

Supplementary Materials

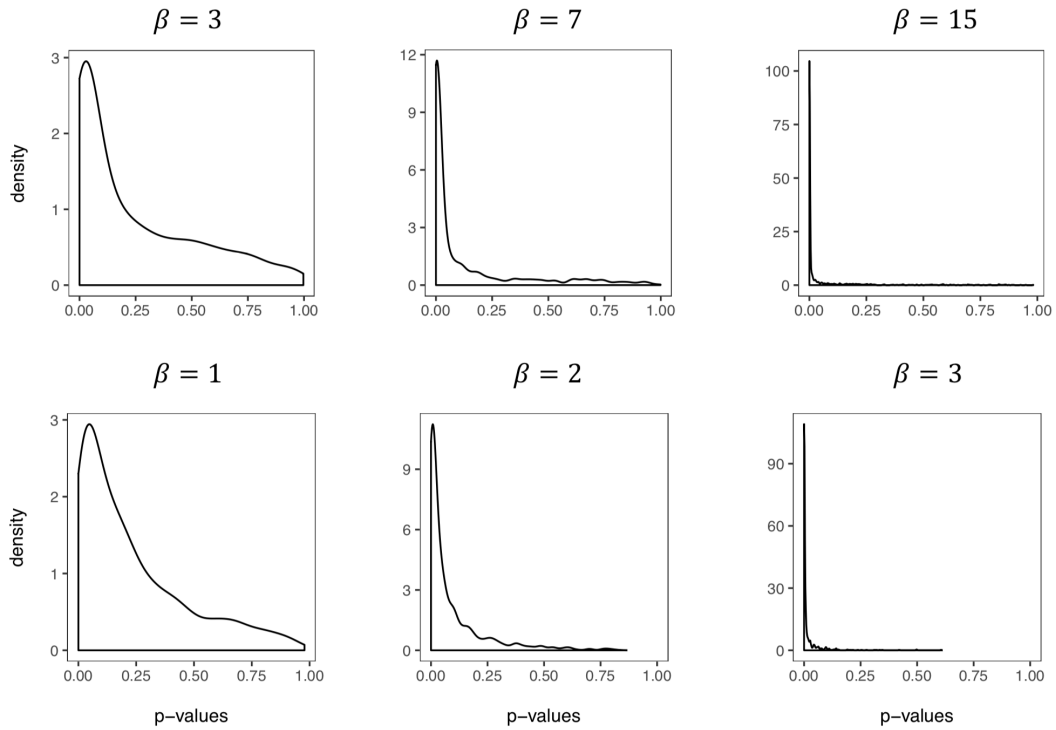


Figure S1: Density functions of p -values generated from the Beta($1/\beta, 1$) distribution (upper panel) and the Gaussian-tailed model (lower panel). The two plots in each column have comparable “height” at around zero but the upper ones always have heavier right tails.

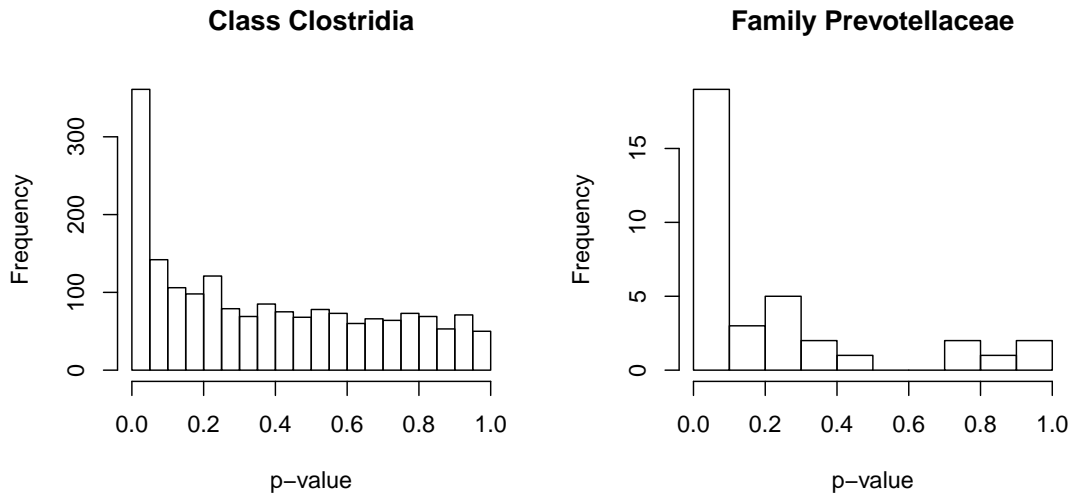


Figure S2: Empirical distributions of p -values for OTUs in class *Clostridia* and family *Prevotellaceae* in the IBD data. These two taxa were detected to be driver taxa by the bottom-up test and contain the most OTUs.

