -0.09 | 0.03 | -0.12 | -0.16 | -0.07 | 0.00 | 0.28 |
| Ruminococcus1.id.11373               | genus | Homa-IR | -0.11 | 0.03 | 0.06  | 0.03 | -0.03 | -0.08 | 0.02  | 0.19 | 0.92 |
| Ruminococcus2.id.11374               | genus | Homa-IR | -0.02 | 0.03 | 0.05  | 0.03 | 0.01  | -0.03 | 0.06  | 0.52 | 0.55 |
| Sellimonas.id.14369                  | genus | Homa-IR | 0.03  | 0.03 | 0.05  | 0.03 | 0.04  | -0.01 | 0.09  | 0.09 | 0.00 |
| Senegalimassilia.id.11160            | genus | Homa-IR | -0.01 | 0.03 | -0.05 | 0.03 | -0.03 | -0.08 | 0.01  | 0.17 | 0.00 |
| Slackia.id.825                       | genus | Homa-IR | 0.05  | 0.03 | -0.06 | 0.03 | 0.00  | -0.05 | 0.04  | 0.95 | 0.81 |
| Streptococcus.id.1853                | genus | Homa-IR | 0.10  | 0.03 | 0.06  | 0.03 | 0.08  | 0.04  | 0.13  | 0.00 | 0.00 |
| Subdoligranulum.id.2070              | genus | Homa-IR | 0.01  | 0.03 | 0.02  | 0.03 | 0.01  | -0.03 | 0.06  | 0.58 | 0.00 |
| Succiniclasticum.id.2169             | genus | Homa-IR | -0.03 | 0.03 | 0.00  | 0.03 | -0.02 | -0.06 | 0.03  | 0.52 | 0.00 |
| Sutterella.id.2896                   | genus | Homa-IR | -0.02 | 0.03 | -0.05 | 0.03 | -0.04 | -0.08 | 0.01  | 0.14 | 0.00 |
| Terrisporobacter.id.11348            | genus | Homa-IR | -0.04 | 0.03 | -0.02 | 0.04 | -0.03 | -0.07 | 0.02  | 0.22 | 0.00 |
| Turicibacter.id.2162                 | genus | Homa-IR | -0.05 | 0.03 | -0.05 | 0.03 | -0.05 | -0.09 | 0.00  | 0.04 | 0.00 |
| Tyzzereila3.id.11335                 | genus | Homa-IR | 0.08  | 0.03 | 0.02  | 0.03 | 0.05  | 0.01  | 0.10  | 0.02 | 0.42 |
| Veillonella.id.2198                  | genus | Homa-IR | 0.01  | 0.03 | -0.04 | 0.03 | -0.01 | -0.06 | 0.03  | 0.63 | 0.00 |
| unknowngenus.id.1000000073           | genus | Homa-IR | -0.16 | 0.03 | -0.08 | 0.03 | -0.12 | -0.17 | -0.08 | 0.00 | 0.70 |
| unknowngenus.id.1000001215           | genus | Homa-IR | -0.13 | 0.03 | -0.03 | 0.03 | -0.08 | -0.13 | -0.04 | 0.00 | 0.77 |
| unknowngenus.id.1000005472           | genus | Homa-IR | -0.12 | 0.03 | -0.10 | 0.03 | -0.11 | -0.15 | -0.06 | 0.00 | 0.00 |
| unknowngenus.id.1000005479           | genus | Homa-IR | -0.05 | 0.03 | -0.05 | 0.03 | -0.05 | -0.10 | 0.00  | 0.03 | 0.00 |
| unknowngenus.id.1000013899           | genus | Homa-IR | 0.01  | 0.03 | -0.04 | 0.03 | -0.01 | -0.06 | 0.03  | 0.58 | 0.37 |
| unknowngenus.id.2071                 | genus | Homa-IR | -0.17 | 0.03 | -0.06 | 0.03 | -0.12 | -0.16 | -0.07 | 0.00 | 0.82 |
| unknowngenus.id.2755                 | genus | Homa-IR | -0.13 | 0.03 | -0.03 | 0.03 | -0.08 | -0.13 | -0.04 | 0.00 | 0.79 |
| unknowngenus.id.826                  | genus | Homa-IR | -0.05 | 0.03 | -0.01 | 0.04 | -0.03 | -0.07 | 0.02  | 0.25 | 0.00 |
| unknowngenus.id.964                  | genus | Homa-IR | 0.04  | 0.03 | 0.02  | 0.03 | 0.03  | -0.02 | 0.08  | 0.20 | 0.00 |

| Taxa in RS only                            | Clade  | Phenotype | Beta_RS | Se_RS |
|--------------------------------------------|--------|-----------|---------|-------|
| BacteroidalesS247group.id.11173            | family | Homa-IR   | -0.05   | 0.03  |
| Veillonellaceae.id.2172                    | family | Homa-IR   | 0.08    | 0.03  |
| Bacteroidespectinophilusgroup.id.14371     | genus  | Homa-IR   | -0.06   | 0.03  |
| Enterobacter.id.3502                       | genus  | Homa-IR   | 0.08    | 0.04  |
| EscherichiaShigella.id.3504                | genus  | Homa-IR   | -0.05   | 0.03  |
| Eubacteriumcoprostanoligenesgroup.id.11375 | genus  | Homa-IR   | -0.03   | 0.03  |
| Eubacteriumeligensgroup.id.14372           | genus  | Homa-IR   | -0.13   | 0.03  |
| Eubacteriumhalliigroup.id.11338            | genus  | Homa-IR   | 0.09    | 0.03  |
| Eubacteriumoxidoreducensgroup.id.11339     | genus  | Homa-IR   | -0.18   | 0.03  |
| Eubacteriumxylanophilumgroup.id.14375      | genus  | Homa-IR   | -0.13   | 0.03  |
| Hungatella.id.11306                        | genus  | Homa-IR   | -0.02   | 0.03  |
| Klebsiella.id.3507                         | genus  | Homa-IR   | 0.05    | 0.03  |
| LachnospiraceaeNC2004group.id.11316        | genus  | Homa-IR   | -0.13   | 0.03  |
| LachnospiraceaeUCG008.id.11328             | genus  | Homa-IR   | -0.05   | 0.03  |
| unknowngenus.id.1868                       | genus  | Homa-IR   | -0.14   | 0.03  |

| Taxa in LLD only                 | Clade  | Phenotype | Beta_RS | Se_RS |
|----------------------------------|--------|-----------|---------|-------|
| Archaea.id.2                     | domain | Homa-IR   | -0.14   | 0.03  |
| Euryarchaeota.id.55              | phylum | Homa-IR   | -0.13   | 0.03  |
| Lentisphaerae.id.2238            | phylum | Homa-IR   | -0.05   | 0.03  |
| Actinomycetales.id.420           | order  | Homa-IR   | 0.05    | 0.03  |
| Mycoplasmatales.id.3946          | order  | Homa-IR   | -0.03   | 0.03  |
| NB1.n.id.3953                    | order  | Homa-IR   | -0.04   | 0.03  |
| Pseudomonadales.id.3709          | order  | Homa-IR   | -0.02   | 0.03  |
| Spirochaetales.id.3870           | order  | Homa-IR   | -0.02   | 0.03  |
| Synergistales.id.3900            | order  | Homa-IR   | -0.06   | 0.03  |
| Thermoplasmatales.id.220         | order  | Homa-IR   | -0.03   | 0.03  |
| unknownorder.id.1000000003       | order  | Homa-IR   | 0.01    | 0.03  |
| Verrucomicrobiales.id.4030       | order  | Homa-IR   | -0.06   | 0.03  |
| Victivallales.id.2254            | order  | Homa-IR   | -0.05   | 0.03  |
| Xanthomonadales.id.3786          | order  | Homa-IR   | -0.02   | 0.03  |
| Spirochaetes.id.3856             | class  | Homa-IR   | -0.02   | 0.03  |
| Synergistia.id.3899              | class  | Homa-IR   | -0.06   | 0.03  |
| Thermoplasmata.id.210            | class  | Homa-IR   | -0.03   | 0.03  |
| Actinomycetaceae.id.421          | family | Homa-IR   | 0.05    | 0.03  |
| BacteroidalesS24.7group.id.11173 | family | Homa-IR   | -0.05   | 0.03  |
| Christensenellaceae.id.1866      | family | Homa-IR   | -0.14   | 0.03  |
| FamilyXI.id.1936                 | family | Homa-IR   | 0.00    | 0.03  |
| unknownfamily.id.1000000004      | family | Homa-IR   | 0.01    | 0.03  |
| unknownfamily.id.1000006161      | family | Homa-IR   | -0.04   | 0.03  |
| unknownfamily.id.1855            | family | Homa-IR   | -0.01   | 0.03  |
| vadinBE97.id.14446               | family | Homa-IR   | -0.04   | 0.03  |
| Veillonellaceae.id.2172          | family | Homa-IR   | -0.02   | 0.03  |

|                                   |        |         |       |      |
|-----------------------------------|--------|---------|-------|------|
| Xanthomonadaceae.id.3799          | family | Homa-IR | -0.02 | 0.03 |
| Clostridiuminnocuumgroup.id.14397 | genus  | Homa-IR | 0.01  | 0.03 |
| Eubacteriumbrachygroup.id.11296   | genus  | Homa-IR | 0.06  | 0.03 |

|                                     |       |         |       |      |
|-------------------------------------|-------|---------|-------|------|
| Abiotrophia.id.1803                 | genus | Homa-IR | 0.01  | 0.03 |
| Actinomyces.id.423                  | genus | Homa-IR | 0.06  | 0.03 |
| Actinotignum.id.11137               | genus | Homa-IR | -0.04 | 0.03 |
| Allisonella.id.2174                 | genus | Homa-IR | 0.09  | 0.03 |
| Arcanobacterium.id.424              | genus | Homa-IR | -0.01 | 0.03 |
| Asaccharobacter.id.813              | genus | Homa-IR | 0.04  | 0.03 |
| Bilophila.id.3170                   | genus | Homa-IR | -0.02 | 0.03 |
| CandidatusMethanogranum.id.11110    | genus | Homa-IR | -0.01 | 0.03 |
| Catenisphaera.id.14395              | genus | Homa-IR | 0.00  | 0.03 |
| Cellulosilyticum.id.1995            | genus | Homa-IR | -0.06 | 0.03 |
| Cetobacterium.id.2209               | genus | Homa-IR | 0.07  | 0.03 |
| Cloacibacillus.id.3908              | genus | Homa-IR | -0.05 | 0.03 |
| Coprobacillus.id.2154               | genus | Homa-IR | 0.02  | 0.03 |
| CoriobacteriaceaeUCG.002.id.11158   | genus | Homa-IR | -0.04 | 0.03 |
| CoriobacteriaceaeUCG.003.id.11159   | genus | Homa-IR | 0.03  | 0.03 |
| Denitrobacterium.id.818             | genus | Homa-IR | -0.02 | 0.03 |
| dgA.11gutgroup.id.978               | genus | Homa-IR | 0.02  | 0.03 |
| Dielma.id.11380                     | genus | Homa-IR | -0.01 | 0.03 |
| Epulopiscium.id.1998                | genus | Homa-IR | 0.03  | 0.03 |
| ErysipelotrichaceaeUCG006.id.11386  | genus | Homa-IR | 0.01  | 0.03 |
| ErysipelotrichaceaeUCG009.id.11389  | genus | Homa-IR | 0.04  | 0.03 |
| Escherichia.Shigella.id.3504        | genus | Homa-IR | 0.00  | 0.03 |
| Eubacterium.id.1932                 | genus | Homa-IR | 0.05  | 0.03 |
| Faecalicoccus.id.11391              | genus | Homa-IR | 0.01  | 0.03 |
| Faecalitalea.id.11392               | genus | Homa-IR | 0.05  | 0.03 |
| Flavonifractor.id.2059              | genus | Homa-IR | 0.00  | 0.03 |
| Gardnerella.id.437                  | genus | Homa-IR | 0.01  | 0.03 |
| Gordonibacter.id.821                | genus | Homa-IR | 0.00  | 0.03 |
| Hafnia.Obesumbacterium.id.14636     | genus | Homa-IR | 0.01  | 0.03 |
| Howardella.id.2000                  | genus | Homa-IR | 0.02  | 0.03 |
| LachnospiraceaeNK3A20group.id.11318 | genus | Homa-IR | 0.00  | 0.03 |
| Lactococcus.id.1851                 | genus | Homa-IR | -0.02 | 0.03 |
| Lautropia.id.2905                   | genus | Homa-IR | 0.01  | 0.03 |
| Leuconostoc.id.1841                 | genus | Homa-IR | 0.00  | 0.03 |
| Methanobrevibacter.id.123           | genus | Homa-IR | -0.13 | 0.03 |
| Methanosphaera.id.124               | genus | Homa-IR | -0.07 | 0.03 |
| Mogibacterium.id.1960               | genus | Homa-IR | -0.01 | 0.03 |
| Morganella.id.3512                  | genus | Homa-IR | 0.05  | 0.03 |
| Porphyromonas.id.956                | genus | Homa-IR | -0.02 | 0.03 |
| Prevotella1.id.11179                | genus | Homa-IR | 0.02  | 0.03 |
| PrevotellaceaeUCG003.id.11187       | genus | Homa-IR | 0.07  | 0.03 |
| PrevotellaceaeUCG004.id.11188       | genus | Homa-IR | -0.05 | 0.03 |
| Pseudomonas.id.3723                 | genus | Homa-IR | -0.02 | 0.03 |
| Rikenella.id.973                    | genus | Homa-IR | 0.01  | 0.03 |

|                                      |       |         |       |      |
|--------------------------------------|-------|---------|-------|------|
| RuminococcaceaeNK4A214group.id.11358 | genus | Homa-IR | -0.15 | 0.03 |
| RuminococcaceaeUCG005.id.11363       | genus | Homa-IR | -0.11 | 0.03 |
| RuminococcaceaeUCG008.id.11365       | genus | Homa-IR | -0.06 | 0.03 |



|                                |       |         |       |      |
|--------------------------------|-------|---------|-------|------|
| RuminococcaceaeUCG010.id.11367 | genus | Homa-IR | -0.13 | 0.03 |
| Sarcina.id.1896                | genus | Homa-IR | 0.05  | 0.03 |
| Solobacterium.id.2161          | genus | Homa-IR | 0.06  | 0.03 |
| Staphylococcus.id.1780         | genus | Homa-IR | 0.04  | 0.03 |
| Stenotrophomonas.id.3818       | genus | Homa-IR | -0.02 | 0.03 |
| Succinivibrio.id.3331          | genus | Homa-IR | 0.04  | 0.03 |
| Synergistes.id.3913            | genus | Homa-IR | -0.03 | 0.03 |
| Syntrophococcus.id.2016        | genus | Homa-IR | 0.00  | 0.03 |
| Treponema2.id.11577            | genus | Homa-IR | -0.02 | 0.03 |
| Tyzzerella4.id.11336           | genus | Homa-IR | 0.05  | 0.03 |
| unknowngenus.id.1000000005     | genus | Homa-IR | 0.01  | 0.03 |
| unknowngenus.id.1000027565     | genus | Homa-IR | -0.04 | 0.03 |
| unknowngenus.id.1000043796     | genus | Homa-IR | -0.01 | 0.03 |
| unknowngenus.id.1854           | genus | Homa-IR | -0.03 | 0.03 |
| unknowngenus.id.2163           | genus | Homa-IR | -0.05 | 0.03 |
| unknowngenus.id.3332           | genus | Homa-IR | 0.05  | 0.03 |
| unknowngenus.id.441            | genus | Homa-IR | -0.09 | 0.03 |
| Ureaplasma.id.3951             | genus | Homa-IR | -0.03 | 0.03 |
| Varibaculum.id.427             | genus | Homa-IR | 0.01  | 0.03 |
| Veillonella.id.2198            | genus | Homa-IR | -0.04 | 0.03 |
| Weissella.id.1843              | genus | Homa-IR | 0.01  | 0.03 |

**Supplementary Table 2 - Associations of taxa and insulin resistance**

Effect estimates in RS and LLD were calculated using linear regression; pooled estimates were calculated based on a mixed-effect meta-analysis.

Model 3: Adjusted for age, sex, Time in mail (RS), Batch (RS), smoking, education level (RS), physical activity, alcohol intake, total energy intake, and BMI.

Abbreviation, RS, Rotterdam Study, LLD, Lifelines-Deep Study. P<0.0005 indicates statistical significance

| Overlapping taxa in RS and LLD | Clade  | Phenotype | Beta_RS | Se_RS | Beta_LLD | Se_LLD | Beta_Meta | Lower95%CI_Meta | Upper95%CI_Meta | p_Meta | I <sup>2</sup> |
|--------------------------------|--------|-----------|---------|-------|----------|--------|-----------|-----------------|-----------------|--------|----------------|
| Bacteria.id.3                  | domain | Homa-IR   | 0.00    | 0.03  | 0.07     | 0.03   | 0.04      | 0.00            | 0.08            | 0.03   | 0.554          |
| Actinobacteria.id.400          | phylum | Homa-IR   | 0.02    | 0.03  | 0.00     | 0.03   | 0.01      | -0.03           | 0.05            | 0.54   | 0.069          |
| Bacteroidetes.id.905           | phylum | Homa-IR   | -0.04   | 0.03  | -0.02    | 0.03   | -0.03     | -0.07           | 0.01            | 0.11   | 0              |
| Cyanobacteria.id.1500          | phylum | Homa-IR   | -0.09   | 0.03  | 0.02     | 0.03   | -0.04     | -0.08           | 0.00            | 0.07   | 0.778          |
| Firmicutes.id.1672             | phylum | Homa-IR   | 0.00    | 0.03  | 0.04     | 0.03   | 0.02      | -0.02           | 0.06            | 0.28   | 0.702          |
| Proteobacteria.id.2375         | phylum | Homa-IR   | 0.00    | 0.03  | -0.01    | 0.03   | 0.00      | -0.04           | 0.04            | 0.88   | 0              |
| Tenericutes.id.3919            | phylum | Homa-IR   | -0.08   | 0.03  | -0.06    | 0.03   | -0.07     | -0.11           | -0.03           | 0.00   | 0              |
| Verrucomicrobia.id.3982        | phylum | Homa-IR   | 0.02    | 0.03  | -0.01    | 0.03   | 0.01      | -0.03           | 0.05            | 0.79   | 0              |
| Actinobacteria.id.419          | class  | Homa-IR   | 0.02    | 0.03  | 0.01     | 0.03   | 0.02      | -0.03           | 0.06            | 0.46   | 0.06           |
| Alphaproteobacteria.id.2379    | class  | Homa-IR   | -0.08   | 0.03  | 0.01     | 0.03   | -0.04     | -0.08           | 0.00            | 0.05   | 0.394          |
| Bacilli.id.1673                | class  | Homa-IR   | 0.03    | 0.03  | 0.03     | 0.03   | 0.03      | -0.01           | 0.07            | 0.12   | 0              |
| Bacteroidia.id.912             | class  | Homa-IR   | -0.04   | 0.03  | -0.02    | 0.03   | -0.03     | -0.07           | 0.01            | 0.12   | 0              |
| Betaproteobacteria.id.2867     | class  | Homa-IR   | -0.01   | 0.03  | 0.01     | 0.03   | 0.00      | -0.04           | 0.04            | 0.96   | 0              |
| Clostridia.id.1859             | class  | Homa-IR   | -0.03   | 0.03  | 0.02     | 0.03   | -0.01     | -0.05           | 0.04            | 0.79   | 0.712          |
| Coriobacteriia.id.809          | class  | Homa-IR   | 0.00    | 0.03  | -0.01    | 0.03   | -0.01     | -0.05           | 0.03            | 0.73   | 0              |
| Deltaproteobacteria.id.3087    | class  | Homa-IR   | -0.03   | 0.03  | -0.01    | 0.03   | -0.02     | -0.06           | 0.02            | 0.34   | 0.151          |
| Erysipelotrichia.id.2147       | class  | Homa-IR   | 0.05    | 0.03  | 0.04     | 0.03   | 0.05      | 0.00            | 0.09            | 0.03   | 0              |
| Gammaproteobacteria.id.3303    | class  | Homa-IR   | 0.00    | 0.03  | -0.01    | 0.03   | 0.00      | -0.04           | 0.04            | 0.83   | 0              |
| Melainabacteria.id.1589        | class  | Homa-IR   | -0.08   | 0.03  | 0.01     | 0.03   | -0.04     | -0.08           | 0.01            | 0.09   | 0.677          |
| Mollicutes.id.3920             | class  | Homa-IR   | -0.08   | 0.03  | -0.06    | 0.03   | -0.07     | -0.11           | -0.03           | 0.00   | 0              |
| Negativicutes.id.2164          | class  | Homa-IR   | 0.01    | 0.03  | -0.02    | 0.03   | 0.00      | -0.04           | 0.04            | 0.84   | 0              |
| Verrucomicrobiae.id.4029       | class  | Homa-IR   | 0.02    | 0.03  | -0.01    | 0.03   | 0.01      | -0.03           | 0.05            | 0.78   | 0              |
| Aeromonadales.id.3316          | order  | Homa-IR   | -0.03   | 0.03  | 0.01     | 0.03   | -0.01     | -0.05           | 0.03            | 0.66   | 0.55           |
| Bacteroidales.id.913           | order  | Homa-IR   | -0.04   | 0.03  | -0.02    | 0.03   | -0.03     | -0.07           | 0.01            | 0.12   | 0              |
| Bifidobacteriales.id.432       | order  | Homa-IR   | 0.02    | 0.03  | 0.01     | 0.03   | 0.01      | -0.03           | 0.05            | 0.59   | 0              |
| Burkholderiales.id.2874        | order  | Homa-IR   | -0.01   | 0.03  | 0.01     | 0.03   | 0.00      | -0.04           | 0.04            | 0.95   | 0              |
| Clostridiales.id.1863          | order  | Homa-IR   | -0.03   | 0.03  | 0.02     | 0.03   | -0.01     | -0.05           | 0.04            | 0.79   | 0.714          |

|                            |       |         |       |      |       |      |       |       |      |      |       |
|----------------------------|-------|---------|-------|------|-------|------|-------|-------|------|------|-------|
| Coriobacteriales.id.810    | order | Homa-IR | 0.00  | 0.03 | -0.01 | 0.03 | -0.01 | -0.05 | 0.03 | 0.73 | 0     |
| Desulfovibrionales.id.3156 | order | Homa-IR | -0.03 | 0.03 | -0.01 | 0.03 | -0.02 | -0.06 | 0.02 | 0.35 | 0.163 |

|                                      |        |         |       |      |       |      |       |       |       |      |       |
|--------------------------------------|--------|---------|-------|------|-------|------|-------|-------|-------|------|-------|
| Enterobacteriales.id.3468            | order  | Homa-IR | 0.02  | 0.03 | 0.01  | 0.03 | 0.01  | -0.03 | 0.05  | 0.52 | 0     |
| Erysipelotrichales.id.2148           | order  | Homa-IR | 0.05  | 0.03 | 0.04  | 0.03 | 0.05  | 0.00  | 0.09  | 0.03 | 0     |
| Gastranaerophilales.id.1591          | order  | Homa-IR | -0.08 | 0.03 | 0.01  | 0.03 | -0.03 | -0.08 | 0.01  | 0.09 | 0.673 |
| Lactobacillales.id.1800              | order  | Homa-IR | 0.03  | 0.03 | 0.03  | 0.03 | 0.03  | -0.01 | 0.07  | 0.13 | 0     |
| MollicutesRF9.id.11579               | order  | Homa-IR | -0.06 | 0.03 | -0.06 | 0.03 | -0.06 | -0.10 | -0.02 | 0.00 | 0     |
| Pasteurellales.id.3688               | order  | Homa-IR | -0.02 | 0.03 | -0.05 | 0.03 | -0.03 | -0.07 | 0.01  | 0.09 | 0.547 |
| Rhodospirillales.id.2667             | order  | Homa-IR | -0.08 | 0.03 | 0.01  | 0.03 | -0.04 | -0.08 | 0.00  | 0.05 | 0.444 |
| Selenomonadales.id.2165              | order  | Homa-IR | 0.01  | 0.03 | -0.02 | 0.03 | 0.00  | -0.04 | 0.04  | 0.84 | 0     |
| Verrucomicrobiales.id.4030           | order  | Homa-IR | 0.02  | 0.03 | -0.01 | 0.03 | 0.01  | -0.03 | 0.05  | 0.78 | 0     |
| Acidaminococcaceae.id.2166           | family | Homa-IR | -0.05 | 0.03 | -0.02 | 0.03 | -0.04 | -0.08 | 0.00  | 0.07 | 0     |
| Alcaligenaceae.id.2875               | family | Homa-IR | 0.00  | 0.03 | 0.02  | 0.03 | 0.01  | -0.03 | 0.05  | 0.66 | 0     |
| Bacteroidaceae.id.917                | family | Homa-IR | -0.04 | 0.03 | -0.01 | 0.03 | -0.03 | -0.07 | 0.02  | 0.22 | 0     |
| Bifidobacteriaceae.id.433            | family | Homa-IR | 0.02  | 0.03 | 0.01  | 0.03 | 0.01  | -0.03 | 0.05  | 0.59 | 0     |
| Christensenellaceae.id.1866          | family | Homa-IR | -0.10 | 0.03 | -0.07 | 0.03 | -0.08 | -0.12 | -0.04 | 0.00 | 0     |
| Clostridiaceae1.id.1869              | family | Homa-IR | -0.03 | 0.03 | -0.01 | 0.03 | -0.02 | -0.06 | 0.02  | 0.35 | 0     |
| ClostridialesvadinBB60group.id.11286 | family | Homa-IR | -0.11 | 0.03 | -0.03 | 0.03 | -0.07 | -0.11 | -0.03 | 0.00 | 0.613 |
| Coriobacteriaceae.id.811             | family | Homa-IR | 0.00  | 0.03 | -0.01 | 0.03 | -0.01 | -0.05 | 0.03  | 0.73 | 0     |
| Desulfovibrionaceae.id.3169          | family | Homa-IR | -0.03 | 0.03 | -0.01 | 0.03 | -0.02 | -0.06 | 0.02  | 0.34 | 0.135 |
| Enterobacteriaceae.id.3469           | family | Homa-IR | 0.02  | 0.03 | 0.01  | 0.03 | 0.01  | -0.03 | 0.05  | 0.52 | 0     |
| Enterococcaceae.id.1828              | family | Homa-IR | 0.05  | 0.03 | -0.03 | 0.03 | 0.01  | -0.02 | 0.05  | 0.45 | 0.068 |
| Erysipelotrichaceae.id.2149          | family | Homa-IR | 0.05  | 0.03 | 0.04  | 0.03 | 0.05  | 0.00  | 0.09  | 0.03 | 0     |
| FamilyXIII.id.1957                   | family | Homa-IR | -0.03 | 0.03 | -0.02 | 0.03 | -0.03 | -0.07 | 0.01  | 0.17 | 0.699 |
| Lachnospiraceae.id.1987              | family | Homa-IR | 0.04  | 0.03 | 0.03  | 0.03 | 0.04  | 0.00  | 0.08  | 0.07 | 0     |
| Lactobacillaceae.id.1836             | family | Homa-IR | -0.02 | 0.03 | -0.04 | 0.03 | -0.03 | -0.07 | 0.01  | 0.11 | 0     |
| Pasteurellaceae.id.3689              | family | Homa-IR | -0.02 | 0.03 | -0.05 | 0.03 | -0.03 | -0.07 | 0.01  | 0.09 | 0.547 |
| Peptococcaceae.id.2024               | family | Homa-IR | -0.03 | 0.03 | -0.01 | 0.03 | -0.02 | -0.06 | 0.02  | 0.33 | 0.629 |
| Peptostreptococcaceae.id.2042        | family | Homa-IR | -0.04 | 0.03 | 0.00  | 0.03 | -0.02 | -0.06 | 0.02  | 0.30 | 0     |
| Porphyromonadaceae.id.943            | family | Homa-IR | -0.06 | 0.03 | -0.05 | 0.03 | -0.05 | -0.09 | -0.01 | 0.01 | 0     |
| Prevotellaceae.id.960                | family | Homa-IR | -0.02 | 0.03 | 0.02  | 0.03 | 0.00  | -0.04 | 0.04  | 0.95 | 0.181 |
| Rhodospirillaceae.id.2717            | family | Homa-IR | -0.08 | 0.03 | 0.01  | 0.03 | -0.04 | -0.08 | 0.00  | 0.06 | 0.446 |
| Rikenellaceae.id.967                 | family | Homa-IR | -0.07 | 0.03 | -0.04 | 0.03 | -0.05 | -0.10 | -0.01 | 0.01 | 0     |
| Ruminococcaceae.id.2050              | family | Homa-IR | -0.09 | 0.03 | 0.00  | 0.03 | -0.05 | -0.09 | -0.01 | 0.02 | 0.851 |

|                             |        |         |       |      |      |      |       |       |      |      |       |
|-----------------------------|--------|---------|-------|------|------|------|-------|-------|------|------|-------|
| Streptococcaceae.id.1850    | family | Homa-IR | 0.04  | 0.03 | 0.06 | 0.03 | 0.05  | 0.01  | 0.09 | 0.02 | 0     |
| Succinivibrionaceae.id.3326 | family | Homa-IR | -0.03 | 0.03 | 0.01 | 0.03 | -0.01 | -0.05 | 0.03 | 0.64 | 0.558 |

|                                            |        |         |       |      |       |      |       |       |       |      |       |
|--------------------------------------------|--------|---------|-------|------|-------|------|-------|-------|-------|------|-------|
| Veillonellaceae.id.2172                    | family | Homa-IR | 0.06  | 0.03 | -0.02 | 0.03 | 0.02  | -0.02 | 0.07  | 0.22 | 0.71  |
| Verrucomicrobiaceae.id.4036                | family | Homa-IR | 0.02  | 0.03 | -0.01 | 0.03 | 0.01  | -0.03 | 0.05  | 0.78 | 0     |
| unknownfamily.id.1000001214                | family | Homa-IR | -0.08 | 0.03 | 0.01  | 0.03 | -0.03 | -0.08 | 0.01  | 0.09 | 0.673 |
| unknownfamily.id.1000005471                | family | Homa-IR | -0.06 | 0.03 | -0.06 | 0.03 | -0.06 | -0.10 | -0.02 | 0.00 | 0     |
| unknownfamily.id.987                       | family | Homa-IR | 0.01  | 0.03 | -0.06 | 0.03 | -0.02 | -0.06 | 0.02  | 0.31 | 0     |
| Bacteroidespectinophilusgroup.id.14371     | genus  | Homa-IR | -0.02 | 0.03 | -0.01 | 0.03 | -0.02 | -0.06 | 0.02  | 0.36 | 0     |
| Eubacteriumcoprostanoligenesgroup.id.11375 | genus  | Homa-IR | -0.02 | 0.03 | -0.02 | 0.03 | -0.02 | -0.06 | 0.02  | 0.38 | 0.082 |
| Eubacteriumeligensgroup.id.14372           | genus  | Homa-IR | -0.09 | 0.03 | -0.05 | 0.03 | -0.07 | -0.11 | -0.03 | 0.00 | 0.658 |
| Eubacteriumhalliigroup.id.11338            | genus  | Homa-IR | 0.07  | 0.03 | 0.02  | 0.03 | 0.05  | 0.00  | 0.09  | 0.03 | 0.294 |
| Eubacteriumrectalegroup.id.14374           | genus  | Homa-IR | 0.01  | 0.03 | 0.03  | 0.03 | 0.02  | -0.02 | 0.06  | 0.33 | 0     |
| Eubacteriumruminantiumgroup.id.11340       | genus  | Homa-IR | -0.04 | 0.03 | -0.03 | 0.03 | -0.04 | -0.07 | 0.00  | 0.08 | 0     |
| Eubacteriumventriosumgroup.id.11341        | genus  | Homa-IR | 0.03  | 0.03 | 0.03  | 0.03 | 0.03  | -0.01 | 0.07  | 0.14 | 0.269 |
| Eubacteriumxylanophilumgroup.id.14375      | genus  | Homa-IR | -0.07 | 0.03 | -0.03 | 0.03 | -0.05 | -0.09 | -0.01 | 0.01 | 0.716 |
| Ruminococcusgauvreauigroup.id.11342        | genus  | Homa-IR | 0.00  | 0.03 | 0.01  | 0.03 | 0.00  | -0.04 | 0.04  | 0.97 | 0.683 |
| Ruminococcusgnavusgroup.id.14376           | genus  | Homa-IR | 0.02  | 0.03 | 0.07  | 0.03 | 0.05  | 0.01  | 0.09  | 0.02 | 0.492 |
| Ruminococcustorquesgroup.id.14377          | genus  | Homa-IR | 0.06  | 0.03 | 0.00  | 0.03 | 0.03  | -0.01 | 0.07  | 0.09 | 0     |
| Acidaminococcus.id.2167                    | genus  | Homa-IR | 0.02  | 0.03 | 0.03  | 0.03 | 0.02  | -0.02 | 0.06  | 0.25 | 0     |
| Adlercreutzia.id.812                       | genus  | Homa-IR | 0.05  | 0.03 | 0.02  | 0.03 | 0.04  | 0.00  | 0.08  | 0.08 | 0     |
| Akkermansia.id.4037                        | genus  | Homa-IR | 0.02  | 0.03 | -0.01 | 0.03 | 0.01  | -0.03 | 0.05  | 0.78 | 0     |
| Alistipes.id.968                           | genus  | Homa-IR | -0.08 | 0.03 | -0.03 | 0.03 | -0.05 | -0.09 | -0.01 | 0.01 | 0     |
| Alloprevotella.id.961                      | genus  | Homa-IR | -0.05 | 0.03 | 0.04  | 0.03 | 0.00  | -0.04 | 0.04  | 0.90 | 0.488 |
| Anaerostipes.id.1991                       | genus  | Homa-IR | 0.03  | 0.03 | 0.00  | 0.03 | 0.01  | -0.03 | 0.05  | 0.50 | 0     |
| Anaerotruncus.id.2054                      | genus  | Homa-IR | -0.08 | 0.03 | -0.03 | 0.03 | -0.06 | -0.10 | -0.02 | 0.01 | 0.601 |
| Bacteroides.id.918                         | genus  | Homa-IR | -0.04 | 0.03 | -0.01 | 0.03 | -0.03 | -0.07 | 0.02  | 0.22 | 0     |
| Barnesiella.id.944                         | genus  | Homa-IR | -0.05 | 0.03 | -0.02 | 0.03 | -0.04 | -0.08 | 0.00  | 0.07 | 0     |
| Bifidobacterium.id.436                     | genus  | Homa-IR | 0.02  | 0.03 | 0.01  | 0.03 | 0.01  | -0.03 | 0.05  | 0.51 | 0     |
| Blautia.id.1992                            | genus  | Homa-IR | 0.05  | 0.03 | 0.03  | 0.03 | 0.04  | 0.00  | 0.08  | 0.04 | 0     |
| Butyricicoccus.id.2055                     | genus  | Homa-IR | -0.02 | 0.03 | 0.00  | 0.03 | -0.01 | -0.05 | 0.03  | 0.62 | 0     |
| Butyricimonas.id.945                       | genus  | Homa-IR | -0.05 | 0.03 | -0.02 | 0.03 | -0.04 | -0.08 | 0.00  | 0.06 | 0     |
| Butyrivibrio.id.1993                       | genus  | Homa-IR | -0.05 | 0.03 | -0.01 | 0.03 | -0.03 | -0.07 | 0.01  | 0.13 | 0.375 |
| Catenibacterium.id.2153                    | genus  | Homa-IR | 0.01  | 0.03 | -0.01 | 0.03 | 0.00  | -0.04 | 0.04  | 0.88 | 0     |
| ChristensenellaceaeR7group.id.11283        | genus  | Homa-IR | -0.10 | 0.03 | -0.06 | 0.03 | -0.08 | -0.12 | -0.04 | 0.00 | 0     |

|                                     |       |         |       |      |       |      |       |       |      |      |       |
|-------------------------------------|-------|---------|-------|------|-------|------|-------|-------|------|------|-------|
| Clostridium sensu stricto 1.id.1873 | genus | Homa-IR | -0.03 | 0.03 | -0.01 | 0.03 | -0.02 | -0.06 | 0.02 | 0.33 | 0     |
| Collinsella.id.815                  | genus | Homa-IR | 0.01  | 0.03 | -0.01 | 0.03 | 0.00  | -0.04 | 0.04 | 0.99 | 0.123 |

