

Table S1. List of ASVs detected with mean relative abundances (%) over 0.1% in the group not exposed to antibiotics (n=27).

ASV name	Not exposed (mean Relative Abundance %)	Not exposed (sd)
<i>ASV1_Moraxella</i>	17.40	22.87
<i>ASV2_Streptococcus</i>	17.15	22.54
<i>ASV10_Haemophilus_influenzae</i>	8.53	18.67
<i>ASV7_Moraxella</i>	5.75	7.52
<i>ASV11_Streptococcus</i>	5.51	7.24
<i>ASV5_Moraxella_nonliquefaciens</i>	5.14	14.13
<i>ASV26_Haemophilus</i>	4.27	14.33
<i>ASV4_Haemophilus</i>	2.74	8.60
<i>ASV51_Streptococcus_pneumoniae</i>	2.46	9.73
<i>ASV30_Haemophilus</i>	2.34	4.91
<i>ASV3_Streptococcus</i>	1.82	5.16
<i>ASV13_Moraxella</i>	1.48	4.29
<i>ASV699_Neisseria</i>	1.26	6.56
<i>ASV5408_Haemophilus</i>	1.20	4.14
<i>ASV9_Haemophilus</i>	1.15	5.75
<i>ASV16_Haemophilus_influenzae</i>	0.93	2.76
<i>ASV9291_Streptococcus</i>	0.90	3.69
<i>ASV1146_Phyllobacterium</i>	0.88	4.55
<i>ASV6_Dolosigranulum_pigrum</i>	0.84	2.37
<i>ASV19_Moraxella</i>	0.80	3.89
<i>ASV14_Haemophilus</i>	0.61	1.82
<i>ASV5415_Streptococcus</i>	0.61	3.16
<i>ASV8641_Moraxella_nonliquefaciens</i>	0.56	2.91
<i>ASV8_Moraxella_lincolnii</i>	0.54	2.01
<i>ASV78_Haemophilus_influenzae</i>	0.51	2.27
<i>ASV34_Haemophilus_influenzae</i>	0.44	1.47
<i>ASV393_Neisseria</i>	0.41	2.12
<i>ASV29_Haemophilus</i>	0.39	1.98
<i>ASV22_Streptococcus_pneumoniae</i>	0.39	2.01
<i>ASV31_Haemophilus_influenzae</i>	0.38	1.93
<i>ASV12_Streptococcus</i>	0.37	1.38
<i>ASV102_Neisseria</i>	0.34	1.65
<i>ASV37_Staphylococcus</i>	0.34	1.09
<i>ASV23_Corynebacterium</i>	0.33	0.90
<i>ASV57_Veillonella_dispar</i>	0.32	0.83
<i>ASV5429_Neisseria</i>	0.31	1.61
<i>ASV1117_Haemophilus_haemolyticus</i>	0.30	1.54
<i>ASV258_Haemophilus</i>	0.30	1.54
<i>ASV64_Granulicatella</i>	0.27	0.77
<i>ASV47_Prevotella_melaninogenica</i>	0.26	0.65
<i>ASV17_Dolosigranulum</i>	0.26	0.81
<i>ASV18_Staphylococcus</i>	0.26	1.07
<i>ASV118_Haemophilus_parainfluenzae</i>	0.20	0.96
<i>ASV85_Streptococcus_peroris</i>	0.19	0.93

<i>ASV94_Streptococcus_salivarius</i>	0.19	0.97
<i>ASV271_Streptococcus_sanguinis</i>	0.19	0.93
<i>ASV121_Veillonella</i>	0.17	0.63
<i>ASV8638_Haemophilus</i>	0.16	0.58
<i>ASV606_Caulobacter</i>	0.16	0.82
<i>ASV114_Alloprevotella</i>	0.15	0.76
<i>ASV89_Alloprevotella</i>	0.12	0.43
<i>ASV21_Moraxella</i>	0.12	0.63
<i>ASV260_Veillonella</i>	0.12	0.46
<i>ASV197_Fusobacterium</i>	0.11	0.53
<i>ASV46_Staphylococcus</i>	0.10	0.27
<i>ASV42_Gemella</i>	0.10	0.35
<i>ASV109_Moraxella</i>	0.10	0.53

Abbreviations: ASV; Amplicon Sequence Variant. SD; Standard Deviation.