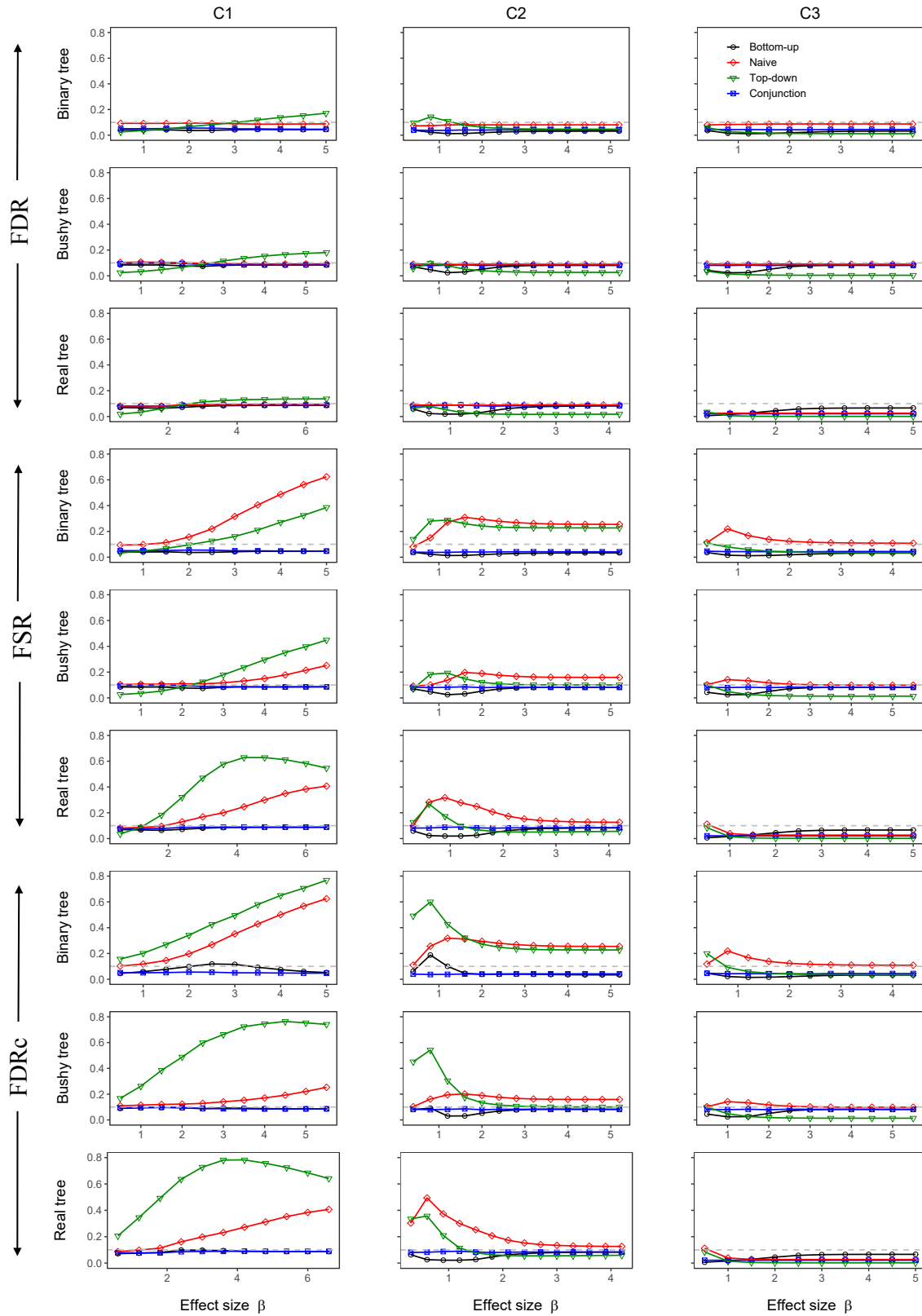


Figure S3: Error rates for testing all nodes in the tree. The non-null p -values at leaf nodes were simulated from the Gaussian-tailed model.