|                                      |       |         |       |      |       |      |       |       |       |      |       |
|--------------------------------------|-------|---------|-------|------|-------|------|-------|-------|-------|------|-------|
| Coprococcus1.id.11301                | genus | Homa-IR | -0.06 | 0.03 | -0.03 | 0.03 | -0.04 | -0.08 | 0.00  | 0.04 | 0     |
| Coprococcus2.id.11302                | genus | Homa-IR | -0.05 | 0.03 | -0.01 | 0.03 | -0.03 | -0.07 | 0.01  | 0.14 | 0     |
| Coprococcus3.id.11303                | genus | Homa-IR | 0.01  | 0.03 | 0.01  | 0.03 | 0.01  | -0.03 | 0.05  | 0.68 | 0     |
| Desulfovibrio.id.3173                | genus | Homa-IR | -0.02 | 0.03 | -0.01 | 0.03 | -0.02 | -0.06 | 0.02  | 0.43 | 0.33  |
| Dialister.id.2183                    | genus | Homa-IR | 0.05  | 0.03 | -0.02 | 0.03 | 0.02  | -0.02 | 0.06  | 0.45 | 0.635 |
| Dorea.id.1997                        | genus | Homa-IR | 0.02  | 0.03 | -0.02 | 0.03 | 0.00  | -0.04 | 0.04  | 0.98 | 0.45  |
| Eggerthella.id.819                   | genus | Homa-IR | 0.00  | 0.03 | 0.07  | 0.03 | 0.04  | -0.01 | 0.08  | 0.09 | 0.739 |
| Eisenbergiella.id.11304              | genus | Homa-IR | -0.02 | 0.03 | 0.03  | 0.03 | 0.00  | -0.04 | 0.04  | 0.94 | 0.249 |
| Enterococcus.id.1831                 | genus | Homa-IR | 0.05  | 0.03 | -0.02 | 0.03 | 0.02  | -0.02 | 0.06  | 0.35 | 0     |
| Enterorhabdus.id.820                 | genus | Homa-IR | -0.04 | 0.03 | -0.02 | 0.03 | -0.03 | -0.07 | 0.01  | 0.11 | 0     |
| Erysipelatoclostridium.id.11381      | genus | Homa-IR | -0.01 | 0.03 | 0.06  | 0.03 | 0.02  | -0.02 | 0.06  | 0.27 | 0.396 |
| ErysipelotrichaceaeUCG003.id.11384   | genus | Homa-IR | 0.03  | 0.03 | 0.01  | 0.03 | 0.02  | -0.02 | 0.06  | 0.36 | 0     |
| Faecalibacterium.id.2057             | genus | Homa-IR | -0.03 | 0.03 | 0.02  | 0.03 | 0.00  | -0.04 | 0.04  | 0.86 | 0.613 |
| FamilyXIIAD3011group.id.11293        | genus | Homa-IR | -0.05 | 0.03 | -0.06 | 0.03 | -0.06 | -0.10 | -0.02 | 0.00 | 0     |
| FamilyXIIICUG001.id.11294            | genus | Homa-IR | 0.00  | 0.03 | -0.03 | 0.03 | -0.01 | -0.05 | 0.03  | 0.52 | 0     |
| Fusicatenibacter.id.11305            | genus | Homa-IR | 0.03  | 0.03 | 0.02  | 0.03 | 0.03  | -0.02 | 0.07  | 0.22 | 0     |
| Haemophilus.id.3698                  | genus | Homa-IR | -0.02 | 0.03 | -0.05 | 0.03 | -0.03 | -0.07 | 0.01  | 0.09 | 0.432 |
| Holdemanella.id.11393                | genus | Homa-IR | 0.01  | 0.03 | 0.06  | 0.03 | 0.04  | 0.00  | 0.08  | 0.07 | 0     |
| Intestinibacter.id.11345             | genus | Homa-IR | -0.01 | 0.03 | 0.01  | 0.03 | 0.00  | -0.04 | 0.04  | 0.98 | 0     |
| Intestinimonas.id.2062               | genus | Homa-IR | -0.07 | 0.03 | -0.01 | 0.03 | -0.04 | -0.08 | 0.00  | 0.03 | 0     |
| Lachnoclostridium.id.11308           | genus | Homa-IR | 0.00  | 0.03 | 0.04  | 0.03 | 0.02  | -0.02 | 0.06  | 0.41 | 0.668 |
| Lachnospira.id.2004                  | genus | Homa-IR | -0.03 | 0.03 | 0.03  | 0.03 | 0.00  | -0.04 | 0.04  | 0.98 | 0     |
| LachnospiraceaeFCS020group.id.11314  | genus | Homa-IR | -0.03 | 0.03 | -0.08 | 0.03 | -0.05 | -0.09 | -0.01 | 0.01 | 0.346 |
| LachnospiraceaeND3007group.id.11317  | genus | Homa-IR | -0.04 | 0.03 | 0.00  | 0.03 | -0.02 | -0.06 | 0.02  | 0.26 | 0     |
| LachnospiraceaeNK4A136group.id.11319 | genus | Homa-IR | -0.07 | 0.03 | -0.03 | 0.03 | -0.05 | -0.09 | -0.01 | 0.02 | 0.686 |
| LachnospiraceaeUCG001.id.11321       | genus | Homa-IR | -0.02 | 0.03 | -0.01 | 0.03 | -0.02 | -0.06 | 0.02  | 0.46 | 0     |
| LachnospiraceaeUCG004.id.11324       | genus | Homa-IR | -0.03 | 0.03 | -0.04 | 0.03 | -0.03 | -0.07 | 0.01  | 0.10 | 0     |
| LachnospiraceaeUCG010.id.11330       | genus | Homa-IR | -0.02 | 0.03 | -0.05 | 0.03 | -0.03 | -0.07 | 0.01  | 0.10 | 0     |
| Lactobacillus.id.1837                | genus | Homa-IR | -0.02 | 0.03 | -0.03 | 0.03 | -0.03 | -0.07 | 0.01  | 0.19 | 0     |
| Marvinbryantia.id.2005               | genus | Homa-IR | -0.08 | 0.03 | -0.07 | 0.03 | -0.08 | -0.12 | -0.04 | 0.00 | 0     |
| Megamonas.id.2184                    | genus | Homa-IR | 0.02  | 0.03 | -0.01 | 0.03 | 0.01  | -0.03 | 0.05  | 0.62 | 0     |
| Megasphaera.id.2185                  | genus | Homa-IR | 0.01  | 0.03 | 0.01  | 0.03 | 0.01  | -0.03 | 0.05  | 0.62 | 0.135 |



|                     |       |         |       |      |       |      |       |       |       |      |   |
|---------------------|-------|---------|-------|------|-------|------|-------|-------|-------|------|---|
| Mitsuokella.id.2186 | genus | Homa-IR | 0.07  | 0.03 | 0.01  | 0.03 | 0.04  | 0.00  | 0.08  | 0.04 | 0 |
| Odoribacter.id.952  | genus | Homa-IR | -0.10 | 0.03 | -0.03 | 0.03 | -0.06 | -0.10 | -0.02 | 0.00 | 0 |

|                                      |       |         |       |      |       |      |       |       |       |      |       |
|--------------------------------------|-------|---------|-------|------|-------|------|-------|-------|-------|------|-------|
| Olsenella.id.822                     | genus | Homa-IR | 0.00  | 0.03 | -0.05 | 0.03 | -0.02 | -0.06 | 0.02  | 0.28 | 0.557 |
| Oscillospira.id.2064                 | genus | Homa-IR | -0.05 | 0.03 | -0.01 | 0.03 | -0.03 | -0.07 | 0.01  | 0.19 | 0     |
| Parabacteroides.id.954               | genus | Homa-IR | -0.03 | 0.03 | -0.05 | 0.03 | -0.04 | -0.08 | 0.00  | 0.03 | 0     |
| Paraprevotella.id.962                | genus | Homa-IR | -0.03 | 0.03 | -0.02 | 0.03 | -0.02 | -0.06 | 0.02  | 0.28 | 0     |
| Parasutterella.id.2892               | genus | Homa-IR | 0.00  | 0.03 | 0.04  | 0.03 | 0.02  | -0.02 | 0.06  | 0.30 | 0.214 |
| Peptococcus.id.2037                  | genus | Homa-IR | -0.01 | 0.03 | 0.00  | 0.03 | -0.01 | -0.05 | 0.03  | 0.66 | 0     |
| Phascolarctobacterium.id.2168        | genus | Homa-IR | -0.06 | 0.03 | -0.03 | 0.03 | -0.04 | -0.08 | 0.00  | 0.03 | 0     |
| Prevotella2.id.11180                 | genus | Homa-IR | 0.00  | 0.03 | -0.02 | 0.03 | -0.01 | -0.05 | 0.03  | 0.75 | 0     |
| Prevotella7.id.11182                 | genus | Homa-IR | -0.02 | 0.03 | -0.01 | 0.03 | -0.02 | -0.06 | 0.02  | 0.43 | 0     |
| Prevotella9.id.11183                 | genus | Homa-IR | -0.01 | 0.03 | 0.01  | 0.03 | 0.00  | -0.04 | 0.04  | 1.00 | 0     |
| PrevotellaceaeNK3B31group.id.11185   | genus | Homa-IR | 0.01  | 0.03 | 0.06  | 0.03 | 0.03  | -0.01 | 0.07  | 0.10 | 0     |
| PrevotellaceaeUCG001.id.11186        | genus | Homa-IR | -0.01 | 0.03 | 0.02  | 0.03 | 0.00  | -0.04 | 0.04  | 0.88 | 0.757 |
| RikenellaceaeRC9gutgroup.id.11191    | genus | Homa-IR | 0.00  | 0.03 | -0.04 | 0.03 | -0.02 | -0.06 | 0.02  | 0.37 | 0     |
| Romboutsia.id.11347                  | genus | Homa-IR | -0.05 | 0.03 | 0.00  | 0.03 | -0.03 | -0.07 | 0.01  | 0.19 | 0.064 |
| Roseburia.id.2012                    | genus | Homa-IR | 0.01  | 0.03 | 0.02  | 0.03 | 0.02  | -0.02 | 0.06  | 0.43 | 0     |
| Ruminiclostridium5.id.11355          | genus | Homa-IR | -0.07 | 0.03 | -0.02 | 0.03 | -0.04 | -0.09 | 0.00  | 0.03 | 0.791 |
| Ruminiclostridium6.id.11356          | genus | Homa-IR | -0.09 | 0.03 | 0.01  | 0.03 | -0.04 | -0.08 | 0.00  | 0.04 | 0.869 |
| Ruminiclostridium9.id.11357          | genus | Homa-IR | -0.04 | 0.03 | -0.08 | 0.03 | -0.06 | -0.10 | -0.02 | 0.00 | 0.294 |
| RuminococcaceaeNK4A214group.id.11358 | genus | Homa-IR | -0.10 | 0.03 | -0.08 | 0.03 | -0.09 | -0.13 | -0.05 | 0.00 | 0     |
| RuminococcaceaeUCG002.id.11360       | genus | Homa-IR | -0.07 | 0.03 | -0.08 | 0.03 | -0.07 | -0.11 | -0.03 | 0.00 | 0     |
| RuminococcaceaeUCG003.id.11361       | genus | Homa-IR | -0.05 | 0.03 | -0.09 | 0.03 | -0.07 | -0.11 | -0.03 | 0.00 | 0.392 |
| RuminococcaceaeUCG004.id.11362       | genus | Homa-IR | 0.02  | 0.03 | 0.02  | 0.03 | 0.02  | -0.02 | 0.06  | 0.33 | 0     |
| RuminococcaceaeUCG005.id.11363       | genus | Homa-IR | -0.12 | 0.03 | -0.07 | 0.03 | -0.10 | -0.14 | -0.05 | 0.00 | 0.324 |
| RuminococcaceaeUCG008.id.11365       | genus | Homa-IR | -0.09 | 0.03 | -0.04 | 0.03 | -0.07 | -0.10 | -0.03 | 0.00 | 0.328 |
| RuminococcaceaeUCG010.id.11367       | genus | Homa-IR | -0.11 | 0.03 | -0.06 | 0.03 | -0.09 | -0.13 | -0.05 | 0.00 | 0     |
| RuminococcaceaeUCG013.id.11370       | genus | Homa-IR | -0.02 | 0.03 | 0.04  | 0.03 | 0.01  | -0.03 | 0.05  | 0.57 | 0.666 |
| RuminococcaceaeUCG014.id.11371       | genus | Homa-IR | -0.07 | 0.03 | -0.07 | 0.03 | -0.07 | -0.11 | -0.03 | 0.00 | 0     |
| Ruminococcus1.id.11373               | genus | Homa-IR | -0.07 | 0.03 | 0.03  | 0.03 | -0.02 | -0.06 | 0.02  | 0.31 | 0.895 |
| Ruminococcus2.id.11374               | genus | Homa-IR | -0.04 | 0.03 | 0.03  | 0.03 | 0.00  | -0.04 | 0.04  | 0.86 | 0     |
| Sellimonas.id.14369                  | genus | Homa-IR | 0.04  | 0.03 | 0.04  | 0.03 | 0.04  | 0.00  | 0.08  | 0.06 | 0     |
| Senegalimassilia.id.11160            | genus | Homa-IR | -0.01 | 0.03 | -0.05 | 0.03 | -0.03 | -0.07 | 0.01  | 0.12 | 0.388 |
| Slackia.id.825                       | genus | Homa-IR | 0.03  | 0.03 | -0.04 | 0.03 | -0.01 | -0.05 | 0.03  | 0.80 | 0.855 |

|                         |       |         |       |      |      |      |       |       |      |      |   |
|-------------------------|-------|---------|-------|------|------|------|-------|-------|------|------|---|
| Streptococcus.id.1853   | genus | Homa-IR | 0.04  | 0.03 | 0.06 | 0.03 | 0.05  | 0.01  | 0.09 | 0.02 | 0 |
| Subdoligranulum.id.2070 | genus | Homa-IR | -0.01 | 0.03 | 0.00 | 0.03 | -0.01 | -0.05 | 0.03 | 0.73 | 0 |

|                            |       |         |       |      |       |      |       |       |       |      |       |
|----------------------------|-------|---------|-------|------|-------|------|-------|-------|-------|------|-------|
| Succiniclasticum.id.2169   | genus | Homa-IR | 0.00  | 0.03 | 0.00  | 0.03 | 0.00  | -0.04 | 0.04  | 1.00 | 0     |
| Sutterella.id.2896         | genus | Homa-IR | -0.01 | 0.03 | -0.02 | 0.03 | -0.02 | -0.06 | 0.02  | 0.40 | 0     |
| Terrisporobacter.id.11348  | genus | Homa-IR | -0.05 | 0.03 | -0.02 | 0.03 | -0.04 | -0.08 | 0.00  | 0.08 | 0     |
| Turicibacter.id.2162       | genus | Homa-IR | -0.03 | 0.03 | -0.01 | 0.03 | -0.02 | -0.06 | 0.02  | 0.27 | 0     |
| Tyzzerella3.id.11335       | genus | Homa-IR | 0.03  | 0.03 | 0.00  | 0.03 | 0.02  | -0.02 | 0.06  | 0.38 | 0     |
| Veillonella.id.2198        | genus | Homa-IR | -0.02 | 0.03 | -0.03 | 0.03 | -0.03 | -0.07 | 0.01  | 0.21 | 0.475 |
| unknowngenus.id.1000000073 | genus | Homa-IR | -0.11 | 0.03 | -0.03 | 0.03 | -0.07 | -0.11 | -0.03 | 0.00 | 0.613 |
| unknowngenus.id.1000001215 | genus | Homa-IR | -0.08 | 0.03 | 0.01  | 0.03 | -0.03 | -0.08 | 0.01  | 0.09 | 0.673 |
| unknowngenus.id.1000005472 | genus | Homa-IR | -0.06 | 0.03 | -0.06 | 0.03 | -0.06 | -0.10 | -0.02 | 0.00 | 0     |
| unknowngenus.id.1000005479 | genus | Homa-IR | -0.04 | 0.03 | -0.05 | 0.03 | -0.04 | -0.08 | 0.00  | 0.03 | 0     |
| unknowngenus.id.1000013899 | genus | Homa-IR | 0.01  | 0.03 | -0.06 | 0.03 | -0.02 | -0.06 | 0.02  | 0.31 | 0     |
| unknowngenus.id.2071       | genus | Homa-IR | -0.09 | 0.03 | -0.03 | 0.03 | -0.06 | -0.10 | -0.02 | 0.01 | 0.81  |
| unknowngenus.id.2755       | genus | Homa-IR | -0.08 | 0.03 | 0.01  | 0.03 | -0.04 | -0.08 | 0.00  | 0.06 | 0.459 |
| unknowngenus.id.826        | genus | Homa-IR | -0.03 | 0.03 | 0.01  | 0.03 | -0.01 | -0.05 | 0.03  | 0.54 | 0.291 |
| unknowngenus.id.964        | genus | Homa-IR | 0.05  | 0.03 | 0.01  | 0.03 | 0.03  | -0.01 | 0.07  | 0.11 | 0     |

| Taxa in RS only                            | Clade  | Phenotype | Beta_RS | Se_RS |
|--------------------------------------------|--------|-----------|---------|-------|
| BacteroidalesS247group.id.11173            | family | Homa-IR   | -0.05   | 0.03  |
| Veillonellaceae.id.2172                    | family | Homa-IR   | 0.06    | 0.03  |
| Bacteroidespectinophilusgroup.id.14371     | genus  | Homa-IR   | -0.02   | 0.03  |
| Enterobacter.id.3502                       | genus  | Homa-IR   | 0.04    | 0.03  |
| EscherichiaShigella.id.3504                | genus  | Homa-IR   | 0.01    | 0.03  |
| Eubacteriumcoprostanoligenesgroup.id.11375 | genus  | Homa-IR   | -0.07   | 0.03  |
| Eubacteriumeligensgroup.id.14372           | genus  | Homa-IR   | -0.09   | 0.03  |
| Eubacteriumhalliigroup.id.11338            | genus  | Homa-IR   | 0.07    | 0.03  |
| Eubacteriumoxidoreducensgroup.id.11339     | genus  | Homa-IR   | -0.10   | 0.03  |
| Eubacteriumxylanophilumgroup.id.14375      | genus  | Homa-IR   | -0.07   | 0.03  |
| Hungatella.id.11306                        | genus  | Homa-IR   | -0.01   | 0.03  |
| Klebsiella.id.3507                         | genus  | Homa-IR   | 0.05    | 0.03  |
| LachnospiraceaeNC2004group.id.11316        | genus  | Homa-IR   | -0.08   | 0.03  |

|                                |       |         |       |      |
|--------------------------------|-------|---------|-------|------|
| LachnospiraceaeUCG008.id.11328 | genus | Homa-IR | -0.03 | 0.03 |
| unknowngenus.id.1868           | genus | Homa-IR | -0.06 | 0.03 |

| Taxa in LLD only                  | Clade  | Phenotype | Beta_LLD | Se_LLD |
|-----------------------------------|--------|-----------|----------|--------|
| Archaea.id.2                      | domain | Homa-IR   | -0.07    | 0.03   |
| Euryarchaeota.id.55               | phylum | Homa-IR   | -0.07    | 0.03   |
| Lentisphaerae.id.2238             | phylum | Homa-IR   | -0.02    | 0.03   |
| Actinomycetales.id.420            | order  | Homa-IR   | 0.05     | 0.03   |
| Mycoplasmatales.id.3946           | order  | Homa-IR   | -0.03    | 0.03   |
| NB1.n.id.3953                     | order  | Homa-IR   | 0.00     | 0.03   |
| Pseudomonadales.id.3709           | order  | Homa-IR   | -0.03    | 0.03   |
| Spirochaetales.id.3870            | order  | Homa-IR   | 0.00     | 0.03   |
| Synergistales.id.3900             | order  | Homa-IR   | -0.02    | 0.03   |
| Thermoplasmatales.id.220          | order  | Homa-IR   | -0.02    | 0.03   |
| unknownorder.id.1000000003        | order  | Homa-IR   | 0.01     | 0.03   |
| Verrucomicrobiales.id.4030        | order  | Homa-IR   | -0.01    | 0.03   |
| Victivallales.id.2254             | order  | Homa-IR   | -0.02    | 0.03   |
| Xanthomonadales.id.3786           | order  | Homa-IR   | -0.03    | 0.03   |
| Spirochaetes.id.3856              | class  | Homa-IR   | 0.00     | 0.03   |
| Synergistia.id.3899               | class  | Homa-IR   | -0.02    | 0.03   |
| Thermoplasmata.id.210             | class  | Homa-IR   | -0.02    | 0.03   |
| Actinomycetaceae.id.421           | family | Homa-IR   | 0.05     | 0.03   |
| BacteroidalesS24.7group.id.11173  | family | Homa-IR   | -0.05    | 0.03   |
| Christensenellaceae.id.1866       | family | Homa-IR   | -0.07    | 0.03   |
| FamilyXI.id.1936                  | family | Homa-IR   | 0.01     | 0.03   |
| unknownfamily.id.1000000004       | family | Homa-IR   | 0.01     | 0.03   |
| unknownfamily.id.1000006161       | family | Homa-IR   | 0.00     | 0.03   |
| unknownfamily.id.1855             | family | Homa-IR   | -0.03    | 0.03   |
| vadinBE97.id.14446                | family | Homa-IR   | -0.02    | 0.03   |
| Veillonellaceae.id.2172           | family | Homa-IR   | -0.02    | 0.03   |
| Xanthomonadaceae.id.3799          | family | Homa-IR   | -0.03    | 0.03   |
| Clostridiuminnocuumgroup.id.14397 | genus  | Homa-IR   | 0.05     | 0.03   |
| Eubacteriumbrachygroup.id.11296   | genus  | Homa-IR   | 0.05     | 0.03   |
| Abiotrophia.id.1803               | genus  | Homa-IR   | 0.00     | 0.03   |
| Actinomyces.id.423                | genus  | Homa-IR   | 0.05     | 0.03   |

|                       |       |         |       |      |
|-----------------------|-------|---------|-------|------|
| Actinotignum.id.11137 | genus | Homa-IR | -0.02 | 0.03 |
| Allisonella.id.2174   | genus | Homa-IR | 0.04  | 0.03 |

|                                     |       |         |       |      |
|-------------------------------------|-------|---------|-------|------|
| Arcanobacterium.id.424              | genus | Homa-IR | 0.00  | 0.03 |
| Asaccharobacter.id.813              | genus | Homa-IR | 0.02  | 0.03 |
| Bilophila.id.3170                   | genus | Homa-IR | 0.00  | 0.03 |
| CandidatusMethanogranum.id.11110    | genus | Homa-IR | -0.02 | 0.03 |
| Catenisphaera.id.14395              | genus | Homa-IR | -0.03 | 0.03 |
| Cellulosilyticum.id.1995            | genus | Homa-IR | -0.05 | 0.03 |
| Cetobacterium.id.2209               | genus | Homa-IR | 0.02  | 0.03 |
| Cloacibacillus.id.3908              | genus | Homa-IR | -0.01 | 0.03 |
| Coprobacillus.id.2154               | genus | Homa-IR | -0.01 | 0.03 |
| CoriobacteriaceaeUCG.002.id.11158   | genus | Homa-IR | -0.03 | 0.03 |
| CoriobacteriaceaeUCG.003.id.11159   | genus | Homa-IR | 0.05  | 0.03 |
| Denitrobacterium.id.818             | genus | Homa-IR | -0.03 | 0.03 |
| dgA.11gutgroup.id.978               | genus | Homa-IR | 0.02  | 0.03 |
| Dielma.id.11380                     | genus | Homa-IR | 0.00  | 0.03 |
| Epulopiscium.id.1998                | genus | Homa-IR | 0.03  | 0.03 |
| ErysipelotrichaceaeUCG006.id.11386  | genus | Homa-IR | 0.02  | 0.03 |
| ErysipelotrichaceaeUCG009.id.11389  | genus | Homa-IR | 0.04  | 0.03 |
| Escherichia.Shigella.id.3504        | genus | Homa-IR | 0.00  | 0.03 |
| Eubacterium.id.1932                 | genus | Homa-IR | 0.04  | 0.03 |
| Faecalicoccus.id.11391              | genus | Homa-IR | 0.00  | 0.03 |
| Faecalitalea.id.11392               | genus | Homa-IR | 0.05  | 0.03 |
| Flavonifractor.id.2059              | genus | Homa-IR | 0.00  | 0.03 |
| Gardnerella.id.437                  | genus | Homa-IR | 0.00  | 0.03 |
| Gordonibacter.id.821                | genus | Homa-IR | 0.03  | 0.03 |
| Hafnia.Obesumbacterium.id.14636     | genus | Homa-IR | 0.00  | 0.03 |
| Howardella.id.2000                  | genus | Homa-IR | -0.01 | 0.03 |
| LachnospiraceaeNK3A20group.id.11318 | genus | Homa-IR | 0.03  | 0.03 |
| Lactococcus.id.1851                 | genus | Homa-IR | 0.00  | 0.03 |
| Lautropia.id.2905                   | genus | Homa-IR | 0.01  | 0.03 |
| Leuconostoc.id.1841                 | genus | Homa-IR | -0.02 | 0.03 |
| Methanobrevibacter.id.123           | genus | Homa-IR | -0.07 | 0.03 |
| Methanosphaera.id.124               | genus | Homa-IR | -0.04 | 0.03 |



|                       |       |         |       |      |
|-----------------------|-------|---------|-------|------|
| Mogibacterium.id.1960 | genus | Homa-IR | -0.02 | 0.03 |
| Morganella.id.3512    | genus | Homa-IR | -0.03 | 0.03 |

|                                      |       |         |       |      |
|--------------------------------------|-------|---------|-------|------|
| Porphyromonas.id.956                 | genus | Homa-IR | 0.01  | 0.03 |
| Prevotella1.id.11179                 | genus | Homa-IR | 0.01  | 0.03 |
| PrevotellaceaeUCG003.id.11187        | genus | Homa-IR | 0.07  | 0.03 |
| PrevotellaceaeUCG004.id.11188        | genus | Homa-IR | -0.05 | 0.03 |
| Pseudomonas.id.3723                  | genus | Homa-IR | -0.03 | 0.03 |
| Rikenella.id.973                     | genus | Homa-IR | -0.01 | 0.03 |
| RuminococcaceaeNK4A214group.id.11358 | genus | Homa-IR | -0.08 | 0.03 |
| RuminococcaceaeUCG005.id.11363       | genus | Homa-IR | -0.07 | 0.03 |
| RuminococcaceaeUCG008.id.11365       | genus | Homa-IR | -0.04 | 0.03 |
| RuminococcaceaeUCG010.id.11367       | genus | Homa-IR | -0.06 | 0.03 |
| Sarcina.id.1896                      | genus | Homa-IR | 0.06  | 0.03 |
| Solobacterium.id.2161                | genus | Homa-IR | 0.02  | 0.03 |
| Staphylococcus.id.1780               | genus | Homa-IR | 0.05  | 0.03 |
| Stenotrophomonas.id.3818             | genus | Homa-IR | -0.03 | 0.03 |
| Succinivibrio.id.3331                | genus | Homa-IR | 0.01  | 0.03 |
| Synergistes.id.3913                  | genus | Homa-IR | -0.01 | 0.03 |
| Syntrophococcus.id.2016              | genus | Homa-IR | -0.01 | 0.03 |
| Treponema2.id.11577                  | genus | Homa-IR | 0.00  | 0.03 |
| Tyzzerella4.id.11336                 | genus | Homa-IR | 0.05  | 0.03 |
| unknowngenus.id.1000000005           | genus | Homa-IR | 0.01  | 0.03 |
| unknowngenus.id.1000027565           | genus | Homa-IR | -0.02 | 0.03 |
| unknowngenus.id.1000043796           | genus | Homa-IR | -0.03 | 0.03 |
| unknowngenus.id.1854                 | genus | Homa-IR | -0.04 | 0.03 |
| unknowngenus.id.2163                 | genus | Homa-IR | -0.04 | 0.03 |
| unknowngenus.id.3332                 | genus | Homa-IR | 0.02  | 0.03 |
| unknowngenus.id.441                  | genus | Homa-IR | -0.06 | 0.03 |
| Ureaplasma.id.3951                   | genus | Homa-IR | -0.03 | 0.03 |
| Varibaculum.id.427                   | genus | Homa-IR | 0.04  | 0.03 |
| Veillonella.id.2198                  | genus | Homa-IR | -0.03 | 0.03 |
| Weissella.id.1843                    | genus | Homa-IR | 0.01  | 0.03 |

**Supplementary Table 2 - Associations of taxa and insulin resistance**

Effect estimates in RS and LLD were calculated using linear regression; pooled estimates were calculated based on a mixed-effect meta-analysis.

Model 4: Adjusted for age, sex, Time in mail (RS), Batch (RS), smoking, education level (RS), physical activity, alcohol intake, total energy intake, BMI, PPI, and lipid-lowering medication.

Abbreviation, RS, Rotterdam Study, LLD, Lifelines-Deep Study. P<0.0005 indicates statistical significance

| Overlapping taxa in RS and LLD | Clade  | Phenotype | Beta_RS | Se_RS | Beta_LLD | Se_LLD | Beta_Meta | Lower95%CI_Meta | Upper95%CI_Meta | p_Meta | I <sup>2</sup> |
|--------------------------------|--------|-----------|---------|-------|----------|--------|-----------|-----------------|-----------------|--------|----------------|
| Bacteria.id.3                  | domain | Homa-IR   | 0.00    | 0.03  | 0.03     | 0.02   | 0.02      | -0.03           | 0.07            | 0.46   | 0.00           |
| Actinobacteria.id.400          | phylum | Homa-IR   | 0.02    | 0.03  | 0.00     | 0.03   | 0.01      | -0.03           | 0.05            | 0.49   | 0.00           |
| Bacteroidetes.id.905           | phylum | Homa-IR   | -0.03   | 0.03  | -0.02    | 0.03   | -0.03     | -0.07           | 0.02            | 0.22   | 0.00           |
| Cyanobacteria.id.1500          | phylum | Homa-IR   | -0.08   | 0.03  | 0.02     | 0.03   | -0.03     | -0.07           | 0.01            | 0.13   | 0.82           |
| Firmicutes.id.1672             | phylum | Homa-IR   | 0.00    | 0.03  | 0.04     | 0.03   | 0.02      | -0.02           | 0.06            | 0.31   | 0.00           |
| Proteobacteria.id.2375         | phylum | Homa-IR   | 0.00    | 0.03  | -0.02    | 0.03   | -0.01     | -0.05           | 0.03            | 0.56   | 0.00           |
| Tenericutes.id.3919            | phylum | Homa-IR   | -0.07   | 0.03  | -0.06    | 0.03   | -0.06     | -0.10           | -0.02           | 0.00   | 0.00           |
| Verrucomicrobia.id.3982        | phylum | Homa-IR   | 0.02    | 0.03  | -0.02    | 0.03   | 0.00      | -0.04           | 0.04            | 0.92   | 0.02           |
| Actinobacteria.id.419          | class  | Homa-IR   | 0.02    | 0.03  | 0.01     | 0.03   | 0.01      | -0.03           | 0.05            | 0.50   | 0.00           |
| Alphaproteobacteria.id.2379    | class  | Homa-IR   | -0.08   | 0.03  | 0.00     | 0.03   | -0.04     | -0.08           | 0.00            | 0.05   | 0.75           |
| Bacilli.id.1673                | class  | Homa-IR   | 0.02    | 0.03  | 0.03     | 0.03   | 0.02      | -0.02           | 0.06            | 0.32   | 0.00           |
| Bacteroidia.id.912             | class  | Homa-IR   | -0.03   | 0.03  | -0.02    | 0.03   | -0.03     | -0.07           | 0.02            | 0.22   | 0.00           |
| Betaproteobacteria.id.2867     | class  | Homa-IR   | -0.01   | 0.03  | 0.01     | 0.03   | 0.00      | -0.04           | 0.04            | 0.87   | 0.00           |
| Clostridia.id.1859             | class  | Homa-IR   | -0.02   | 0.03  | 0.02     | 0.03   | 0.00      | -0.04           | 0.04            | 0.91   | 0.00           |
| Coriobacteriia.id.809          | class  | Homa-IR   | 0.00    | 0.03  | -0.01    | 0.03   | 0.00      | -0.04           | 0.04            | 0.91   | 0.00           |
| Deltaproteobacteria.id.3087    | class  | Homa-IR   | -0.02   | 0.03  | -0.01    | 0.03   | -0.01     | -0.05           | 0.03            | 0.53   | 0.00           |
| Erysipelotrichia.id.2147       | class  | Homa-IR   | 0.04    | 0.03  | 0.04     | 0.03   | 0.04      | 0.00            | 0.08            | 0.05   | 0.00           |
| Gammaproteobacteria.id.3303    | class  | Homa-IR   | -0.01   | 0.03  | -0.02    | 0.03   | -0.02     | -0.06           | 0.02            | 0.44   | 0.00           |
| Melainabacteria.id.1589        | class  | Homa-IR   | -0.07   | 0.03  | 0.02     | 0.03   | -0.03     | -0.07           | 0.01            | 0.16   | 0.76           |
| Mollicutes.id.3920             | class  | Homa-IR   | -0.07   | 0.03  | -0.06    | 0.03   | -0.06     | -0.10           | -0.02           | 0.00   | 0.00           |
| Negativicutes.id.2164          | class  | Homa-IR   | 0.01    | 0.03  | -0.02    | 0.03   | 0.00      | -0.04           | 0.04            | 0.90   | 0.00           |
| Verrucomicrobiae.id.4029       | class  | Homa-IR   | 0.02    | 0.03  | -0.02    | 0.03   | 0.00      | -0.04           | 0.04            | 0.91   | 0.03           |
| Aeromonadales.id.3316          | order  | Homa-IR   | -0.02   | 0.03  | 0.00     | 0.03   | -0.01     | -0.05           | 0.03            | 0.76   | 0.00           |
| Bacteroidales.id.913           | order  | Homa-IR   | -0.03   | 0.03  | -0.02    | 0.03   | -0.03     | -0.07           | 0.02            | 0.22   | 0.00           |
| Bifidobacteriales.id.432       | order  | Homa-IR   | 0.01    | 0.03  | 0.01     | 0.03   | 0.01      | -0.03           | 0.05            | 0.60   | 0.00           |
| Burkholderiales.id.2874        | order  | Homa-IR   | 0.00    | 0.03  | 0.01     | 0.03   | 0.01      | -0.03           | 0.05            | 0.78   | 0.00           |
| Clostridiales.id.1863          | order  | Homa-IR   | -0.02   | 0.03  | 0.02     | 0.03   | 0.00      | -0.04           | 0.04            | 0.92   | 0.00           |

|                            |       |         |       |      |       |      |       |       |      |      |      |
|----------------------------|-------|---------|-------|------|-------|------|-------|-------|------|------|------|
| Coriobacteriales.id.810    | order | Homa-IR | 0.00  | 0.03 | -0.01 | 0.03 | 0.00  | -0.04 | 0.04 | 0.91 | 0.00 |
| Desulfovibrionales.id.3156 | order | Homa-IR | -0.02 | 0.03 | -0.01 | 0.03 | -0.01 | -0.05 | 0.03 | 0.54 | 0.00 |

|                                      |        |         |       |      |       |      |       |       |       |      |      |
|--------------------------------------|--------|---------|-------|------|-------|------|-------|-------|-------|------|------|
| Enterobacteriales.id.3468            | order  | Homa-IR | 0.01  | 0.03 | 0.01  | 0.03 | 0.01  | -0.03 | 0.05  | 0.77 | 0.00 |
| Erysipelotrichales.id.2148           | order  | Homa-IR | 0.04  | 0.03 | 0.04  | 0.03 | 0.04  | 0.00  | 0.08  | 0.05 | 0.00 |
| Gastranaerophilales.id.1591          | order  | Homa-IR | -0.07 | 0.03 | 0.02  | 0.03 | -0.03 | -0.07 | 0.01  | 0.17 | 0.76 |
| Lactobacillales.id.1800              | order  | Homa-IR | 0.02  | 0.03 | 0.03  | 0.03 | 0.02  | -0.02 | 0.06  | 0.31 | 0.00 |
| MollicutesRF9.id.11579               | order  | Homa-IR | -0.06 | 0.03 | -0.06 | 0.03 | -0.06 | -0.10 | -0.02 | 0.00 | 0.00 |
| Pasteurellales.id.3688               | order  | Homa-IR | -0.03 | 0.03 | -0.05 | 0.03 | -0.04 | -0.08 | 0.00  | 0.06 | 0.00 |
| Rhodospirillales.id.2667             | order  | Homa-IR | -0.08 | 0.03 | 0.00  | 0.03 | -0.04 | -0.08 | 0.00  | 0.05 | 0.76 |
| Selenomonadales.id.2165              | order  | Homa-IR | 0.01  | 0.03 | -0.02 | 0.03 | 0.00  | -0.04 | 0.04  | 0.90 | 0.00 |
| Verrucomicrobiales.id.4030           | order  | Homa-IR | 0.02  | 0.03 | -0.02 | 0.03 | 0.00  | -0.04 | 0.04  | 0.91 | 0.03 |
| Acidaminococcaceae.id.2166           | family | Homa-IR | -0.04 | 0.03 | -0.02 | 0.03 | -0.03 | -0.07 | 0.01  | 0.12 | 0.00 |
| Alcaligenaceae.id.2875               | family | Homa-IR | 0.01  | 0.03 | 0.02  | 0.03 | 0.01  | -0.03 | 0.05  | 0.54 | 0.00 |
| Bacteroidaceae.id.917                | family | Homa-IR | -0.02 | 0.03 | -0.02 | 0.03 | -0.02 | -0.06 | 0.02  | 0.33 | 0.00 |
| Bifidobacteriaceae.id.433            | family | Homa-IR | 0.01  | 0.03 | 0.01  | 0.03 | 0.01  | -0.03 | 0.05  | 0.60 | 0.00 |
| Christensenellaceae.id.1866          | family | Homa-IR | -0.09 | 0.03 | -0.06 | 0.03 | -0.08 | -0.12 | -0.03 | 0.00 | 0.00 |
| Clostridiaceae1.id.1869              | family | Homa-IR | -0.03 | 0.03 | 0.00  | 0.03 | -0.02 | -0.06 | 0.02  | 0.37 | 0.00 |
| ClostridialesvadinBB60group.id.11286 | family | Homa-IR | -0.10 | 0.03 | -0.03 | 0.03 | -0.06 | -0.10 | -0.02 | 0.00 | 0.63 |
| Coriobacteriaceae.id.811             | family | Homa-IR | 0.00  | 0.03 | -0.01 | 0.03 | 0.00  | -0.04 | 0.04  | 0.91 | 0.00 |
| Desulfovibrionaceae.id.3169          | family | Homa-IR | -0.02 | 0.03 | -0.01 | 0.03 | -0.01 | -0.05 | 0.03  | 0.53 | 0.00 |
| Enterobacteriaceae.id.3469           | family | Homa-IR | 0.01  | 0.03 | 0.01  | 0.03 | 0.01  | -0.03 | 0.05  | 0.77 | 0.00 |
| Enterococcaceae.id.1828              | family | Homa-IR | 0.03  | 0.03 | -0.04 | 0.03 | 0.00  | -0.03 | 0.04  | 0.84 | 0.68 |
| Erysipelotrichaceae.id.2149          | family | Homa-IR | 0.04  | 0.03 | 0.04  | 0.03 | 0.04  | 0.00  | 0.08  | 0.05 | 0.00 |
| FamilyXIII.id.1957                   | family | Homa-IR | -0.03 | 0.03 | -0.02 | 0.03 | -0.03 | -0.07 | 0.01  | 0.20 | 0.00 |
| Lachnospiraceae.id.1987              | family | Homa-IR | 0.04  | 0.03 | 0.03  | 0.03 | 0.04  | 0.00  | 0.08  | 0.08 | 0.00 |
| Lactobacillaceae.id.1836             | family | Homa-IR | -0.02 | 0.03 | -0.04 | 0.03 | -0.03 | -0.07 | 0.01  | 0.13 | 0.00 |
| Pasteurellaceae.id.3689              | family | Homa-IR | -0.03 | 0.03 | -0.05 | 0.03 | -0.04 | -0.08 | 0.00  | 0.06 | 0.00 |
| Peptococcaceae.id.2024               | family | Homa-IR | -0.03 | 0.03 | 0.00  | 0.03 | -0.02 | -0.06 | 0.02  | 0.36 | 0.00 |
| Peptostreptococcaceae.id.2042        | family | Homa-IR | -0.04 | 0.03 | 0.01  | 0.03 | -0.02 | -0.06 | 0.02  | 0.33 | 0.27 |
| Porphyromonadaceae.id.943            | family | Homa-IR | -0.04 | 0.03 | -0.05 | 0.03 | -0.05 | -0.09 | -0.01 | 0.02 | 0.00 |
| Prevotellaceae.id.960                | family | Homa-IR | -0.01 | 0.03 | 0.02  | 0.03 | 0.00  | -0.04 | 0.04  | 0.93 | 0.00 |
| Rhodospirillaceae.id.2717            | family | Homa-IR | -0.08 | 0.03 | 0.00  | 0.03 | -0.04 | -0.08 | 0.00  | 0.06 | 0.75 |
| Rikenellaceae.id.967                 | family | Homa-IR | -0.06 | 0.03 | -0.04 | 0.03 | -0.05 | -0.09 | -0.01 | 0.02 | 0.00 |
| Ruminococcaceae.id.2050              | family | Homa-IR | -0.07 | 0.03 | 0.00  | 0.03 | -0.04 | -0.08 | 0.00  | 0.05 | 0.70 |

|                             |        |         |       |      |      |      |       |       |      |      |      |
|-----------------------------|--------|---------|-------|------|------|------|-------|-------|------|------|------|
| Streptococcaceae.id.1850    | family | Homa-IR | 0.03  | 0.03 | 0.05 | 0.03 | 0.04  | 0.00  | 0.08 | 0.07 | 0.00 |
| Succinivibrionaceae.id.3326 | family | Homa-IR | -0.02 | 0.03 | 0.00 | 0.03 | -0.01 | -0.05 | 0.03 | 0.74 | 0.00 |