Table S2. List of ASVs detected with mean relative abundances (%) over 0.1% in the group exposed to antibiotics.

ASV name	Exposed (mean Relative Abundance %)	Exposed (sd)
<i>ASV3_Streptococcus</i>	9.30	17.33
<i>ASV2_Streptococcus</i>	8.54	18.38
<i>ASV1_Moraxella</i>	6.54	13.29
<i>ASV4_Haemophilus</i>	4.18	9.76
<i>ASV10_Haemophilus_influenzae</i>	3.60	12.18
<i>ASV18_Staphylococcus</i>	3.11	8.80
<i>ASV22_Streptococcus_pneumoniae</i>	3.07	10.82
<i>ASV11_Streptococcus</i>	2.61	5.58
<i>ASV7_Moraxella</i>	2.36	4.76
<i>ASV12_Streptococcus</i>	2.32	4.51
<i>ASV37_Staphylococcus</i>	1.95	5.61
<i>ASV87_Streptococcus</i>	1.67	10.35
<i>ASV6_Dolosigranulum_pigrum</i>	1.42	4.13
<i>ASV5_Moraxella_nonliquefaciens</i>	1.36	4.77
<i>ASV23_Corynebacterium</i>	1.29	3.20
<i>ASV16_Haemophilus_influenzae</i>	1.26	4.03
<i>ASV15_Chryseobacterium</i>	1.22	8.98
<i>ASV608_Moraxella</i>	1.21	8.89
<i>ASV14_Haemophilus</i>	1.19	2.93
<i>ASV30_Haemophilus</i>	1.13	3.97
<i>ASV43_Staphylococcus</i>	0.97	2.75
<i>ASV28_Delftia</i>	0.96	6.70
<i>ASV85_Streptococcus_peroris</i>	0.95	5.47
<i>ASV57_Veillonella_dispar</i>	0.93	2.15
<i>ASV9_Haemophilus</i>	0.84	2.95

ASV27_ <i>Streptobacillus_hongkongensis</i>	0.76	5.10
ASV183_ <i>Mycoplasma_pneumoniae</i>	0.73	5.38
ASV46_ <i>Staphylococcus</i>	0.66	3.17
ASV58_ <i>Pantoea</i>	0.66	4.83
ASV5411_ <i>Moraxella</i>	0.65	4.78
ASV94_ <i>Streptococcus_salivarius</i>	0.62	2.12
ASV47_ <i>Prevotella_melaninogenica</i>	0.60	1.44
ASV1610_ <i>Peptoniphilus_gorbachii</i>	0.56	4.14
ASV35_ <i>Chryseobacterium_gleum</i>	0.56	4.15
ASV5418_ <i>Staphylococcus</i>	0.56	1.83
ASV8_ <i>Moraxella_lincolnii</i>	0.49	2.07
ASV5410_ <i>Streptococcus</i>	0.47	2.49
ASV78_ <i>Haemophilus_influenzae</i>	0.47	1.86
ASV5971_ <i>Pseudomonas</i>	0.42	1.53
ASV17_ <i>Dolosigranulum</i>	0.40	1.36
ASV121_ <i>Veillonella</i>	0.40	1.70
ASV5407_ <i>Moraxella</i>	0.39	2.88
ASV64_ <i>Granulicatella</i>	0.37	0.66
ASV13_ <i>Moraxella</i>	0.36	1.12
ASV8638_ <i>Haemophilus</i>	0.34	1.53
ASV522_ <i>Rothia_mucilaginosa</i>	0.34	2.17
ASV109_ <i>Moraxella</i>	0.33	2.45
ASV29_ <i>Haemophilus</i>	0.33	1.23
ASV9299_ <i>Streptococcus</i>	0.33	1.63
ASV86_ <i>Prevotella_nanceiensis</i>	0.31	1.87
ASV40_ <i>Chryseobacterium</i>	0.31	2.27
ASV50_ <i>Acinetobacter_junii</i>	0.30	2.18
ASV2154_ <i>Haemophilus_influenzae</i>	0.30	2.11
ASV5420_ <i>Moraxella</i>	0.27	2.02
ASV5436_ <i>Porphyromonas</i>	0.26	1.46
ASV75_ <i>Lautropia_mirabilis</i>	0.26	1.52
ASV54_ <i>Dolosigranulum</i>	0.26	1.84
ASV49_ <i>Lachnospiraceae</i>	0.25	1.82
ASV62_ <i>Delftia</i>	0.23	1.62
ASV95_ <i>Dolosigranulum</i>	0.22	1.64
ASV53_ <i>Veillonella</i>	0.22	0.95
ASV236_ <i>Snodgrassella</i>	0.22	1.04
ASV124_ <i>Abiotrophia_defectiva</i>	0.22	0.63
ASV554_ <i>Fusobacterium_necrophorum</i>	0.22	1.58
ASV491_ <i>Mycoplasma</i>	0.20	1.48
ASV60_ <i>Acinetobacter</i>	0.20	1.47
ASV9298_ <i>Streptococcus</i>	0.20	1.17
ASV80_ <i>Kingella</i>	0.20	1.41
ASV38_ <i>Alloprevotella</i>	0.19	0.71
ASV144_ <i>Pantoea</i>	0.18	1.34
ASV88_ <i>Corynebacterium</i>	0.18	0.40
ASV626_ <i>Corynebacterium</i>	0.18	0.98
ASV26_ <i>Haemophilus</i>	0.18	0.79
ASV9289_ <i>Corynebacterium</i>	0.18	0.83
ASV697_ <i>Staphylococcus_hominis</i>	0.16	0.83