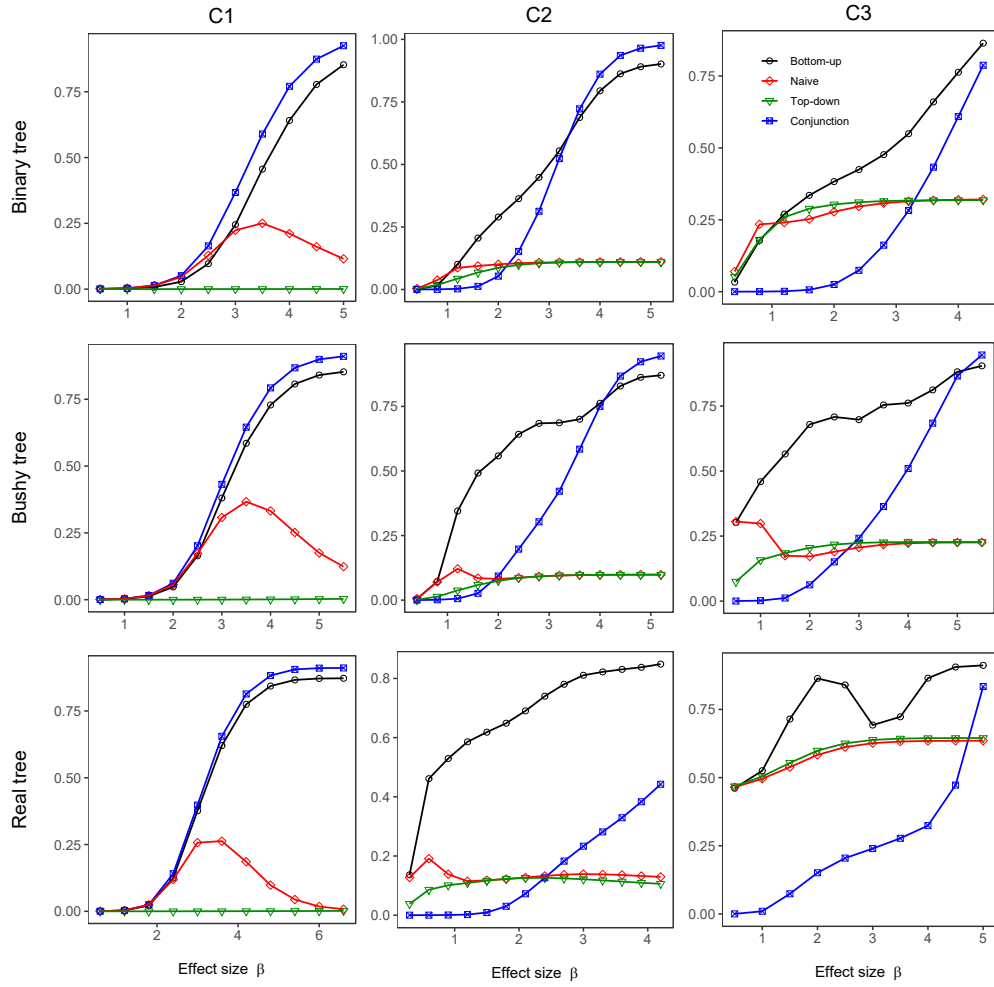


Figure S4: Accuracy (weighted Jaccard similarity) for detecting all associated nodes (including the driver nodes and all of their descendants at all levels). The non-null p -values at leaf nodes were simulated from the Gaussian-tailed model.