|                                            |        |         |       |      |       |      |       |       |       |      |      |
|--------------------------------------------|--------|---------|-------|------|-------|------|-------|-------|-------|------|------|
| Veillonellaceae.id.2172                    | family | Homa-IR | 0.05  | 0.03 | -0.02 | 0.03 | 0.02  | -0.02 | 0.06  | 0.32 | 0.63 |
| Verrucomicrobiaceae.id.4036                | family | Homa-IR | 0.02  | 0.03 | -0.02 | 0.03 | 0.00  | -0.04 | 0.04  | 0.91 | 0.03 |
| unknownfamily.id.1000001214                | family | Homa-IR | -0.07 | 0.03 | 0.02  | 0.03 | -0.03 | -0.07 | 0.01  | 0.17 | 0.76 |
| unknownfamily.id.1000005471                | family | Homa-IR | -0.06 | 0.03 | -0.06 | 0.03 | -0.06 | -0.10 | -0.02 | 0.00 | 0.00 |
| unknownfamily.id.987                       | family | Homa-IR | 0.01  | 0.03 | -0.05 | 0.03 | -0.02 | -0.06 | 0.02  | 0.35 | 0.61 |
| Bacteroidespectinophilusgroup.id.14371     | genus  | Homa-IR | -0.02 | 0.03 | -0.01 | 0.03 | -0.02 | -0.06 | 0.02  | 0.41 | 0.00 |
| Eubacteriumcoprostanoligenesgroup.id.11375 | genus  | Homa-IR | 0.00  | 0.03 | -0.02 | 0.03 | -0.01 | -0.05 | 0.03  | 0.65 | 0.00 |
| Eubacteriumeligensgroup.id.14372           | genus  | Homa-IR | -0.09 | 0.03 | -0.05 | 0.03 | -0.07 | -0.11 | -0.03 | 0.00 | 0.00 |
| Eubacteriumhalliigroup.id.11338            | genus  | Homa-IR | 0.06  | 0.03 | 0.02  | 0.03 | 0.04  | 0.00  | 0.08  | 0.04 | 0.18 |
| Eubacteriumrectalegroup.id.14374           | genus  | Homa-IR | 0.03  | 0.03 | 0.03  | 0.03 | 0.03  | -0.01 | 0.07  | 0.19 | 0.00 |
| Eubacteriumruminantiumgroup.id.11340       | genus  | Homa-IR | -0.03 | 0.03 | -0.03 | 0.03 | -0.03 | -0.07 | 0.01  | 0.11 | 0.00 |
| Eubacteriumventriosumgroup.id.11341        | genus  | Homa-IR | 0.04  | 0.03 | 0.03  | 0.03 | 0.04  | 0.00  | 0.08  | 0.07 | 0.00 |
| Eubacteriumxylanophilumgroup.id.14375      | genus  | Homa-IR | -0.05 | 0.03 | -0.03 | 0.03 | -0.04 | -0.08 | 0.00  | 0.05 | 0.00 |
| Ruminococcusgauvreauigroup.id.11342        | genus  | Homa-IR | 0.00  | 0.03 | 0.01  | 0.03 | 0.00  | -0.04 | 0.04  | 0.86 | 0.00 |
| Ruminococcusgnavusgroup.id.14376           | genus  | Homa-IR | 0.01  | 0.03 | 0.07  | 0.03 | 0.04  | 0.00  | 0.08  | 0.05 | 0.56 |
| Ruminococcustorquesgroup.id.14377          | genus  | Homa-IR | 0.06  | 0.03 | 0.00  | 0.03 | 0.04  | 0.00  | 0.07  | 0.08 | 0.59 |
| Acidaminococcus.id.2167                    | genus  | Homa-IR | 0.02  | 0.03 | 0.03  | 0.03 | 0.02  | -0.02 | 0.06  | 0.26 | 0.00 |
| Adlercreutzia.id.812                       | genus  | Homa-IR | 0.05  | 0.03 | 0.02  | 0.03 | 0.04  | 0.00  | 0.08  | 0.06 | 0.00 |
| Akkermansia.id.4037                        | genus  | Homa-IR | 0.02  | 0.03 | -0.02 | 0.03 | 0.00  | -0.04 | 0.04  | 0.92 | 0.03 |
| Alistipes.id.968                           | genus  | Homa-IR | -0.06 | 0.03 | -0.03 | 0.03 | -0.05 | -0.09 | -0.01 | 0.02 | 0.00 |
| Alloprevotella.id.961                      | genus  | Homa-IR | -0.04 | 0.03 | 0.04  | 0.03 | 0.00  | -0.04 | 0.04  | 0.87 | 0.73 |
| Anaerostipes.id.1991                       | genus  | Homa-IR | 0.02  | 0.03 | 0.00  | 0.03 | 0.01  | -0.03 | 0.05  | 0.59 | 0.00 |
| Anaerotruncus.id.2054                      | genus  | Homa-IR | -0.07 | 0.03 | -0.03 | 0.03 | -0.05 | -0.09 | -0.01 | 0.01 | 0.00 |
| Bacteroides.id.918                         | genus  | Homa-IR | -0.02 | 0.03 | -0.02 | 0.03 | -0.02 | -0.06 | 0.02  | 0.33 | 0.00 |
| Barnesiella.id.944                         | genus  | Homa-IR | -0.04 | 0.03 | -0.02 | 0.03 | -0.03 | -0.07 | 0.01  | 0.11 | 0.00 |
| Bifidobacterium.id.436                     | genus  | Homa-IR | 0.01  | 0.03 | 0.02  | 0.03 | 0.01  | -0.03 | 0.05  | 0.52 | 0.00 |
| Blautia.id.1992                            | genus  | Homa-IR | 0.04  | 0.03 | 0.03  | 0.03 | 0.04  | -0.01 | 0.08  | 0.09 | 0.00 |
| Butyricoccus.id.2055                       | genus  | Homa-IR | -0.02 | 0.03 | 0.00  | 0.03 | -0.01 | -0.05 | 0.03  | 0.52 | 0.00 |
| Butyricimonas.id.945                       | genus  | Homa-IR | -0.05 | 0.03 | -0.02 | 0.03 | -0.03 | -0.07 | 0.01  | 0.10 | 0.00 |
| Butyrivibrio.id.1993                       | genus  | Homa-IR | -0.04 | 0.03 | -0.01 | 0.03 | -0.03 | -0.07 | 0.01  | 0.20 | 0.00 |
| Catenibacterium.id.2153                    | genus  | Homa-IR | 0.01  | 0.03 | -0.01 | 0.03 | 0.00  | -0.04 | 0.04  | 0.94 | 0.00 |
| ChristensenellaceaeR7group.id.11283        | genus  | Homa-IR | -0.09 | 0.03 | -0.06 | 0.03 | -0.07 | -0.12 | -0.03 | 0.00 | 0.00 |

|                                  |       |         |       |      |       |      |       |       |      |      |      |
|----------------------------------|-------|---------|-------|------|-------|------|-------|-------|------|------|------|
| Clostridiumsensustricto1.id.1873 | genus | Homa-IR | -0.03 | 0.03 | 0.00  | 0.03 | -0.02 | -0.06 | 0.02 | 0.35 | 0.00 |
| Collinsella.id.815               | genus | Homa-IR | 0.01  | 0.03 | -0.01 | 0.03 | 0.00  | -0.04 | 0.04 | 0.95 | 0.00 |



|                                      |       |         |       |      |       |      |       |       |       |      |      |
|--------------------------------------|-------|---------|-------|------|-------|------|-------|-------|-------|------|------|
| Coprococcus1.id.11301                | genus | Homa-IR | -0.05 | 0.03 | -0.03 | 0.03 | -0.04 | -0.08 | 0.00  | 0.05 | 0.00 |
| Coprococcus2.id.11302                | genus | Homa-IR | -0.04 | 0.03 | 0.00  | 0.03 | -0.02 | -0.06 | 0.02  | 0.25 | 0.09 |
| Coprococcus3.id.11303                | genus | Homa-IR | 0.01  | 0.03 | 0.01  | 0.03 | 0.01  | -0.03 | 0.05  | 0.65 | 0.00 |
| Desulfovibrio.id.3173                | genus | Homa-IR | -0.01 | 0.03 | -0.01 | 0.03 | -0.01 | -0.05 | 0.03  | 0.58 | 0.00 |
| Dialister.id.2183                    | genus | Homa-IR | 0.04  | 0.03 | -0.02 | 0.03 | 0.01  | -0.03 | 0.05  | 0.59 | 0.44 |
| Dorea.id.1997                        | genus | Homa-IR | 0.03  | 0.03 | -0.02 | 0.03 | 0.01  | -0.03 | 0.05  | 0.73 | 0.35 |
| Eggerthella.id.819                   | genus | Homa-IR | 0.00  | 0.03 | 0.07  | 0.03 | 0.03  | -0.01 | 0.08  | 0.09 | 0.68 |
| Eisenbergiella.id.11304              | genus | Homa-IR | -0.03 | 0.03 | 0.03  | 0.03 | 0.00  | -0.04 | 0.04  | 0.95 | 0.44 |
| Enterococcus.id.1831                 | genus | Homa-IR | 0.03  | 0.03 | -0.02 | 0.03 | 0.01  | -0.03 | 0.05  | 0.62 | 0.45 |
| Enterorhabdus.id.820                 | genus | Homa-IR | -0.04 | 0.03 | -0.02 | 0.03 | -0.03 | -0.07 | 0.01  | 0.15 | 0.00 |
| Erysipelatoclostridium.id.11381      | genus | Homa-IR | -0.02 | 0.03 | 0.06  | 0.03 | 0.02  | -0.02 | 0.06  | 0.38 | 0.70 |
| ErysipelotrichaceaeUCG003.id.11384   | genus | Homa-IR | 0.04  | 0.03 | 0.01  | 0.03 | 0.03  | -0.01 | 0.07  | 0.21 | 0.00 |
| Faecalibacterium.id.2057             | genus | Homa-IR | -0.01 | 0.03 | 0.03  | 0.03 | 0.01  | -0.03 | 0.05  | 0.74 | 0.00 |
| FamilyXIIAD3011group.id.11293        | genus | Homa-IR | -0.05 | 0.03 | -0.06 | 0.03 | -0.06 | -0.10 | -0.02 | 0.01 | 0.00 |
| FamilyXIIICUG001.id.11294            | genus | Homa-IR | 0.01  | 0.03 | -0.02 | 0.03 | -0.01 | -0.05 | 0.03  | 0.78 | 0.00 |
| Fusicatenibacter.id.11305            | genus | Homa-IR | 0.04  | 0.03 | 0.02  | 0.03 | 0.03  | -0.01 | 0.07  | 0.19 | 0.00 |
| Haemophilus.id.3698                  | genus | Homa-IR | -0.03 | 0.03 | -0.05 | 0.03 | -0.04 | -0.08 | 0.00  | 0.05 | 0.00 |
| Holdemanella.id.11393                | genus | Homa-IR | 0.01  | 0.03 | 0.06  | 0.03 | 0.03  | -0.01 | 0.07  | 0.09 | 0.38 |
| Intestinibacter.id.11345             | genus | Homa-IR | -0.02 | 0.03 | 0.02  | 0.03 | 0.00  | -0.04 | 0.04  | 0.88 | 0.05 |
| Intestinimonas.id.2062               | genus | Homa-IR | -0.06 | 0.03 | -0.02 | 0.03 | -0.04 | -0.08 | 0.00  | 0.04 | 0.31 |
| Lachnoclostridium.id.11308           | genus | Homa-IR | 0.00  | 0.03 | 0.03  | 0.03 | 0.01  | -0.03 | 0.05  | 0.55 | 0.00 |
| Lachnospira.id.2004                  | genus | Homa-IR | -0.02 | 0.03 | 0.03  | 0.03 | 0.01  | -0.03 | 0.05  | 0.78 | 0.13 |
| LachnospiraceaeFCS020group.id.11314  | genus | Homa-IR | -0.02 | 0.03 | -0.07 | 0.03 | -0.05 | -0.09 | -0.01 | 0.03 | 0.45 |
| LachnospiraceaeND3007group.id.11317  | genus | Homa-IR | -0.03 | 0.03 | 0.00  | 0.03 | -0.02 | -0.06 | 0.02  | 0.42 | 0.00 |
| LachnospiraceaeNK4A136group.id.11319 | genus | Homa-IR | -0.05 | 0.03 | -0.03 | 0.03 | -0.04 | -0.08 | 0.00  | 0.04 | 0.00 |
| LachnospiraceaeUCG001.id.11321       | genus | Homa-IR | -0.01 | 0.03 | -0.01 | 0.03 | -0.01 | -0.05 | 0.03  | 0.64 | 0.00 |
| LachnospiraceaeUCG004.id.11324       | genus | Homa-IR | -0.02 | 0.03 | -0.03 | 0.03 | -0.03 | -0.07 | 0.01  | 0.20 | 0.00 |
| LachnospiraceaeUCG010.id.11330       | genus | Homa-IR | -0.01 | 0.03 | -0.05 | 0.03 | -0.03 | -0.07 | 0.01  | 0.14 | 0.00 |
| Lactobacillus.id.1837                | genus | Homa-IR | -0.02 | 0.03 | -0.03 | 0.03 | -0.02 | -0.06 | 0.02  | 0.23 | 0.00 |
| Marvinbryantia.id.2005               | genus | Homa-IR | -0.07 | 0.03 | -0.08 | 0.03 | -0.07 | -0.11 | -0.03 | 0.00 | 0.00 |
| Megamonas.id.2184                    | genus | Homa-IR | 0.03  | 0.03 | 0.00  | 0.03 | 0.01  | -0.03 | 0.05  | 0.54 | 0.00 |
| Megasphaera.id.2185                  | genus | Homa-IR | 0.01  | 0.03 | 0.01  | 0.03 | 0.01  | -0.03 | 0.05  | 0.56 | 0.00 |

|                     |       |         |       |      |       |      |       |       |       |      |      |
|---------------------|-------|---------|-------|------|-------|------|-------|-------|-------|------|------|
| Mitsuokella.id.2186 | genus | Homa-IR | 0.07  | 0.03 | 0.01  | 0.03 | 0.04  | 0.00  | 0.08  | 0.03 | 0.46 |
| Odoribacter.id.952  | genus | Homa-IR | -0.08 | 0.03 | -0.03 | 0.03 | -0.06 | -0.10 | -0.02 | 0.01 | 0.44 |

|                                      |       |         |       |      |       |      |       |       |       |      |      |
|--------------------------------------|-------|---------|-------|------|-------|------|-------|-------|-------|------|------|
| Olsenella.id.822                     | genus | Homa-IR | 0.00  | 0.03 | -0.05 | 0.03 | -0.02 | -0.06 | 0.02  | 0.31 | 0.27 |
| Oscillospira.id.2064                 | genus | Homa-IR | -0.04 | 0.03 | -0.01 | 0.03 | -0.02 | -0.06 | 0.02  | 0.28 | 0.00 |
| Parabacteroides.id.954               | genus | Homa-IR | -0.02 | 0.03 | -0.06 | 0.03 | -0.04 | -0.08 | 0.00  | 0.05 | 0.00 |
| Paraprevotella.id.962                | genus | Homa-IR | -0.02 | 0.03 | -0.01 | 0.03 | -0.02 | -0.06 | 0.02  | 0.33 | 0.00 |
| Parasutterella.id.2892               | genus | Homa-IR | 0.00  | 0.03 | 0.04  | 0.03 | 0.02  | -0.02 | 0.06  | 0.27 | 0.00 |
| Peptococcus.id.2037                  | genus | Homa-IR | -0.01 | 0.03 | 0.00  | 0.03 | -0.01 | -0.05 | 0.03  | 0.70 | 0.00 |
| Phascolarctobacterium.id.2168        | genus | Homa-IR | -0.05 | 0.03 | -0.02 | 0.03 | -0.04 | -0.08 | 0.00  | 0.05 | 0.00 |
| Prevotella2.id.11180                 | genus | Homa-IR | 0.01  | 0.03 | -0.01 | 0.03 | 0.00  | -0.04 | 0.04  | 0.85 | 0.00 |
| Prevotella7.id.11182                 | genus | Homa-IR | -0.01 | 0.03 | -0.01 | 0.03 | -0.01 | -0.05 | 0.03  | 0.54 | 0.00 |
| Prevotella9.id.11183                 | genus | Homa-IR | -0.01 | 0.03 | 0.01  | 0.03 | 0.00  | -0.04 | 0.04  | 1.00 | 0.00 |
| PrevotellaceaeNK3B31group.id.11185   | genus | Homa-IR | 0.01  | 0.03 | 0.06  | 0.03 | 0.03  | -0.01 | 0.07  | 0.12 | 0.38 |
| PrevotellaceaeUCG001.id.11186        | genus | Homa-IR | 0.00  | 0.03 | 0.02  | 0.03 | 0.01  | -0.03 | 0.05  | 0.75 | 0.00 |
| RikenellaceaeRC9gutgroup.id.11191    | genus | Homa-IR | 0.00  | 0.03 | -0.03 | 0.03 | -0.02 | -0.06 | 0.02  | 0.42 | 0.00 |
| Romboutsia.id.11347                  | genus | Homa-IR | -0.04 | 0.03 | 0.00  | 0.03 | -0.02 | -0.06 | 0.02  | 0.27 | 0.13 |
| Roseburia.id.2012                    | genus | Homa-IR | 0.02  | 0.03 | 0.03  | 0.03 | 0.02  | -0.02 | 0.06  | 0.27 | 0.00 |
| Ruminiclostridium5.id.11355          | genus | Homa-IR | -0.07 | 0.03 | -0.02 | 0.03 | -0.05 | -0.09 | -0.01 | 0.03 | 0.02 |
| Ruminiclostridium6.id.11356          | genus | Homa-IR | -0.08 | 0.03 | 0.01  | 0.03 | -0.04 | -0.08 | 0.00  | 0.08 | 0.79 |
| Ruminiclostridium9.id.11357          | genus | Homa-IR | -0.04 | 0.03 | -0.09 | 0.03 | -0.06 | -0.10 | -0.02 | 0.00 | 0.31 |
| RuminococcaceaeNK4A214group.id.11358 | genus | Homa-IR | -0.09 | 0.03 | -0.08 | 0.03 | -0.09 | -0.13 | -0.05 | 0.00 | 0.00 |
| RuminococcaceaeUCG002.id.11360       | genus | Homa-IR | -0.06 | 0.03 | -0.07 | 0.03 | -0.06 | -0.10 | -0.02 | 0.00 | 0.00 |
| RuminococcaceaeUCG003.id.11361       | genus | Homa-IR | -0.03 | 0.03 | -0.08 | 0.03 | -0.06 | -0.10 | -0.02 | 0.00 | 0.27 |
| RuminococcaceaeUCG004.id.11362       | genus | Homa-IR | 0.02  | 0.03 | 0.02  | 0.03 | 0.02  | -0.02 | 0.06  | 0.36 | 0.00 |
| RuminococcaceaeUCG005.id.11363       | genus | Homa-IR | -0.11 | 0.03 | -0.07 | 0.03 | -0.09 | -0.13 | -0.05 | 0.00 | 0.08 |
| RuminococcaceaeUCG008.id.11365       | genus | Homa-IR | -0.10 | 0.03 | -0.04 | 0.03 | -0.07 | -0.11 | -0.03 | 0.00 | 0.56 |
| RuminococcaceaeUCG010.id.11367       | genus | Homa-IR | -0.10 | 0.03 | -0.06 | 0.03 | -0.08 | -0.12 | -0.04 | 0.00 | 0.09 |
| RuminococcaceaeUCG013.id.11370       | genus | Homa-IR | -0.01 | 0.03 | 0.04  | 0.03 | 0.01  | -0.03 | 0.05  | 0.58 | 0.25 |
| RuminococcaceaeUCG014.id.11371       | genus | Homa-IR | -0.06 | 0.03 | -0.06 | 0.03 | -0.06 | -0.10 | -0.02 | 0.00 | 0.00 |
| Ruminococcus1.id.11373               | genus | Homa-IR | -0.05 | 0.03 | 0.03  | 0.03 | -0.01 | -0.05 | 0.03  | 0.59 | 0.72 |
| Ruminococcus2.id.11374               | genus | Homa-IR | -0.02 | 0.03 | 0.04  | 0.03 | 0.01  | -0.03 | 0.05  | 0.72 | 0.44 |
| Sellimonas.id.14369                  | genus | Homa-IR | 0.03  | 0.03 | 0.03  | 0.03 | 0.03  | -0.01 | 0.07  | 0.13 | 0.00 |
| Senegalimassilia.id.11160            | genus | Homa-IR | -0.01 | 0.03 | -0.05 | 0.03 | -0.03 | -0.07 | 0.01  | 0.14 | 0.10 |
| Slackia.id.825                       | genus | Homa-IR | 0.03  | 0.03 | -0.05 | 0.03 | -0.01 | -0.05 | 0.03  | 0.71 | 0.69 |

|                         |       |         |      |      |      |      |      |       |      |      |      |
|-------------------------|-------|---------|------|------|------|------|------|-------|------|------|------|
| Streptococcus.id.1853   | genus | Homa-IR | 0.03 | 0.03 | 0.05 | 0.03 | 0.04 | 0.00  | 0.08 | 0.06 | 0.00 |
| Subdoligranulum.id.2070 | genus | Homa-IR | 0.00 | 0.03 | 0.00 | 0.03 | 0.00 | -0.04 | 0.04 | 0.86 | 0.00 |

|                            |       |         |       |      |       |      |       |       |       |      |      |
|----------------------------|-------|---------|-------|------|-------|------|-------|-------|-------|------|------|
| Succiniclasticum.id.2169   | genus | Homa-IR | 0.01  | 0.03 | 0.00  | 0.03 | 0.00  | -0.04 | 0.04  | 0.88 | 0.00 |
| Sutterella.id.2896         | genus | Homa-IR | 0.00  | 0.03 | -0.02 | 0.03 | -0.01 | -0.05 | 0.03  | 0.56 | 0.00 |
| Terrisporobacter.id.11348  | genus | Homa-IR | -0.05 | 0.03 | -0.02 | 0.03 | -0.04 | -0.08 | 0.00  | 0.06 | 0.00 |
| Turicibacter.id.2162       | genus | Homa-IR | -0.04 | 0.03 | -0.01 | 0.03 | -0.02 | -0.06 | 0.02  | 0.22 | 0.00 |
| Tyzzerella3.id.11335       | genus | Homa-IR | 0.04  | 0.03 | 0.00  | 0.03 | 0.02  | -0.02 | 0.06  | 0.26 | 0.00 |
| Veillonella.id.2198        | genus | Homa-IR | -0.04 | 0.03 | -0.03 | 0.03 | -0.04 | -0.08 | 0.01  | 0.09 | 0.00 |
| unknowngenus.id.1000000073 | genus | Homa-IR | -0.10 | 0.03 | -0.03 | 0.03 | -0.06 | -0.10 | -0.02 | 0.00 | 0.63 |
| unknowngenus.id.1000001215 | genus | Homa-IR | -0.07 | 0.03 | 0.02  | 0.03 | -0.03 | -0.07 | 0.01  | 0.17 | 0.76 |
| unknowngenus.id.1000005472 | genus | Homa-IR | -0.06 | 0.03 | -0.06 | 0.03 | -0.06 | -0.10 | -0.02 | 0.00 | 0.00 |
| unknowngenus.id.1000005479 | genus | Homa-IR | -0.03 | 0.03 | -0.05 | 0.03 | -0.04 | -0.08 | 0.00  | 0.06 | 0.00 |
| unknowngenus.id.1000013899 | genus | Homa-IR | 0.01  | 0.03 | -0.05 | 0.03 | -0.02 | -0.06 | 0.02  | 0.35 | 0.61 |
| unknowngenus.id.2071       | genus | Homa-IR | -0.08 | 0.03 | -0.03 | 0.03 | -0.06 | -0.10 | -0.02 | 0.01 | 0.31 |
| unknowngenus.id.2755       | genus | Homa-IR | -0.08 | 0.03 | 0.01  | 0.03 | -0.04 | -0.08 | 0.00  | 0.07 | 0.75 |
| unknowngenus.id.826        | genus | Homa-IR | -0.02 | 0.03 | 0.01  | 0.03 | -0.01 | -0.05 | 0.03  | 0.67 | 0.00 |
| unknowngenus.id.964        | genus | Homa-IR | 0.06  | 0.03 | 0.01  | 0.03 | 0.04  | 0.00  | 0.08  | 0.06 | 0.26 |

| Taxa in RS only                            | Clade  | Phenotype | Beta_RS | Se_RS |
|--------------------------------------------|--------|-----------|---------|-------|
| BacteroidalesS247group.id.11173            | family | Homa-IR   | -0.03   | 0.03  |
| Veillonellaceae.id.2172                    | family | Homa-IR   | 0.05    | 0.03  |
| Bacteroidespectinophilusgroup.id.14371     | genus  | Homa-IR   | -0.02   | 0.03  |
| Enterobacter.id.3502                       | genus  | Homa-IR   | 0.02    | 0.03  |
| EscherichiaShigella.id.3504                | genus  | Homa-IR   | 0.00    | 0.03  |
| Eubacteriumcoprostanoligenesgroup.id.11375 | genus  | Homa-IR   | 0.00    | 0.03  |
| Eubacteriumeligensgroup.id.14372           | genus  | Homa-IR   | -0.09   | 0.03  |
| Eubacteriumhalliigroup.id.11338            | genus  | Homa-IR   | 0.06    | 0.03  |
| Eubacteriumoxidoreducensgroup.id.11339     | genus  | Homa-IR   | -0.09   | 0.03  |
| Eubacteriumxylanophilumgroup.id.14375      | genus  | Homa-IR   | -0.05   | 0.03  |
| Hungatella.id.11306                        | genus  | Homa-IR   | -0.02   | 0.03  |
| Klebsiella.id.3507                         | genus  | Homa-IR   | 0.04    | 0.03  |
| LachnospiraceaeNC2004group.id.11316        | genus  | Homa-IR   | -0.07   | 0.03  |

|                                |       |         |       |      |
|--------------------------------|-------|---------|-------|------|
| LachnospiraceaeUCG008.id.11328 | genus | Homa-IR | -0.02 | 0.03 |
| unknowngenus.id.1868           | genus | Homa-IR | -0.05 | 0.03 |

| Taxa in LLD only                  | Clade  | Phenotype | Beta_LLD | Se_LLD |
|-----------------------------------|--------|-----------|----------|--------|
| Archaea.id.2                      | domain | Homa-IR   | -0.07    | 0.03   |
| Euryarchaeota.id.55               | phylum | Homa-IR   | -0.07    | 0.03   |
| Lentisphaerae.id.2238             | phylum | Homa-IR   | -0.02    | 0.03   |
| Actinomycetales.id.420            | order  | Homa-IR   | 0.05     | 0.03   |
| Mycoplasmatales.id.3946           | order  | Homa-IR   | -0.03    | 0.03   |
| NB1.n.id.3953                     | order  | Homa-IR   | 0.00     | 0.03   |
| Pseudomonadales.id.3709           | order  | Homa-IR   | -0.04    | 0.03   |
| Spirochaetales.id.3870            | order  | Homa-IR   | 0.00     | 0.03   |
| Synergistales.id.3900             | order  | Homa-IR   | -0.01    | 0.03   |
| Thermoplasmatales.id.220          | order  | Homa-IR   | -0.02    | 0.03   |
| unknownorder.id.1000000003        | order  | Homa-IR   | 0.02     | 0.03   |
| Verrucomicrobiales.id.4030        | order  | Homa-IR   | -0.02    | 0.03   |
| Victivallales.id.2254             | order  | Homa-IR   | -0.02    | 0.03   |
| Xanthomonadales.id.3786           | order  | Homa-IR   | -0.04    | 0.03   |
| Spirochaetes.id.3856              | class  | Homa-IR   | 0.00     | 0.03   |
| Synergistia.id.3899               | class  | Homa-IR   | -0.01    | 0.03   |
| Thermoplasmata.id.210             | class  | Homa-IR   | -0.02    | 0.03   |
| Actinomycetaceae.id.421           | family | Homa-IR   | 0.05     | 0.03   |
| BacteroidalesS24.7group.id.11173  | family | Homa-IR   | -0.05    | 0.03   |
| Christensenellaceae.id.1866       | family | Homa-IR   | -0.06    | 0.03   |
| FamilyXI.id.1936                  | family | Homa-IR   | 0.01     | 0.03   |
| unknownfamily.id.1000000004       | family | Homa-IR   | 0.02     | 0.03   |
| unknownfamily.id.1000006161       | family | Homa-IR   | 0.00     | 0.03   |
| unknownfamily.id.1855             | family | Homa-IR   | -0.03    | 0.03   |
| vadinBE97.id.14446                | family | Homa-IR   | -0.02    | 0.03   |
| Veillonellaceae.id.2172           | family | Homa-IR   | -0.02    | 0.03   |
| Xanthomonadaceae.id.3799          | family | Homa-IR   | -0.04    | 0.03   |
| Clostridiuminnocuumgroup.id.14397 | genus  | Homa-IR   | 0.04     | 0.03   |
| Eubacteriumbrachygroup.id.11296   | genus  | Homa-IR   | 0.05     | 0.03   |
| Abiotrophia.id.1803               | genus  | Homa-IR   | 0.00     | 0.03   |
| Actinomyces.id.423                | genus  | Homa-IR   | 0.05     | 0.03   |

|                       |       |         |       |      |
|-----------------------|-------|---------|-------|------|
| Actinotignum.id.11137 | genus | Homa-IR | -0.02 | 0.03 |
| Allisonella.id.2174   | genus | Homa-IR | 0.04  | 0.03 |



|                                     |       |         |       |      |
|-------------------------------------|-------|---------|-------|------|
| Arcanobacterium.id.424              | genus | Homa-IR | 0.00  | 0.03 |
| Asaccharobacter.id.813              | genus | Homa-IR | 0.02  | 0.03 |
| Bilophila.id.3170                   | genus | Homa-IR | 0.00  | 0.03 |
| CandidatusMethanogranum.id.11110    | genus | Homa-IR | -0.02 | 0.03 |
| Catenisphaera.id.14395              | genus | Homa-IR | -0.03 | 0.03 |
| Cellulosilyticum.id.1995            | genus | Homa-IR | -0.05 | 0.03 |
| Cetobacterium.id.2209               | genus | Homa-IR | 0.02  | 0.03 |
| Cloacibacillus.id.3908              | genus | Homa-IR | -0.01 | 0.03 |
| Coprobacillus.id.2154               | genus | Homa-IR | 0.00  | 0.03 |
| CoriobacteriaceaeUCG.002.id.11158   | genus | Homa-IR | -0.03 | 0.03 |
| CoriobacteriaceaeUCG.003.id.11159   | genus | Homa-IR | 0.05  | 0.03 |
| Denitrobacterium.id.818             | genus | Homa-IR | -0.02 | 0.03 |
| dgA.11gutgroup.id.978               | genus | Homa-IR | 0.02  | 0.03 |
| Dielma.id.11380                     | genus | Homa-IR | 0.00  | 0.03 |
| Epulopiscium.id.1998                | genus | Homa-IR | 0.03  | 0.03 |
| ErysipelotrichaceaeUCG006.id.11386  | genus | Homa-IR | 0.02  | 0.03 |
| ErysipelotrichaceaeUCG009.id.11389  | genus | Homa-IR | 0.04  | 0.03 |
| Escherichia.Shigella.id.3504        | genus | Homa-IR | 0.00  | 0.03 |
| Eubacterium.id.1932                 | genus | Homa-IR | 0.04  | 0.03 |
| Faecalicoccus.id.11391              | genus | Homa-IR | 0.00  | 0.03 |
| Faecalitalea.id.11392               | genus | Homa-IR | 0.05  | 0.03 |
| Flavonifractor.id.2059              | genus | Homa-IR | 0.00  | 0.03 |
| Gardnerella.id.437                  | genus | Homa-IR | 0.00  | 0.03 |
| Gordonibacter.id.821                | genus | Homa-IR | 0.03  | 0.03 |
| Hafnia.Obesumbacterium.id.14636     | genus | Homa-IR | -0.01 | 0.03 |
| Howardella.id.2000                  | genus | Homa-IR | -0.02 | 0.03 |
| LachnospiraceaeNK3A20group.id.11318 | genus | Homa-IR | 0.03  | 0.03 |
| Lactococcus.id.1851                 | genus | Homa-IR | 0.00  | 0.03 |
| Lautropia.id.2905                   | genus | Homa-IR | 0.01  | 0.03 |
| Leuconostoc.id.1841                 | genus | Homa-IR | -0.02 | 0.03 |
| Methanobrevibacter.id.123           | genus | Homa-IR | -0.07 | 0.03 |
| Methanosphaera.id.124               | genus | Homa-IR | -0.04 | 0.03 |

|                       |       |         |       |      |
|-----------------------|-------|---------|-------|------|
| Mogibacterium.id.1960 | genus | Homa-IR | -0.02 | 0.03 |
| Morganella.id.3512    | genus | Homa-IR | -0.03 | 0.03 |

|                                      |       |         |       |      |
|--------------------------------------|-------|---------|-------|------|
| Porphyromonas.id.956                 | genus | Homa-IR | 0.01  | 0.03 |
| Prevotella1.id.11179                 | genus | Homa-IR | 0.01  | 0.03 |
| PrevotellaceaeUCG003.id.11187        | genus | Homa-IR | 0.07  | 0.03 |
| PrevotellaceaeUCG004.id.11188        | genus | Homa-IR | -0.05 | 0.03 |
| Pseudomonas.id.3723                  | genus | Homa-IR | -0.04 | 0.03 |
| Rikenella.id.973                     | genus | Homa-IR | -0.01 | 0.03 |
| RuminococcaceaeNK4A214group.id.11358 | genus | Homa-IR | -0.08 | 0.03 |
| RuminococcaceaeUCG005.id.11363       | genus | Homa-IR | -0.07 | 0.03 |
| RuminococcaceaeUCG008.id.11365       | genus | Homa-IR | -0.04 | 0.03 |
| RuminococcaceaeUCG010.id.11367       | genus | Homa-IR | -0.06 | 0.03 |
| Sarcina.id.1896                      | genus | Homa-IR | 0.05  | 0.03 |
| Solobacterium.id.2161                | genus | Homa-IR | 0.02  | 0.03 |
| Staphylococcus.id.1780               | genus | Homa-IR | 0.04  | 0.03 |
| Stenotrophomonas.id.3818             | genus | Homa-IR | -0.04 | 0.03 |
| Succinivibrio.id.3331                | genus | Homa-IR | 0.00  | 0.03 |
| Synergistes.id.3913                  | genus | Homa-IR | -0.01 | 0.03 |
| Syntrophococcus.id.2016              | genus | Homa-IR | -0.01 | 0.03 |
| Treponema2.id.11577                  | genus | Homa-IR | 0.00  | 0.03 |
| Tyzzerella4.id.11336                 | genus | Homa-IR | 0.05  | 0.03 |
| unknowngenus.id.1000000005           | genus | Homa-IR | 0.02  | 0.03 |
| unknowngenus.id.1000027565           | genus | Homa-IR | -0.02 | 0.03 |
| unknowngenus.id.1000043796           | genus | Homa-IR | -0.03 | 0.03 |
| unknowngenus.id.1854                 | genus | Homa-IR | -0.04 | 0.03 |
| unknowngenus.id.2163                 | genus | Homa-IR | -0.05 | 0.03 |
| unknowngenus.id.3332                 | genus | Homa-IR | 0.02  | 0.03 |
| unknowngenus.id.441                  | genus | Homa-IR | -0.06 | 0.03 |
| Ureaplasma.id.3951                   | genus | Homa-IR | -0.03 | 0.03 |
| Varibaculum.id.427                   | genus | Homa-IR | 0.04  | 0.03 |
| Veillonella.id.2198                  | genus | Homa-IR | -0.03 | 0.03 |
| Weissella.id.1843                    | genus | Homa-IR | 0.01  | 0.03 |

**eTable 3.** Associations of Taxa and Type 2 Diabetes

Effect estimates in RS and LLD were calculated using logistic regression; pooled estimates were calculated based on a mixed-effect meta-analysis.

Model 1: Adjusted for age, sex, Time in mail (RS), and Batch (RS).