<i>ASV25_Haemophilus_influenzae</i>	0.16	1.20
<i>ASV5444_Peptoniphilus</i>	0.16	1.20
<i>ASV34_Haemophilus_influenzae</i>	0.16	1.19
<i>ASV475_Prevotella</i>	0.16	1.14
<i>ASV166_Enterobacteriaceae</i>	0.16	1.15
<i>ASV103_Streptophyta</i>	0.15	0.89
<i>ASV5428_Haemophilus</i>	0.15	1.11
<i>ASV265_Staphylococcus_epidermidis</i>	0.15	0.69
<i>ASV100_Porphyrromonas</i>	0.14	0.48
<i>ASV5423_Haemophilus</i>	0.14	1.03
<i>ASV9295_Haemophilus</i>	0.14	1.01
<i>ASV31_Haemophilus_influenzae</i>	0.13	0.68
<i>ASV9312_Staphylococcus</i>	0.13	0.97
<i>ASV2294_Staphylococcus</i>	0.13	0.71
<i>ASV9297_Streptobacillus</i>	0.13	0.96
<i>ASV150_Oribacterium_sinus</i>	0.13	0.83
<i>ASV2126_Haemophilus_influenzae</i>	0.13	0.95
<i>ASV73_Acinetobacter</i>	0.13	0.74
<i>ASV98_Acidovorax</i>	0.12	0.46
<i>ASV111_Veillonella</i>	0.12	0.79
<i>ASV118_Haemophilus_parainfluenzae</i>	0.12	0.30
<i>ASV167_Porphyrromonas</i>	0.12	0.60
<i>ASV374_Streptobacillus</i>	0.12	0.81
<i>ASV247_Staphylococcus</i>	0.12	0.51
<i>ASV1299_Sphingomonas</i>	0.11	0.30
<i>ASV9294_Haemophilus</i>	0.11	0.82
<i>ASV546_Mycoplasma</i>	0.11	0.83
<i>ASV102_Neisseria</i>	0.11	0.39
<i>ASV188_Staphylococcus_hominis</i>	0.11	0.42
<i>ASV257_Rothia_mucilaginosa</i>	0.11	0.50
<i>ASV114_Alloprevotella</i>	0.11	0.79
<i>ASV89_Alloprevotella</i>	0.11	0.24
<i>ASV130_Veillonella</i>	0.10	0.26
<i>ASV32_Haemophilus_influenzae</i>	0.10	0.76
<i>ASV728_Neisseria</i>	0.10	0.73
<i>ASV9305_Veillonella</i>	0.10	0.43
<i>ASV5409_Moraxella</i>	0.10	0.74

Abbreviations: ASV; Amplicon Sequence Variant. SD; Standard Deviation.