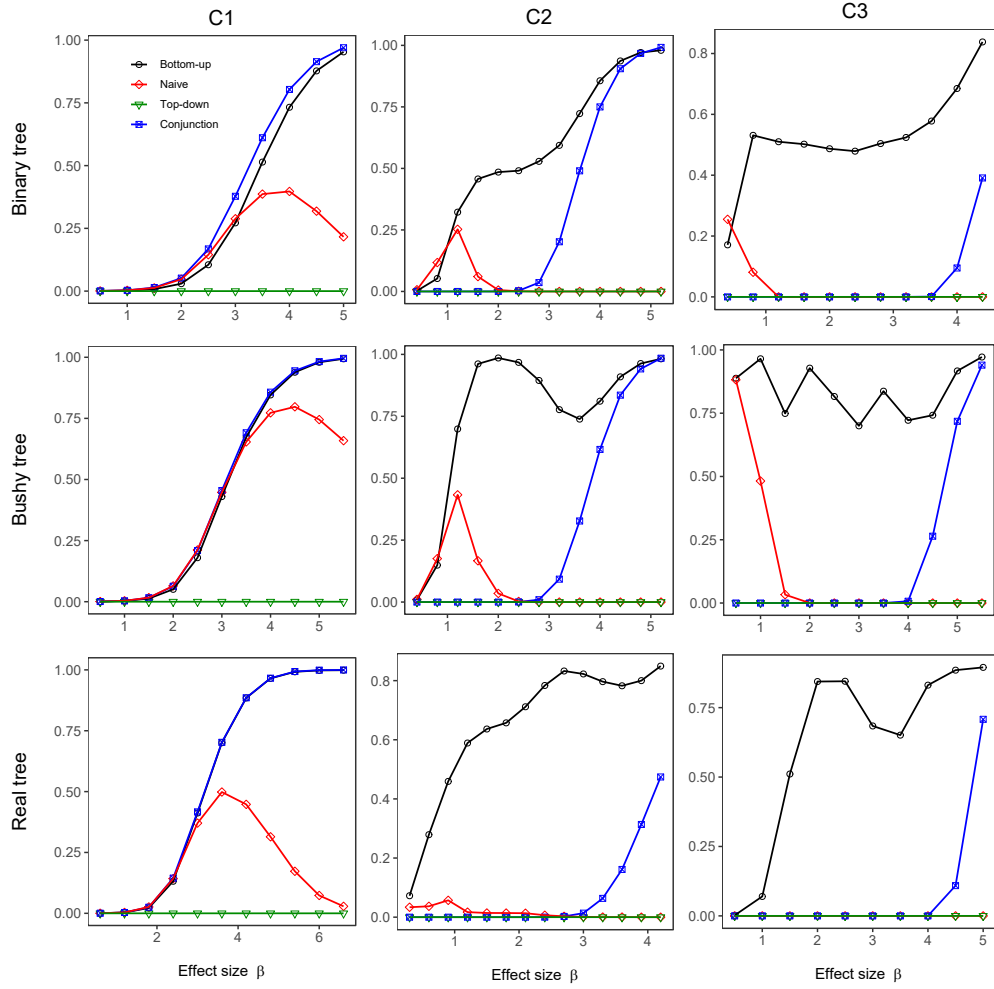


Figure S5: Percentage of driver nodes that were pinpointed. The non-null p -values at leaf nodes were simulated from the Gaussian-tailed model.