Abbreviation, RS, Rotterdam Study, LLD, Lifelines-Deep Study. P<0.0005 indicates statistical significance

| Overlapping taxa in RS and LLD | Clade  | Phenotype | Beta_RS | Se_RS | Beta_LLD | Se_LLD | OR_Meta | Lower95%CI_Meta | Upper95%CI_Meta | P_Meta | I <sup>2</sup> |
|--------------------------------|--------|-----------|---------|-------|----------|--------|---------|-----------------|-----------------|--------|----------------|
| Bacteria.id.3                  | domain | T2D       | 0.12    | 0.09  | 0.29     | 0.23   | 1.15    | 0.97            | 1.37            | 0.10   | 0.00           |
| Actinobacteria.id.400          | phylum | T2D       | -0.03   | 0.09  | -0.08    | 0.31   | 0.97    | 0.81            | 1.16            | 0.73   | 0.00           |
| Bacteroidetes.id.905           | phylum | T2D       | 0.36    | 0.09  | 0.40     | 0.16   | 1.45    | 1.24            | 1.70            | 0.00   | 0.00           |
| Cyanobacteria.id.1500          | phylum | T2D       | -0.02   | 0.09  | -0.53    | 0.36   | 0.95    | 0.80            | 1.13            | 0.57   | 0.47           |
| Firmicutes.id.1672             | phylum | T2D       | -0.06   | 0.09  | 0.04     | 0.26   | 0.95    | 0.80            | 1.13            | 0.58   | 0.00           |
| Proteobacteria.id.2375         | phylum | T2D       | -0.13   | 0.08  | -0.17    | 0.22   | 0.87    | 0.75            | 1.02            | 0.09   | 0.00           |
| Tenericutes.id.3919            | phylum | T2D       | 0.05    | 0.09  | -0.02    | 0.24   | 1.04    | 0.88            | 1.23            | 0.65   | 0.00           |
| Verrucomicrobia.id.3982        | phylum | T2D       | 0.07    | 0.09  | -0.03    | 0.29   | 1.06    | 0.90            | 1.26            | 0.49   | 0.00           |
| Actinobacteria.id.419          | class  | T2D       | 0.05    | 0.09  | -0.21    | 0.28   | 1.03    | 0.87            | 1.21            | 0.77   | 0.00           |
| Alphaproteobacteria.id.2379    | class  | T2D       | 0.11    | 0.09  | 0.08     | 0.14   | 1.10    | 0.95            | 1.28            | 0.20   | 0.00           |
| Bacilli.id.1673                | class  | T2D       | -0.01   | 0.09  | 0.08     | 0.22   | 1.01    | 0.85            | 1.18            | 0.95   | 0.00           |
| Bacteroidia.id.912             | class  | T2D       | -0.16   | 0.09  | -0.31    | 0.36   | 0.85    | 0.71            | 1.01            | 0.07   | 0.00           |
| Betaproteobacteria.id.2867     | class  | T2D       | -0.04   | 0.09  | 0.08     | 0.26   | 0.98    | 0.83            | 1.15            | 0.77   | 0.00           |
| Clostridia.id.1859             | class  | T2D       | 0.00    | 0.09  | 0.03     | 0.23   | 1.01    | 0.85            | 1.19            | 0.95   | 0.00           |
| Coriobacteriia.id.809          | class  | T2D       | -0.07   | 0.08  | -0.06    | 0.22   | 1.02    | 0.97            | 1.08            | 0.37   | 0.00           |
| Deltaproteobacteria.id.3087    | class  | T2D       | -0.21   | 0.09  | -1.12    | 0.67   | 0.79    | 0.67            | 0.95            | 0.01   | 0.45           |
| Erysipelotrichia.id.2147       | class  | T2D       | -0.06   | 0.09  | 0.04     | 0.26   | 0.95    | 0.80            | 1.13            | 0.58   | 0.00           |
| Gammaproteobacteria.id.3303    | class  | T2D       | 0.03    | 0.09  | -0.34    | 0.34   | 1.01    | 0.85            | 1.20            | 0.94   | 0.07           |
| Melainabacteria.id.1589        | class  | T2D       | 0.07    | 0.09  | 0.28     | 0.23   | 1.11    | 0.93            | 1.31            | 0.24   | 0.00           |
| Mollicutes.id.3920             | class  | T2D       | -0.30   | 0.08  | -0.38    | 0.34   | 0.74    | 0.63            | 0.87            | 0.00   | 0.00           |
| Negativicutes.id.2164          | class  | T2D       | -0.70   | 0.10  | -0.21    | 0.27   | 0.52    | 0.44            | 0.63            | 0.00   | 0.68           |
| Verrucomicrobiae.id.4029       | class  | T2D       | -0.12   | 0.10  | 0.00     | 0.20   | 0.91    | 0.76            | 1.08            | 0.27   | 0.00           |
| Aeromonadales.id.3316          | order  | T2D       | 0.05    | 0.09  | -0.02    | 0.24   | 1.04    | 0.88            | 1.23            | 0.65   | 0.00           |
| Bacteroidales.id.913           | order  | T2D       | 0.07    | 0.09  | -0.03    | 0.29   | 1.06    | 0.90            | 1.26            | 0.49   | 0.00           |
| Bifidobacteriales.id.432       | order  | T2D       | 0.11    | 0.09  | 0.11     | 0.13   | 1.12    | 0.96            | 1.29            | 0.14   | 0.00           |
| Burkholderiales.id.2874        | order  | T2D       | 0.12    | 0.08  | -0.25    | 0.94   | 1.13    | 0.97            | 1.32            | 0.12   | 0.00           |
| Clostridiales.id.1863          | order  | T2D       | 0.05    | 0.09  | -0.21    | 0.28   | 1.03    | 0.87            | 1.21            | 0.77   | 0.00           |
| Coriobacteriales.id.810        | order  | T2D       | -0.22   | 0.08  | -0.42    | 0.34   | 0.79    | 0.68            | 0.93            | 0.00   | 0.00           |

|                                      |        |     |       |      |         |          |      |      |      |      |      |
|--------------------------------------|--------|-----|-------|------|---------|----------|------|------|------|------|------|
| Desulfovibrionales.id.3156           | order  | T2D | 0.21  | 0.10 | -0.04   | 0.25     | 1.19 | 1.00 | 1.43 | 0.05 | 0.00 |
| Enterobacteriales.id.3468            | order  | T2D | 0.32  | 0.08 | 0.10    | 0.14     | 1.31 | 1.14 | 1.50 | 0.00 | 0.45 |
| Erysipelotrichales.id.2148           | order  | T2D | -0.02 | 0.09 | 0.16    | 0.15     | 1.02 | 0.88 | 1.19 | 0.77 | 0.06 |
| Gastranaerophilales.id.1591          | order  | T2D | -0.14 | 0.09 | -0.60   | 0.55     | 0.86 | 0.72 | 1.02 | 0.09 | 0.00 |
| Lactobacillales.id.1800              | order  | T2D | -0.65 | 0.09 | -0.38   | 0.30     | 0.53 | 0.45 | 0.63 | 0.00 | 0.00 |
| MollicutesRF9.id.11579               | order  | T2D | -0.11 | 0.09 | -0.47   | 0.39     | 0.88 | 0.74 | 1.05 | 0.14 | 0.00 |
| Pasteurellales.id.3688               | order  | T2D | 0.04  | 0.09 | -0.47   | 0.53     | 1.03 | 0.86 | 1.22 | 0.77 | 0.00 |
| Rhodospirillales.id.2667             | order  | T2D | -0.02 | 0.09 | -0.05   | 0.28     | 0.98 | 0.82 | 1.16 | 0.78 | 0.00 |
| Selenomonadales.id.2165              | order  | T2D | -0.14 | 0.09 | -0.02   | 0.24     | 0.89 | 0.75 | 1.04 | 0.15 | 0.00 |
| Verrucomicrobiales.id.4030           | order  | T2D | -0.21 | 0.08 | 0.18    | 0.26     | 0.84 | 0.72 | 0.97 | 0.02 | 0.51 |
| Acidaminococcaceae.id.2166           | family | T2D | 0.32  | 0.09 | 0.42    | 0.16     | 1.41 | 1.21 | 1.64 | 0.00 | 0.00 |
| Alcaligenaceae.id.2875               | family | T2D | 0.03  | 0.08 | -386.85 | 40595.94 | 1.03 | 0.88 | 1.21 | 0.71 | 0.00 |
| Bacteroidaceae.id.917                | family | T2D | 0.14  | 0.09 | 0.17    | 0.25     | 1.15 | 0.98 | 1.36 | 0.09 | 0.00 |
| Bifidobacteriaceae.id.433            | family | T2D | 0.00  | 0.09 | 0.03    | 0.23     | 1.01 | 0.85 | 1.19 | 0.95 | 0.00 |
| Christensenellaceae.id.1866          | family | T2D | -0.20 | 0.14 | -0.10   | 0.36     | 0.83 | 0.64 | 1.06 | 0.13 | 0.00 |
| Clostridiaceae1.id.1869              | family | T2D | -0.22 | 0.08 | -0.15   | 0.28     | 0.81 | 0.70 | 0.94 | 0.01 | 0.00 |
| ClostridialesvadinBB60group.id.11286 | family | T2D | -0.34 | 0.09 | 0.24    | 0.18     | 0.80 | 0.69 | 0.94 | 0.01 | 0.88 |
| Coriobacteriaceae.id.811             | family | T2D | 0.14  | 0.10 | -0.14   | 0.28     | 1.11 | 0.92 | 1.33 | 0.27 | 0.00 |
| Desulfovibrionaceae.id.3169          | family | T2D | 0.22  | 0.10 | 0.18    | 0.14     | 1.23 | 1.05 | 1.45 | 0.01 | 0.00 |
| Enterobacteriaceae.id.3469           | family | T2D | -0.24 | 0.10 | 0.16    | 0.21     | 0.85 | 0.71 | 1.01 | 0.07 | 0.65 |
| Enterococcaceae.id.1828              | family | T2D | -0.10 | 0.09 | 0.11    | 0.26     | 0.92 | 0.78 | 1.09 | 0.34 | 0.00 |
| Erysipelotrichaceae.id.2149          | family | T2D | -0.35 | 0.09 | -0.22   | 0.30     | 0.71 | 0.60 | 0.85 | 0.00 | 0.00 |
| FamilyXIII.id.1957                   | family | T2D | -0.19 | 0.09 | -1.11   | 0.55     | 0.81 | 0.68 | 0.96 | 0.01 | 0.63 |
| Lachnospiraceae.id.1987              | family | T2D | -0.03 | 0.09 | 0.01    | 0.29     | 0.97 | 0.82 | 1.15 | 0.75 | 0.00 |
| Lactobacillaceae.id.1836             | family | T2D | 0.30  | 0.10 | -0.38   | 0.40     | 1.30 | 1.08 | 1.57 | 0.01 | 0.63 |
| Pasteurellaceae.id.3689              | family | T2D | 0.14  | 0.08 | -2.49   | 3.85     | 1.15 | 0.99 | 1.34 | 0.07 | 0.00 |
| Peptococcaceae.id.2024               | family | T2D | 0.03  | 0.09 | -0.11   | 0.26     | 1.01 | 0.86 | 1.19 | 0.90 | 0.00 |
| Peptostreptococcaceae.id.2042        | family | T2D | 0.00  | 0.09 | 0.03    | 0.23     | 1.01 | 0.85 | 1.19 | 0.95 | 0.00 |
| Porphyromonadaceae.id.943            | family | T2D | -0.10 | 0.09 | -0.04   | 0.25     | 0.91 | 0.77 | 1.07 | 0.25 | 0.00 |
| Prevotellaceae.id.960                | family | T2D | 0.05  | 0.09 | -3.15   | 4.55     | 1.05 | 0.88 | 1.24 | 0.60 | 0.00 |
| Rhodospirillaceae.id.2717            | family | T2D | -0.17 | 0.09 | -0.01   | 0.24     | 0.86 | 0.73 | 1.01 | 0.07 | 0.00 |
| Rikenellaceae.id.967                 | family | T2D | -0.23 | 0.09 | -0.09   | 0.27     | 0.81 | 0.69 | 0.95 | 0.01 | 0.00 |
| Ruminococcaceae.id.2050              | family | T2D | 0.03  | 0.09 | -0.34   | 0.34     | 1.01 | 0.85 | 1.20 | 0.94 | 0.07 |

|                                            |        |     |       |      |       |      |      |      |      |      |      |
|--------------------------------------------|--------|-----|-------|------|-------|------|------|------|------|------|------|
| Streptococcaceae.id.1850                   | family | T2D | -0.14 | 0.09 | -0.47 | 0.41 | 0.86 | 0.72 | 1.03 | 0.09 | 0.00 |
| Succinivibrionaceae.id.3326                | family | T2D | 0.07  | 0.09 | 0.26  | 0.23 | 1.10 | 0.93 | 1.30 | 0.26 | 0.00 |
| Veillonellaceae.id.2172                    | family | T2D | 0.22  | 0.10 | -0.14 | 0.28 | 1.20 | 1.00 | 1.44 | 0.04 | 0.33 |
| Verrucomicrobiaceae.id.4036                | family | T2D | 0.12  | 0.09 | -0.81 | 0.45 | 1.09 | 0.91 | 1.30 | 0.37 | 0.76 |
| unknownfamily.id.1000001214                | family | T2D | 0.01  | 0.09 | -0.25 | 0.44 | 1.00 | 0.84 | 1.19 | 0.98 | 0.00 |
| unknownfamily.id.1000005471                | family | T2D | -0.20 | 0.11 | -0.37 | 0.56 | 0.82 | 0.67 | 1.00 | 0.05 | 0.00 |
| unknownfamily.id.987                       | family | T2D | 0.06  | 0.08 | -1.46 | 1.47 | 1.05 | 0.90 | 1.24 | 0.52 | 0.05 |
| Bacteroidespectinophilusgroup.id.14371     | genus  | T2D | -0.28 | 0.08 | -0.36 | 0.34 | 0.75 | 0.64 | 0.88 | 0.00 | 0.00 |
| Eubacteriumcoprostanoligenesgroup.id.11375 | genus  | T2D | -0.72 | 0.10 | -0.21 | 0.27 | 0.52 | 0.43 | 0.62 | 0.00 | 0.67 |
| Eubacteriumeligensgroup.id.14372           | genus  | T2D | 0.07  | 0.09 | 0.13  | 0.21 | 1.08 | 0.92 | 1.27 | 0.36 | 0.00 |
| Eubacteriumhalliigroup.id.11338            | genus  | T2D | 0.14  | 0.10 | 0.10  | 0.24 | 1.14 | 0.95 | 1.36 | 0.15 | 0.00 |
| Eubacteriumrectalegroup.id.14374           | genus  | T2D | -0.15 | 0.09 | -0.26 | 0.33 | 0.86 | 0.72 | 1.02 | 0.08 | 0.00 |
| Eubacteriumruminantiumgroup.id.11340       | genus  | T2D | 0.08  | 0.10 | -0.57 | 0.33 | 1.03 | 0.86 | 1.23 | 0.77 | 0.72 |
| Eubacteriumventriosumgroup.id.11341        | genus  | T2D | 0.02  | 0.09 | -0.13 | 0.33 | 1.01 | 0.85 | 1.20 | 0.91 | 0.00 |
| Eubacteriumxylanophilumgroup.id.14375      | genus  | T2D | 0.09  | 0.09 | 0.19  | 0.24 | 1.11 | 0.94 | 1.31 | 0.21 | 0.00 |
| Ruminococcusgavvreauiigroup.id.11342       | genus  | T2D | -0.07 | 0.09 | -0.40 | 0.30 | 0.91 | 0.77 | 1.07 | 0.27 | 0.13 |
| Ruminococcusgnavusgroup.id.14376           | genus  | T2D | 0.14  | 0.08 | -0.70 | 0.89 | 1.14 | 0.97 | 1.35 | 0.11 | 0.00 |
| Ruminococcusstorquesgroup.id.14377         | genus  | T2D | 0.16  | 0.08 | 0.15  | 0.14 | 1.17 | 1.02 | 1.35 | 0.03 | 0.00 |
| Acidaminococcus.id.2167                    | genus  | T2D | 0.12  | 0.08 | -3.65 | 8.88 | 1.12 | 0.96 | 1.31 | 0.14 | 0.00 |
| Adlercreutzia.id.812                       | genus  | T2D | -0.04 | 0.09 | -0.48 | 0.37 | 0.94 | 0.79 | 1.11 | 0.46 | 0.24 |
| Akkermansia.id.4037                        | genus  | T2D | -0.02 | 0.09 | 0.19  | 0.15 | 1.04 | 0.89 | 1.21 | 0.63 | 0.31 |
| Alistipes.id.968                           | genus  | T2D | -0.13 | 0.09 | -0.11 | 0.31 | 0.88 | 0.74 | 1.04 | 0.14 | 0.00 |
| Alloprevotella.id.961                      | genus  | T2D | -0.14 | 0.08 | -0.09 | 0.26 | 0.87 | 0.74 | 1.02 | 0.08 | 0.00 |
| Anaerostipes.id.1991                       | genus  | T2D | -0.15 | 0.09 | -0.95 | 0.46 | 0.84 | 0.71 | 1.00 | 0.04 | 0.66 |
| Anaerotruncus.id.2054                      | genus  | T2D | -0.21 | 0.09 | -0.14 | 0.27 | 0.81 | 0.69 | 0.96 | 0.01 | 0.00 |
| Bacteroides.id.918                         | genus  | T2D | -0.11 | 0.09 | 0.28  | 0.17 | 0.97 | 0.83 | 1.12 | 0.65 | 0.76 |
| Barnesiella.id.944                         | genus  | T2D | -0.02 | 0.09 | 0.16  | 0.15 | 1.03 | 0.89 | 1.20 | 0.71 | 0.00 |
| Bifidobacterium.id.436                     | genus  | T2D | 0.13  | 0.09 | -0.07 | 0.25 | 1.12 | 0.95 | 1.31 | 0.17 | 0.00 |
| Blautia.id.1992                            | genus  | T2D | -0.57 | 0.10 | -0.12 | 0.24 | 0.60 | 0.51 | 0.72 | 0.00 | 0.67 |
| Butyricicoccus.id.2055                     | genus  | T2D | -0.13 | 0.09 | 0.10  | 0.21 | 0.91 | 0.78 | 1.07 | 0.25 | 0.02 |
| Butyricimonas.id.945                       | genus  | T2D | 0.16  | 0.09 | 0.28  | 0.18 | 1.20 | 1.02 | 1.41 | 0.03 | 0.00 |
| Butyrivibrio.id.1993                       | genus  | T2D | -0.24 | 0.09 | -0.34 | 0.37 | 0.78 | 0.66 | 0.93 | 0.00 | 0.00 |
| Catenibacterium.id.2153                    | genus  | T2D | -0.07 | 0.09 | 0.27  | 0.16 | 1.01 | 0.86 | 1.17 | 0.93 | 0.69 |

|                                      |       |     |       |      |         |          |      |      |      |      |      |
|--------------------------------------|-------|-----|-------|------|---------|----------|------|------|------|------|------|
| ChristensenellaceaeR7group.id.11283  | genus | T2D | -0.27 | 0.08 | 0.17    | 0.22     | 0.81 | 0.69 | 0.95 | 0.01 | 0.71 |
| Clostridiumsensustricto1.id.1873     | genus | T2D | -0.25 | 0.09 | 0.03    | 0.24     | 0.81 | 0.69 | 0.95 | 0.01 | 0.17 |
| Collinsella.id.815                   | genus | T2D | 0.08  | 0.09 | 0.01    | 0.20     | 1.07 | 0.91 | 1.25 | 0.42 | 0.00 |
| Coproccoccus1.id.11301               | genus | T2D | -0.09 | 0.09 | -0.59   | 0.49     | 0.90 | 0.76 | 1.08 | 0.26 | 0.00 |
| Coproccoccus2.id.11302               | genus | T2D | 0.04  | 0.09 | -0.31   | 0.41     | 1.03 | 0.86 | 1.22 | 0.77 | 0.00 |
| Coproccoccus3.id.11303               | genus | T2D | 0.31  | 0.08 | 0.07    | 0.17     | 1.30 | 1.13 | 1.50 | 0.00 | 0.41 |
| Desulfovibrio.id.3173                | genus | T2D | -0.13 | 0.09 | -0.67   | 0.43     | 0.86 | 0.73 | 1.02 | 0.08 | 0.34 |
| Dialister.id.2183                    | genus | T2D | 0.01  | 0.09 | -704.30 | 70799.55 | 1.01 | 0.84 | 1.20 | 0.93 | 0.00 |
| Dorea.id.1997                        | genus | T2D | -0.05 | 0.09 | -0.34   | 0.69     | 0.95 | 0.79 | 1.14 | 0.56 | 0.00 |
| Eggerthella.id.819                   | genus | T2D | 0.04  | 0.08 | -0.20   | 0.54     | 1.04 | 0.88 | 1.22 | 0.65 | 0.00 |
| Eisenbergiella.id.11304              | genus | T2D | 0.05  | 0.09 | -0.08   | 0.28     | 1.04 | 0.87 | 1.23 | 0.67 | 0.00 |
| Enterococcus.id.1831                 | genus | T2D | 0.15  | 0.08 | -9.09   | 6.52     | 1.16 | 0.99 | 1.36 | 0.08 | 0.50 |
| Enterorhabdus.id.820                 | genus | T2D | -0.21 | 0.10 | -0.02   | 0.28     | 0.82 | 0.69 | 0.98 | 0.03 | 0.00 |
| Erysipelatoclostridium.id.11381      | genus | T2D | -0.09 | 0.09 | -0.37   | 0.40     | 0.90 | 0.76 | 1.08 | 0.25 | 0.00 |
| ErysipelotrichaceaeUCG003.id.11384   | genus | T2D | 0.04  | 0.09 | -0.15   | 0.34     | 1.03 | 0.87 | 1.22 | 0.72 | 0.00 |
| Faecalibacterium.id.2057             | genus | T2D | -0.07 | 0.09 | 0.18    | 0.19     | 0.98 | 0.83 | 1.16 | 0.83 | 0.33 |
| FamilyXIIID3011group.id.11293        | genus | T2D | -0.02 | 0.09 | -0.65   | 0.58     | 0.97 | 0.81 | 1.15 | 0.71 | 0.14 |
| FamilyXIIID3001.id.11294             | genus | T2D | -0.20 | 0.09 | -0.90   | 0.60     | 0.81 | 0.67 | 0.96 | 0.02 | 0.24 |
| Fusicatenibacter.id.11305            | genus | T2D | 0.06  | 0.08 | -366.30 | 30802.74 | 1.06 | 0.90 | 1.24 | 0.49 | 0.00 |
| Haemophilus.id.3698                  | genus | T2D | -0.02 | 0.09 | 0.01    | 0.18     | 0.98 | 0.84 | 1.15 | 0.82 | 0.00 |
| Holdemanella.id.11393                | genus | T2D | 0.03  | 0.09 | -0.33   | 0.51     | 1.02 | 0.86 | 1.21 | 0.79 | 0.00 |
| Intestinibacter.id.11345             | genus | T2D | -0.10 | 0.10 | -0.33   | 0.76     | 0.90 | 0.74 | 1.10 | 0.31 | 0.00 |
| Intestinimonas.id.2062               | genus | T2D | -0.05 | 0.10 | -0.97   | 2.57     | 0.95 | 0.79 | 1.15 | 0.62 | 0.00 |
| Lachnoclostridium.id.11308           | genus | T2D | -0.05 | 0.09 | 0.07    | 0.20     | 0.98 | 0.83 | 1.15 | 0.77 | 0.00 |
| Lachnospira.id.2004                  | genus | T2D | -0.66 | 0.09 | -1.19   | 0.61     | 0.51 | 0.43 | 0.61 | 0.00 | 0.00 |
| LachnospiraceaeFCS020group.id.11314  | genus | T2D | -0.01 | 0.09 | -0.38   | 0.34     | 0.96 | 0.81 | 1.15 | 0.68 | 0.10 |
| LachnospiraceaeND3007group.id.11317  | genus | T2D | -0.23 | 0.09 | 0.30    | 0.15     | 0.91 | 0.79 | 1.06 | 0.22 | 0.89 |
| LachnospiraceaeNK4A136group.id.11319 | genus | T2D | -0.30 | 0.09 | -0.04   | 0.25     | 0.77 | 0.65 | 0.91 | 0.00 | 0.00 |
| LachnospiraceaeUCG001.id.11321       | genus | T2D | -0.16 | 0.09 | -0.05   | 0.26     | 0.86 | 0.73 | 1.01 | 0.07 | 0.00 |
| LachnospiraceaeUCG004.id.11324       | genus | T2D | -0.30 | 0.09 | -0.44   | 0.39     | 0.73 | 0.62 | 0.87 | 0.00 | 0.00 |
| LachnospiraceaeUCG010.id.11330       | genus | T2D | -0.21 | 0.08 | -0.25   | 0.31     | 0.81 | 0.69 | 0.94 | 0.01 | 0.00 |
| Lactobacillus.id.1837                | genus | T2D | -0.17 | 0.09 | -0.18   | 0.30     | 0.84 | 0.71 | 1.00 | 0.06 | 0.00 |
| Marvinbryantia.id.2005               | genus | T2D | 0.06  | 0.09 | 0.02    | 0.25     | 1.06 | 0.90 | 1.25 | 0.49 | 0.00 |

|                                      |       |     |       |      |         |          |      |      |      |      |      |
|--------------------------------------|-------|-----|-------|------|---------|----------|------|------|------|------|------|
| Megamonas.id.2184                    | genus | T2D | -0.31 | 0.09 | -0.20   | 0.31     | 0.74 | 0.63 | 0.87 | 0.00 | 0.00 |
| Megasphaera.id.2185                  | genus | T2D | -0.18 | 0.10 | 0.00    | 0.22     | 0.86 | 0.72 | 1.03 | 0.10 | 0.00 |
| Mitsuokella.id.2186                  | genus | T2D | -0.33 | 0.10 | -0.11   | 0.27     | 0.74 | 0.62 | 0.88 | 0.00 | 0.00 |
| Odoribacter.id.952                   | genus | T2D | -0.03 | 0.09 | -0.31   | 0.31     | 0.95 | 0.80 | 1.12 | 0.53 | 0.00 |
| Olsenella.id.822                     | genus | T2D | -0.17 | 0.09 | 0.02    | 0.24     | 0.86 | 0.74 | 1.01 | 0.07 | 0.00 |
| Oscillospira.id.2064                 | genus | T2D | -0.21 | 0.09 | 0.09    | 0.22     | 0.85 | 0.72 | 0.99 | 0.04 | 0.39 |
| Parabacteroides.id.954               | genus | T2D | -0.09 | 0.09 | 0.15    | 0.22     | 0.95 | 0.81 | 1.11 | 0.51 | 0.03 |
| Paraprevotella.id.962                | genus | T2D | -0.05 | 0.09 | 0.10    | 0.17     | 0.99 | 0.84 | 1.16 | 0.86 | 0.00 |
| Parasutterella.id.2892               | genus | T2D | -0.08 | 0.09 | 0.13    | 0.19     | 0.96 | 0.82 | 1.13 | 0.62 | 0.08 |
| Peptococcus.id.2037                  | genus | T2D | -0.07 | 0.09 | -0.40   | 0.38     | 0.91 | 0.77 | 1.09 | 0.30 | 0.00 |
| Phascolarctobacterium.id.2168        | genus | T2D | 0.33  | 0.09 | 0.42    | 0.16     | 1.42 | 1.22 | 1.65 | 0.00 | 0.00 |
| Prevotella2.id.11180                 | genus | T2D | -0.01 | 0.09 | 0.31    | 0.21     | 1.05 | 0.89 | 1.23 | 0.59 | 0.50 |
| Prevotella7.id.11182                 | genus | T2D | -0.10 | 0.11 | -290.23 | 22660.60 | 0.90 | 0.73 | 1.11 | 0.33 | 0.00 |
| Prevotella9.id.11183                 | genus | T2D | -0.06 | 0.09 | -0.70   | 0.65     | 0.93 | 0.77 | 1.11 | 0.41 | 0.00 |
| PrevotellaceaeNK3B31group.id.11185   | genus | T2D | -0.33 | 0.10 | 0.24    | 0.11     | 0.94 | 0.81 | 1.09 | 0.40 | 0.93 |
| PrevotellaceaeUCG001.id.11186        | genus | T2D | -0.19 | 0.09 | 0.07    | 0.19     | 0.87 | 0.74 | 1.03 | 0.11 | 0.29 |
| RikenellaceaeRC9gutgroup.id.11191    | genus | T2D | 0.10  | 0.08 | -132.55 | 10703.92 | 1.11 | 0.94 | 1.31 | 0.23 | 0.00 |
| Romboutsia.id.11347                  | genus | T2D | 0.12  | 0.08 | 0.17    | 0.13     | 1.15 | 1.00 | 1.32 | 0.05 | 0.00 |
| Roseburia.id.2012                    | genus | T2D | 0.03  | 0.08 | -386.83 | 40583.02 | 1.03 | 0.88 | 1.21 | 0.71 | 0.00 |
| Ruminiclostridium5.id.11355          | genus | T2D | -0.02 | 0.09 | -0.53   | 0.36     | 0.95 | 0.80 | 1.13 | 0.57 | 0.47 |
| Ruminiclostridium6.id.11356          | genus | T2D | 0.07  | 0.09 | 0.28    | 0.23     | 1.11 | 0.93 | 1.31 | 0.24 | 0.00 |
| Ruminiclostridium9.id.11357          | genus | T2D | -0.06 | 0.09 | 0.04    | 0.26     | 0.95 | 0.80 | 1.13 | 0.58 | 0.00 |
| RuminococcaceaeNK4A214group.id.11358 | genus | T2D | -0.13 | 0.08 | -0.17   | 0.22     | 0.87 | 0.75 | 1.02 | 0.09 | 0.00 |
| RuminococcaceaeUCG002.id.11360       | genus | T2D | 0.05  | 0.09 | -0.02   | 0.24     | 1.04 | 0.88 | 1.23 | 0.65 | 0.00 |
| RuminococcaceaeUCG003.id.11361       | genus | T2D | 0.07  | 0.09 | -0.02   | 0.29     | 1.06 | 0.90 | 1.26 | 0.48 | 0.00 |
| RuminococcaceaeUCG004.id.11362       | genus | T2D | 0.11  | 0.09 | 0.11    | 0.13     | 1.12 | 0.96 | 1.29 | 0.14 | 0.00 |
| RuminococcaceaeUCG005.id.11363       | genus | T2D | 0.05  | 0.09 | -0.21   | 0.28     | 1.03 | 0.87 | 1.21 | 0.77 | 0.00 |
| RuminococcaceaeUCG008.id.11365       | genus | T2D | -0.01 | 0.09 | 0.08    | 0.22     | 1.01 | 0.85 | 1.19 | 0.94 | 0.00 |
| RuminococcaceaeUCG010.id.11367       | genus | T2D | 0.36  | 0.09 | 0.40    | 0.16     | 1.45 | 1.24 | 1.70 | 0.00 | 0.00 |
| RuminococcaceaeUCG013.id.11370       | genus | T2D | -0.13 | 0.09 | -0.32   | 0.37     | 0.87 | 0.73 | 1.04 | 0.13 | 0.00 |
| RuminococcaceaeUCG014.id.11371       | genus | T2D | -0.02 | 0.09 | 0.16    | 0.15     | 1.02 | 0.88 | 1.19 | 0.77 | 0.06 |
| Ruminococcus1.id.11373               | genus | T2D | -0.02 | 0.09 | -0.05   | 0.28     | 0.98 | 0.83 | 1.17 | 0.82 | 0.00 |
| Ruminococcus2.id.11374               | genus | T2D | -0.04 | 0.09 | 0.08    | 0.26     | 0.98 | 0.83 | 1.15 | 0.77 | 0.00 |



|                            |       |     |       |      |         |          |      |      |      |      |      |
|----------------------------|-------|-----|-------|------|---------|----------|------|------|------|------|------|
| Sellimonas.id.14369        | genus | T2D | 0.00  | 0.09 | 0.03    | 0.23     | 1.01 | 0.85 | 1.19 | 0.95 | 0.00 |
| Senegalimassilia.id.11160  | genus | T2D | 0.09  | 0.09 | 0.23    | 0.24     | 1.11 | 0.94 | 1.32 | 0.20 | 0.00 |
| Slackia.id.825             | genus | T2D | -0.02 | 0.09 | -0.51   | 0.35     | 0.95 | 0.80 | 1.13 | 0.56 | 0.45 |
| Streptococcus.id.1853      | genus | T2D | 0.01  | 0.09 | 0.03    | 0.26     | 1.01 | 0.86 | 1.19 | 0.89 | 0.00 |
| Subdoligranulum.id.2070    | genus | T2D | -0.01 | 0.09 | -0.03   | 0.23     | 0.98 | 0.83 | 1.16 | 0.84 | 0.00 |
| Succiniclasticum.id.2169   | genus | T2D | 0.07  | 0.09 | 0.08    | 0.14     | 1.07 | 0.92 | 1.24 | 0.36 | 0.00 |
| Sutterella.id.2896         | genus | T2D | -0.16 | 0.09 | -0.31   | 0.36     | 0.85 | 0.71 | 1.01 | 0.07 | 0.00 |
| Terrisporobacter.id.11348  | genus | T2D | 0.00  | 0.09 | 0.03    | 0.23     | 1.00 | 0.85 | 1.18 | 0.99 | 0.00 |
| Turicibacter.id.2162       | genus | T2D | -0.01 | 0.09 | 0.08    | 0.22     | 1.01 | 0.85 | 1.19 | 0.94 | 0.00 |
| Tyzzerella3.id.11335       | genus | T2D | -0.13 | 0.09 | -0.32   | 0.37     | 0.87 | 0.73 | 1.04 | 0.13 | 0.00 |
| Veillonella.id.2198        | genus | T2D | -0.07 | 0.09 | -0.81   | 1.00     | 0.92 | 0.77 | 1.11 | 0.39 | 0.00 |
| unknowngenus.id.1000000073 | genus | T2D | -0.12 | 0.10 | 0.00    | 0.20     | 0.91 | 0.76 | 1.08 | 0.27 | 0.00 |
| unknowngenus.id.1000001215 | genus | T2D | -0.01 | 0.09 | 0.08    | 0.22     | 1.01 | 0.85 | 1.19 | 0.94 | 0.00 |
| unknowngenus.id.1000005472 | genus | T2D | -0.13 | 0.09 | -0.32   | 0.37     | 0.87 | 0.73 | 1.04 | 0.13 | 0.00 |
| unknowngenus.id.1000005479 | genus | T2D | -0.06 | 0.09 | -0.75   | 0.73     | 0.93 | 0.78 | 1.11 | 0.42 | 0.00 |
| unknowngenus.id.1000013899 | genus | T2D | -0.07 | 0.09 | -0.81   | 1.00     | 0.92 | 0.77 | 1.11 | 0.39 | 0.00 |
| unknowngenus.id.2071       | genus | T2D | -0.24 | 0.10 | 0.12    | 0.19     | 0.85 | 0.72 | 1.01 | 0.06 | 0.66 |
| unknowngenus.id.2755       | genus | T2D | -0.02 | 0.09 | -0.07   | 0.30     | 0.97 | 0.82 | 1.16 | 0.75 | 0.00 |
| unknowngenus.id.826        | genus | T2D | -0.03 | 0.09 | -0.27   | 0.31     | 0.96 | 0.81 | 1.13 | 0.60 | 0.00 |
| unknowngenus.id.964        | genus | T2D | -0.03 | 0.09 | -233.51 | 24550.24 | 0.97 | 0.80 | 1.16 | 0.72 | 0.00 |

| Taxa in RS only                              | Clade  | Phenotype | Beta_RS | Se_RS |
|----------------------------------------------|--------|-----------|---------|-------|
| family.BacteroidalesS247group.id.11173       | family | T2D       | -0.06   | 0.09  |
| family.Veillonellaceae.id.2172               | family | T2D       | 0.14    | 0.09  |
| genus..Bacteroidespectinophilusgroup.id.1437 | family | T2D       | -0.20   | 0.14  |
| genus.Enterobacter.id.3502                   | genus  | T2D       | 0.00    | 0.10  |
| genus.EscherichiaShigella.id.3504            | genus  | T2D       | 0.03    | 0.09  |
| genus..Eubacteriumcoprostanoligenesgroup.id  | genus  | T2D       | -0.22   | 0.08  |
| genus..Eubacteriumeligenesgroup.id.14372     | genus  | T2D       | -0.34   | 0.09  |
| genus..Eubacteriumhalliigroup.id.11338       | genus  | T2D       | 0.14    | 0.10  |
| genus..Eubacteriumoxidoreducensgroup.id.113  | genus  | T2D       | -0.19   | 0.09  |

|                                             |              |                  |                 |               |
|---------------------------------------------|--------------|------------------|-----------------|---------------|
| genus..Eubacteriumxylanophilumgroup.id.1437 | genus        | T2D              | -0.35           | 0.09          |
| genus.Hungatella.id.11306                   | genus        | T2D              | 0.07            | 0.09          |
| genus.Klebsiella.id.3507                    | genus        | T2D              | 0.19            | 0.07          |
| genus.LachnospiraceaeNC2004group.id.11316   | genus        | T2D              | -0.23           | 0.09          |
| genus.LachnospiraceaeUCG008.id.11328        | genus        | T2D              | -0.08           | 0.09          |
| genus.unknowngenus.id.1868                  | genus        | T2D              | -0.25           | 0.09          |
| <b>Taxa in LLD only</b>                     | <b>Clade</b> | <b>Phenotype</b> | <b>Beta_LLD</b> | <b>Se_LLD</b> |
| domain.Archaea.id.2                         | Clade        | T2D              | 0.06            | 0.22          |
| phylum.Euryarchaeota.id.55                  | domain       | T2D              | 0.06            | 0.22          |
| phylum.Lentisphaerae.id.2238                | phylum       | T2D              | -0.04           | 0.25          |
| order.Actinomycetales.id.420                | phylum       | T2D              | 0.12            | 0.15          |
| order.Mycoplasmatales.id.3946               | order        | T2D              | -0.42           | 53.21         |
| order.NB1.n.id.3953                         | order        | T2D              | 0.06            | 0.18          |
| order.Pseudomonadales.id.3709               | order        | T2D              | -0.22           | 3.03          |
| order.Spirochaetales.id.3870                | order        | T2D              | -17.98          | 1882.17       |
| order.Synergistales.id.3900                 | order        | T2D              | -1.18           | 1.67          |
| order.Thermoplasmatales.id.220              | order        | T2D              | 0.15            | 0.09          |
| order.unknownorder.id.1000000003            | order        | T2D              | -0.33           | 0.70          |
| order.Verrucomicrobiales.id.4030            | order        | T2D              | 0.03            | 0.23          |
| order.Victivallales.id.2254                 | order        | T2D              | -0.04           | 0.25          |
| order.Xanthomonadales.id.3786               | order        | T2D              | -23.17          | 2531.04       |
| class.Spirochaetes.id.3856                  | order        | T2D              | -17.98          | 1882.17       |
| class.Synergistia.id.3899                   | class        | T2D              | -1.18           | 1.67          |
| class.Thermoplasmata.id.210                 | class        | T2D              | 0.15            | 0.09          |
| family.Actinomycetaceae.id.421              | class        | T2D              | 0.12            | 0.15          |
| family.BacteroidalesS24.7group.id.11173     | family       | T2D              | -0.75           | 0.73          |
| family.Christensenellaceae.id.1866          | family       | T2D              | -0.38           | 0.34          |
| family.FamilyXI.id.1936                     | family       | T2D              | -0.60           | 0.88          |
| family.unknownfamily.id.1000000004          | family       | T2D              | -0.33           | 0.70          |
| family.unknownfamily.id.1000006161          | family       | T2D              | 0.06            | 0.18          |
| family.unknownfamily.id.1855                | family       | T2D              | 0.16            | 0.08          |
| family.vadinBE97.id.14446                   | family       | T2D              | -0.88           | 1.74          |
| family.Veillonellaceae.id.2172              | family       | T2D              | 0.17            | 0.25          |

|                                          |        |     |         |          |
|------------------------------------------|--------|-----|---------|----------|
| family.Xanthomonadaceae.id.3799          | family | T2D | -23.17  | 2531.04  |
| genus..Clostridiuminnocuumgroup.id.14397 | family | T2D | 0.20    | 0.12     |
| genus..Eubacteriumbrachygroup.id.11296   | family | T2D | 0.32    | 0.13     |
| genus.Abiotrophia.id.1803                | genus  | T2D | -13.05  | 1002.76  |
| genus.Actinomyces.id.423                 | genus  | T2D | 0.07    | 0.16     |
| genus.Actinotignum.id.11137              | genus  | T2D | -14.86  | 1183.52  |
| genus.Allisonella.id.2174                | genus  | T2D | -0.19   | 0.35     |
| genus.Arcanobacterium.id.424             | genus  | T2D | -16.17  | 1632.63  |
| genus.Asaccharobacter.id.813             | genus  | T2D | 0.10    | 0.23     |
| genus.Bilophila.id.3170                  | genus  | T2D | 0.18    | 0.22     |
| genus.CandidatusMethanogranum.id.11110   | genus  | T2D | -4.17   | 431.66   |
| genus.Catenisphaera.id.14395             | genus  | T2D | -797.38 | 71752.59 |
| genus.Cellulosilyticum.id.1995           | genus  | T2D | -82.67  | 6750.72  |
| genus.Cetobacterium.id.2209              | genus  | T2D | -0.44   | 53.21    |
| genus.Cloacibacillus.id.3908             | genus  | T2D | -0.58   | 0.91     |
| genus.Coprobacillus.id.2154              | genus  | T2D | -0.78   | 1.59     |
| genus.CoriobacteriaceaeUCG.002.id.11158  | genus  | T2D | -0.40   | 0.58     |
| genus.CoriobacteriaceaeUCG.003.id.11159  | genus  | T2D | -287.68 | 30911.31 |
| genus.Denitrobacterium.id.818            | genus  | T2D | 0.25    | 0.09     |
| genus.dgA.11gutgroup.id.978              | genus  | T2D | -0.47   | 53.21    |
| genus.Dielma.id.11380                    | genus  | T2D | -0.30   | 1.72     |
| genus.Epulopiscium.id.1998               | genus  | T2D | -1.76   | 2.84     |
| genus.ErysipelotrichaceaeUCG006.id.11386 | genus  | T2D | -6.67   | 599.88   |
| genus.ErysipelotrichaceaeUCG009.id.11389 | genus  | T2D | -0.47   | 53.21    |
| genus.Escherichia.Shigella.id.3504       | genus  | T2D | 0.09    | 0.13     |
| genus.Eubacterium.id.1932                | genus  | T2D | 0.26    | 0.24     |
| genus.Faecalicoccus.id.11391             | genus  | T2D | -70.76  | 5178.86  |
| genus.Faecalitalea.id.11392              | genus  | T2D | 0.14    | 0.09     |
| genus.Flavonifractor.id.2059             | genus  | T2D | -0.16   | 0.49     |
| genus.Gardnerella.id.437                 | genus  | T2D | -15.95  | 1515.01  |
| genus.Gordonibacter.id.821               | genus  | T2D | -0.27   | 0.42     |
| genus.Hafnia.Obesumbacterium.id.14636    | genus  | T2D | 0.33    | 0.47     |
| genus.Howardella.id.2000                 | genus  | T2D | -0.49   | 0.39     |

|                                           |       |     |          |          |
|-------------------------------------------|-------|-----|----------|----------|
| genus.LachnospiraceaeNK3A20group.id.11318 | genus | T2D | -2.78    | 336.53   |
| genus.Lactococcus.id.1851                 | genus | T2D | -0.39    | 0.71     |
| genus.Lautropia.id.2905                   | genus | T2D | -46.78   | 5123.76  |
| genus.Leuconostoc.id.1841                 | genus | T2D | -0.77    | 0.73     |
| genus.Methanobrevibacter.id.123           | genus | T2D | 0.11     | 0.22     |
| genus.Methanosphaera.id.124               | genus | T2D | -0.35    | 0.46     |
| genus.Mogibacterium.id.1960               | genus | T2D | -1.50    | 1.55     |
| genus.Morganella.id.3512                  | genus | T2D | -0.37    | 53.21    |
| genus.Porphyromonas.id.956                | genus | T2D | -1.36    | 1.78     |
| genus.Prevotella1.id.11179                | genus | T2D | -1.02    | 95.11    |
| genus.PrevotellaceaeUCG003.id.11187       | genus | T2D | -59.54   | 6966.22  |
| genus.PrevotellaceaeUCG004.id.11188       | genus | T2D | -4.99    | 486.22   |
| genus.Pseudomonas.id.3723                 | genus | T2D | -1019.69 | 75983.98 |
| genus.Rikenella.id.973                    | genus | T2D | -15.54   | 1318.59  |
| genus.RuminococcaceaeNK4A214group.id.113  | genus | T2D | -0.44    | 0.39     |
| genus.RuminococcaceaeUCG005.id.11363      | genus | T2D | -0.20    | 0.31     |
| genus.RuminococcaceaeUCG008.id.11365      | genus | T2D | 0.00     | 0.22     |
| genus.RuminococcaceaeUCG010.id.11367      | genus | T2D | -0.11    | 0.27     |
| genus.Sarcina.id.1896                     | genus | T2D | -61.45   | 5551.30  |
| genus.Solobacterium.id.2161               | genus | T2D | -3.46    | 5.10     |
| genus.Staphylococcus.id.1780              | genus | T2D | -0.03    | 0.29     |
| genus.Stenotrophomonas.id.3818            | genus | T2D | -0.46    | 53.21    |
| genus.Succinivibrio.id.3331               | genus | T2D | -242.11  | 22249.13 |
| genus.Synergistes.id.3913                 | genus | T2D | -24.53   | 2041.02  |
| genus.Syntrophococcus.id.2016             | genus | T2D | -0.85    | 92.21    |
| genus.Treponema2.id.11577                 | genus | T2D | -15.37   | 1902.38  |
| genus.Tyzzerella4.id.11336                | genus | T2D | -4.55    | 8.93     |
| genus.unknowngenus.id.1000000005          | genus | T2D | -0.33    | 0.70     |
| genus.unknowngenus.id.1000027565          | genus | T2D | -0.88    | 1.74     |
| genus.unknowngenus.id.1000043796          | genus | T2D | 0.16     | 0.08     |
| genus.unknowngenus.id.1854                | genus | T2D | -41.58   | 2981.31  |
| genus.unknowngenus.id.2163                | genus | T2D | 0.15     | 0.10     |
| genus.unknowngenus.id.3332                | genus | T2D | -32.60   | 2665.47  |

|                           |       |     |       |       |
|---------------------------|-------|-----|-------|-------|
| genus.unknowngenus.id.441 | genus | T2D | -0.11 | 0.37  |
| genus.Ureaplasma.id.3951  | genus | T2D | -0.42 | 53.21 |
| genus.Varibaculum.id.427  | genus | T2D | 0.23  | 0.14  |
| genus.Veillonella.id.2198 | genus | T2D | 0.17  | 0.13  |
| genus.Weissella.id.1843   | genus | T2D | 0.06  | 0.14  |

**Supplementary Table 3 - Associations of taxa and type 2 diabetes**

Effect estimates in RS and LLD were calculated using logistic regression; pooled estimates were calculated based on a mixed-effect meta-analysis.