Figure S1. Phylogenetic tree of streptococcal type-strains. Phylogenetic tree showing the positions of main streptococcal ASVs detected in our study (ASV2, ASV3, ASV11 and ASV12) relative to other type-strains within the genus *Streptococcus*. The tree was reconstructed by the maximum-likelihood method based on V3-V4 region of 16S rRNA gene sequences. The cell collection precedence and their corresponding GenBank accession numbers for 16S rRNA genes are included for each type-strain.

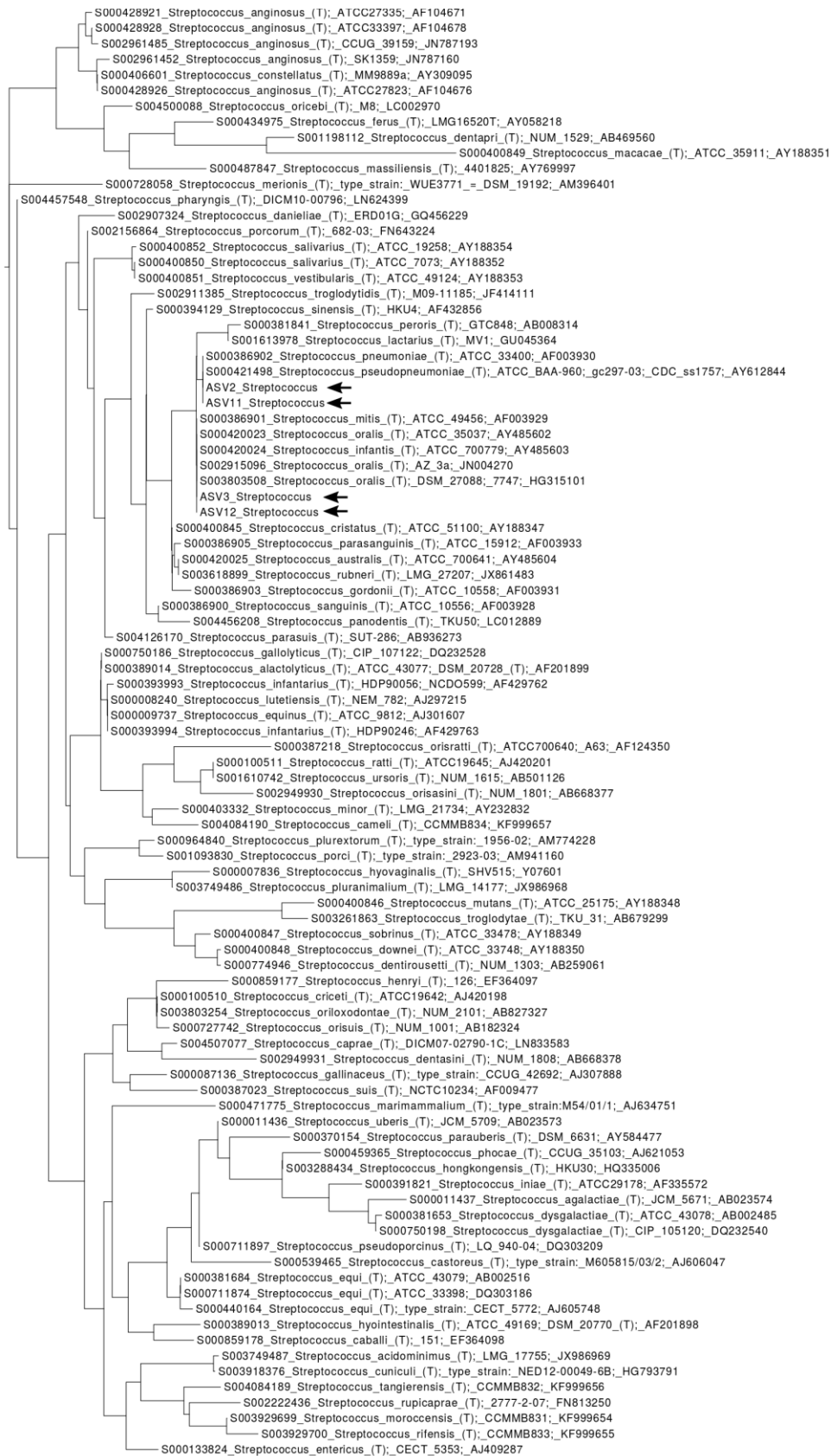


Figure S2. Classification of children with IPD according to antibiotic-exposure using a Random Forest model based on nasopharyngeal microbiota composition at the genus level. The 16S rRNA data was merged at the genus level and all 344 genera detected were included as explanatory variables in the model. Confounding variables including age, gender, seasonality, vaccination, ICU admission, and length of hospital stay were also included in the model as copredictors. **A)** ROC curve showing the performance of the RF model for patient's classification using relative abundances of bacterial genera and confounding variables. **B)** Barplot showing top 25 most important features to class separation according to Mean Decrease Accuracy score (confounding variables were not found among the top important