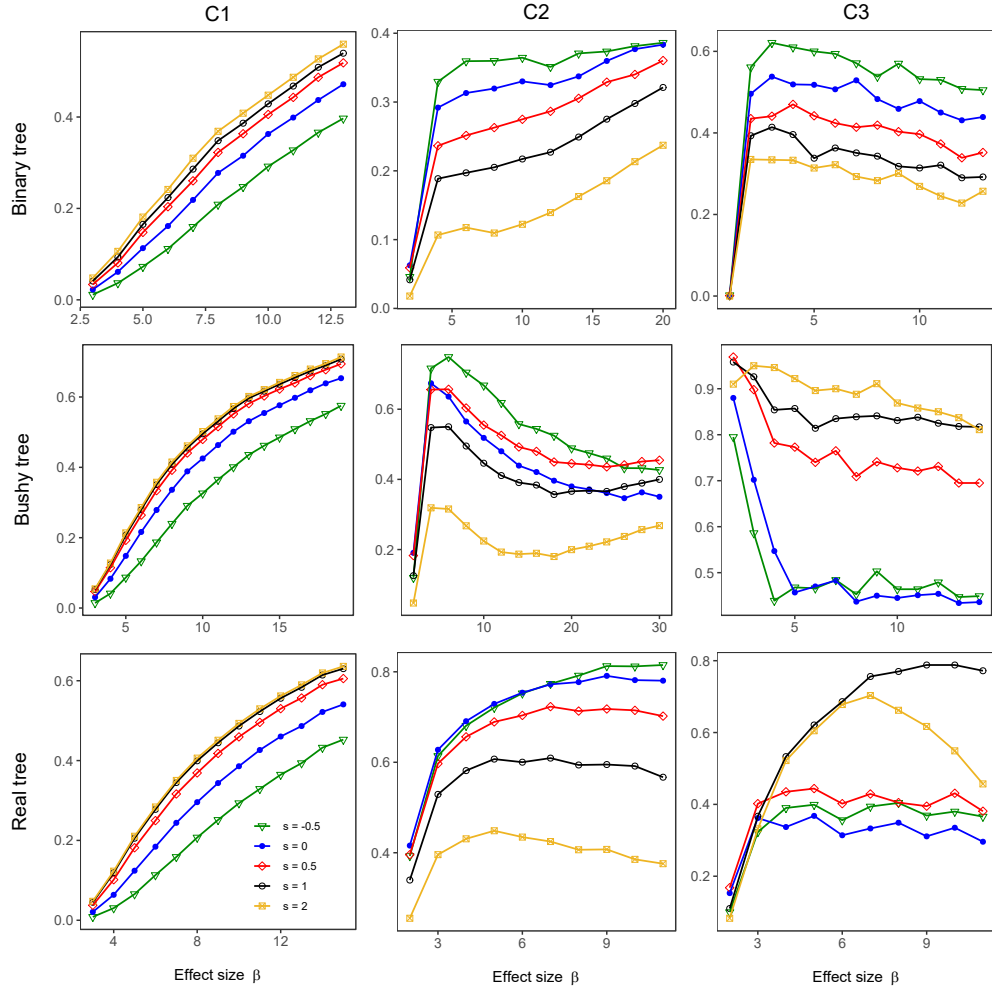


Figure S6: Percentage of driver nodes that were pinpointed by our bottom-up test with different schemes that partition the total error rate q into q_1, \dots, q_L . We considered partitioning schemes that set q_l proportional to n_l^s , where $s \in \{-0.5, 0, 0.5, 1, 2\}$. Thus, $s = 1$ corresponds to the default partition in our bottom-up test. Compared to the default partition, $s = 2$ gives higher q_l to lower levels and $s = -0.5$ gives higher q_l to higher levels. The non-null p -values at leaf nodes were simulated from a $\text{Beta}(1/\beta, 1)$ distribution.