Model 2: Adjusted for age, sex, Time in mail (RS), Batch (RS), smoking, education level (RS), physical activity, alcohol intake, and total energy intake.

Abbreviation, RS, Rotterdam Study, LLD, Lifelines-Deep Study. P<0.0005 indicates statistical significance

| Overlapping taxa in RS and LLD | Clade  | Phenotype | Beta_RS | Se_RS | Beta_LLD | Se_LLD | OR_Meta | Lower95%CI_Meta | Upper95%CI_Meta | P_Meta | I <sup>2</sup> |
|--------------------------------|--------|-----------|---------|-------|----------|--------|---------|-----------------|-----------------|--------|----------------|
| Bacteria.id.3                  | domain | T2D       | 0.11    | 0.12  | 0.26     | 0.23   | 1.15    | 0.94            | 1.41            | 0.18   | 0.00           |
| Actinobacteria.id.400          | phylum | T2D       | -0.05   | 0.11  | -0.06    | 0.31   | 0.95    | 0.77            | 1.17            | 0.61   | 0.00           |
| Bacteroidetes.id.905           | phylum | T2D       | 0.36    | 0.11  | 0.36     | 0.17   | 1.43    | 1.20            | 1.72            | 0.00   | 0.00           |
| Cyanobacteria.id.1500          | phylum | T2D       | -0.08   | 0.11  | -0.57    | 0.35   | 0.88    | 0.72            | 1.09            | 0.25   | 0.44           |
| Firmicutes.id.1672             | phylum | T2D       | -0.02   | 0.12  | -0.07    | 0.26   | 0.98    | 0.79            | 1.20            | 0.82   | 0.00           |
| Proteobacteria.id.2375         | phylum | T2D       | -0.19   | 0.10  | -0.15    | 0.22   | 0.84    | 0.70            | 1.00            | 0.05   | 0.00           |
| Tenericutes.id.3919            | phylum | T2D       | -0.07   | 0.11  | 0.14     | 0.24   | 0.97    | 0.79            | 1.19            | 0.77   | 0.00           |
| Verrucomicrobia.id.3982        | phylum | T2D       | 0.04    | 0.11  | -0.04    | 0.32   | 1.03    | 0.84            | 1.27            | 0.76   | 0.00           |
| Actinobacteria.id.419          | class  | T2D       | 0.00    | 0.11  | -0.18    | 0.28   | 0.98    | 0.80            | 1.20            | 0.83   | 0.00           |
| Alphaproteobacteria.id.2379    | class  | T2D       | 0.08    | 0.11  | 0.11     | 0.15   | 1.10    | 0.92            | 1.31            | 0.31   | 0.00           |
| Bacilli.id.1673                | class  | T2D       | -0.11   | 0.12  | -0.01    | 0.25   | 0.91    | 0.74            | 1.13            | 0.40   | 0.00           |
| Bacteroidia.id.912             | class  | T2D       | -0.23   | 0.12  | -0.27    | 0.38   | 0.79    | 0.64            | 0.99            | 0.04   | 0.00           |
| Betaproteobacteria.id.2867     | class  | T2D       | -0.13   | 0.11  | 0.09     | 0.28   | 0.91    | 0.74            | 1.11            | 0.33   | 0.00           |
| Clostridia.id.1859             | class  | T2D       | 0.00    | 0.11  | 0.01     | 0.23   | 1.00    | 0.82            | 1.22            | 0.98   | 0.00           |
| Coriobacteriia.id.809          | class  | T2D       | -0.06   | 0.10  | -0.07    | 0.22   | 1.02    | 0.97            | 1.08            | 0.39   | 0.00           |
| Deltaproteobacteria.id.3087    | class  | T2D       | -0.13   | 0.11  | -1.17    | 0.69   | 0.85    | 0.69            | 1.06            | 0.15   | 0.54           |
| Erysipelotrichia.id.2147       | class  | T2D       | -0.01   | 0.12  | -0.09    | 0.27   | 0.97    | 0.79            | 1.20            | 0.81   | 0.00           |
| Gammaproteobacteria.id.3303    | class  | T2D       | -0.01   | 0.12  | -0.42    | 0.34   | 0.95    | 0.76            | 1.17            | 0.61   | 0.24           |
| Melainabacteria.id.1589        | class  | T2D       | 0.07    | 0.12  | 0.25     | 0.23   | 1.11    | 0.90            | 1.36            | 0.32   | 0.00           |
| Mollicutes.id.3920             | class  | T2D       | -0.36   | 0.10  | -0.33    | 0.34   | 0.70    | 0.58            | 0.85            | 0.00   | 0.00           |
| Negativicutes.id.2164          | class  | T2D       | -0.83   | 0.13  | -0.14    | 0.25   | 0.50    | 0.40            | 0.62            | 0.00   | 0.83           |
| Verrucomicrobiae.id.4029       | class  | T2D       | -0.19   | 0.13  | 0.03     | 0.23   | 0.87    | 0.70            | 1.08            | 0.22   | 0.00           |
| Aeromonadales.id.3316          | order  | T2D       | -0.07   | 0.11  | 0.14     | 0.24   | 0.97    | 0.79            | 1.19            | 0.77   | 0.00           |
| Bacteroidales.id.913           | order  | T2D       | 0.04    | 0.11  | -0.04    | 0.32   | 1.03    | 0.84            | 1.27            | 0.75   | 0.00           |
| Bifidobacteriales.id.432       | order  | T2D       | 0.09    | 0.11  | 0.12     | 0.14   | 1.11    | 0.93            | 1.32            | 0.24   | 0.00           |
| Burkholderiales.id.2874        | order  | T2D       | 0.17    | 0.09  | -0.48    | 1.13   | 1.18    | 0.99            | 1.41            | 0.06   | 0.00           |
| Clostridiales.id.1863          | order  | T2D       | 0.00    | 0.11  | -0.18    | 0.28   | 0.98    | 0.80            | 1.20            | 0.83   | 0.00           |

|                            |       |     |       |      |       |      |      |      |      |      |      |
|----------------------------|-------|-----|-------|------|-------|------|------|------|------|------|------|
| Coriobacteriales.id.810    | order | T2D | -0.25 | 0.10 | -0.40 | 0.34 | 0.77 | 0.64 | 0.93 | 0.01 | 0.00 |
| Desulfovibrionales.id.3156 | order | T2D | 0.16  | 0.12 | -0.07 | 0.24 | 1.12 | 0.91 | 1.39 | 0.27 | 0.00 |

|                                      |        |     |       |      |         |          |      |      |      |      |      |
|--------------------------------------|--------|-----|-------|------|---------|----------|------|------|------|------|------|
| Enterobacteriales.id.3468            | order  | T2D | 0.27  | 0.10 | 0.01    | 0.14     | 1.20 | 1.02 | 1.40 | 0.03 | 0.59 |
| Erysipelotrichales.id.2148           | order  | T2D | -0.09 | 0.12 | 0.18    | 0.16     | 1.01 | 0.84 | 1.22 | 0.89 | 0.45 |
| Gastranaerophilales.id.1591          | order  | T2D | -0.12 | 0.11 | -0.59   | 0.55     | 0.87 | 0.70 | 1.08 | 0.21 | 0.00 |
| Lactobacillales.id.1800              | order  | T2D | -0.70 | 0.11 | -0.33   | 0.29     | 0.52 | 0.43 | 0.64 | 0.00 | 0.27 |
| MollicutesRF9.id.11579               | order  | T2D | -0.16 | 0.11 | -0.56   | 0.39     | 0.83 | 0.67 | 1.02 | 0.08 | 0.00 |
| Pasteurellales.id.3688               | order  | T2D | 0.05  | 0.11 | -0.34   | 0.47     | 1.03 | 0.83 | 1.27 | 0.81 | 0.00 |
| Rhodospirillales.id.2667             | order  | T2D | -0.05 | 0.11 | -0.03   | 0.28     | 0.95 | 0.78 | 1.17 | 0.65 | 0.00 |
| Selenomonadales.id.2165              | order  | T2D | -0.16 | 0.11 | -0.02   | 0.25     | 0.87 | 0.71 | 1.06 | 0.17 | 0.00 |
| Verrucomicrobiales.id.4030           | order  | T2D | -0.23 | 0.10 | 0.22    | 0.27     | 0.84 | 0.70 | 1.01 | 0.06 | 0.58 |
| Acidaminococcaceae.id.2166           | family | T2D | 0.34  | 0.11 | 0.41    | 0.16     | 1.43 | 1.20 | 1.71 | 0.00 | 0.00 |
| Alcaligenaceae.id.2875               | family | T2D | 0.04  | 0.10 | -399.26 | 40432.95 | 1.04 | 0.84 | 1.27 | 0.74 | 0.00 |
| Bacteroidaceae.id.917                | family | T2D | -0.03 | 0.11 | 0.18    | 0.26     | 1.00 | 0.82 | 1.23 | 0.97 | 0.00 |
| Bifidobacteriaceae.id.433            | family | T2D | 0.00  | 0.11 | 0.01    | 0.23     | 1.00 | 0.82 | 1.22 | 0.98 | 0.00 |
| Christensenellaceae.id.1866          | family | T2D | -0.81 | 0.57 | -0.15   | 0.44     | 0.67 | 0.34 | 1.33 | 0.25 | 0.00 |
| Clostridiaceae1.id.1869              | family | T2D | -0.30 | 0.10 | -0.20   | 0.29     | 0.75 | 0.63 | 0.90 | 0.00 | 0.00 |
| ClostridialesvadinBB60group.id.11286 | family | T2D | -0.33 | 0.11 | 0.23    | 0.18     | 0.84 | 0.70 | 1.01 | 0.07 | 0.86 |
| Coriobacteriaceae.id.811             | family | T2D | 0.08  | 0.12 | -0.10   | 0.27     | 1.06 | 0.86 | 1.30 | 0.61 | 0.00 |
| Desulfovibrionaceae.id.3169          | family | T2D | 0.13  | 0.12 | 0.09    | 0.15     | 1.12 | 0.93 | 1.35 | 0.22 | 0.00 |
| Enterobacteriaceae.id.3469           | family | T2D | -0.18 | 0.12 | 0.17    | 0.20     | 0.92 | 0.75 | 1.12 | 0.39 | 0.56 |
| Enterococcaceae.id.1828              | family | T2D | -0.11 | 0.11 | 0.07    | 0.23     | 0.92 | 0.76 | 1.13 | 0.43 | 0.00 |
| Erysipelotrichaceae.id.2149          | family | T2D | -0.40 | 0.12 | -0.26   | 0.33     | 0.68 | 0.55 | 0.84 | 0.00 | 0.00 |
| FamilyXIII.id.1957                   | family | T2D | -0.16 | 0.11 | -1.01   | 0.53     | 0.82 | 0.67 | 1.02 | 0.07 | 0.59 |
| Lachnospiraceae.id.1987              | family | T2D | -0.05 | 0.11 | -0.06   | 0.38     | 0.95 | 0.77 | 1.17 | 0.62 | 0.00 |
| Lactobacillaceae.id.1836             | family | T2D | 0.26  | 0.12 | -0.28   | 0.37     | 1.23 | 0.98 | 1.54 | 0.07 | 0.48 |
| Pasteurellaceae.id.3689              | family | T2D | 0.13  | 0.09 | -3.16   | 4.59     | 1.14 | 0.95 | 1.37 | 0.17 | 0.00 |
| Peptococcaceae.id.2024               | family | T2D | 0.04  | 0.11 | -0.02   | 0.26     | 1.04 | 0.85 | 1.26 | 0.73 | 0.00 |
| Peptostreptococcaceae.id.2042        | family | T2D | 0.00  | 0.11 | 0.01    | 0.23     | 1.00 | 0.82 | 1.22 | 0.98 | 0.00 |
| Porphyromonadaceae.id.943            | family | T2D | -0.11 | 0.11 | -0.05   | 0.26     | 0.90 | 0.74 | 1.10 | 0.31 | 0.00 |
| Prevotellaceae.id.960                | family | T2D | -0.03 | 0.12 | -2.68   | 4.20     | 0.97 | 0.77 | 1.22 | 0.79 | 0.00 |
| Rhodospirillaceae.id.2717            | family | T2D | -0.05 | 0.11 | 0.02    | 0.23     | 0.96 | 0.79 | 1.17 | 0.70 | 0.00 |
| Rikenellaceae.id.967                 | family | T2D | -0.33 | 0.11 | -0.10   | 0.29     | 0.74 | 0.61 | 0.90 | 0.00 | 0.00 |
| Ruminococcaceae.id.2050              | family | T2D | -0.01 | 0.12 | -0.42   | 0.34     | 0.95 | 0.76 | 1.17 | 0.61 | 0.24 |



|                             |        |     |       |      |       |      |      |      |      |      |      |
|-----------------------------|--------|-----|-------|------|-------|------|------|------|------|------|------|
| Streptococcaceae.id.1850    | family | T2D | -0.15 | 0.11 | -0.59 | 0.44 | 0.84 | 0.67 | 1.04 | 0.11 | 0.00 |
| Succinivibrionaceae.id.3326 | family | T2D | 0.06  | 0.12 | 0.26  | 0.23 | 1.11 | 0.90 | 1.36 | 0.32 | 0.00 |

|                                           |        |     |       |      |       |      |      |      |      |      |      |
|-------------------------------------------|--------|-----|-------|------|-------|------|------|------|------|------|------|
| Veillonellaceae.id.2172                   | family | T2D | 0.28  | 0.12 | -0.13 | 0.29 | 1.24 | 1.00 | 1.55 | 0.05 | 0.40 |
| Verrucomicrobiaceae.id.4036               | family | T2D | 0.10  | 0.11 | -0.62 | 0.44 | 1.06 | 0.86 | 1.31 | 0.59 | 0.59 |
| unknownfamily.id.1000001214               | family | T2D | 0.06  | 0.11 | -0.24 | 0.40 | 1.04 | 0.84 | 1.28 | 0.73 | 0.00 |
| unknownfamily.id.1000005471               | family | T2D | -0.15 | 0.12 | -0.48 | 0.64 | 0.85 | 0.67 | 1.07 | 0.17 | 0.00 |
| unknownfamily.id.987                      | family | T2D | 0.08  | 0.10 | -1.58 | 1.56 | 1.07 | 0.88 | 1.31 | 0.50 | 0.12 |
| Bacteroidespectinophilusgroup.id.14371    | genus  | T2D | -0.34 | 0.10 | -0.32 | 0.35 | 0.71 | 0.58 | 0.86 | 0.00 | 0.00 |
| Eubacteriumcoprostanoligenesgroup.id.1137 | genus  | T2D | -0.85 | 0.13 | -0.14 | 0.26 | 0.49 | 0.39 | 0.61 | 0.00 | 0.83 |
| Eubacteriumeligensgroup.id.14372          | genus  | T2D | 0.08  | 0.11 | 0.26  | 0.22 | 1.12 | 0.92 | 1.36 | 0.25 | 0.00 |
| Eubacteriumhalliigroup.id.11338           | genus  | T2D | 0.06  | 0.12 | 0.12  | 0.24 | 1.08 | 0.88 | 1.32 | 0.47 | 0.00 |
| Eubacteriumrectalegroup.id.14374          | genus  | T2D | -0.19 | 0.11 | -0.22 | 0.35 | 0.83 | 0.67 | 1.02 | 0.08 | 0.00 |
| Eubacteriumruminantiumgroup.id.11340      | genus  | T2D | 0.10  | 0.12 | -0.51 | 0.34 | 1.03 | 0.83 | 1.29 | 0.77 | 0.66 |
| Eubacteriumventriosumgroup.id.11341       | genus  | T2D | -0.03 | 0.11 | -0.14 | 0.36 | 0.96 | 0.78 | 1.19 | 0.74 | 0.00 |
| Eubacteriumxylanophilumgroup.id.14375     | genus  | T2D | -0.05 | 0.11 | 0.22  | 0.25 | 0.99 | 0.81 | 1.22 | 0.95 | 0.00 |
| Ruminococcusgauvreauigroup.id.11342       | genus  | T2D | -0.07 | 0.11 | -0.25 | 0.29 | 0.91 | 0.75 | 1.11 | 0.35 | 0.00 |
| Ruminococcusgnavusgroup.id.14376          | genus  | T2D | 0.07  | 0.11 | -0.72 | 0.91 | 1.06 | 0.86 | 1.32 | 0.59 | 0.00 |
| Ruminococcustorquesgroup.id.14377         | genus  | T2D | 0.05  | 0.11 | 0.21  | 0.15 | 1.11 | 0.94 | 1.32 | 0.21 | 0.00 |
| Acidaminococcus.id.2167                   | genus  | T2D | 0.16  | 0.09 | -3.22 | 8.23 | 1.17 | 0.98 | 1.40 | 0.08 | 0.00 |
| Adlercreutzia.id.812                      | genus  | T2D | 0.03  | 0.11 | -0.33 | 0.37 | 1.00 | 0.81 | 1.22 | 0.97 | 0.00 |
| Akkermansia.id.4037                       | genus  | T2D | -0.10 | 0.11 | 0.24  | 0.14 | 1.04 | 0.87 | 1.23 | 0.70 | 0.71 |
| Alistipes.id.968                          | genus  | T2D | -0.14 | 0.11 | -0.02 | 0.31 | 0.88 | 0.72 | 1.08 | 0.23 | 0.00 |
| Alloprevotella.id.961                     | genus  | T2D | -0.11 | 0.10 | -0.05 | 0.27 | 0.90 | 0.74 | 1.09 | 0.27 | 0.00 |
| Anaerostipes.id.1991                      | genus  | T2D | -0.17 | 0.11 | -0.92 | 0.47 | 0.82 | 0.67 | 1.00 | 0.05 | 0.59 |
| Anaerotruncus.id.2054                     | genus  | T2D | -0.16 | 0.11 | -0.10 | 0.27 | 0.86 | 0.70 | 1.05 | 0.14 | 0.00 |
| Bacteroides.id.918                        | genus  | T2D | -0.13 | 0.10 | 0.25  | 0.18 | 0.96 | 0.81 | 1.15 | 0.67 | 0.70 |
| Barnesiella.id.944                        | genus  | T2D | -0.08 | 0.12 | 0.17  | 0.15 | 1.02 | 0.85 | 1.23 | 0.82 | 0.42 |
| Bifidobacterium.id.436                    | genus  | T2D | 0.12  | 0.11 | -0.06 | 0.26 | 1.10 | 0.90 | 1.33 | 0.36 | 0.00 |
| Blautia.id.1992                           | genus  | T2D | -0.69 | 0.13 | -0.11 | 0.22 | 0.58 | 0.47 | 0.72 | 0.00 | 0.81 |
| Butyricicoccus.id.2055                    | genus  | T2D | -0.13 | 0.11 | 0.18  | 0.22 | 0.93 | 0.77 | 1.13 | 0.47 | 0.35 |
| Butyricimonas.id.945                      | genus  | T2D | 0.04  | 0.11 | 0.14  | 0.19 | 1.07 | 0.88 | 1.29 | 0.50 | 0.00 |
| Butyrivibrio.id.1993                      | genus  | T2D | -0.28 | 0.11 | -0.32 | 0.37 | 0.75 | 0.61 | 0.93 | 0.01 | 0.00 |
| Catenibacterium.id.2153                   | genus  | T2D | -0.10 | 0.11 | 0.26  | 0.18 | 1.00 | 0.83 | 1.20 | 1.00 | 0.64 |
| ChristensenellaceaeR7group.id.11283       | genus  | T2D | -0.35 | 0.10 | 0.27  | 0.23 | 0.79 | 0.65 | 0.95 | 0.01 | 0.83 |

|                                  |       |     |       |      |      |      |      |      |      |      |      |
|----------------------------------|-------|-----|-------|------|------|------|------|------|------|------|------|
| Clostridiumsensustricto1.id.1873 | genus | T2D | -0.31 | 0.11 | 0.03 | 0.22 | 0.78 | 0.65 | 0.95 | 0.01 | 0.47 |
| Collinsella.id.815               | genus | T2D | 0.03  | 0.11 | 0.04 | 0.19 | 1.03 | 0.86 | 1.25 | 0.72 | 0.00 |

|                                      |       |     |       |      |         |          |      |      |      |      |      |
|--------------------------------------|-------|-----|-------|------|---------|----------|------|------|------|------|------|
| Coprococcus1.id.11301                | genus | T2D | -0.05 | 0.11 | -0.67   | 0.51     | 0.92 | 0.75 | 1.15 | 0.47 | 0.31 |
| Coprococcus2.id.11302                | genus | T2D | 0.10  | 0.11 | -0.29   | 0.41     | 1.07 | 0.87 | 1.32 | 0.51 | 0.00 |
| Coprococcus3.id.11303                | genus | T2D | 0.25  | 0.10 | -0.02   | 0.15     | 1.18 | 1.01 | 1.39 | 0.04 | 0.53 |
| Desulfovibrio.id.3173                | genus | T2D | -0.11 | 0.11 | -0.56   | 0.42     | 0.87 | 0.71 | 1.07 | 0.19 | 0.09 |
| Dialister.id.2183                    | genus | T2D | -0.03 | 0.11 | -716.05 | 68684.93 | 0.97 | 0.78 | 1.21 | 0.76 | 0.00 |
| Dorea.id.1997                        | genus | T2D | -0.11 | 0.12 | -0.60   | 0.89     | 0.89 | 0.70 | 1.13 | 0.34 | 0.00 |
| Eggerthella.id.819                   | genus | T2D | -0.01 | 0.11 | -0.35   | 0.58     | 0.98 | 0.80 | 1.20 | 0.84 | 0.00 |
| Eisenbergiella.id.11304              | genus | T2D | 0.06  | 0.11 | -0.11   | 0.31     | 1.04 | 0.84 | 1.28 | 0.71 | 0.00 |
| Enterococcus.id.1831                 | genus | T2D | 0.12  | 0.11 | -8.32   | 6.35     | 1.13 | 0.92 | 1.39 | 0.26 | 0.43 |
| Enterorhabdus.id.820                 | genus | T2D | -0.14 | 0.12 | 0.04    | 0.27     | 0.89 | 0.72 | 1.10 | 0.28 | 0.00 |
| Erysipelatoclostridium.id.11381      | genus | T2D | -0.13 | 0.11 | -0.44   | 0.41     | 0.86 | 0.69 | 1.06 | 0.16 | 0.00 |
| ErysipelotrichaceaeUCG003.id.11384   | genus | T2D | -0.06 | 0.11 | -0.13   | 0.35     | 0.94 | 0.76 | 1.15 | 0.55 | 0.00 |
| Faecalibacterium.id.2057             | genus | T2D | -0.04 | 0.12 | 0.13    | 0.21     | 1.00 | 0.82 | 1.22 | 1.00 | 0.00 |
| FamilyXIIIAD3011group.id.11293       | genus | T2D | 0.00  | 0.11 | -0.66   | 0.59     | 0.97 | 0.79 | 1.21 | 0.81 | 0.17 |
| FamilyXIIIUCG001.id.11294            | genus | T2D | -0.12 | 0.11 | -0.91   | 0.62     | 0.86 | 0.70 | 1.07 | 0.18 | 0.37 |
| Fusicatenibacter.id.11305            | genus | T2D | 0.07  | 0.11 | -371.34 | 31676.30 | 1.08 | 0.87 | 1.33 | 0.50 | 0.00 |
| Haemophilus.id.3698                  | genus | T2D | -0.03 | 0.11 | 0.00    | 0.17     | 0.98 | 0.81 | 1.17 | 0.80 | 0.00 |
| Holdemanella.id.11393                | genus | T2D | 0.05  | 0.11 | -0.24   | 0.47     | 1.03 | 0.84 | 1.27 | 0.76 | 0.00 |
| Intestinibacter.id.11345             | genus | T2D | -0.01 | 0.11 | -0.41   | 0.88     | 0.98 | 0.79 | 1.22 | 0.88 | 0.00 |
| Intestinimonas.id.2062               | genus | T2D | -0.01 | 0.11 | -1.33   | 3.97     | 0.99 | 0.79 | 1.24 | 0.90 | 0.00 |
| Lachnoclostridium.id.11308           | genus | T2D | -0.06 | 0.11 | 0.10    | 0.20     | 0.98 | 0.80 | 1.18 | 0.80 | 0.00 |
| Lachnospira.id.2004                  | genus | T2D | -0.67 | 0.11 | -1.08   | 0.61     | 0.51 | 0.41 | 0.63 | 0.00 | 0.00 |
| LachnospiraceaeFCS020group.id.11314  | genus | T2D | -0.03 | 0.11 | -0.35   | 0.33     | 0.94 | 0.77 | 1.15 | 0.55 | 0.00 |
| LachnospiraceaeND3007group.id.11317  | genus | T2D | -0.36 | 0.11 | 0.23    | 0.17     | 0.84 | 0.70 | 1.00 | 0.05 | 0.88 |
| LachnospiraceaeNK4A136group.id.11319 | genus | T2D | -0.36 | 0.11 | 0.01    | 0.27     | 0.74 | 0.60 | 0.91 | 0.00 | 0.36 |
| LachnospiraceaeUCG001.id.11321       | genus | T2D | -0.16 | 0.11 | -0.01   | 0.28     | 0.87 | 0.72 | 1.07 | 0.19 | 0.00 |
| LachnospiraceaeUCG004.id.11324       | genus | T2D | -0.31 | 0.11 | -0.38   | 0.41     | 0.73 | 0.60 | 0.90 | 0.00 | 0.00 |
| LachnospiraceaeUCG010.id.11330       | genus | T2D | -0.19 | 0.10 | -0.23   | 0.33     | 0.83 | 0.68 | 1.01 | 0.06 | 0.00 |
| Lactobacillus.id.1837                | genus | T2D | -0.12 | 0.11 | -0.12   | 0.32     | 0.89 | 0.72 | 1.10 | 0.27 | 0.00 |
| Marvinbryantia.id.2005               | genus | T2D | 0.02  | 0.11 | 0.01    | 0.25     | 1.02 | 0.84 | 1.24 | 0.84 | 0.00 |
| Megamonas.id.2184                    | genus | T2D | -0.30 | 0.11 | -0.20   | 0.31     | 0.75 | 0.62 | 0.91 | 0.00 | 0.00 |
| Megasphaera.id.2185                  | genus | T2D | -0.14 | 0.12 | 0.02    | 0.21     | 0.90 | 0.74 | 1.10 | 0.33 | 0.00 |

|                     |       |     |       |      |       |      |      |      |      |      |      |
|---------------------|-------|-----|-------|------|-------|------|------|------|------|------|------|
| Mitsuokella.id.2186 | genus | T2D | -0.33 | 0.12 | -0.03 | 0.28 | 0.75 | 0.61 | 0.93 | 0.01 | 0.00 |
| Odoribacter.id.952  | genus | T2D | -0.14 | 0.11 | -0.31 | 0.31 | 0.86 | 0.70 | 1.05 | 0.13 | 0.00 |

|                                      |       |     |       |      |         |          |      |      |      |      |      |
|--------------------------------------|-------|-----|-------|------|---------|----------|------|------|------|------|------|
| Olsenella.id.822                     | genus | T2D | -0.16 | 0.11 | 0.05    | 0.24     | 0.89 | 0.73 | 1.07 | 0.21 | 0.00 |
| Oscillospira.id.2064                 | genus | T2D | -0.18 | 0.11 | 0.07    | 0.24     | 0.87 | 0.72 | 1.06 | 0.17 | 0.00 |
| Parabacteroides.id.954               | genus | T2D | -0.11 | 0.11 | 0.15    | 0.24     | 0.93 | 0.77 | 1.13 | 0.46 | 0.00 |
| Paraprevotella.id.962                | genus | T2D | -0.16 | 0.13 | 0.05    | 0.17     | 0.92 | 0.76 | 1.13 | 0.43 | 0.02 |
| Parasutterella.id.2892               | genus | T2D | -0.13 | 0.12 | 0.22    | 0.19     | 0.96 | 0.79 | 1.17 | 0.70 | 0.60 |
| Peptococcus.id.2037                  | genus | T2D | -0.17 | 0.12 | -0.34   | 0.38     | 0.83 | 0.67 | 1.03 | 0.10 | 0.00 |
| Phascolarctobacterium.id.2168        | genus | T2D | 0.34  | 0.11 | 0.41    | 0.16     | 1.43 | 1.20 | 1.71 | 0.00 | 0.00 |
| Prevotella2.id.11180                 | genus | T2D | 0.04  | 0.11 | 0.34    | 0.21     | 1.11 | 0.91 | 1.35 | 0.29 | 0.33 |
| Prevotella7.id.11182                 | genus | T2D | -0.01 | 0.11 | -295.81 | 23456.74 | 0.99 | 0.79 | 1.22 | 0.90 | 0.00 |
| Prevotella9.id.11183                 | genus | T2D | -0.03 | 0.12 | -0.69   | 0.67     | 0.95 | 0.76 | 1.19 | 0.65 | 0.00 |
| PrevotellaceaeNK3B31group.id.11185   | genus | T2D | -0.42 | 0.13 | 0.15    | 0.12     | 0.89 | 0.74 | 1.06 | 0.19 | 0.90 |
| PrevotellaceaeUCG001.id.11186        | genus | T2D | -0.25 | 0.12 | 0.05    | 0.19     | 0.84 | 0.69 | 1.03 | 0.09 | 0.44 |
| RikenellaceaeRC9gutgroup.id.11191    | genus | T2D | 0.14  | 0.10 | -133.93 | 10258.92 | 1.15 | 0.94 | 1.40 | 0.17 | 0.00 |
| Romboutsia.id.11347                  | genus | T2D | 0.01  | 0.11 | 0.13    | 0.15     | 1.05 | 0.89 | 1.25 | 0.56 | 0.00 |
| Roseburia.id.2012                    | genus | T2D | 0.03  | 0.10 | -399.25 | 40424.84 | 1.04 | 0.84 | 1.27 | 0.74 | 0.00 |
| Ruminiclostridium5.id.11355          | genus | T2D | -0.08 | 0.11 | -0.57   | 0.35     | 0.88 | 0.72 | 1.09 | 0.25 | 0.44 |
| Ruminiclostridium6.id.11356          | genus | T2D | 0.07  | 0.12 | 0.25    | 0.23     | 1.11 | 0.90 | 1.36 | 0.32 | 0.00 |
| Ruminiclostridium9.id.11357          | genus | T2D | -0.02 | 0.12 | -0.07   | 0.27     | 0.97 | 0.79 | 1.19 | 0.78 | 0.00 |
| RuminococcaceaeNK4A214group.id.11358 | genus | T2D | -0.19 | 0.10 | -0.15   | 0.22     | 0.84 | 0.70 | 1.00 | 0.05 | 0.00 |
| RuminococcaceaeUCG002.id.11360       | genus | T2D | -0.07 | 0.11 | 0.14    | 0.24     | 0.97 | 0.79 | 1.19 | 0.77 | 0.00 |
| RuminococcaceaeUCG003.id.11361       | genus | T2D | 0.04  | 0.11 | -0.04   | 0.31     | 1.03 | 0.84 | 1.27 | 0.75 | 0.00 |
| RuminococcaceaeUCG004.id.11362       | genus | T2D | 0.09  | 0.11 | 0.12    | 0.14     | 1.11 | 0.93 | 1.32 | 0.24 | 0.00 |
| RuminococcaceaeUCG005.id.11363       | genus | T2D | 0.00  | 0.11 | -0.18   | 0.28     | 0.98 | 0.80 | 1.20 | 0.83 | 0.00 |
| RuminococcaceaeUCG008.id.11365       | genus | T2D | -0.11 | 0.12 | -0.01   | 0.25     | 0.92 | 0.74 | 1.13 | 0.41 | 0.00 |
| RuminococcaceaeUCG010.id.11367       | genus | T2D | 0.35  | 0.11 | 0.36    | 0.17     | 1.43 | 1.19 | 1.71 | 0.00 | 0.00 |
| RuminococcaceaeUCG013.id.11370       | genus | T2D | -0.19 | 0.12 | -0.29   | 0.39     | 0.82 | 0.66 | 1.02 | 0.08 | 0.00 |
| RuminococcaceaeUCG014.id.11371       | genus | T2D | -0.09 | 0.12 | 0.18    | 0.16     | 1.01 | 0.84 | 1.22 | 0.89 | 0.45 |
| Ruminococcus1.id.11373               | genus | T2D | -0.05 | 0.11 | -0.03   | 0.28     | 0.95 | 0.78 | 1.17 | 0.65 | 0.00 |
| Ruminococcus2.id.11374               | genus | T2D | -0.13 | 0.11 | 0.09    | 0.28     | 0.91 | 0.74 | 1.11 | 0.33 | 0.00 |
| Sellimonas.id.14369                  | genus | T2D | 0.00  | 0.11 | 0.01    | 0.23     | 1.00 | 0.82 | 1.22 | 0.98 | 0.00 |
| Senegalimassilia.id.11160            | genus | T2D | 0.04  | 0.11 | 0.29    | 0.24     | 1.09 | 0.89 | 1.32 | 0.41 | 0.00 |
| Slackia.id.825                       | genus | T2D | -0.08 | 0.11 | -0.57   | 0.35     | 0.88 | 0.72 | 1.09 | 0.25 | 0.43 |

|                         |       |     |       |      |       |      |      |      |      |      |      |
|-------------------------|-------|-----|-------|------|-------|------|------|------|------|------|------|
| Streptococcus.id.1853   | genus | T2D | -0.08 | 0.12 | -0.05 | 0.27 | 0.93 | 0.75 | 1.14 | 0.47 | 0.00 |
| Subdoligranulum.id.2070 | genus | T2D | -0.06 | 0.12 | -0.03 | 0.23 | 0.95 | 0.78 | 1.16 | 0.62 | 0.00 |