features). Color-coding shows directionality of the association for each of the 25 top features to either the not-exposed (yellow) or ATB-exposed (blue) group based on a post-hoc analyses with cliff's delta estimation of the effect size. In addition, a heatmap displaying relative abundance (%) of these top 25 features across samples is shown at the right. Each column represents a sample, while each row represents a different feature. In the x axis, samples are split by group and ordered according to hierarchical clustering using a Bray-Curtis dissimilarity measure.

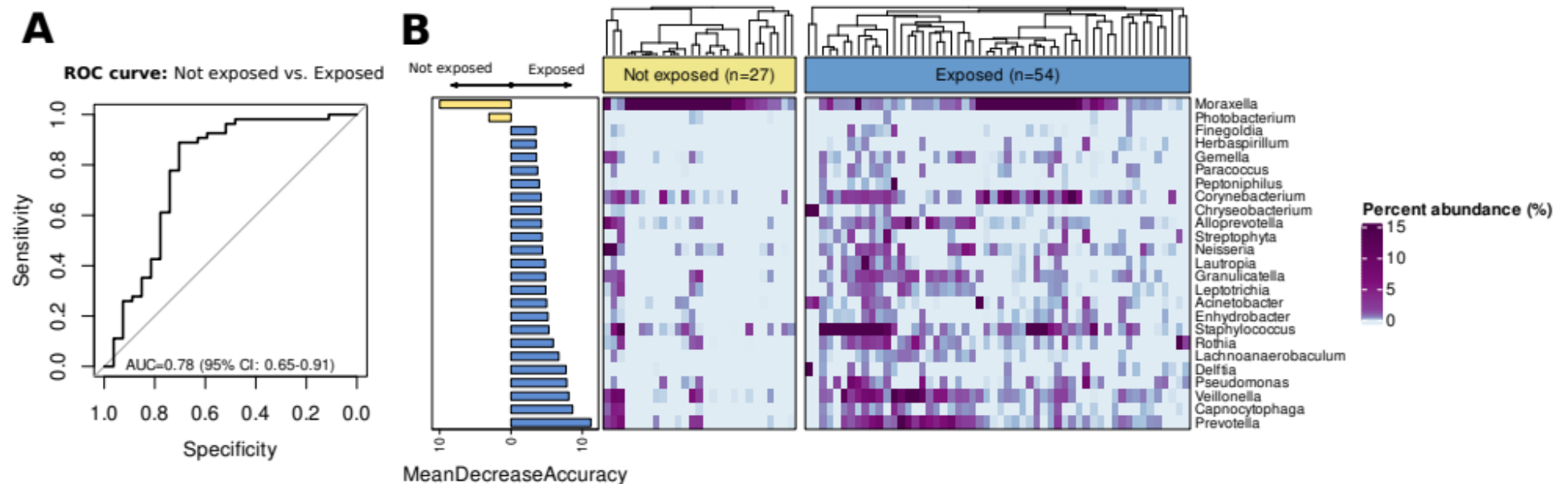


Figure S3. Differential ranking analysis with Songbird. Samples from the group of patients with IPD exposed to antibiotics were utilized as the reference to infer differentially abundant ASVs according to antibiotic exposure. The ASVs with the highest differentials (differentials >1) are colored according to the direction of the association; features colored in blue are more abundant in samples from patients exposed to antibiotics, while features colored in yellow are more abundant in samples from patients not exposed to antibiotics. Differential ranking analysis was performed with the Songbird standalone tool (<https://github.com/biocore/songbird>) using default parameters and results were plotted with ggplot2.