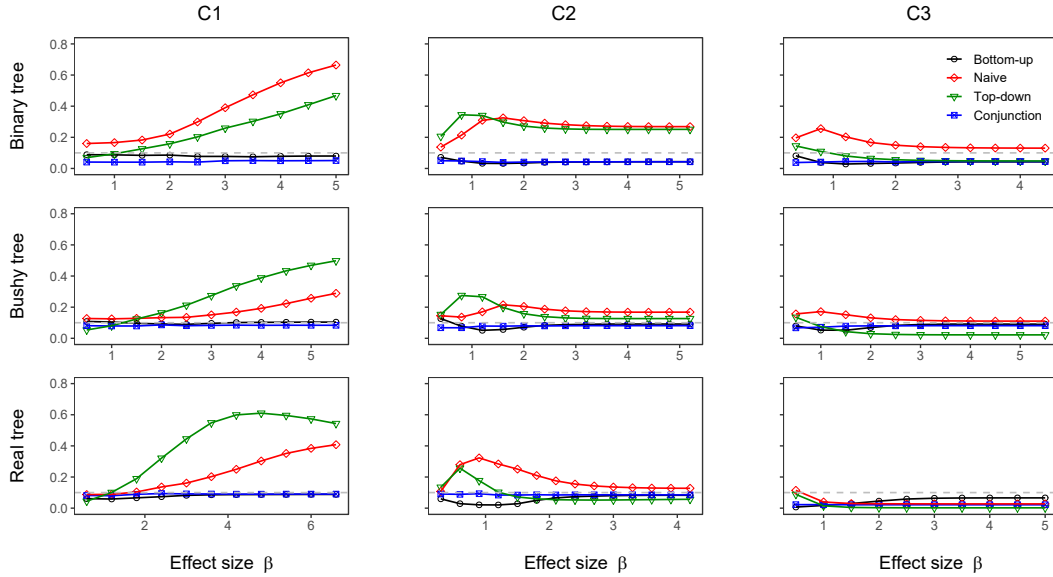


Figure S7: FSR for testing all nodes in the tree where there are weak dependencies among null leaf nodes. The non-null p -values at leaf nodes were simulated from the Gaussian-tailed model. For null OTUs, a vector Z was first drawn from $Z \sim N(0, \Sigma)$, where Σ has 1's for diagonal elements, 0.1 for off-diagonal elements whose row index j and column index k satisfy $|j - k| \leq 4$, and 0 for the remaining off-diagonal elements; then each p -value was converted from each element in Z by $p_i = 1 - \Phi(Z_i)$, where Φ is the standard normal cumulative distribution function. This simulation model resulted in dependent OTUs if they are “adjacent”.

Table S1: Taxa detected by the weighted bottom-up test to be differential abundant between the UC and control groups