|                            |       |     |       |      |         |          |      |      |      |      |      |
|----------------------------|-------|-----|-------|------|---------|----------|------|------|------|------|------|
| Succiniclasticum.id.2169   | genus | T2D | 0.05  | 0.11 | 0.11    | 0.16     | 1.07 | 0.89 | 1.28 | 0.46 | 0.00 |
| Sutterella.id.2896         | genus | T2D | -0.23 | 0.12 | -0.27   | 0.38     | 0.79 | 0.64 | 0.99 | 0.04 | 0.00 |
| Terrisporobacter.id.11348  | genus | T2D | -0.01 | 0.11 | 0.01    | 0.23     | 1.00 | 0.82 | 1.22 | 0.98 | 0.00 |
| Turicibacter.id.2162       | genus | T2D | -0.11 | 0.12 | -0.01   | 0.25     | 0.92 | 0.74 | 1.13 | 0.41 | 0.00 |
| Tyzzerella3.id.11335       | genus | T2D | -0.19 | 0.12 | -0.29   | 0.39     | 0.82 | 0.66 | 1.02 | 0.08 | 0.00 |
| Veillonella.id.2198        | genus | T2D | -0.07 | 0.12 | -0.67   | 0.96     | 0.92 | 0.73 | 1.16 | 0.49 | 0.00 |
| unknowngenus.id.1000000073 | genus | T2D | -0.19 | 0.13 | 0.03    | 0.23     | 0.87 | 0.70 | 1.08 | 0.22 | 0.00 |
| unknowngenus.id.1000001215 | genus | T2D | -0.11 | 0.12 | -0.01   | 0.25     | 0.92 | 0.74 | 1.13 | 0.41 | 0.00 |
| unknowngenus.id.1000005472 | genus | T2D | -0.19 | 0.12 | -0.29   | 0.39     | 0.82 | 0.66 | 1.02 | 0.08 | 0.00 |
| unknowngenus.id.1000005479 | genus | T2D | -0.05 | 0.11 | -1.02   | 0.85     | 0.93 | 0.75 | 1.16 | 0.53 | 0.21 |
| unknowngenus.id.1000013899 | genus | T2D | -0.07 | 0.12 | -0.67   | 0.96     | 0.92 | 0.73 | 1.16 | 0.49 | 0.00 |
| unknowngenus.id.2071       | genus | T2D | -0.33 | 0.12 | 0.11    | 0.19     | 0.81 | 0.66 | 0.99 | 0.04 | 0.73 |
| unknowngenus.id.2755       | genus | T2D | -0.05 | 0.11 | -0.05   | 0.31     | 0.95 | 0.77 | 1.17 | 0.62 | 0.00 |
| unknowngenus.id.826        | genus | T2D | -0.06 | 0.11 | -0.16   | 0.30     | 0.93 | 0.76 | 1.14 | 0.50 | 0.00 |
| unknowngenus.id.964        | genus | T2D | -0.06 | 0.12 | -228.80 | 24024.42 | 0.95 | 0.74 | 1.20 | 0.65 | 0.00 |

| Taxa in RS only                             | Clade  | Phenotype | Beta_RS | Se_RS |
|---------------------------------------------|--------|-----------|---------|-------|
| family.BacteroidalesS247group.id.11173      | family | T2D       | -0.03   | 0.06  |
| family.Veillonellaceae.id.2172              | family | T2D       | -0.01   | 0.05  |
| genus..Bacteroidespectinophilusgroup.id.143 | family | T2D       | -0.99   | 0.69  |
| genus.Enterobacter.id.3502                  | genus  | T2D       | 0.22    | 0.15  |
| genus.EscherichiaShigella.id.3504           | genus  | T2D       | 0.01    | 0.04  |
| genus..Eubacteriumcoprostanoligenesgroup.i  | genus  | T2D       | -0.25   | 0.08  |
| genus..Eubacteriumeligensgroup.id.14372     | genus  | T2D       | -0.18   | 0.06  |
| genus..Eubacteriumhalliigroup.id.11338      | genus  | T2D       | 0.08    | 0.12  |
| genus..Eubacteriumoxidoreducensgroup.id.1   | genus  | T2D       | -0.18   | 0.11  |
| genus..Eubacteriumxylanophilumgroup.id.14   | genus  | T2D       | -0.27   | 0.08  |
| genus.Hungatella.id.11306                   | genus  | T2D       | -0.03   | 0.14  |
| genus.Klebsiella.id.3507                    | genus  | T2D       | 0.13    | 0.09  |
| genus.LachnospiraceaeNC2004group.id.1131    | genus  | T2D       | -0.34   | 0.11  |



|                                      |       |     |       |      |
|--------------------------------------|-------|-----|-------|------|
| genus.LachnospiraceaeUCG008.id.11328 | genus | T2D | -0.09 | 0.13 |
| genus.unknowngenus.id.1868           | genus | T2D | -0.27 | 0.12 |

| Taxa in LLD only                         | Clade  | Phenotype | Beta_LLD | Se_LLD  |
|------------------------------------------|--------|-----------|----------|---------|
| domain.Archaea.id.2                      | Clade  | T2D       | 0.07     | 0.22    |
| phylum.Euryarchaeota.id.55               | domain | T2D       | 0.07     | 0.22    |
| phylum.Lentisphaerae.id.2238             | phylum | T2D       | -0.04    | 0.22    |
| order.Actinomycetales.id.420             | phylum | T2D       | 0.12     | 0.15    |
| order.Mycoplasmatales.id.3946            | order  | T2D       | -0.40    | 53.21   |
| order.NB1.n.id.3953                      | order  | T2D       | 0.07     | 0.17    |
| order.Pseudomonadales.id.3709            | order  | T2D       | -0.16    | 2.54    |
| order.Spirochaetales.id.3870             | order  | T2D       | -17.48   | 2064.40 |
| order.Synergistales.id.3900              | order  | T2D       | -1.18    | 1.73    |
| order.Thermoplasmatales.id.220           | order  | T2D       | 0.20     | 0.10    |
| order.unknownorder.id.1000000003         | order  | T2D       | -0.27    | 0.66    |
| order.Verrucomicrobiales.id.4030         | order  | T2D       | 0.01     | 0.23    |
| order.Victivallales.id.2254              | order  | T2D       | -0.04    | 0.22    |
| order.Xanthomonadales.id.3786            | order  | T2D       | -21.14   | 2353.29 |
| class.Spirochaetes.id.3856               | order  | T2D       | -17.48   | 2064.40 |
| class.Synergistia.id.3899                | class  | T2D       | -1.18    | 1.73    |
| class.Thermoplasmata.id.210              | class  | T2D       | 0.20     | 0.10    |
| family.Actinomycetaceae.id.421           | class  | T2D       | 0.12     | 0.15    |
| family.BacteroidalesS24.7group.id.11173  | family | T2D       | -1.02    | 0.85    |
| family.Christensenellaceae.id.1866       | family | T2D       | -0.33    | 0.34    |
| family.FamilyXI.id.1936                  | family | T2D       | -0.54    | 0.82    |
| family.unknownfamily.id.1000000004       | family | T2D       | -0.27    | 0.66    |
| family.unknownfamily.id.1000006161       | family | T2D       | 0.07     | 0.17    |
| family.unknownfamily.id.1855             | family | T2D       | 0.14     | 0.08    |
| family.vadinBE97.id.14446                | family | T2D       | -0.53    | 1.53    |
| family.Veillonellaceae.id.2172           | family | T2D       | 0.18     | 0.26    |
| family.Xanthomonadaceae.id.3799          | family | T2D       | -21.14   | 2353.29 |
| genus..Clostridiuminnocuumgroup.id.14397 | family | T2D       | 0.14     | 0.12    |
| genus..Eubacteriumbrachygroup.id.11296   | family | T2D       | 0.36     | 0.13    |
| genus.Abiotrophia.id.1803                | genus  | T2D       | -12.81   | 1010.99 |
| genus.Actinomyces.id.423                 | genus  | T2D       | 0.08     | 0.15    |

|                             |       |     |        |         |
|-----------------------------|-------|-----|--------|---------|
| genus.Actinotignum.id.11137 | genus | T2D | -13.70 | 1171.94 |
| genus.Allisonella.id.2174   | genus | T2D | -0.23  | 0.36    |

|                                          |       |     |         |          |
|------------------------------------------|-------|-----|---------|----------|
| genus.Arcanobacterium.id.424             | genus | T2D | -17.67  | 1662.07  |
| genus.Asaccharobacter.id.813             | genus | T2D | 0.15    | 0.22     |
| genus.Bilophila.id.3170                  | genus | T2D | 0.14    | 0.24     |
| genus.CandidatusMethanogranum.id.11110   | genus | T2D | -4.30   | 423.74   |
| genus.Catenisphaera.id.14395             | genus | T2D | -796.47 | 70906.35 |
| genus.Cellulosilyticum.id.1995           | genus | T2D | -81.38  | 6776.06  |
| genus.Cetobacterium.id.2209              | genus | T2D | -0.40   | 53.21    |
| genus.Cloacibacillus.id.3908             | genus | T2D | -0.57   | 0.94     |
| genus.Coprobacillus.id.2154              | genus | T2D | -0.74   | 1.62     |
| genus.CoriobacteriaceaeUCG.002.id.11158  | genus | T2D | -0.36   | 0.59     |
| genus.CoriobacteriaceaeUCG.003.id.11159  | genus | T2D | -286.12 | 29432.75 |
| genus.Denitrobacterium.id.818            | genus | T2D | 0.19    | 0.13     |
| genus.dgA.11gutgroup.id.978              | genus | T2D | -0.46   | 53.21    |
| genus.Dielma.id.11380                    | genus | T2D | -0.21   | 1.79     |
| genus.Epulopiscium.id.1998               | genus | T2D | -2.27   | 3.23     |
| genus.ErysipelotrichaceaeUCG006.id.11386 | genus | T2D | -6.92   | 589.73   |
| genus.ErysipelotrichaceaeUCG009.id.11389 | genus | T2D | -0.49   | 53.21    |
| genus.Escherichia.Shigella.id.3504       | genus | T2D | 0.10    | 0.14     |
| genus.Eubacterium.id.1932                | genus | T2D | 0.26    | 0.19     |
| genus.Faecalicoccus.id.11391             | genus | T2D | -70.01  | 4858.27  |
| genus.Faecalitalea.id.11392              | genus | T2D | 0.16    | 0.10     |
| genus.Flavonifractor.id.2059             | genus | T2D | -0.13   | 0.47     |
| genus.Gardnerella.id.437                 | genus | T2D | -15.75  | 1536.96  |
| genus.Gordonibacter.id.821               | genus | T2D | -0.29   | 0.44     |
| genus.Hafnia.Obesumbacterium.id.14636    | genus | T2D | 0.31    | 0.48     |
| genus.Howardella.id.2000                 | genus | T2D | -0.48   | 0.41     |
| genus.LachnospiraceaeNK3A20group.id.1131 | genus | T2D | -2.54   | 322.11   |
| genus.Lactococcus.id.1851                | genus | T2D | -0.36   | 0.67     |
| genus.Lautropia.id.2905                  | genus | T2D | -38.98  | 5070.09  |
| genus.Leuconostoc.id.1841                | genus | T2D | -0.71   | 0.77     |
| genus.Methanobrevibacter.id.123          | genus | T2D | 0.10    | 0.21     |
| genus.Methanosphaera.id.124              | genus | T2D | -0.37   | 0.52     |

|                             |       |     |       |       |
|-----------------------------|-------|-----|-------|-------|
| genus.Mogibacterium.id.1960 | genus | T2D | -1.64 | 1.50  |
| genus.Morganella.id.3512    | genus | T2D | -0.33 | 53.21 |

|                                         |       |     |          |          |
|-----------------------------------------|-------|-----|----------|----------|
| genus.Porphyromonas.id.956              | genus | T2D | -1.66    | 1.96     |
| genus.Prevotella1.id.11179              | genus | T2D | -1.06    | 156.90   |
| genus.PrevotellaceaeUCG003.id.11187     | genus | T2D | -58.76   | 7137.04  |
| genus.PrevotellaceaeUCG004.id.11188     | genus | T2D | -6.17    | 507.98   |
| genus.Pseudomonas.id.3723               | genus | T2D | -1030.30 | 83303.57 |
| genus.Rikenella.id.973                  | genus | T2D | -15.35   | 1241.32  |
| genus.RuminococcaceaeNK4A214group.id.11 | genus | T2D | -0.38    | 0.41     |
| genus.RuminococcaceaeUCG005.id.11363    | genus | T2D | -0.20    | 0.31     |
| genus.RuminococcaceaeUCG008.id.11365    | genus | T2D | 0.02     | 0.21     |
| genus.RuminococcaceaeUCG010.id.11367    | genus | T2D | -0.03    | 0.28     |
| genus.Sarcina.id.1896                   | genus | T2D | -55.99   | 5591.92  |
| genus.Solobacterium.id.2161             | genus | T2D | -2.95    | 4.22     |
| genus.Staphylococcus.id.1780            | genus | T2D | 0.00     | 0.25     |
| genus.Stenotrophomonas.id.3818          | genus | T2D | -0.42    | 53.21    |
| genus.Succinivibrio.id.3331             | genus | T2D | -260.73  | 22878.78 |
| genus.Synergistes.id.3913               | genus | T2D | -25.46   | 2062.61  |
| genus.Syntrophococcus.id.2016           | genus | T2D | -0.87    | 89.99    |
| genus.Treponema2.id.11577               | genus | T2D | -15.52   | 1932.94  |
| genus.Tyzzerella4.id.11336              | genus | T2D | -2.95    | 7.15     |
| genus.unknowngenus.id.1000000005        | genus | T2D | -0.27    | 0.66     |
| genus.unknowngenus.id.1000027565        | genus | T2D | -0.53    | 1.53     |
| genus.unknowngenus.id.1000043796        | genus | T2D | 0.14     | 0.08     |
| genus.unknowngenus.id.1854              | genus | T2D | -41.03   | 3041.97  |
| genus.unknowngenus.id.2163              | genus | T2D | 0.15     | 0.11     |
| genus.unknowngenus.id.3332              | genus | T2D | -35.59   | 4287.44  |
| genus.unknowngenus.id.441               | genus | T2D | -0.18    | 0.38     |
| genus.Ureaplasma.id.3951                | genus | T2D | -0.40    | 53.21    |
| genus.Varibaculum.id.427                | genus | T2D | 0.28     | 0.14     |
| genus.Veillonella.id.2198               | genus | T2D | 0.13     | 0.15     |
| genus.Weissella.id.1843                 | genus | T2D | 0.09     | 0.14     |

**Supplementary Table 3 - Associations of taxa and type 2 diabetes**

Effect estimates in RS and LLD were calculated using logistic regression; pooled estimates were calculated based on a mixed-effect meta-analysis.

Model 3: Adjusted for age, sex, Time in mail (RS), Batch (RS), smoking, education level (RS), physical activity, alcohol intake, total energy intake, and BMI.

Abbreviation RS, Rotterdam Study, LLD, Lifelines-Deep Study. P<0.0005 indicates statistical significance

| Overlapping taxa in RS and LLD | Clade  | Phenotype | Beta_RS | Se_RS | Beta_LLD | Se_LLD   | OR_Meta | Lower95%CI_Meta | Upper95%CI_Meta | P_Meta | I <sup>2</sup> |
|--------------------------------|--------|-----------|---------|-------|----------|----------|---------|-----------------|-----------------|--------|----------------|
| Bacteria.id.3                  | domain | T2D       | -0.09   | 0.11  | 0.22     | 0.50     | 1.02    | 0.97            | 1.08            | 0.37   | 0.00           |
| Actinobacteria.id.400          | phylum | T2D       | 0.02    | 0.11  | 0.31     | 0.24     | 1.08    | 0.88            | 1.32            | 0.47   | 0.12           |
| Bacteroidetes.id.905           | phylum | T2D       | -0.05   | 0.11  | -0.49    | 0.34     | 0.91    | 0.74            | 1.13            | 0.39   | 0.36           |
| Cyanobacteria.id.1500          | phylum | T2D       | -0.02   | 0.12  | -0.02    | 0.27     | 0.98    | 0.79            | 1.22            | 0.87   | 0.00           |
| Firmicutes.id.1672             | phylum | T2D       | -0.08   | 0.12  | -0.11    | 0.24     | 0.92    | 0.75            | 1.13            | 0.43   | 0.00           |
| Proteobacteria.id.2375         | phylum | T2D       | 0.10    | 0.12  | 0.12     | 0.15     | 1.12    | 0.93            | 1.34            | 0.23   | 0.00           |
| Tenericutes.id.3919            | phylum | T2D       | -0.09   | 0.12  | -0.19    | 0.36     | 0.90    | 0.72            | 1.13            | 0.36   | 0.00           |
| Verrucomicrobia.id.3982        | phylum | T2D       | 0.06    | 0.12  | 0.09     | 0.23     | 1.07    | 0.87            | 1.30            | 0.53   | 0.00           |
| Actinobacteria.id.419          | class  | T2D       | 0.08    | 0.12  | 0.31     | 0.23     | 1.14    | 0.92            | 1.40            | 0.23   | 0.00           |
| Alphaproteobacteria.id.2379    | class  | T2D       | 0.02    | 0.12  | -0.01    | 0.32     | 1.01    | 0.81            | 1.26            | 0.91   | 0.00           |
| Bacilli.id.1673                | class  | T2D       | 0.26    | 0.12  | 0.31     | 0.18     | 1.32    | 1.09            | 1.59            | 0.00   | 0.00           |
| Bacteroidia.id.912             | class  | T2D       | -0.05   | 0.11  | -0.50    | 0.34     | 0.91    | 0.74            | 1.13            | 0.39   | 0.37           |
| Betaproteobacteria.id.2867     | class  | T2D       | 0.06    | 0.12  | -0.02    | 0.26     | 1.05    | 0.85            | 1.30            | 0.64   | 0.00           |
| Clostridia.id.1859             | class  | T2D       | -0.17   | 0.11  | -0.20    | 0.23     | 0.84    | 0.70            | 1.02            | 0.07   | 0.00           |
| Coriobacteriia.id.809          | class  | T2D       | -0.06   | 0.12  | 0.11     | 0.25     | 0.97    | 0.79            | 1.19            | 0.78   | 0.00           |
| Deltaproteobacteria.id.3087    | class  | T2D       | 0.10    | 0.12  | 0.00     | 0.30     | 1.10    | 0.89            | 1.36            | 0.40   | 0.00           |
| Erysipelotrichia.id.2147       | class  | T2D       | -0.02   | 0.12  | -0.24    | 0.30     | 0.95    | 0.77            | 1.18            | 0.66   | 0.00           |
| Gammaproteobacteria.id.3303    | class  | T2D       | 0.11    | 0.12  | 0.12     | 0.14     | 1.12    | 0.94            | 1.34            | 0.21   | 0.00           |
| Melainabacteria.id.1589        | class  | T2D       | -0.05   | 0.12  | 0.02     | 0.25     | 0.96    | 0.78            | 1.19            | 0.73   | 0.00           |
| Mollicutes.id.3920             | class  | T2D       | -0.09   | 0.12  | -0.19    | 0.36     | 0.90    | 0.72            | 1.13            | 0.36   | 0.00           |
| Negativicutes.id.2164          | class  | T2D       | -0.11   | 0.11  | 0.14     | 0.27     | 0.93    | 0.76            | 1.14            | 0.48   | 0.00           |
| Verrucomicrobiae.id.4029       | class  | T2D       | 0.06    | 0.12  | 0.09     | 0.23     | 1.07    | 0.87            | 1.31            | 0.51   | 0.00           |
| Aeromonadales.id.3316          | order  | T2D       | 0.07    | 0.11  | -413.18  | 40214.87 | 1.07    | 0.87            | 1.32            | 0.52   | 0.00           |
| Bacteroidales.id.913           | order  | T2D       | -0.05   | 0.11  | -0.50    | 0.34     | 0.91    | 0.74            | 1.13            | 0.39   | 0.37           |
| Bifidobacteriales.id.432       | order  | T2D       | 0.04    | 0.12  | 0.30     | 0.24     | 1.09    | 0.89            | 1.35            | 0.40   | 0.00           |
| Burkholderiales.id.2874        | order  | T2D       | 0.06    | 0.12  | -0.02    | 0.26     | 1.05    | 0.85            | 1.30            | 0.66   | 0.00           |
| Clostridiales.id.1863          | order  | T2D       | -0.17   | 0.11  | -0.20    | 0.23     | 0.84    | 0.70            | 1.02            | 0.07   | 0.00           |
| Coriobacteriales.id.810        | order  | T2D       | -0.06   | 0.12  | 0.11     | 0.25     | 0.97    | 0.79            | 1.19            | 0.78   | 0.00           |
| Desulfovibrionales.id.3156     | order  | T2D       | 0.10    | 0.12  | 0.01     | 0.30     | 1.10    | 0.89            | 1.36            | 0.40   | 0.00           |

|                                      |        |     |       |      |       |      |      |      |      |      |      |
|--------------------------------------|--------|-----|-------|------|-------|------|------|------|------|------|------|
| Enterobacteriales.id.3468            | order  | T2D | 0.12  | 0.12 | 0.14  | 0.14 | 1.14 | 0.95 | 1.36 | 0.16 | 0.00 |
| Erysipelotrichales.id.2148           | order  | T2D | -0.02 | 0.12 | -0.24 | 0.30 | 0.95 | 0.77 | 1.18 | 0.66 | 0.00 |
| Gastranaerophilales.id.1591          | order  | T2D | -0.05 | 0.12 | 0.02  | 0.25 | 0.96 | 0.78 | 1.20 | 0.73 | 0.00 |
| Lactobacillales.id.1800              | order  | T2D | 0.25  | 0.12 | 0.32  | 0.18 | 1.31 | 1.08 | 1.58 | 0.01 | 0.00 |
| MollicutesRF9.id.11579               | order  | T2D | -0.07 | 0.12 | -0.20 | 0.37 | 0.92 | 0.74 | 1.15 | 0.48 | 0.00 |
| Pasteurellales.id.3688               | order  | T2D | -0.07 | 0.12 | 0.19  | 0.16 | 1.03 | 0.85 | 1.24 | 0.79 | 0.45 |
| Rhodospirillales.id.2667             | order  | T2D | 0.03  | 0.12 | 0.01  | 0.29 | 1.03 | 0.83 | 1.27 | 0.82 | 0.00 |
| Selenomonadales.id.2165              | order  | T2D | -0.11 | 0.11 | 0.14  | 0.27 | 0.93 | 0.76 | 1.14 | 0.48 | 0.00 |
| Verrucomicrobiales.id.4030           | order  | T2D | 0.06  | 0.12 | 0.09  | 0.23 | 1.07 | 0.87 | 1.31 | 0.51 | 0.00 |
| Acidaminococcaceae.id.2166           | family | T2D | -0.11 | 0.11 | -1.26 | 0.72 | 0.87 | 0.70 | 1.09 | 0.23 | 0.60 |
| Alcaligenaceae.id.2875               | family | T2D | 0.05  | 0.12 | -0.04 | 0.27 | 1.04 | 0.84 | 1.28 | 0.72 | 0.00 |
| Bacteroidaceae.id.917                | family | T2D | 0.00  | 0.12 | -0.36 | 0.33 | 0.96 | 0.77 | 1.19 | 0.70 | 0.03 |
| Bifidobacteriaceae.id.433            | family | T2D | 0.04  | 0.12 | 0.30  | 0.24 | 1.09 | 0.89 | 1.35 | 0.40 | 0.00 |
| Christensenellaceae.id.1866          | family | T2D | -0.25 | 0.11 | -0.24 | 0.35 | 0.78 | 0.64 | 0.96 | 0.02 | 0.00 |
| Clostridiaceae1.id.1869              | family | T2D | -0.83 | 0.13 | -0.11 | 0.25 | 0.51 | 0.40 | 0.64 | 0.00 | 0.84 |
| ClostridialesvadinBB60group.id.11286 | family | T2D | -0.08 | 0.13 | 0.08  | 0.22 | 0.96 | 0.77 | 1.19 | 0.71 | 0.00 |
| Coriobacteriaceae.id.811             | family | T2D | -0.06 | 0.12 | 0.11  | 0.25 | 0.97 | 0.79 | 1.19 | 0.78 | 0.00 |
| Desulfovibrionaceae.id.3169          | family | T2D | 0.10  | 0.12 | 0.00  | 0.30 | 1.10 | 0.89 | 1.36 | 0.40 | 0.00 |
| Enterobacteriaceae.id.3469           | family | T2D | 0.12  | 0.12 | 0.14  | 0.14 | 1.14 | 0.95 | 1.36 | 0.16 | 0.00 |
| Enterococcaceae.id.1828              | family | T2D | 0.12  | 0.09 | -0.44 | 1.11 | 1.13 | 0.94 | 1.36 | 0.21 | 0.00 |
| Erysipelotrichaceae.id.2149          | family | T2D | -0.02 | 0.12 | -0.24 | 0.30 | 0.95 | 0.77 | 1.18 | 0.66 | 0.00 |
| FamilyXIII.id.1957                   | family | T2D | -0.16 | 0.11 | -0.41 | 0.34 | 0.84 | 0.68 | 1.02 | 0.08 | 0.00 |
| Lachnospiraceae.id.1987              | family | T2D | 0.09  | 0.12 | -0.16 | 0.26 | 1.05 | 0.84 | 1.30 | 0.68 | 0.00 |
| Lactobacillaceae.id.1836             | family | T2D | 0.20  | 0.10 | -0.06 | 0.14 | 1.11 | 0.94 | 1.30 | 0.21 | 0.59 |
| Pasteurellaceae.id.3689              | family | T2D | -0.07 | 0.12 | 0.19  | 0.16 | 1.03 | 0.85 | 1.24 | 0.79 | 0.45 |
| Peptococcaceae.id.2024               | family | T2D | -0.08 | 0.12 | -0.55 | 0.55 | 0.90 | 0.72 | 1.13 | 0.37 | 0.00 |
| Peptostreptococcaceae.id.2042        | family | T2D | -0.67 | 0.11 | -0.33 | 0.30 | 0.53 | 0.43 | 0.66 | 0.00 | 0.13 |
| Porphyromonadaceae.id.943            | family | T2D | -0.09 | 0.12 | -0.44 | 0.36 | 0.88 | 0.71 | 1.10 | 0.28 | 0.00 |
| Prevotellaceae.id.960                | family | T2D | 0.04  | 0.12 | -0.40 | 0.48 | 1.02 | 0.82 | 1.27 | 0.86 | 0.00 |
| Rhodospirillaceae.id.2717            | family | T2D | 0.03  | 0.12 | 0.01  | 0.29 | 1.03 | 0.83 | 1.27 | 0.82 | 0.00 |
| Rikenellaceae.id.967                 | family | T2D | -0.10 | 0.11 | 0.10  | 0.25 | 0.93 | 0.76 | 1.14 | 0.50 | 0.00 |
| Ruminococcaceae.id.2050              | family | T2D | -0.18 | 0.11 | 0.20  | 0.28 | 0.88 | 0.72 | 1.07 | 0.19 | 0.37 |



|                             |        |     |      |      |         |          |      |      |      |      |      |
|-----------------------------|--------|-----|------|------|---------|----------|------|------|------|------|------|
| Streptococcaceae.id.1850    | family | T2D | 0.23 | 0.11 | 0.39    | 0.17     | 1.32 | 1.10 | 1.59 | 0.00 | 0.00 |
| Succinivibrionaceae.id.3326 | family | T2D | 0.07 | 0.11 | -413.19 | 40223.44 | 1.07 | 0.87 | 1.32 | 0.52 | 0.00 |

|                                            |        |     |       |      |       |      |      |      |      |      |      |
|--------------------------------------------|--------|-----|-------|------|-------|------|------|------|------|------|------|
| Veillonellaceae.id.2172                    | family | T2D | -0.08 | 0.12 | 0.22  | 0.25 | 0.97 | 0.79 | 1.19 | 0.78 | 0.15 |
| Verrucomicrobiaceae.id.4036                | family | T2D | 0.06  | 0.12 | 0.09  | 0.23 | 1.07 | 0.87 | 1.31 | 0.51 | 0.00 |
| unknownfamily.id.1000001214                | family | T2D | -0.05 | 0.12 | 0.02  | 0.25 | 0.96 | 0.78 | 1.20 | 0.73 | 0.00 |
| unknownfamily.id.1000005471                | family | T2D | -0.07 | 0.12 | -0.20 | 0.37 | 0.92 | 0.74 | 1.15 | 0.48 | 0.00 |
| unknownfamily.id.987                       | family | T2D | -0.09 | 0.12 | -0.90 | 1.09 | 0.91 | 0.71 | 1.15 | 0.43 | 0.00 |
| Bacteroidespectinophilusgroup.id.14371     | genus  | T2D | -0.74 | 0.57 | -0.08 | 0.35 | 0.77 | 0.43 | 1.38 | 0.38 | 0.00 |
| Eubacteriumcoprostanoligenesgroup.id.11375 | genus  | T2D | -0.25 | 0.10 | -0.31 | 0.31 | 0.77 | 0.64 | 0.93 | 0.01 | 0.00 |
| Eubacteriumeligensgroup.id.14372           | genus  | T2D | -0.27 | 0.12 | 0.20  | 0.18 | 0.88 | 0.73 | 1.07 | 0.20 | 0.79 |
| Eubacteriumhalliigroup.id.11338            | genus  | T2D | 0.03  | 0.12 | -0.21 | 0.29 | 0.99 | 0.80 | 1.23 | 0.95 | 0.00 |
| Eubacteriumrectalegroup.id.14374           | genus  | T2D | 0.02  | 0.12 | 0.09  | 0.16 | 1.05 | 0.87 | 1.27 | 0.62 | 0.00 |
| Eubacteriumruminantiumgroup.id.11340       | genus  | T2D | -0.15 | 0.12 | 0.17  | 0.20 | 0.94 | 0.77 | 1.16 | 0.58 | 0.46 |
| Eubacteriumventriosumgroup.id.11341        | genus  | T2D | -0.12 | 0.12 | 0.06  | 0.22 | 0.92 | 0.75 | 1.13 | 0.43 | 0.00 |
| Eubacteriumxylanophilumgroup.id.14375      | genus  | T2D | -0.30 | 0.12 | -0.26 | 0.34 | 0.75 | 0.60 | 0.93 | 0.01 | 0.00 |
| Ruminococcusgauvreauigroup.id.11342        | genus  | T2D | -0.19 | 0.11 | -1.29 | 0.54 | 0.79 | 0.64 | 0.98 | 0.03 | 0.75 |
| Ruminococcusgnavusgroup.id.14376           | genus  | T2D | -0.09 | 0.12 | -0.08 | 0.39 | 0.92 | 0.74 | 1.14 | 0.44 | 0.00 |
| Ruminococcustorquesgroup.id.14377          | genus  | T2D | 0.23  | 0.12 | -0.39 | 0.42 | 1.20 | 0.95 | 1.51 | 0.13 | 0.51 |
| Acidaminococcus.id.2167                    | genus  | T2D | 0.09  | 0.10 | -4.15 | 5.19 | 1.10 | 0.91 | 1.33 | 0.34 | 0.00 |
| Adlercreutzia.id.812                       | genus  | T2D | 0.03  | 0.11 | -0.08 | 0.27 | 1.01 | 0.83 | 1.24 | 0.89 | 0.00 |
| Akkermansia.id.4037                        | genus  | T2D | 0.06  | 0.12 | 0.09  | 0.23 | 1.07 | 0.87 | 1.31 | 0.51 | 0.00 |
| Alistipes.id.968                           | genus  | T2D | -0.06 | 0.12 | 0.06  | 0.26 | 0.96 | 0.78 | 1.18 | 0.72 | 0.00 |
| Alloprevotella.id.961                      | genus  | T2D | -0.03 | 0.12 | -2.54 | 4.04 | 0.97 | 0.76 | 1.23 | 0.79 | 0.00 |
| Anaerostipes.id.1991                       | genus  | T2D | -0.07 | 0.11 | -0.02 | 0.24 | 0.94 | 0.77 | 1.15 | 0.54 | 0.00 |
| Anaerotruncus.id.2054                      | genus  | T2D | -0.26 | 0.11 | -0.10 | 0.30 | 0.79 | 0.64 | 0.97 | 0.02 | 0.00 |
| Bacteroides.id.918                         | genus  | T2D | 0.00  | 0.12 | -0.36 | 0.33 | 0.96 | 0.77 | 1.19 | 0.70 | 0.03 |
| Barnesiella.id.944                         | genus  | T2D | -0.09 | 0.12 | -0.49 | 0.42 | 0.88 | 0.71 | 1.11 | 0.28 | 0.00 |
| Bifidobacterium.id.436                     | genus  | T2D | 0.04  | 0.12 | 0.29  | 0.24 | 1.09 | 0.89 | 1.35 | 0.41 | 0.00 |
| Blautia.id.1992                            | genus  | T2D | 0.21  | 0.12 | -0.21 | 0.31 | 1.17 | 0.93 | 1.47 | 0.17 | 0.37 |
| Butyricicoccus.id.2055                     | genus  | T2D | 0.02  | 0.11 | -0.63 | 0.45 | 0.98 | 0.79 | 1.22 | 0.88 | 0.50 |
| Butyricimonas.id.945                       | genus  | T2D | 0.13  | 0.12 | -0.20 | 0.41 | 1.11 | 0.89 | 1.38 | 0.35 | 0.00 |
| Butyrivibrio.id.1993                       | genus  | T2D | -0.09 | 0.13 | -0.37 | 0.60 | 0.90 | 0.71 | 1.15 | 0.40 | 0.00 |
| Catenibacterium.id.2153                    | genus  | T2D | 0.04  | 0.11 | -1.87 | 1.52 | 1.03 | 0.83 | 1.27 | 0.80 | 0.36 |
| ChristensenellaceaeR7group.id.11283        | genus  | T2D | -0.24 | 0.11 | -0.24 | 0.36 | 0.79 | 0.64 | 0.97 | 0.02 | 0.00 |

|                                     |       |     |       |      |       |      |      |      |      |      |      |
|-------------------------------------|-------|-----|-------|------|-------|------|------|------|------|------|------|
| Clostridium sensu stricto 1.id.1873 | genus | T2D | -0.84 | 0.13 | -0.11 | 0.26 | 0.50 | 0.40 | 0.63 | 0.00 | 0.84 |
| Collinsella.id.815                  | genus | T2D | 0.01  | 0.12 | 0.21  | 0.23 | 1.05 | 0.86 | 1.29 | 0.63 | 0.00 |

|                                      |       |     |       |      |         |          |      |      |      |      |      |
|--------------------------------------|-------|-----|-------|------|---------|----------|------|------|------|------|------|
| Coprococcus1.id.11301                | genus | T2D | 0.06  | 0.12 | 0.14    | 0.25     | 1.07 | 0.87 | 1.32 | 0.50 | 0.00 |
| Coprococcus2.id.11302                | genus | T2D | -0.14 | 0.12 | -0.18   | 0.34     | 0.86 | 0.69 | 1.07 | 0.18 | 0.00 |
| Coprococcus3.id.11303                | genus | T2D | 0.05  | 0.12 | -0.60   | 0.35     | 0.98 | 0.78 | 1.23 | 0.86 | 0.68 |
| Desulfovibrio.id.3173                | genus | T2D | 0.04  | 0.12 | -0.11   | 0.35     | 1.03 | 0.83 | 1.27 | 0.81 | 0.00 |
| Dialister.id.2183                    | genus | T2D | -0.07 | 0.12 | 0.27    | 0.24     | 0.99 | 0.80 | 1.22 | 0.92 | 0.36 |
| Dorea.id.1997                        | genus | T2D | -0.15 | 0.11 | -0.29   | 0.30     | 0.85 | 0.69 | 1.03 | 0.10 | 0.00 |
| Eggerthella.id.819                   | genus | T2D | 0.04  | 0.12 | -1.16   | 1.15     | 1.03 | 0.82 | 1.30 | 0.78 | 0.08 |
| Eisenbergiella.id.11304              | genus | T2D | 0.11  | 0.11 | 0.22    | 0.15     | 1.16 | 0.97 | 1.37 | 0.10 | 0.00 |
| Enterococcus.id.1831                 | genus | T2D | 0.11  | 0.10 | -2.68   | 7.94     | 1.11 | 0.92 | 1.35 | 0.26 | 0.00 |
| Enterorhabdus.id.820                 | genus | T2D | 0.07  | 0.11 | -0.29   | 0.37     | 1.04 | 0.84 | 1.29 | 0.72 | 0.00 |
| Erysipelatoclostridium.id.11381      | genus | T2D | -0.06 | 0.12 | 0.22    | 0.15     | 1.05 | 0.87 | 1.26 | 0.61 | 0.57 |
| ErysipelotrichaceaeUCG003.id.11384   | genus | T2D | -0.15 | 0.11 | -0.12   | 0.32     | 0.87 | 0.70 | 1.07 | 0.18 | 0.00 |
| Faecalibacterium.id.2057             | genus | T2D | -0.13 | 0.10 | -0.12   | 0.28     | 0.88 | 0.73 | 1.06 | 0.19 | 0.00 |
| FamilyXIIAD3011group.id.11293        | genus | T2D | -0.08 | 0.11 | -0.84   | 0.47     | 0.89 | 0.72 | 1.10 | 0.28 | 0.60 |
| FamilyXIIICUG001.id.11294            | genus | T2D | -0.12 | 0.12 | -0.10   | 0.28     | 0.89 | 0.72 | 1.09 | 0.26 | 0.00 |
| Fusicatenibacter.id.11305            | genus | T2D | -0.22 | 0.11 | 0.22    | 0.19     | 0.89 | 0.74 | 1.07 | 0.22 | 0.75 |
| Haemophilus.id.3698                  | genus | T2D | -0.07 | 0.12 | 0.18    | 0.15     | 1.03 | 0.85 | 1.24 | 0.77 | 0.40 |
| Holdemanella.id.11393                | genus | T2D | 0.07  | 0.11 | -0.04   | 0.26     | 1.06 | 0.86 | 1.30 | 0.59 | 0.00 |
| Intestinibacter.id.11345             | genus | T2D | -0.67 | 0.13 | -0.10   | 0.23     | 0.59 | 0.47 | 0.74 | 0.00 | 0.80 |
| Intestinimonas.id.2062               | genus | T2D | -0.10 | 0.11 | 0.15    | 0.23     | 0.95 | 0.78 | 1.16 | 0.62 | 0.00 |
| Lachnoclostridium.id.11308           | genus | T2D | -0.02 | 0.12 | 0.13    | 0.20     | 1.02 | 0.84 | 1.24 | 0.85 | 0.00 |
| Lachnospira.id.2004                  | genus | T2D | -0.26 | 0.11 | -0.33   | 0.38     | 0.76 | 0.62 | 0.94 | 0.01 | 0.00 |
| LachnospiraceaeFCS020group.id.11314  | genus | T2D | -0.10 | 0.12 | 0.23    | 0.18     | 0.99 | 0.82 | 1.20 | 0.94 | 0.57 |
| LachnospiraceaeND3007group.id.11317  | genus | T2D | -0.32 | 0.11 | 0.26    | 0.24     | 0.80 | 0.66 | 0.98 | 0.03 | 0.80 |
| LachnospiraceaeNK4A136group.id.11319 | genus | T2D | -0.31 | 0.11 | -0.05   | 0.23     | 0.77 | 0.63 | 0.94 | 0.01 | 0.00 |
| LachnospiraceaeUCG001.id.11321       | genus | T2D | 0.04  | 0.12 | 0.03    | 0.19     | 1.04 | 0.85 | 1.26 | 0.72 | 0.00 |
| LachnospiraceaeUCG004.id.11324       | genus | T2D | -0.06 | 0.12 | -0.60   | 0.50     | 0.92 | 0.73 | 1.15 | 0.44 | 0.10 |
| LachnospiraceaeUCG010.id.11330       | genus | T2D | 0.12  | 0.11 | -0.32   | 0.41     | 1.09 | 0.88 | 1.35 | 0.44 | 0.04 |
| Lactobacillus.id.1837                | genus | T2D | 0.18  | 0.10 | -0.09   | 0.15     | 1.09 | 0.93 | 1.29 | 0.29 | 0.53 |
| Marvinbryantia.id.2005               | genus | T2D | -0.06 | 0.11 | -0.54   | 0.42     | 0.91 | 0.73 | 1.13 | 0.39 | 0.19 |
| Megamonas.id.2184                    | genus | T2D | -0.04 | 0.11 | -710.93 | 69209.72 | 0.96 | 0.77 | 1.20 | 0.73 | 0.00 |
| Megasphaera.id.2185                  | genus | T2D | -0.13 | 0.13 | -0.72   | 0.86     | 0.87 | 0.68 | 1.12 | 0.28 | 0.00 |

|                     |       |     |       |      |       |      |      |      |      |      |      |
|---------------------|-------|-----|-------|------|-------|------|------|------|------|------|------|
| Mitsuokella.id.2186 | genus | T2D | -0.07 | 0.12 | -0.31 | 0.58 | 0.92 | 0.74 | 1.16 | 0.50 | 0.00 |
| Odoribacter.id.952  | genus | T2D | 0.11  | 0.12 | -0.06 | 0.31 | 1.09 | 0.88 | 1.36 | 0.43 | 0.00 |

|                                      |       |     |       |      |         |          |      |      |      |      |      |
|--------------------------------------|-------|-----|-------|------|---------|----------|------|------|------|------|------|
| Olsenella.id.822                     | genus | T2D | 0.08  | 0.11 | -8.31   | 6.43     | 1.08 | 0.87 | 1.35 | 0.48 | 0.41 |
| Oscillospira.id.2064                 | genus | T2D | -0.10 | 0.12 | 0.09    | 0.26     | 0.93 | 0.75 | 1.15 | 0.52 | 0.00 |
| Parabacteroides.id.954               | genus | T2D | -0.08 | 0.12 | -0.36   | 0.36     | 0.90 | 0.72 | 1.13 | 0.36 | 0.00 |
| Paraprevotella.id.962                | genus | T2D | -0.04 | 0.11 | -0.10   | 0.35     | 0.95 | 0.77 | 1.18 | 0.66 | 0.00 |
| Parasutterella.id.2892               | genus | T2D | -0.02 | 0.12 | 0.15    | 0.20     | 1.02 | 0.84 | 1.25 | 0.81 | 0.00 |
| Peptococcus.id.2037                  | genus | T2D | -0.02 | 0.12 | -0.64   | 0.60     | 0.96 | 0.77 | 1.20 | 0.72 | 0.03 |
| Phascolarctobacterium.id.2168        | genus | T2D | -0.10 | 0.11 | -1.01   | 0.65     | 0.88 | 0.71 | 1.10 | 0.26 | 0.49 |
| Prevotella2.id.11180                 | genus | T2D | 0.08  | 0.11 | -396.57 | 30961.40 | 1.08 | 0.87 | 1.35 | 0.47 | 0.00 |
| Prevotella7.id.11182                 | genus | T2D | -0.05 | 0.12 | -0.05   | 0.21     | 0.95 | 0.78 | 1.16 | 0.61 | 0.00 |
| Prevotella9.id.11183                 | genus | T2D | 0.02  | 0.11 | -0.28   | 0.46     | 1.00 | 0.81 | 1.24 | 1.00 | 0.00 |
| PrevotellaceaeNK3B31group.id.11185   | genus | T2D | -0.02 | 0.12 | -0.37   | 0.88     | 0.98 | 0.78 | 1.23 | 0.85 | 0.00 |
| PrevotellaceaeUCG001.id.11186        | genus | T2D | 0.00  | 0.12 | -1.01   | 3.17     | 1.00 | 0.80 | 1.26 | 0.98 | 0.00 |
| RikenellaceaeRC9gutgroup.id.11191    | genus | T2D | -0.05 | 0.12 | 0.11    | 0.20     | 0.99 | 0.82 | 1.21 | 0.95 | 0.00 |
| Romboutsia.id.11347                  | genus | T2D | -0.63 | 0.12 | -1.06   | 0.61     | 0.52 | 0.42 | 0.66 | 0.00 | 0.00 |
| Roseburia.id.2012                    | genus | T2D | -0.07 | 0.11 | -0.47   | 0.36     | 0.90 | 0.72 | 1.11 | 0.31 | 0.08 |
| Ruminiclostridium5.id.11355          | genus | T2D | -0.32 | 0.11 | 0.21    | 0.17     | 0.86 | 0.71 | 1.03 | 0.10 | 0.85 |
| Ruminiclostridium6.id.11356          | genus | T2D | -0.22 | 0.12 | -0.01   | 0.29     | 0.83 | 0.67 | 1.02 | 0.08 | 0.00 |
| Ruminiclostridium9.id.11357          | genus | T2D | -0.05 | 0.12 | 0.09    | 0.27     | 0.98 | 0.79 | 1.20 | 0.81 | 0.00 |
| RuminococcaceaeNK4A214group.id.11358 | genus | T2D | -0.22 | 0.11 | -0.28   | 0.41     | 0.80 | 0.64 | 0.99 | 0.04 | 0.00 |
| RuminococcaceaeUCG002.id.11360       | genus | T2D | -0.12 | 0.11 | -0.15   | 0.33     | 0.89 | 0.72 | 1.09 | 0.25 | 0.00 |
| RuminococcaceaeUCG003.id.11361       | genus | T2D | -0.08 | 0.12 | -0.08   | 0.32     | 0.92 | 0.74 | 1.15 | 0.48 | 0.00 |
| RuminococcaceaeUCG004.id.11362       | genus | T2D | 0.05  | 0.12 | 0.07    | 0.25     | 1.05 | 0.86 | 1.29 | 0.63 | 0.00 |
| RuminococcaceaeUCG005.id.11363       | genus | T2D | -0.19 | 0.11 | -0.11   | 0.29     | 0.84 | 0.68 | 1.03 | 0.10 | 0.00 |
| RuminococcaceaeUCG008.id.11365       | genus | T2D | -0.05 | 0.12 | 0.05    | 0.21     | 0.97 | 0.80 | 1.19 | 0.80 | 0.00 |
| RuminococcaceaeUCG010.id.11367       | genus | T2D | -0.20 | 0.12 | 0.05    | 0.27     | 0.85 | 0.69 | 1.06 | 0.15 | 0.00 |
| RuminococcaceaeUCG013.id.11370       | genus | T2D | -0.17 | 0.11 | -0.39   | 0.33     | 0.82 | 0.67 | 1.02 | 0.07 | 0.00 |
| RuminococcaceaeUCG014.id.11371       | genus | T2D | -0.06 | 0.11 | 0.09    | 0.23     | 0.97 | 0.79 | 1.18 | 0.75 | 0.00 |
| Ruminococcus1.id.11373               | genus | T2D | -0.12 | 0.12 | 0.08    | 0.24     | 0.92 | 0.75 | 1.12 | 0.41 | 0.00 |
| Ruminococcus2.id.11374               | genus | T2D | -0.07 | 0.11 | 0.10    | 0.25     | 0.96 | 0.79 | 1.17 | 0.70 | 0.00 |
| Sellimonas.id.14369                  | genus | T2D | -0.15 | 0.13 | 0.05    | 0.17     | 0.92 | 0.75 | 1.13 | 0.44 | 0.00 |
| Senegalimassilia.id.11160            | genus | T2D | -0.10 | 0.12 | 0.20    | 0.20     | 0.97 | 0.80 | 1.19 | 0.80 | 0.41 |
| Slackia.id.825                       | genus | T2D | -0.17 | 0.12 | -0.35   | 0.38     | 0.83 | 0.66 | 1.04 | 0.11 | 0.00 |

|                         |       |     |      |      |      |      |      |      |      |      |      |
|-------------------------|-------|-----|------|------|------|------|------|------|------|------|------|
| Streptococcus.id.1853   | genus | T2D | 0.23 | 0.11 | 0.39 | 0.17 | 1.32 | 1.10 | 1.59 | 0.00 | 0.00 |
| Subdoligranulum.id.2070 | genus | T2D | 0.03 | 0.12 | 0.33 | 0.22 | 1.10 | 0.90 | 1.34 | 0.36 | 0.35 |

|                            |       |     |       |      |         |          |      |      |      |      |      |
|----------------------------|-------|-----|-------|------|---------|----------|------|------|------|------|------|
| Succiniclasicum.id.2169    | genus | T2D | 0.01  | 0.12 | -287.75 | 23111.13 | 1.01 | 0.80 | 1.29 | 0.92 | 0.00 |
| Sutterella.id.2896         | genus | T2D | 0.04  | 0.12 | -0.72   | 0.69     | 1.02 | 0.81 | 1.28 | 0.89 | 0.16 |
| Terrisporobacter.id.11348  | genus | T2D | -0.43 | 0.13 | 0.15    | 0.13     | 0.89 | 0.74 | 1.06 | 0.20 | 0.90 |
| Turicibacter.id.2162       | genus | T2D | -0.23 | 0.12 | 0.11    | 0.20     | 0.87 | 0.71 | 1.07 | 0.19 | 0.54 |
| Tyzzerella3.id.11335       | genus | T2D | 0.09  | 0.11 | -130.98 | 9906.14  | 1.09 | 0.89 | 1.35 | 0.40 | 0.00 |
| Veillonella.id.2198        | genus | T2D | -0.01 | 0.11 | 0.15    | 0.15     | 1.04 | 0.88 | 1.24 | 0.62 | 0.00 |
| unknowngenus.id.1000000073 | genus | T2D | -0.08 | 0.13 | 0.08    | 0.22     | 0.96 | 0.77 | 1.19 | 0.71 | 0.00 |
| unknowngenus.id.1000001215 | genus | T2D | -0.05 | 0.12 | 0.02    | 0.25     | 0.96 | 0.78 | 1.20 | 0.73 | 0.00 |
| unknowngenus.id.1000005472 | genus | T2D | -0.07 | 0.12 | -0.20   | 0.37     | 0.92 | 0.74 | 1.15 | 0.48 | 0.00 |
| unknowngenus.id.1000005479 | genus | T2D | -0.06 | 0.12 | -1.11   | 0.87     | 0.92 | 0.73 | 1.16 | 0.50 | 0.30 |
| unknowngenus.id.1000013899 | genus | T2D | -0.09 | 0.12 | -0.90   | 1.09     | 0.91 | 0.71 | 1.15 | 0.43 | 0.00 |
| unknowngenus.id.2071       | genus | T2D | -0.23 | 0.13 | 0.17    | 0.19     | 0.89 | 0.73 | 1.10 | 0.28 | 0.68 |
| unknowngenus.id.2755       | genus | T2D | 0.02  | 0.12 | -0.01   | 0.32     | 1.02 | 0.82 | 1.27 | 0.86 | 0.00 |
| unknowngenus.id.826        | genus | T2D | -0.04 | 0.12 | -0.12   | 0.30     | 0.95 | 0.77 | 1.18 | 0.64 | 0.00 |
| unknowngenus.id.964        | genus | T2D | -0.01 | 0.13 | -223.38 | 23574.05 | 0.99 | 0.77 | 1.27 | 0.95 | 0.00 |

| Taxa in RS only                              | Clade  | Phenotype | Beta_RS | Se_RS |
|----------------------------------------------|--------|-----------|---------|-------|
| family.BacteroidalesS247group.id.11173       | family | T2D       | -0.06   | 0.12  |
| family.Veillonellaceae.id.2172               | family | T2D       | -0.08   | 0.12  |
| genus..Bacteroidespectinophilusgroup.id.1437 | family | T2D       | -0.74   | 0.57  |
| genus.Enterobacter.id.3502                   | genus  | T2D       | 0.15    | 0.11  |
| genus.EscherichiaShigella.id.3504            | genus  | T2D       | 0.03    | 0.12  |
| genus..Eubacteriumcoprostanoligenesgroup.id  | genus  | T2D       | -0.25   | 0.10  |
| genus..Eubacteriumeligensgroup.id.14372      | genus  | T2D       | -0.27   | 0.12  |
| genus..Eubacteriumhalliigroup.id.11338       | genus  | T2D       | 0.03    | 0.12  |
| genus..Eubacteriumoxidoreducensgroup.id.11   | genus  | T2D       | -0.06   | 0.12  |
| genus..Eubacteriumxylanophilumgroup.id.143   | genus  | T2D       | -0.30   | 0.12  |
| genus.Hungatella.id.11306                    | genus  | T2D       | 0.02    | 0.13  |
| genus.Klebsiella.id.3507                     | genus  | T2D       | 0.13    | 0.09  |
| genus.LachnospiraceaeNC2004group.id.11316    | genus  | T2D       | -0.26   | 0.12  |



|                                      |       |     |       |      |
|--------------------------------------|-------|-----|-------|------|
| genus.LachnospiraceaeUCG008.id.11328 | genus | T2D | -0.05 | 0.12 |
| genus.unknowngenus.id.1868           | genus | T2D | -0.23 | 0.09 |

| Taxa in LLD only                         | Clade  | Phenotype | Beta_LLD | Se_LLD  |
|------------------------------------------|--------|-----------|----------|---------|
| domain.Archaea.id.2                      | Clade  | T2D       | 0.15     | 0.22    |
| phylum.Euryarchaeota.id.55               | domain | T2D       | 0.15     | 0.22    |
| phylum.Lentisphaerae.id.2238             | phylum | T2D       | -0.02    | 0.20    |
| order.Actinomycetales.id.420             | phylum | T2D       | 0.09     | 0.17    |
| order.Mycoplasmatales.id.3946            | order  | T2D       | -0.41    | 53.21   |
| order.NB1.n.id.3953                      | order  | T2D       | 0.09     | 0.16    |
| order.Pseudomonadales.id.3709            | order  | T2D       | -0.18    | 2.68    |
| order.Spirochaetales.id.3870             | order  | T2D       | -17.61   | 2014.59 |
| order.Synergistales.id.3900              | order  | T2D       | -0.96    | 1.66    |
| order.Thermoplasmatales.id.220           | order  | T2D       | 0.21     | 0.09    |
| order.unknownorder.id.1000000003         | order  | T2D       | -0.27    | 0.68    |
| order.Verrucomicrobiales.id.4030         | order  | T2D       | 0.09     | 0.23    |
| order.Victivallales.id.2254              | order  | T2D       | -0.02    | 0.20    |
| order.Xanthomonadales.id.3786            | order  | T2D       | -21.18   | 2344.91 |
| class.Spirochaetes.id.3856               | order  | T2D       | -17.61   | 2014.59 |
| class.Synergistia.id.3899                | class  | T2D       | -0.96    | 1.66    |
| class.Thermoplasmata.id.210              | class  | T2D       | 0.21     | 0.09    |
| family.Actinomycetaceae.id.421           | class  | T2D       | 0.09     | 0.17    |
| family.BacteroidalesS24.7group.id.11173  | family | T2D       | -1.11    | 0.87    |
| family.Christensenellaceae.id.1866       | family | T2D       | -0.24    | 0.35    |
| family.FamilyXI.id.1936                  | family | T2D       | -0.49    | 0.81    |
| family.unknownfamily.id.1000000004       | family | T2D       | -0.27    | 0.68    |
| family.unknownfamily.id.1000006161       | family | T2D       | 0.09     | 0.16    |
| family.unknownfamily.id.1855             | family | T2D       | 0.13     | 0.08    |
| family.vadinBE97.id.14446                | family | T2D       | -0.39    | 1.41    |
| family.Veillonellaceae.id.2172           | family | T2D       | 0.22     | 0.25    |
| family.Xanthomonadaceae.id.3799          | family | T2D       | -21.18   | 2344.91 |
| genus..Clostridiuminnocuumgroup.id.14397 | family | T2D       | 0.17     | 0.12    |
| genus..Eubacteriumbrachygroup.id.11296   | family | T2D       | 0.39     | 0.14    |
| genus.Abiotrophia.id.1803                | genus  | T2D       | -12.52   | 953.72  |
| genus.Actinomyces.id.423                 | genus  | T2D       | 0.03     | 0.19    |

|                             |       |     |        |         |
|-----------------------------|-------|-----|--------|---------|
| genus.Actinotignum.id.11137 | genus | T2D | -13.58 | 1197.75 |
| genus.Allisonella.id.2174   | genus | T2D | -0.27  | 0.36    |

|                                           |       |     |         |          |
|-------------------------------------------|-------|-----|---------|----------|
| genus.Arcanobacterium.id.424              | genus | T2D | -17.45  | 1669.68  |
| genus.Asaccharobacter.id.813              | genus | T2D | 0.12    | 0.23     |
| genus.Bilophila.id.3170                   | genus | T2D | 0.19    | 0.23     |
| genus.CandidatusMethanogranum.id.11110    | genus | T2D | -4.21   | 436.67   |
| genus.Catenisphaera.id.14395              | genus | T2D | -807.94 | 70837.85 |
| genus.Cellulosilyticum.id.1995            | genus | T2D | -84.84  | 7287.37  |
| genus.Cetobacterium.id.2209               | genus | T2D | -0.43   | 53.21    |
| genus.Cloacibacillus.id.3908              | genus | T2D | -0.44   | 0.89     |
| genus.Coprobacillus.id.2154               | genus | T2D | -0.74   | 1.64     |
| genus.CoriobacteriaceaeUCG.002.id.11158   | genus | T2D | -0.29   | 0.57     |
| genus.CoriobacteriaceaeUCG.003.id.11159   | genus | T2D | -279.82 | 29054.73 |
| genus.Denitrobacterium.id.818             | genus | T2D | 0.18    | 0.13     |
| genus.dgA.11gutgroup.id.978               | genus | T2D | -0.46   | 53.21    |
| genus.Dielma.id.11380                     | genus | T2D | -0.16   | 1.79     |
| genus.Epulopiscium.id.1998                | genus | T2D | -2.20   | 3.28     |
| genus.ErysipelotrichaceaeUCG006.id.11386  | genus | T2D | -7.03   | 579.02   |
| genus.ErysipelotrichaceaeUCG009.id.11389  | genus | T2D | -0.49   | 53.21    |
| genus.Escherichia.Shigella.id.3504        | genus | T2D | 0.11    | 0.14     |
| genus.Eubacterium.id.1932                 | genus | T2D | 0.27    | 0.20     |
| genus.Faecalicoccus.id.11391              | genus | T2D | -70.19  | 5031.35  |
| genus.Faecalitalea.id.11392               | genus | T2D | 0.14    | 0.10     |
| genus.Flavonifractor.id.2059              | genus | T2D | -0.15   | 0.49     |
| genus.Gardnerella.id.437                  | genus | T2D | -15.54  | 1509.59  |
| genus.Gordonibacter.id.821                | genus | T2D | -0.30   | 0.47     |
| genus.Hafnia.Obesumbacterium.id.14636     | genus | T2D | 0.29    | 0.47     |
| genus.Howardella.id.2000                  | genus | T2D | -0.54   | 0.43     |
| genus.LachnospiraceaeNK3A20group.id.11318 | genus | T2D | -2.52   | 318.19   |
| genus.Lactococcus.id.1851                 | genus | T2D | -0.32   | 0.68     |
| genus.Lautropia.id.2905                   | genus | T2D | -37.88  | 5179.50  |
| genus.Leuconostoc.id.1841                 | genus | T2D | -0.86   | 0.85     |
| genus.Methanobrevibacter.id.123           | genus | T2D | 0.18    | 0.22     |
| genus.Methanosphaera.id.124               | genus | T2D | -0.31   | 0.52     |

|                             |       |     |       |       |
|-----------------------------|-------|-----|-------|-------|
| genus.Mogibacterium.id.1960 | genus | T2D | -2.14 | 1.60  |
| genus.Morganella.id.3512    | genus | T2D | -0.39 | 53.21 |

|                                          |       |     |          |          |
|------------------------------------------|-------|-----|----------|----------|
| genus.Porphyromonas.id.956               | genus | T2D | -1.42    | 1.85     |
| genus.Preotella1.id.11179                | genus | T2D | -1.07    | 156.52   |
| genus.PreoteiaceaeUCG003.id.11187        | genus | T2D | -57.99   | 7076.11  |
| genus.PreoteiaceaeUCG004.id.11188        | genus | T2D | -6.12    | 515.91   |
| genus.Pseudomonas.id.3723                | genus | T2D | -1029.29 | 83993.69 |
| genus.Rikenella.id.973                   | genus | T2D | -15.17   | 1263.33  |
| genus.RuminococcaceaeNK4A214group.id.113 | genus | T2D | -0.28    | 0.41     |
| genus.RuminococcaceaeUCG005.id.11363     | genus | T2D | -0.11    | 0.29     |
| genus.RuminococcaceaeUCG008.id.11365     | genus | T2D | 0.05     | 0.21     |
| genus.RuminococcaceaeUCG010.id.11367     | genus | T2D | 0.05     | 0.27     |
| genus.Sarcina.id.1896                    | genus | T2D | -52.89   | 5540.50  |
| genus.Solobacterium.id.2161              | genus | T2D | -3.26    | 4.06     |
| genus.Staphylococcus.id.1780             | genus | T2D | 0.01     | 0.28     |
| genus.Stenotrophomonas.id.3818           | genus | T2D | -0.43    | 53.21    |
| genus.Succinivibrio.id.3331              | genus | T2D | -258.74  | 22480.30 |
| genus.Synergistes.id.3913                | genus | T2D | -25.30   | 2076.07  |
| genus.Syntrophococcus.id.2016            | genus | T2D | -0.89    | 89.40    |
| genus.Treponema2.id.11577                | genus | T2D | -15.36   | 1910.08  |
| genus.Tyzzerella4.id.11336               | genus | T2D | -3.64    | 8.45     |
| genus.unknowngenus.id.1000000005         | genus | T2D | -0.27    | 0.68     |
| genus.unknowngenus.id.1000027565         | genus | T2D | -0.39    | 1.41     |
| genus.unknowngenus.id.1000043796         | genus | T2D | 0.13     | 0.08     |
| genus.unknowngenus.id.1854               | genus | T2D | -41.00   | 2997.88  |
| genus.unknowngenus.id.2163               | genus | T2D | 0.15     | 0.11     |
| genus.unknowngenus.id.3332               | genus | T2D | -37.00   | 4333.76  |
| genus.unknowngenus.id.441                | genus | T2D | -0.10    | 0.38     |
| genus.Ureaplasma.id.3951                 | genus | T2D | -0.41    | 53.21    |
| genus.Varibaculum.id.427                 | genus | T2D | 0.33     | 0.14     |
| genus.Veillonella.id.2198                | genus | T2D | 0.15     | 0.15     |
| genus.Weissella.id.1843                  | genus | T2D | 0.09     | 0.13     |

**Supplementary Table 3 - Associations of taxa and type 2 diabetes**

Effect estimates in RS and LLD were calculated using logistic regression; pooled estimates were calculated based on a mixed-effect meta-analysis.

Model 4: Adjusted for age, sex, Time in mail (RS), Batch (RS), smoking, education level (RS), physical activity, alcohol intake, total energy intake, BMI, PPI, and lipid-lowering medication.

Abbreviation RS, Rotterdam Study, LLD, Lifelines-Deep Study. P<0.0005 indicates statistical significance

| Overlapping taxa in RS and LLD | Clade  | Phenotype | Beta_RS | Se_RS | Beta_LLD | Se_LLD   | OR_Meta | Lower95%CI_Meta | Upper95%CI_Meta | p_Meta | I <sup>2</sup> |
|--------------------------------|--------|-----------|---------|-------|----------|----------|---------|-----------------|-----------------|--------|----------------|
| Bacteria.id.3                  | domain | T2D       | -0.12   | 0.12  | 0.22     | 0.44     | 1.03    | 0.98            | 1.09            | 0.24   | 0.00           |
| Actinobacteria.id.400          | phylum | T2D       | 0.03    | 0.12  | 0.39     | 0.26     | 1.09    | 0.88            | 1.35            | 0.41   | 0.37           |
| Bacteroidetes.id.905           | phylum | T2D       | 0.00    | 0.12  | -0.56    | 0.35     | 0.94    | 0.76            | 1.18            | 0.61   | 0.57           |
| Cyanobacteria.id.1500          | phylum | T2D       | 0.11    | 0.13  | 0.06     | 0.28     | 1.10    | 0.88            | 1.38            | 0.40   | 0.00           |
| Firmicutes.id.1672             | phylum | T2D       | -0.09   | 0.12  | -0.05    | 0.24     | 0.92    | 0.74            | 1.14            | 0.45   | 0.00           |
| Proteobacteria.id.2375         | phylum | T2D       | 0.06    | 0.12  | 0.03     | 0.17     | 1.05    | 0.87            | 1.28            | 0.61   | 0.00           |
| Tenericutes.id.3919            | phylum | T2D       | -0.05   | 0.13  | -0.09    | 0.35     | 0.95    | 0.75            | 1.19            | 0.63   | 0.00           |
| Verrucomicrobia.id.3982        | phylum | T2D       | 0.07    | 0.12  | -0.10    | 0.26     | 1.04    | 0.84            | 1.28            | 0.70   | 0.00           |
| Actinobacteria.id.419          | class  | T2D       | 0.06    | 0.13  | 0.37     | 0.25     | 1.13    | 0.91            | 1.41            | 0.26   | 0.18           |
| Alphaproteobacteria.id.2379    | class  | T2D       | 0.05    | 0.13  | -0.21    | 0.43     | 1.03    | 0.81            | 1.30            | 0.83   | 0.00           |
| Bacilli.id.1673                | class  | T2D       | 0.21    | 0.13  | 0.22     | 0.18     | 1.24    | 1.01            | 1.51            | 0.04   | 0.00           |
| Bacteroidia.id.912             | class  | T2D       | 0.00    | 0.12  | -0.57    | 0.35     | 0.94    | 0.76            | 1.18            | 0.61   | 0.58           |
| Betaproteobacteria.id.2867     | class  | T2D       | 0.12    | 0.12  | -0.01    | 0.29     | 1.11    | 0.89            | 1.38            | 0.37   | 0.00           |
| Clostridia.id.1859             | class  | T2D       | -0.16   | 0.11  | -0.08    | 0.23     | 0.87    | 0.71            | 1.06            | 0.17   | 0.00           |
| Coriobacteriia.id.809          | class  | T2D       | -0.04   | 0.12  | 0.15     | 0.26     | 0.99    | 0.80            | 1.23            | 0.94   | 0.00           |
| Deltaproteobacteria.id.3087    | class  | T2D       | 0.17    | 0.12  | -0.01    | 0.31     | 1.16    | 0.93            | 1.45            | 0.19   | 0.00           |
| Erysipelotrichia.id.2147       | class  | T2D       | -0.09   | 0.12  | -0.28    | 0.28     | 0.89    | 0.71            | 1.10            | 0.28   | 0.00           |
| Gammaproteobacteria.id.3303    | class  | T2D       | 0.03    | 0.13  | 0.03     | 0.16     | 1.03    | 0.85            | 1.25            | 0.76   | 0.00           |
| Melainabacteria.id.1589        | class  | T2D       | 0.07    | 0.13  | 0.09     | 0.25     | 1.07    | 0.86            | 1.34            | 0.53   | 0.00           |
| Mollicutes.id.3920             | class  | T2D       | -0.05   | 0.13  | -0.09    | 0.35     | 0.95    | 0.75            | 1.19            | 0.63   | 0.00           |
| Negativicutes.id.2164          | class  | T2D       | -0.08   | 0.12  | 0.13     | 0.29     | 0.95    | 0.77            | 1.17            | 0.63   | 0.00           |
| Verrucomicrobiae.id.4029       | class  | T2D       | 0.07    | 0.12  | -0.10    | 0.26     | 1.04    | 0.85            | 1.29            | 0.68   | 0.00           |
| Aeromonadales.id.3316          | order  | T2D       | 0.08    | 0.12  | -412.55  | 39640.87 | 1.08    | 0.86            | 1.35            | 0.51   | 0.00           |
| Bacteroidales.id.913           | order  | T2D       | 0.00    | 0.12  | -0.57    | 0.35     | 0.94    | 0.76            | 1.18            | 0.61   | 0.58           |
| Bifidobacteriales.id.432       | order  | T2D       | 0.02    | 0.12  | 0.37     | 0.25     | 1.09    | 0.88            | 1.36            | 0.42   | 0.33           |
| Burkholderiales.id.2874        | order  | T2D       | 0.12    | 0.12  | -0.02    | 0.29     | 1.11    | 0.89            | 1.38            | 0.37   | 0.00           |
| Clostridiales.id.1863          | order  | T2D       | -0.16   | 0.11  | -0.08    | 0.23     | 0.87    | 0.71            | 1.06            | 0.17   | 0.00           |
| Coriobacteriales.id.810        | order  | T2D       | -0.04   | 0.12  | 0.15     | 0.26     | 0.99    | 0.80            | 1.23            | 0.94   | 0.00           |
| Desulfovibrionales.id.3156     | order  | T2D       | 0.17    | 0.12  | 0.00     | 0.31     | 1.16    | 0.93            | 1.45            | 0.19   | 0.00           |

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|                                      |        |     |       |      |       |      |      |      |      |      |      |
|--------------------------------------|--------|-----|-------|------|-------|------|------|------|------|------|------|
| Enterobacteriales.id.3468            | order  | T2D | 0.04  | 0.13 | 0.10  | 0.16 | 1.06 | 0.87 | 1.29 | 0.54 | 0.00 |
| Erysipelotrichales.id.2148           | order  | T2D | -0.09 | 0.12 | -0.28 | 0.28 | 0.89 | 0.71 | 1.10 | 0.28 | 0.00 |
| Gastranaerophilales.id.1591          | order  | T2D | 0.07  | 0.13 | 0.09  | 0.25 | 1.07 | 0.86 | 1.35 | 0.53 | 0.00 |
| Lactobacillales.id.1800              | order  | T2D | 0.20  | 0.13 | 0.22  | 0.18 | 1.23 | 1.01 | 1.50 | 0.04 | 0.00 |
| MollicutesRF9.id.11579               | order  | T2D | -0.04 | 0.12 | -0.10 | 0.35 | 0.95 | 0.76 | 1.20 | 0.67 | 0.00 |
| Pasteurellales.id.3688               | order  | T2D | -0.11 | 0.13 | 0.17  | 0.17 | 0.99 | 0.81 | 1.21 | 0.91 | 0.40 |
| Rhodospirillales.id.2667             | order  | T2D | 0.06  | 0.12 | -0.17 | 0.40 | 1.04 | 0.82 | 1.31 | 0.74 | 0.00 |
| Selenomonadales.id.2165              | order  | T2D | -0.08 | 0.12 | 0.13  | 0.29 | 0.95 | 0.77 | 1.17 | 0.63 | 0.00 |
| Verrucomicrobiales.id.4030           | order  | T2D | 0.07  | 0.12 | -0.10 | 0.26 | 1.04 | 0.85 | 1.29 | 0.68 | 0.00 |
| Acidaminococcaceae.id.2166           | family | T2D | -0.11 | 0.12 | -1.29 | 0.72 | 0.87 | 0.69 | 1.09 | 0.23 | 0.62 |
| Alcaligenaceae.id.2875               | family | T2D | 0.11  | 0.12 | -0.05 | 0.30 | 1.09 | 0.87 | 1.37 | 0.44 | 0.00 |
| Bacteroidaceae.id.917                | family | T2D | 0.08  | 0.13 | -0.54 | 0.36 | 1.01 | 0.80 | 1.28 | 0.93 | 0.61 |
| Bifidobacteriaceae.id.433            | family | T2D | 0.02  | 0.12 | 0.37  | 0.25 | 1.09 | 0.88 | 1.36 | 0.42 | 0.33 |
| Christensenellaceae.id.1866          | family | T2D | -0.24 | 0.11 | -0.06 | 0.35 | 0.80 | 0.65 | 0.99 | 0.04 | 0.00 |
| Clostridiaceae1.id.1869              | family | T2D | -0.88 | 0.14 | 0.07  | 0.26 | 0.51 | 0.41 | 0.65 | 0.00 | 0.91 |
| ClostridialesvadinBB60group.id.11286 | family | T2D | -0.03 | 0.13 | 0.12  | 0.19 | 1.02 | 0.82 | 1.26 | 0.88 | 0.00 |
| Coriobacteriaceae.id.811             | family | T2D | -0.04 | 0.12 | 0.15  | 0.26 | 0.99 | 0.80 | 1.23 | 0.94 | 0.00 |
| Desulfovibrionaceae.id.3169          | family | T2D | 0.17  | 0.12 | -0.01 | 0.31 | 1.16 | 0.93 | 1.45 | 0.19 | 0.00 |
| Enterobacteriaceae.id.3469           | family | T2D | 0.04  | 0.13 | 0.10  | 0.16 | 1.06 | 0.87 | 1.29 | 0.54 | 0.00 |
| Enterococcaceae.id.1828              | family | T2D | 0.02  | 0.10 | -1.27 | 2.42 | 1.02 | 0.84 | 1.25 | 0.83 | 0.00 |
| Erysipelotrichaceae.id.2149          | family | T2D | -0.09 | 0.12 | -0.28 | 0.28 | 0.89 | 0.71 | 1.10 | 0.28 | 0.00 |
| FamilyXIII.id.1957                   | family | T2D | -0.14 | 0.11 | -0.37 | 0.32 | 0.85 | 0.69 | 1.04 | 0.12 | 0.00 |
| Lachnospiraceae.id.1987              | family | T2D | 0.09  | 0.13 | -0.28 | 0.28 | 1.03 | 0.82 | 1.29 | 0.82 | 0.28 |
| Lactobacillaceae.id.1836             | family | T2D | 0.18  | 0.11 | 0.01  | 0.14 | 1.12 | 0.94 | 1.33 | 0.19 | 0.00 |
| Pasteurellaceae.id.3689              | family | T2D | -0.11 | 0.13 | 0.17  | 0.17 | 0.99 | 0.81 | 1.21 | 0.91 | 0.40 |
| Peptococcaceae.id.2024               | family | T2D | -0.15 | 0.12 | -0.45 | 0.56 | 0.85 | 0.67 | 1.08 | 0.18 | 0.00 |
| Peptostreptococcaceae.id.2042        | family | T2D | -0.65 | 0.12 | -0.11 | 0.29 | 0.56 | 0.45 | 0.70 | 0.00 | 0.65 |
| Porphyromonadaceae.id.943            | family | T2D | -0.05 | 0.12 | -0.57 | 0.36 | 0.90 | 0.72 | 1.13 | 0.37 | 0.45 |
| Prevotellaceae.id.960                | family | T2D | 0.03  | 0.12 | -0.31 | 0.45 | 1.00 | 0.80 | 1.26 | 0.98 | 0.00 |
| Rhodospirillaceae.id.2717            | family | T2D | 0.06  | 0.12 | -0.17 | 0.40 | 1.04 | 0.82 | 1.32 | 0.73 | 0.00 |
| Rikenellaceae.id.967                 | family | T2D | -0.04 | 0.12 | 0.07  | 0.28 | 0.98 | 0.79 | 1.22 | 0.86 | 0.00 |
| Ruminococcaceae.id.2050              | family | T2D | -0.10 | 0.11 | 0.33  | 0.29 | 0.95 | 0.78 | 1.16 | 0.63 | 0.47 |

|                             |        |     |      |      |         |          |      |      |      |      |      |
|-----------------------------|--------|-----|------|------|---------|----------|------|------|------|------|------|
| Streptococcaceae.id.1850    | family | T2D | 0.18 | 0.12 | 0.26    | 0.18     | 1.23 | 1.01 | 1.50 | 0.04 | 0.00 |
| Succinivibrionaceae.id.3326 | family | T2D | 0.08 | 0.12 | -412.58 | 39666.32 | 1.08 | 0.86 | 1.35 | 0.51 | 0.00 |

|                                            |        |     |       |      |       |      |      |      |      |      |      |
|--------------------------------------------|--------|-----|-------|------|-------|------|------|------|------|------|------|
| Veillonellaceae.id.2172                    | family | T2D | -0.10 | 0.12 | 0.20  | 0.28 | 0.95 | 0.76 | 1.18 | 0.64 | 0.00 |
| Verrucomicrobiaceae.id.4036                | family | T2D | 0.07  | 0.12 | -0.10 | 0.26 | 1.04 | 0.85 | 1.29 | 0.68 | 0.00 |
| unknownfamily.id.1000001214                | family | T2D | 0.07  | 1.07 | 0.09  | 0.25 | 1.07 | 0.86 | 1.35 | 0.53 | 0.00 |
| unknownfamily.id.1000005471                | family | T2D | -0.04 | 0.96 | -0.10 | 0.35 | 0.95 | 0.76 | 1.20 | 0.67 | 0.00 |
| unknownfamily.id.987                       | family | T2D | -0.13 | 0.88 | -0.83 | 1.18 | 0.87 | 0.68 | 1.12 | 0.28 | 0.00 |
| Bacteroidespectinophilusgroup.id.14371     | genus  | T2D | -0.84 | 0.62 | -0.13 | 0.55 | 0.64 | 0.29 | 1.44 | 0.28 | 0.00 |
| Eubacteriumcoprostanoligenesgroup.id.11375 | genus  | T2D | -0.20 | 0.11 | -0.25 | 0.32 | 0.82 | 0.67 | 0.99 | 0.04 | 0.00 |
| Eubacteriumeligensgroup.id.14372           | genus  | T2D | -0.27 | 0.12 | 0.20  | 0.18 | 0.88 | 0.72 | 1.07 | 0.21 | 0.79 |
| Eubacteriumhalliigroup.id.11338            | genus  | T2D | 0.01  | 0.12 | -0.37 | 0.30 | 0.96 | 0.77 | 1.19 | 0.71 | 0.26 |
| Eubacteriumrectalegroup.id.14374           | genus  | T2D | 0.06  | 0.12 | 0.11  | 0.16 | 1.09 | 0.90 | 1.31 | 0.40 | 0.00 |
| Eubacteriumruminantiumgroup.id.11340       | genus  | T2D | -0.07 | 0.13 | 0.21  | 0.20 | 1.01 | 0.82 | 1.25 | 0.92 | 0.25 |
| Eubacteriumventriosumgroup.id.11341        | genus  | T2D | -0.08 | 0.12 | 0.01  | 0.27 | 0.94 | 0.75 | 1.16 | 0.55 | 0.00 |
| Eubacteriumxylanophilumgroup.id.14375      | genus  | T2D | -0.18 | 0.13 | -0.01 | 0.30 | 0.86 | 0.68 | 1.08 | 0.19 | 0.00 |
| Ruminococcusgauvreauigroup.id.11342        | genus  | T2D | -0.19 | 0.12 | -1.08 | 0.51 | 0.79 | 0.63 | 0.98 | 0.04 | 0.66 |
| Ruminococcusgnavusgroup.id.14376           | genus  | T2D | -0.06 | 0.12 | -0.35 | 0.50 | 0.93 | 0.74 | 1.16 | 0.51 | 0.00 |
| Ruminococcustorquesgroup.id.14377          | genus  | T2D | 0.19  | 0.12 | -0.63 | 0.45 | 1.14 | 0.90 | 1.44 | 0.28 | 0.67 |
| Acidaminococcus.id.2167                    | genus  | T2D | 0.06  | 0.10 | -3.99 | 5.72 | 1.06 | 0.86 | 1.30 | 0.58 | 0.00 |
| Adlercreutzia.id.812                       | genus  | T2D | 0.02  | 0.12 | -0.04 | 0.28 | 1.01 | 0.82 | 1.25 | 0.91 | 0.00 |
| Akkermansia.id.4037                        | genus  | T2D | 0.07  | 0.12 | -0.10 | 0.26 | 1.04 | 0.85 | 1.29 | 0.68 | 0.00 |
| Alistipes.id.968                           | genus  | T2D | 0.03  | 0.12 | 0.00  | 0.30 | 1.02 | 0.82 | 1.28 | 0.83 | 0.00 |
| Alloprevotella.id.961                      | genus  | T2D | -0.05 | 0.13 | -2.12 | 3.72 | 0.95 | 0.74 | 1.23 | 0.71 | 0.00 |
| Anaerostipes.id.1991                       | genus  | T2D | -0.10 | 0.12 | -0.09 | 0.27 | 0.90 | 0.73 | 1.11 | 0.34 | 0.00 |
| Anaerotruncus.id.2054                      | genus  | T2D | -0.20 | 0.12 | -0.11 | 0.33 | 0.83 | 0.67 | 1.03 | 0.08 | 0.00 |
| Bacteroides.id.918                         | genus  | T2D | 0.08  | 0.13 | -0.54 | 0.36 | 1.01 | 0.80 | 1.28 | 0.93 | 0.61 |
| Barnesiella.id.944                         | genus  | T2D | -0.01 | 0.12 | -0.68 | 0.47 | 0.95 | 0.75 | 1.20 | 0.67 | 0.47 |
| Bifidobacterium.id.436                     | genus  | T2D | 0.02  | 0.12 | 0.36  | 0.25 | 1.09 | 0.88 | 1.36 | 0.42 | 0.30 |
| Blautia.id.1992                            | genus  | T2D | 0.21  | 0.13 | -0.56 | 0.36 | 1.13 | 0.89 | 1.43 | 0.32 | 0.75 |
| Butyricicoccus.id.2055                     | genus  | T2D | 0.02  | 0.12 | -0.70 | 0.49 | 0.98 | 0.78 | 1.23 | 0.86 | 0.50 |
| Butyricimonas.id.945                       | genus  | T2D | 0.19  | 0.12 | -0.14 | 0.45 | 1.18 | 0.93 | 1.49 | 0.17 | 0.00 |
| Butyrivibrio.id.1993                       | genus  | T2D | -0.05 | 0.13 | -0.45 | 0.71 | 0.94 | 0.73 | 1.21 | 0.61 | 0.00 |
| Catenibacterium.id.2153                    | genus  | T2D | -0.05 | 0.11 | -1.45 | 1.55 | 0.94 | 0.75 | 1.18 | 0.59 | 0.00 |
| ChristensenellaceaeR7group.id.11283        | genus  | T2D | -0.23 | 0.11 | -0.04 | 0.35 | 0.81 | 0.66 | 1.00 | 0.05 | 0.00 |