Taxon	p-value
<i>p-Actinobacteria</i> ; <i>c-Coriobacteriia</i> #	1.39×10^{-4}
<i>p-Actinobacteria</i> ; <i>c-Coriobacteriia</i> #; <i>o-Coriobacteriales</i>	1.39×10^{-4}
<i>p-Actinobacteria</i> ; <i>c-Coriobacteriia</i> #; <i>o-Coriobacteriales</i> ; <i>f-Coriobacteriaceae</i>	1.39×10^{-4}
<i>p-Actinobacteria</i> ; <i>c-Coriobacteriia</i> #; <i>o-Coriobacteriales</i> ; <i>f-Coriobacteriaceae</i> ; <i>g-Slackia</i>	3.42×10^{-4}
<i>p-Bacteroidetes</i> ; <i>c-Bacteroidia</i> ; <i>o-Bacteroidales</i> ; <i>f-Bacteroidaceae</i> ; <i>g-Bacteroides</i> ; <i>s-ovatus</i> #	3.09×10^{-5}
<i>p-Bacteroidetes</i> ; <i>c-Bacteroidia</i> ; <i>o-Bacteroidales</i> ; <i>f-[Paraprevotellaceae]</i> ; <i>g-[Prevotella]</i> #	3.44×10^{-4}
<i>p-Bacteroidetes</i> ; <i>c-Bacteroidia</i> ; <i>o-Bacteroidales</i> ; <i>f-Prevotellaceae</i> #	1.64×10^{-3}
<i>p-Bacteroidetes</i> ; <i>c-Bacteroidia</i> ; <i>o-Bacteroidales</i> ; <i>f-Prevotellaceae</i> #; <i>g-Prevotella</i>	1.64×10^{-3}
<i>p-Bacteroidetes</i> ; <i>c-Bacteroidia</i> ; <i>o-Bacteroidales</i> ; <i>f-Prevotellaceae</i> #; <i>g-Prevotella</i> ; <i>s-copri</i>	2.82×10^{-10}
<i>p-Bacteroidetes</i> ; <i>c-Bacteroidia</i> ; <i>o-Bacteroidales</i> ; <i>f-S2J-7</i> #	2.08×10^{-3}
<i>p-Cyanobacteria</i> ; <i>c-Chloroplast</i> #	1.73×10^{-4}
<i>p-Cyanobacteria</i> ; <i>c-Chloroplast</i> #; <i>o-Streptophyta</i>	1.73×10^{-4}
<i>p-Firmicutes</i> ; <i>c-Clostridia</i> #	6.35×10^{-5}
<i>p-Firmicutes</i> ; <i>c-Clostridia</i> #; <i>o-Streptophyta</i>	$< 1 \times 10^{-16}$
<i>p-Firmicutes</i> ; <i>c-Clostridia</i> #; <i>o-Clostridiales</i>	5.13×10^{-4}
<i>p-Firmicutes</i> ; <i>c-Clostridia</i> #; <i>o-Clostridiales</i> ; <i>f-Clostridiaceae</i> ; <i>g-Clostridium</i>	1.29×10^{-13}
<i>p-Firmicutes</i> ; <i>c-Clostridia</i> #; <i>o-Clostridiales</i> ; <i>f-Lachnospiraceae</i>	3.20×10^{-7}
<i>p-Firmicutes</i> ; <i>c-Clostridia</i> #; <i>o-Clostridiales</i> ; <i>f-Lachnospiraceae</i> ; <i>g-Coproccocus</i>	$< 1 \times 10^{-16}$
<i>p-Firmicutes</i> ; <i>c-Clostridia</i> #; <i>o-Clostridiales</i> ; <i>f-Ruminococcaceae</i>	9.50×10^{-5}
<i>p-Firmicutes</i> ; <i>c-Clostridia</i> #; <i>o-Clostridiales</i> ; <i>f-Ruminococcaceae</i> ; <i>g-Faecalibacterium</i> ; <i>s-prausnitzii</i>	2.82×10^{-3}
<i>p-Firmicutes</i> ; <i>c-Clostridia</i> #; <i>o-Clostridiales</i> ; <i>f-Ruminococcaceae</i> ; <i>g-Ruminococcus</i>	2.82×10^{-3}
<i>p-Firmicutes</i> ; <i>c-Clostridia</i> #; <i>o-Clostridiales</i> ; <i>f-Veillonellaceae</i> ; <i>g-Veillonella</i> ; <i>s-parvula</i>	1.00×10^{-4}
<i>p-Firmicutes</i> ; <i>c-Erysipelotrichi</i> #	6.01×10^{-4}
<i>p-Firmicutes</i> ; <i>c-Erysipelotrichi</i> #; <i>o-Erysipelotrichales</i>	6.01×10^{-4}
<i>p-Firmicutes</i> ; <i>c-Erysipelotrichi</i> #; <i>o-Erysipelotrichales</i> ; <i>f-Erysipelotrichaceae</i>	6.01×10^{-4}
<i>p-Firmicutes</i> ; <i>c-Erysipelotrichi</i> #; <i>o-Erysipelotrichales</i> ; <i>f-Erysipelotrichaceae</i> ; <i>g-cc-115</i>	2.80×10^{-3}
<i>p-Proteobacteria</i> ; <i>c-Gammaproteobacteria</i> ; <i>o-Enterobacteriales</i> ; <i>f-Enterobacteriaceae</i> ; <i>g-Morganella</i> #	3.09×10^{-3}
<i>p-Proteobacteria</i> ; <i>c-Gammaproteobacteria</i> ; <i>o-Enterobacteriales</i> ; <i>f-Enterobacteriaceae</i> ; <i>g-Enterobacter</i> ; <i>s-radicincitams</i> #	2.61×10^{-4}
<i>p-Tenericutes</i> ; <i>c-RF3</i> #	4.25×10^{-3}
<i>p-Verrucomicrobia</i> #	1.25×10^{-3}
<i>p-Verrucomicrobia</i> #; <i>c-Verrucomicrobiae</i>	1.25×10^{-3}
<i>p-Verrucomicrobia</i> #; <i>c-Verrucomicrobiae</i> ; <i>o-Verrucomicrobiales</i>	1.25×10^{-3}
<i>p-Verrucomicrobia</i> #; <i>c-Verrucomicrobiae</i> ; <i>o-Verrucomicrobiales</i> ; <i>f-Verrucomicrobiaceae</i>	1.25×10^{-3}
<i>p-Verrucomicrobia</i> #; <i>c-Verrucomicrobiae</i> ; <i>o-Verrucomicrobiales</i> ; <i>f-Verrucomicrobiaceae</i> ; <i>g-Akkermansia</i>	1.25×10^{-3}
<i>p-Verrucomicrobia</i> #; <i>c-Verrucomicrobiae</i> ; <i>o-Verrucomicrobiales</i> ; <i>f-Verrucomicrobiaceae</i> ; <i>g-Akkermansia</i> ; <i>s-muciniphila</i>	1.25×10^{-3}

NOTE: The detected driver taxa are marked with "#". Kingdom *Bacteria* is omitted from the taxon names.