|                                  |       |     |       |      |      |      |      |      |      |      |      |
|----------------------------------|-------|-----|-------|------|------|------|------|------|------|------|------|
| Clostridiumsensustricto1.id.1873 | genus | T2D | -0.88 | 0.14 | 0.08 | 0.26 | 0.51 | 0.40 | 0.65 | 0.00 | 0.90 |
| Collinsella.id.815               | genus | T2D | 0.00  | 0.12 | 0.26 | 0.23 | 1.06 | 0.85 | 1.31 | 0.61 | 0.02 |

|                                      |       |     |       |      |         |          |      |      |      |      |      |
|--------------------------------------|-------|-----|-------|------|---------|----------|------|------|------|------|------|
| Coprococcus1.id.11301                | genus | T2D | 0.09  | 0.12 | 0.18    | 0.26     | 1.11 | 0.90 | 1.36 | 0.34 | 0.00 |
| Coprococcus2.id.11302                | genus | T2D | -0.13 | 0.12 | 0.00    | 0.32     | 0.90 | 0.71 | 1.12 | 0.34 | 0.00 |
| Coprococcus3.id.11303                | genus | T2D | 0.07  | 0.12 | -0.44   | 0.35     | 1.01 | 0.81 | 1.27 | 0.90 | 0.47 |
| Desulfovibrio.id.3173                | genus | T2D | 0.06  | 0.12 | -0.13   | 0.37     | 1.04 | 0.83 | 1.31 | 0.71 | 0.00 |
| Dialister.id.2183                    | genus | T2D | -0.07 | 0.12 | 0.24    | 0.27     | 0.98 | 0.79 | 1.23 | 0.89 | 0.11 |
| Dorea.id.1997                        | genus | T2D | -0.11 | 0.11 | -0.09   | 0.29     | 0.90 | 0.73 | 1.10 | 0.29 | 0.00 |
| Eggerthella.id.819                   | genus | T2D | 0.13  | 0.12 | -1.96   | 1.30     | 1.12 | 0.89 | 1.42 | 0.33 | 0.61 |
| Eisenbergiella.id.11304              | genus | T2D | 0.10  | 0.11 | 0.13    | 0.24     | 1.11 | 0.91 | 1.36 | 0.31 | 0.00 |
| Enterococcus.id.1831                 | genus | T2D | 0.01  | 0.10 | -6.24   | 7.70     | 1.01 | 0.83 | 1.23 | 0.93 | 0.00 |
| Enterorhabdus.id.820                 | genus | T2D | 0.07  | 0.12 | -0.27   | 0.38     | 1.04 | 0.83 | 1.30 | 0.74 | 0.00 |
| Erysipelatoclostridium.id.11381      | genus | T2D | -0.05 | 0.12 | 0.19    | 0.17     | 1.03 | 0.85 | 1.24 | 0.80 | 0.22 |
| ErysipelotrichaceaeUCG003.id.11384   | genus | T2D | -0.10 | 0.12 | -0.12   | 0.34     | 0.91 | 0.73 | 1.13 | 0.37 | 0.00 |
| Faecalibacterium.id.2057             | genus | T2D | -0.08 | 0.11 | -0.04   | 0.28     | 0.93 | 0.76 | 1.12 | 0.43 | 0.00 |
| FamilyXIIAD3011group.id.11293        | genus | T2D | -0.06 | 0.12 | -0.80   | 0.50     | 0.90 | 0.72 | 1.13 | 0.38 | 0.51 |
| FamilyXIIICUG001.id.11294            | genus | T2D | -0.09 | 0.12 | -0.05   | 0.28     | 0.92 | 0.74 | 1.14 | 0.46 | 0.00 |
| Fusicatenibacter.id.11305            | genus | T2D | -0.18 | 0.11 | 0.13    | 0.20     | 0.90 | 0.74 | 1.09 | 0.28 | 0.44 |
| Haemophilus.id.3698                  | genus | T2D | -0.11 | 0.13 | 0.16    | 0.17     | 0.99 | 0.81 | 1.21 | 0.92 | 0.37 |
| Holdemanella.id.11393                | genus | T2D | 0.07  | 0.12 | -0.08   | 0.25     | 1.04 | 0.84 | 1.28 | 0.71 | 0.00 |
| Intestinibacter.id.11345             | genus | T2D | -0.70 | 0.13 | 0.06    | 0.23     | 0.60 | 0.48 | 0.76 | 0.00 | 0.88 |
| Intestinimonas.id.2062               | genus | T2D | -0.05 | 0.11 | 0.19    | 0.23     | 1.00 | 0.82 | 1.22 | 0.98 | 0.00 |
| Lachnoclostridium.id.11308           | genus | T2D | 0.03  | 0.12 | -0.19   | 0.22     | 0.98 | 0.80 | 1.21 | 0.86 | 0.00 |
| Lachnospira.id.2004                  | genus | T2D | -0.22 | 0.12 | -0.22   | 0.38     | 0.80 | 0.65 | 1.00 | 0.05 | 0.00 |
| LachnospiraceaeFCS020group.id.11314  | genus | T2D | -0.07 | 0.12 | 0.22    | 0.21     | 1.00 | 0.82 | 1.22 | 0.99 | 0.34 |
| LachnospiraceaeND3007group.id.11317  | genus | T2D | -0.28 | 0.12 | 0.39    | 0.23     | 0.87 | 0.71 | 1.06 | 0.16 | 0.85 |
| LachnospiraceaeNK4A136group.id.11319 | genus | T2D | -0.25 | 0.12 | -0.11   | 0.26     | 0.80 | 0.65 | 0.99 | 0.04 | 0.00 |
| LachnospiraceaeUCG001.id.11321       | genus | T2D | 0.15  | 0.12 | 0.06    | 0.21     | 1.13 | 0.92 | 1.39 | 0.23 | 0.00 |
| LachnospiraceaeUCG004.id.11324       | genus | T2D | -0.01 | 0.12 | -0.61   | 0.55     | 0.97 | 0.76 | 1.22 | 0.78 | 0.13 |
| LachnospiraceaeUCG010.id.11330       | genus | T2D | 0.14  | 0.12 | -0.29   | 0.46     | 1.12 | 0.88 | 1.41 | 0.36 | 0.00 |
| Lactobacillus.id.1837                | genus | T2D | 0.16  | 0.11 | -0.02   | 0.16     | 1.10 | 0.92 | 1.32 | 0.29 | 0.00 |
| Marvinbryantia.id.2005               | genus | T2D | -0.02 | 0.12 | -0.49   | 0.38     | 0.94 | 0.76 | 1.18 | 0.60 | 0.30 |
| Megamonas.id.2184                    | genus | T2D | -0.04 | 0.12 | -798.63 | 67821.78 | 0.96 | 0.75 | 1.21 | 0.71 | 0.00 |
| Megasphaera.id.2185                  | genus | T2D | -0.15 | 0.14 | -0.48   | 0.86     | 0.85 | 0.66 | 1.11 | 0.24 | 0.00 |

|                     |       |     |       |      |       |      |      |      |      |      |      |
|---------------------|-------|-----|-------|------|-------|------|------|------|------|------|------|
| Mitsuokella.id.2186 | genus | T2D | -0.15 | 0.12 | -0.09 | 0.47 | 0.86 | 0.68 | 1.09 | 0.22 | 0.00 |
| Odoribacter.id.952  | genus | T2D | 0.18  | 0.12 | -0.10 | 0.32 | 1.15 | 0.92 | 1.45 | 0.23 | 0.00 |

|                                      |       |     |       |      |         |          |      |      |      |      |      |
|--------------------------------------|-------|-----|-------|------|---------|----------|------|------|------|------|------|
| Olsenella.id.822                     | genus | T2D | 0.07  | 0.12 | -8.29   | 6.71     | 1.07 | 0.84 | 1.35 | 0.58 | 0.36 |
| Oscillospira.id.2064                 | genus | T2D | -0.09 | 0.12 | 0.08    | 0.29     | 0.94 | 0.75 | 1.17 | 0.58 | 0.00 |
| Parabacteroides.id.954               | genus | T2D | -0.06 | 0.13 | -0.52   | 0.37     | 0.90 | 0.71 | 1.13 | 0.37 | 0.30 |
| Paraprevotella.id.962                | genus | T2D | -0.04 | 0.12 | -0.09   | 0.39     | 0.96 | 0.76 | 1.20 | 0.70 | 0.00 |
| Parasutterella.id.2892               | genus | T2D | 0.05  | 0.12 | 0.11    | 0.23     | 1.07 | 0.87 | 1.31 | 0.54 | 0.00 |
| Peptococcus.id.2037                  | genus | T2D | -0.10 | 0.12 | -0.55   | 0.61     | 0.89 | 0.70 | 1.12 | 0.32 | 0.00 |
| Phascolarctobacterium.id.2168        | genus | T2D | -0.11 | 0.12 | -1.07   | 0.65     | 0.87 | 0.69 | 1.09 | 0.23 | 0.52 |
| Prevotella2.id.11180                 | genus | T2D | 0.10  | 0.12 | -369.75 | 32035.52 | 1.11 | 0.88 | 1.40 | 0.39 | 0.00 |
| Prevotella7.id.11182                 | genus | T2D | -0.01 | 0.13 | -0.13   | 0.31     | 0.97 | 0.77 | 1.23 | 0.82 | 0.00 |
| Prevotella9.id.11183                 | genus | T2D | -0.03 | 0.12 | -0.19   | 0.41     | 0.95 | 0.76 | 1.20 | 0.68 | 0.00 |
| PrevotellaceaeNK3B31group.id.11185   | genus | T2D | -0.05 | 0.12 | -0.23   | 0.83     | 0.95 | 0.75 | 1.21 | 0.68 | 0.00 |
| PrevotellaceaeUCG001.id.11186        | genus | T2D | -0.02 | 0.12 | -0.93   | 3.37     | 0.97 | 0.76 | 1.24 | 0.83 | 0.00 |
| RikenellaceaeRC9gutgroup.id.11191    | genus | T2D | -0.06 | 0.12 | 0.21    | 0.18     | 1.02 | 0.84 | 1.25 | 0.83 | 0.30 |
| Romboutsia.id.11347                  | genus | T2D | -0.58 | 0.12 | -0.82   | 0.61     | 0.55 | 0.44 | 0.70 | 0.00 | 0.00 |
| Roseburia.id.2012                    | genus | T2D | -0.03 | 0.11 | -0.49   | 0.36     | 0.93 | 0.75 | 1.15 | 0.50 | 0.30 |
| Ruminiclostridium5.id.11355          | genus | T2D | -0.27 | 0.12 | 0.13    | 0.19     | 0.85 | 0.70 | 1.03 | 0.10 | 0.71 |
| Ruminiclostridium6.id.11356          | genus | T2D | -0.17 | 0.12 | 0.05    | 0.27     | 0.87 | 0.70 | 1.09 | 0.23 | 0.00 |
| Ruminiclostridium9.id.11357          | genus | T2D | -0.04 | 0.12 | -0.16   | 0.27     | 0.95 | 0.76 | 1.17 | 0.61 | 0.00 |
| RuminococcaceaeNK4A214group.id.11358 | genus | T2D | -0.19 | 0.12 | -0.26   | 0.38     | 0.82 | 0.66 | 1.02 | 0.08 | 0.00 |
| RuminococcaceaeUCG002.id.11360       | genus | T2D | -0.08 | 0.12 | -0.07   | 0.33     | 0.92 | 0.74 | 1.15 | 0.46 | 0.00 |
| RuminococcaceaeUCG003.id.11361       | genus | T2D | 0.01  | 0.13 | 0.03    | 0.32     | 1.01 | 0.80 | 1.27 | 0.94 | 0.00 |
| RuminococcaceaeUCG004.id.11362       | genus | T2D | 0.01  | 0.12 | -0.08   | 0.27     | 1.00 | 0.80 | 1.24 | 0.99 | 0.00 |
| RuminococcaceaeUCG005.id.11363       | genus | T2D | -0.13 | 0.12 | -0.10   | 0.31     | 0.89 | 0.71 | 1.10 | 0.27 | 0.00 |
| RuminococcaceaeUCG008.id.11365       | genus | T2D | -0.08 | 0.13 | 0.08    | 0.23     | 0.96 | 0.77 | 1.19 | 0.68 | 0.00 |
| RuminococcaceaeUCG010.id.11367       | genus | T2D | -0.17 | 0.13 | 0.12    | 0.28     | 0.89 | 0.71 | 1.12 | 0.31 | 0.00 |
| RuminococcaceaeUCG013.id.11370       | genus | T2D | -0.13 | 0.12 | -0.33   | 0.28     | 0.86 | 0.69 | 1.06 | 0.15 | 0.00 |
| RuminococcaceaeUCG014.id.11371       | genus | T2D | 0.00  | 0.12 | 0.21    | 0.24     | 1.04 | 0.84 | 1.28 | 0.71 | 0.00 |
| Ruminococcus1.id.11373               | genus | T2D | -0.04 | 0.12 | 0.10    | 0.25     | 0.99 | 0.80 | 1.22 | 0.92 | 0.00 |
| Ruminococcus2.id.11374               | genus | T2D | 0.01  | 0.12 | 0.28    | 0.27     | 1.05 | 0.86 | 1.30 | 0.62 | 0.00 |
| Sellimonas.id.14369                  | genus | T2D | -0.15 | 0.14 | -0.17   | 0.19     | 0.86 | 0.69 | 1.06 | 0.16 | 0.00 |
| Senegalimassilia.id.11160            | genus | T2D | -0.10 | 0.12 | 0.24    | 0.19     | 0.99 | 0.81 | 1.22 | 0.96 | 0.55 |
| Slackia.id.825                       | genus | T2D | -0.20 | 0.13 | -0.40   | 0.40     | 0.81 | 0.64 | 1.02 | 0.07 | 0.00 |

|                         |       |     |      |      |      |      |      |      |      |      |      |
|-------------------------|-------|-----|------|------|------|------|------|------|------|------|------|
| Streptococcus.id.1853   | genus | T2D | 0.18 | 0.12 | 0.26 | 0.18 | 1.23 | 1.01 | 1.50 | 0.04 | 0.00 |
| Subdoligranulum.id.2070 | genus | T2D | 0.00 | 0.12 | 0.34 | 0.23 | 1.07 | 0.87 | 1.31 | 0.52 | 0.44 |



|                            |       |     |       |      |         |          |      |      |      |      |      |
|----------------------------|-------|-----|-------|------|---------|----------|------|------|------|------|------|
| Succiniclasticum.id.2169   | genus | T2D | 0.03  | 0.13 | -295.78 | 37207.61 | 1.03 | 0.79 | 1.34 | 0.82 | 0.00 |
| Sutterella.id.2896         | genus | T2D | 0.07  | 0.13 | -0.86   | 0.77     | 1.04 | 0.82 | 1.33 | 0.74 | 0.29 |
| Terrisporobacter.id.11348  | genus | T2D | -0.43 | 0.14 | 0.19    | 0.13     | 0.90 | 0.75 | 1.09 | 0.27 | 0.91 |
| Turicibacter.id.2162       | genus | T2D | -0.31 | 0.13 | 0.11    | 0.22     | 0.81 | 0.65 | 1.01 | 0.07 | 0.62 |
| Tyzzerella3.id.11335       | genus | T2D | 0.14  | 0.11 | -127.52 | 10056.91 | 1.15 | 0.92 | 1.44 | 0.21 | 0.00 |
| Veillonella.id.2198        | genus | T2D | -0.02 | 0.12 | 0.11    | 0.16     | 1.02 | 0.85 | 1.23 | 0.80 | 0.00 |
| unknowngenus.id.1000000073 | genus | T2D | -0.03 | 0.97 | 0.12    | 0.19     | 1.02 | 0.82 | 1.26 | 0.88 | 0.00 |
| unknowngenus.id.1000001215 | genus | T2D | 0.07  | 1.07 | 0.09    | 0.25     | 1.07 | 0.86 | 1.35 | 0.53 | 0.00 |
| unknowngenus.id.1000005472 | genus | T2D | -0.04 | 0.96 | -0.10   | 0.35     | 0.95 | 0.76 | 1.20 | 0.67 | 0.00 |
| unknowngenus.id.1000005479 | genus | T2D | -0.05 | 0.95 | -0.65   | 0.73     | 0.94 | 0.73 | 1.19 | 0.59 | 0.00 |
| unknowngenus.id.1000013899 | genus | T2D | -0.13 | 0.88 | -0.83   | 1.18     | 0.87 | 0.68 | 1.12 | 0.28 | 0.00 |
| unknowngenus.id.2071       | genus | T2D | -0.18 | 0.84 | 0.00    | 0.22     | 0.88 | 0.71 | 1.09 | 0.23 | 0.00 |
| unknowngenus.id.2755       | genus | T2D | 0.06  | 1.06 | -0.20   | 0.42     | 1.04 | 0.82 | 1.31 | 0.75 | 0.00 |
| unknowngenus.id.826        | genus | T2D | -0.01 | 0.99 | -0.19   | 0.31     | 0.97 | 0.77 | 1.21 | 0.77 | 0.00 |
| unknowngenus.id.964        | genus | T2D | -0.02 | 0.98 | -221.95 | 24315.54 | 0.98 | 0.75 | 1.28 | 0.89 | 0.00 |

| Taxa in RS only                              | Clade  | Phenotype | Beta_RS | Se_RS |
|----------------------------------------------|--------|-----------|---------|-------|
| family.BacteroidalesS247group.id.11173       | family | T2D       | -0.05   | 0.13  |
| family.Veillonellaceae.id.2172               | family | T2D       | -0.10   | 0.12  |
| genus..Bacteroidespectinophilusgroup.id.1437 | family | T2D       | -0.84   | 0.62  |
| genus.Enterobacter.id.3502                   | genus  | T2D       | 0.08    | 0.12  |
| genus.EscherichiaShigella.id.3504            | genus  | T2D       | -0.04   | 0.13  |
| genus..Eubacteriumcoprostanoligenesgroup.id  | genus  | T2D       | -0.20   | 0.11  |
| genus..Eubacteriumeligensgroup.id.14372      | genus  | T2D       | -0.27   | 0.12  |
| genus..Eubacteriumhalliigroup.id.11338       | genus  | T2D       | 0.01    | 0.12  |
| genus..Eubacteriumoxidoreducensgroup.id.11   | genus  | T2D       | -0.02   | 0.12  |
| genus..Eubacteriumxylanophilumgroup.id.143   | genus  | T2D       | -0.18   | 0.13  |
| genus.Hungatella.id.11306                    | genus  | T2D       | -0.01   | 0.13  |
| genus.Klebsiella.id.3507                     | genus  | T2D       | 0.08    | 0.10  |
| genus.LachnospiraceaeNC2004group.id.11316    | genus  | T2D       | -0.22   | 0.12  |

|                                      |       |     |       |      |
|--------------------------------------|-------|-----|-------|------|
| genus.LachnospiraceaeUCG008.id.11328 | genus | T2D | -0.05 | 0.12 |
| genus.unknowngenus.id.1868           | genus | T2D | -0.10 | 0.12 |

| Taxa in LLD only                         | Clade  | Phenotype | Beta_LLD   | Se_LLD      |
|------------------------------------------|--------|-----------|------------|-------------|
| domain.Archaea.id.2                      | Clade  | T2D       | 0.17       | 0.22        |
| phylum.Euryarchaeota.id.55               | domain | T2D       | 0.17       | 0.22        |
| phylum.Lentisphaerae.id.2238             | phylum | T2D       | 0.03       | 0.19        |
| order.Actinomycetales.id.420             | phylum | T2D       | 0.10       | 0.18        |
| order.Mycoplasmatales.id.3946            | order  | T2D       | -0.39      | 53.21       |
| order.NB1.n.id.3953                      | order  | T2D       | 0.12       | 0.17        |
| order.Pseudomonadales.id.3709            | order  | T2D       | -0.27      | 4.82        |
| order.Spirochaetales.id.3870             | order  | T2D       | -18.00     | 1841.03     |
| order.Synergistales.id.3900              | order  | T2D       | -0.58      | 1.54        |
| order.Thermoplasmatales.id.220           | order  | T2D       | 0.19       | 0.10        |
| order.unknownorder.id.1000000003         | order  | T2D       | -0.17      | 0.59        |
| order.Verrucomicrobiales.id.4030         | order  | T2D       | -27.41     | 68.42       |
| order.Victivallales.id.2254              | order  | T2D       | 717.20     | 4624.75     |
| order.Xanthomonadales.id.3786            | order  | T2D       | -632578.86 | 77911496.93 |
| class.Spirochaetes.id.3856               | order  | T2D       | -956376.20 | 97828537.00 |
| class.Synergistia.id.3899                | class  | T2D       | -16550.50  | 43744.66    |
| class.Thermoplasmata.id.210              | class  | T2D       | 23222.28   | 11796.78    |
| family.Actinomycetaceae.id.421           | class  | T2D       | 636.93     | 1111.03     |
| family.BacteroidalesS24.7group.id.11173  | family | T2D       | -416.06    | 469.83      |
| family.Christensenellaceae.id.1866       | family | T2D       | -35.01     | 202.79      |
| family.FamilyXI.id.1936                  | family | T2D       | -5834.52   | 8493.48     |
| family.unknownfamily.id.1000000004       | family | T2D       | -1961.30   | 6964.64     |
| family.unknownfamily.id.1000006161       | family | T2D       | 2624.03    | 3550.43     |
| family.unknownfamily.id.1855             | family | T2D       | 506.51     | 331.01      |
| family.vadinBE97.id.14446                | family | T2D       | -7888.71   | 33513.17    |
| family.Veillonellaceae.id.2172           | family | T2D       | 43.39      | 59.81       |
| family.Xanthomonadaceae.id.3799          | family | T2D       | -632578.86 | 77911496.93 |
| genus..Clostridiuminnocuumgroup.id.14397 | family | T2D       | 335.52     | 949.03      |
| genus..Eubacteriumbrachygroup.id.11296   | family | T2D       | 1848.96    | 873.58      |
| genus.Abiotrophia.id.1803                | genus  | T2D       | -975887.47 | 112721664.6 |
| genus.Actinomyces.id.423                 | genus  | T2D       | -39212.65  | 56207.71    |
| genus.Actinotignum.id.11137              | genus  | T2D       | -826750.05 | 109361350.9 |
| genus.Allisonella.id.2174                | genus  | T2D       | -4193.58   | 6365.41     |



|                                           |       |     |             |             |
|-------------------------------------------|-------|-----|-------------|-------------|
| genus.Arcanobacterium.id.424              | genus | T2D | -969578.65  | 85708848.26 |
| genus.Asaccharobacter.id.813              | genus | T2D | 859.56      | 2358.04     |
| genus.Bilophila.id.3170                   | genus | T2D | 1621.61     | 1835.24     |
| genus.CandidatusMethanogranum.id.11110    | genus | T2D | -816043.57  | 94649879.58 |
| genus.Catenisphaera.id.14395              | genus | T2D | -979626.26  | 86502192.01 |
| genus.Cellulosilyticum.id.1995            | genus | T2D | -918976.00  | 80526402.25 |
| genus.Cetobacterium.id.2209               | genus | T2D | -224661.26  | 25470189.88 |
| genus.Cloacibacillus.id.3908              | genus | T2D | -12663.56   | 38283.89    |
| genus.Coprobaillus.id.2154                | genus | T2D | -6768.62    | 17082.33    |
| genus.CoriobacteriaceaeUCG.002.id.11158   | genus | T2D | -7714.46    | 16344.32    |
| genus.CoriobacteriaceaeUCG.003.id.11159   | genus | T2D | -901700.07  | 94003494.98 |
| genus.Denitrobacterium.id.818             | genus | T2D | 4375.35     | 2627.08     |
| genus.dgA.11gutgroup.id.978               | genus | T2D | -164915.59  | 20376297.83 |
| genus.Dielma.id.11380                     | genus | T2D | -2576.00    | 35410.43    |
| genus.Epulopiscium.id.1998                | genus | T2D | -8406.69    | 18727.22    |
| genus.ErysipelotrichaceaeUCG006.id.11386  | genus | T2D | -938246.56  | 73676190.55 |
| genus.ErysipelotrichaceaeUCG009.id.11389  | genus | T2D | -76702.17   | 8490547.39  |
| genus.Escherichia.Shigella.id.3504        | genus | T2D | 49.71       | 102.98      |
| genus.Eubacterium.id.1932                 | genus | T2D | 3026.60     | 2853.80     |
| genus.Faecalicoccus.id.11391              | genus | T2D | -1008344.10 | 74862785.76 |
| genus.Faecalitalea.id.11392               | genus | T2D | 389.04      | 412.06      |
| genus.Flavonifractor.id.2059              | genus | T2D | -9983.06    | 8626.36     |
| genus.Gardnerella.id.437                  | genus | T2D | -991197.47  | 91596782.21 |
| genus.Gordonibacter.id.821                | genus | T2D | -3216.79    | 3980.14     |
| genus.Hafnia.Obesumbacterium.id.14636     | genus | T2D | 5464.04     | 6963.80     |
| genus.Howardella.id.2000                  | genus | T2D | -14045.62   | 10452.20    |
| genus.LachnospiraceaeNK3A20group.id.11318 | genus | T2D | -58692.31   | 7722398.64  |
| genus.Lactococcus.id.1851                 | genus | T2D | -1238.62    | 3296.06     |
| genus.Lautropia.id.2905                   | genus | T2D | -704124.14  | 97309311.93 |
| genus.Leuconostoc.id.1841                 | genus | T2D | -12611.55   | 13776.11    |
| genus.Methanobrevibacter.id.123           | genus | T2D | 66.48       | 72.36       |
| genus.Methanosphaera.id.124               | genus | T2D | -378.87     | 786.50      |

|                             |       |     |            |             |
|-----------------------------|-------|-----|------------|-------------|
| genus.Mogibacterium.id.1960 | genus | T2D | -4650.00   | 5006.80     |
| genus.Morganella.id.3512    | genus | T2D | -200910.72 | 25470194.81 |

|                                          |       |     |             |              |
|------------------------------------------|-------|-----|-------------|--------------|
| genus.Porphyromonas.id.956               | genus | T2D | -67060.31   | 80424.85     |
| genus.Prevotella1.id.11179               | genus | T2D | -66010.75   | 9870113.56   |
| genus.PrevotellaceaeUCG003.id.11187      | genus | T2D | -838943.84  | 104622861.12 |
| genus.PrevotellaceaeUCG004.id.11188      | genus | T2D | -871625.55  | 113815325.59 |
| genus.Pseudomonas.id.3723                | genus | T2D | -1003764.38 | 75177987.73  |
| genus.Rikenella.id.973                   | genus | T2D | -881182.24  | 116205322.14 |
| genus.RuminococcaceaeNK4A214group.id.113 | genus | T2D | -384.70     | 570.08       |
| genus.RuminococcaceaeUCG005.id.11363     | genus | T2D | -177.05     | 565.10       |
| genus.RuminococcaceaeUCG008.id.11365     | genus | T2D | 211.84      | 636.44       |
| genus.RuminococcaceaeUCG010.id.11367     | genus | T2D | 494.92      | 1164.56      |
| genus.Sarcina.id.1896                    | genus | T2D | -717210.15  | 74568532.44  |
| genus.Solobacterium.id.2161              | genus | T2D | -4975.45    | 7793.50      |
| genus.Staphylococcus.id.1780             | genus | T2D | -1109.94    | 7560.90      |
| genus.Stenotrophomonas.id.3818           | genus | T2D | -15598.26   | 1727470.73   |
| genus.Succinivibrio.id.3331              | genus | T2D | -895534.84  | 80325652.35  |
| genus.Synergistes.id.3913                | genus | T2D | -819843.93  | 74178755.63  |
| genus.Syntrophococcus.id.2016            | genus | T2D | -88186.74   | 8647650.41   |
| genus.Treponema2.id.11577                | genus | T2D | -791767.74  | 107821373.84 |
| genus.Tyzzerella4.id.11336               | genus | T2D | -9763.48    | 28105.36     |
| genus.unknowngenus.id.1000000005         | genus | T2D | -1961.30    | 6964.64      |
| genus.unknowngenus.id.1000027565         | genus | T2D | -7888.71    | 33513.17     |
| genus.unknowngenus.id.1000043796         | genus | T2D | 506.51      | 331.01       |
| genus.unknowngenus.id.1854               | genus | T2D | -1082778.03 | 117792911.74 |
| genus.unknowngenus.id.2163               | genus | T2D | 3043.76     | 2539.31      |
| genus.unknowngenus.id.3332               | genus | T2D | -946963.07  | 107653357.20 |
| genus.unknowngenus.id.441                | genus | T2D | -795.45     | 4893.94      |
| genus.Ureaplasma.id.3951                 | genus | T2D | -148560.76  | 20376295.13  |
| genus.Varibaculum.id.427                 | genus | T2D | 5314.59     | 2616.19      |
| genus.Veillonella.id.2198                | genus | T2D | 959.99      | 1483.28      |
| genus.Weissella.id.1843                  | genus | T2D | 1024.17     | 1608.10      |

**eTable 4.** Associations of  $\alpha$  and  $\beta$  Diversity With Insulin Resistance and Type 2 Diabetes After Additionally Adjusting for Diet Quality and Blood Pressure

|                       | HOMA-IR                  | T2D                      |
|-----------------------|--------------------------|--------------------------|
|                       | $\beta$ (95% CI)         | OR (95% CI)              |
| Shannon index         | -0.05 (-0.08, -0.02)     | 0.85 (0.70, 1.04)        |
| Richness              | -0.06 (-0.10, -0.02)     | 0.89 (0.79, 1.00)        |
| Inverse Simpson index | -0.03 (-0.07, 0.01)      | 0.95 (0.86, 1.05)        |
|                       | R <sup>2</sup> (p value) | R <sup>2</sup> (p value) |
| Bray-Curtis distance  | 0.004 (0.001)            | 0.003 (0.001)            |

$\beta$  coefficients and 95% confidence intervals (CI) were from linear regression models for associations between Shannon index, richness, and Inverse Simpson index with HOMA-IR. OR and 95% CI were from logistical regression models for associations between Shannon index, Richness, and Inverse Simpson with T2D. R<sup>2</sup> and p value were examined using permutation analysis of variance (PERMANOVA, 1,000 permutations) for associations of beta-diversity (Bray-Curtis distance). These analyses were conducted in the Rotterdam Study and adjusted for age, sex, time in mail, Batch, smoking education, physical activity, alcohol intake, energy intake, BMI, lipid-lowering medication, PPI, blood pressure, and diet quality score.

**eTable 5.** Statistically Significant Associations Between Taxa and Insulin Resistance After Additionally Adjusting for Diet Quality and Blood Pressure

| Taxa                                        | HOMA-IR<br>$\beta$ (95% CI) | P values |
|---------------------------------------------|-----------------------------|----------|
| family.ClostridialesvadinBB60group.id.11286 | -0.08 (-0.12, -0.04)        | P<0.0001 |
| family.Christensenellaceae.id.1866          | -0.09 (-0.14, -0.03)        | P<0.0001 |
| genus. ChristensenellaceaeR7group.id.11283  | -0.09 (-0.15, -0.03)        | P<0.0001 |
| genus.RuminococcaceaeUCG.005.id.11363       | -0.07 (-0.11, -0.04)        | P<0.0001 |
| genus.RuminococcaceaeUCG.008.id.11365       | -0.08 (-0.12, -0.04)        | P<0.0001 |
| genus.RuminococcaceaeUCG.010.id.11367       | -0.07 (-0.10, -0.04)        | P<0.0001 |
| genus.RuminococcaceaeNK4A214group.id.11358  | -0.06 (-0.09, -0.03)        | P<0.0001 |

$\beta$  coefficients and 95% CI were calculated using linear regression model among non-diabetic participants in the Rotterdam Study, adjusted for age, sex, time in mail, Batch, alcohol intake, total energy intake, smoking status, physical activity, BMI, PPI, lipid-lowering medication, and education level, diet quality score, and blood pressure. All P values <0.0005 were set for statistical significance. Null associations were observed for other taxa and insulin resistance.



**eTable 6.** Statistically Significant Associations Between Taxa and Type 2 Diabetes After Additionally Adjusting for Diet Quality and Blood Pressure

| Taxa                                     | T2D<br>OR (95% CI) | P values |
|------------------------------------------|--------------------|----------|
| family.Clostridiaceae1.id.1869           | 0.67 (0.59, 0.76)  | P=0.0003 |
| family.Peptostreptococcaceae.id.2042     | 0.74 (0.65, 0.83)  | P<0.0001 |
| genus.Clostridium sensu stricto1.id.1873 | 0.67 (0.58, 0.76)  | P<0.0001 |
| genus.Intestinibacter.id.11345           | 0.74 (0.65, 0.85)  | P<0.0001 |
| genus.Romboutsia.id.11347                | 0.77 (0.68, 0.88)  | P<0.0001 |

OR and 95% CI were calculated using logistic regression model in the Rotterdam Study, adjusted for age, sex, time in mail, Batch, alcohol intake, total energy intake, smoking status, physical activity, BMI, PPI, lipid-lowering medication, and education level, diet quality score, and blood pressure. All P values <0.0005 were set for statistical significance. Null associations were observed for other taxa and T2D.

#### **eMethods.** Supplementary Methods

##### **Collection of gut microbiome data**

Details on microbiome data collection in the Rotterdam Study [1, 2] and the Lifelines-Deep Study [3, 4] are described elsewhere. Briefly, for the Rotterdam Study, participants were requested to collect a stool sample at their home using a Commode Specimen Collection System (Covidien, Mansfield, MA) and feces collection tube (Minigrip Nederland, Lelystad, The Netherlands) and to send it through regular mail to Erasmus MC. Upon arrival, samples were recorded and stored at -20°C. The time each sample was in the mail was recorded.[5], and adjusted for in our analyses. An automated stool DNA isolation kit (Diasorin, Saluggia, Italy) was used to isolate bacterial DNA. In the Rotterdam Study sample, a confounding effect driven by DNA isolation batches was observed and therefore adjusted for in analyses. The V3 and V4 hypervariable regions of the bacterial 16S rRNA gene were amplified and sequenced on the Illumina MiSeq platform. For the Lifelines-Deep Study, the stool samples were picked up from participants' homes by students of University Medical Center Groningen. DNA was isolated with the AllPrep DNA/RNA Mini Kit (Qiagen; cat. #80204). The V4 hypervariable region of the bacterial 16S rRNA gene were amplified and

sequenced on the Illumina MiSeq platform. To decrease domain-dependent bias related to different hypervariable regions between the two cohorts, a direct classification of 16S sequencing reads using a naive Bayesian classifier from the Ribosomal Database Project (RDP2.12), and SILVA 16S database release 128 was used to reconstruct taxonomic composition of studied communities, with binning posterior probability cutoff of 0.8 [5]. More specifically, all 16S libraries were rarefied to 10,000 reads prior to taxonomy binning. Furthermore, index sequences (12 bp) were removed from each read and concatenated to generate a unique index of 24 bp for each read-pair. Spacer and primer sequences were removed using TAGCleaner. Paired reads were merged using PEAR with the following settings: minimum overlap of 10 bp (default) and an average read quality phred-score of 20 over a 30 bp sliding window. Merged reads shorter than 200 bp were discarded. Reads were de-multiplexed using QIIME including extra quality filtering steps: merged reads were truncated before three consecutive low-quality bases; ambiguous bases were not allowed. Chimeric reads were removed using UCHIME. For each sample at average 5-6% of the total reads were removed [5]. We only analyzed taxonomical results using genus and higher taxonomic levels. All additional steps have been standardized across both cohorts, as aforementioned, including sub-sampling to 10,000 reads with fixed seed to allow for replicability, procedures of transformations, and the thresholds set for bacterial taxa to be included in the analysis (any taxon should be present in more than 10% of the cohort's samples). This filtering effectively reduced the total number of tests and also made cross-validation and meta-analysis among the two cohorts possible [3]. As a result, in the Rotterdam Study, the microbiome data contained information on 2 domains, 8 phyla, 15 classes, 18 orders, 33 families, and 126 genera. In the Lifelines-Deep Study, the microbiome data contained 2 domain, 12 phyla, 21 classes, 27 orders, 48 families, and 184 genera (Supplementary Figure 2). We also calculated a diversity (Shannon, richness, and Inverse Simpson indices), and  $\beta$  diversity (Bray-Curtis dissimilarity matrix) at genus level using the R package 'vegan', in both cohorts separately.

## Assessment of covariates

Information on education, smoking status, dietary intake, and physical activity were assessed through interviews and questionnaires. In the RS, physical activity was assessed with the LASA Physical Activity Questionnaire, activities were weighted by their intensity with Metabolic Equivalent of Task (MET)[6] and expressed in MET-hours per week. In the LLD, physical activity was assessed with the Short Questionnaire to assess Health-enhancing physical activity, and a physical activity composition score per week was calculated[7, 8]. To measure dietary intake, a 389-item food frequency questionnaire was used in the RS[9], a 125-item food questionnaire was used in the LLD, from which dietary risk factors (e.g., total energy intake, alcohol intake) were calculated[8]. Height and weight were measured in each study's research centers and body mass index ( $\text{kg/m}^2$ ) was calculated. In both cohorts, information on medication use was obtained from general practitioners, pharmacies' databases, Nationwide Medical Registry, or follow-up examinations[8, 10].

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