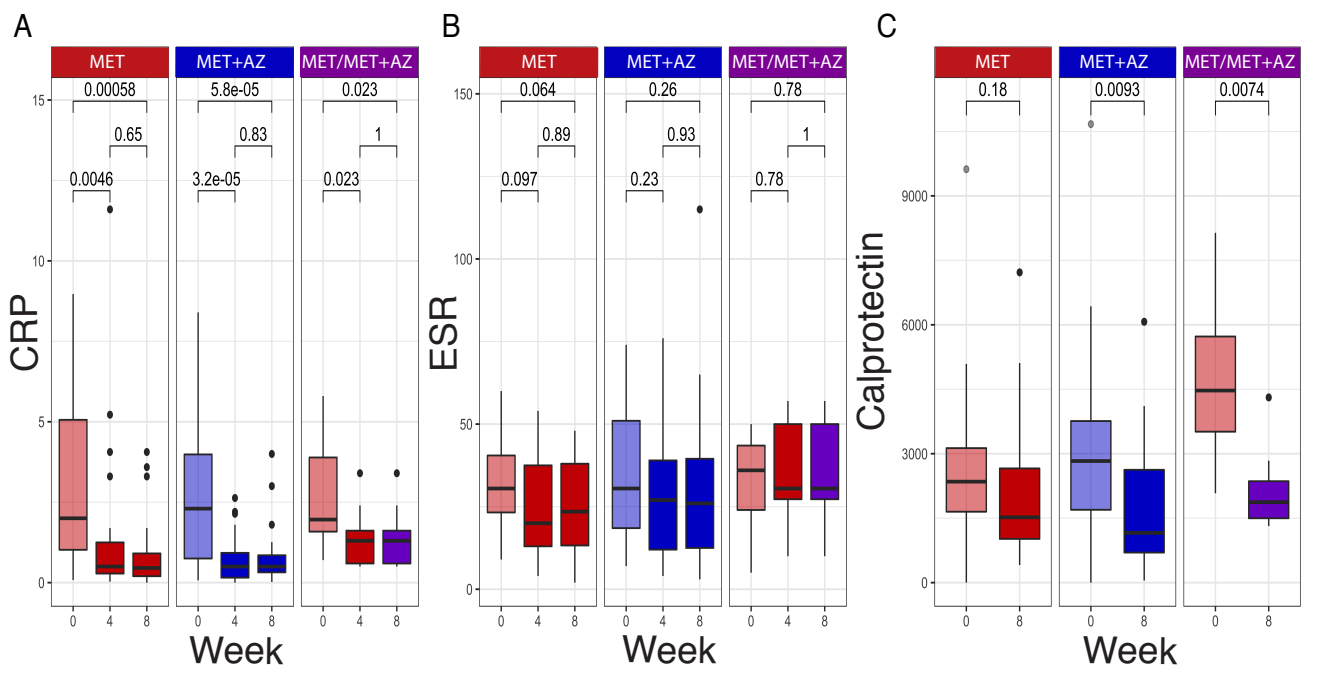
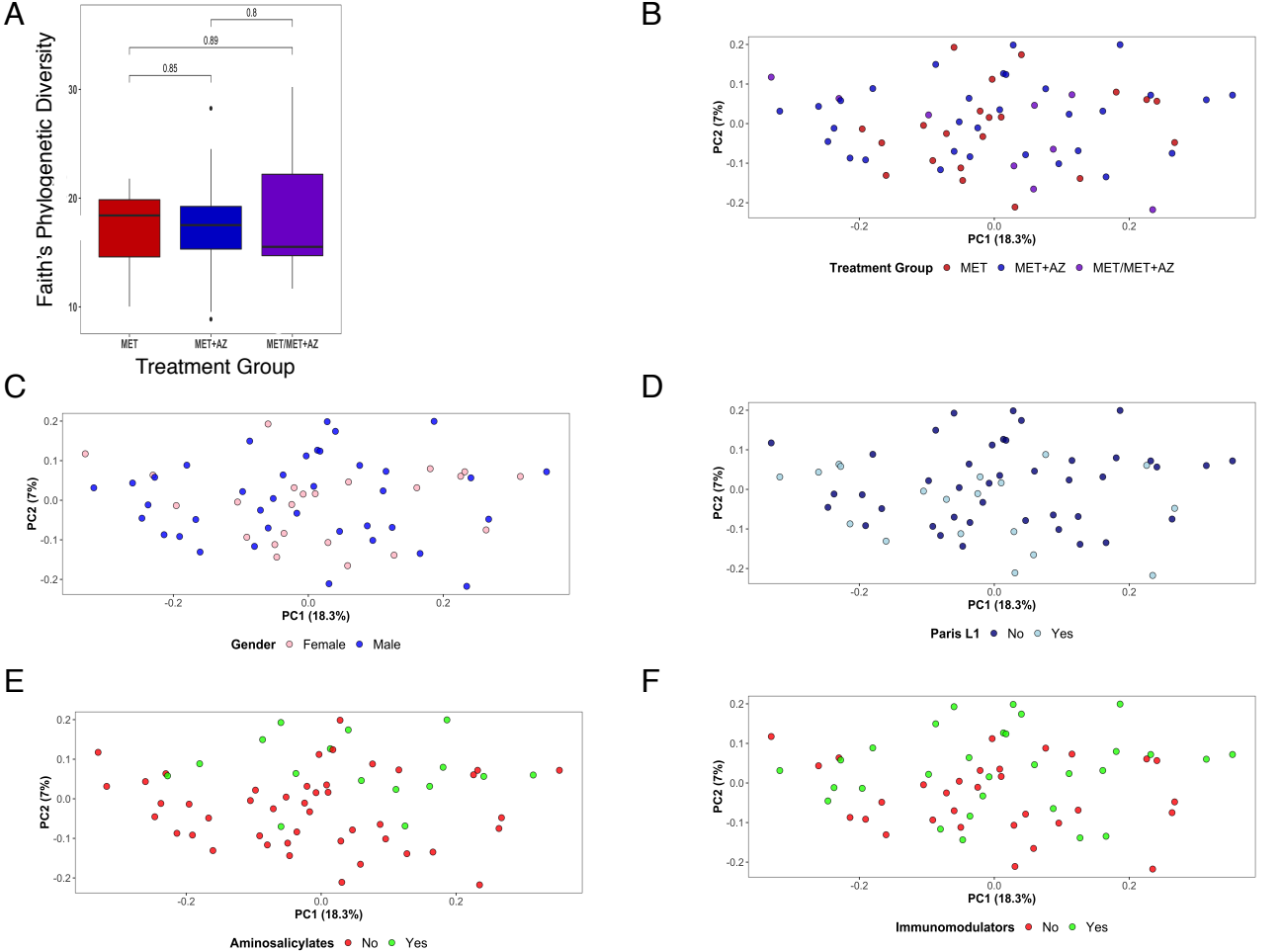
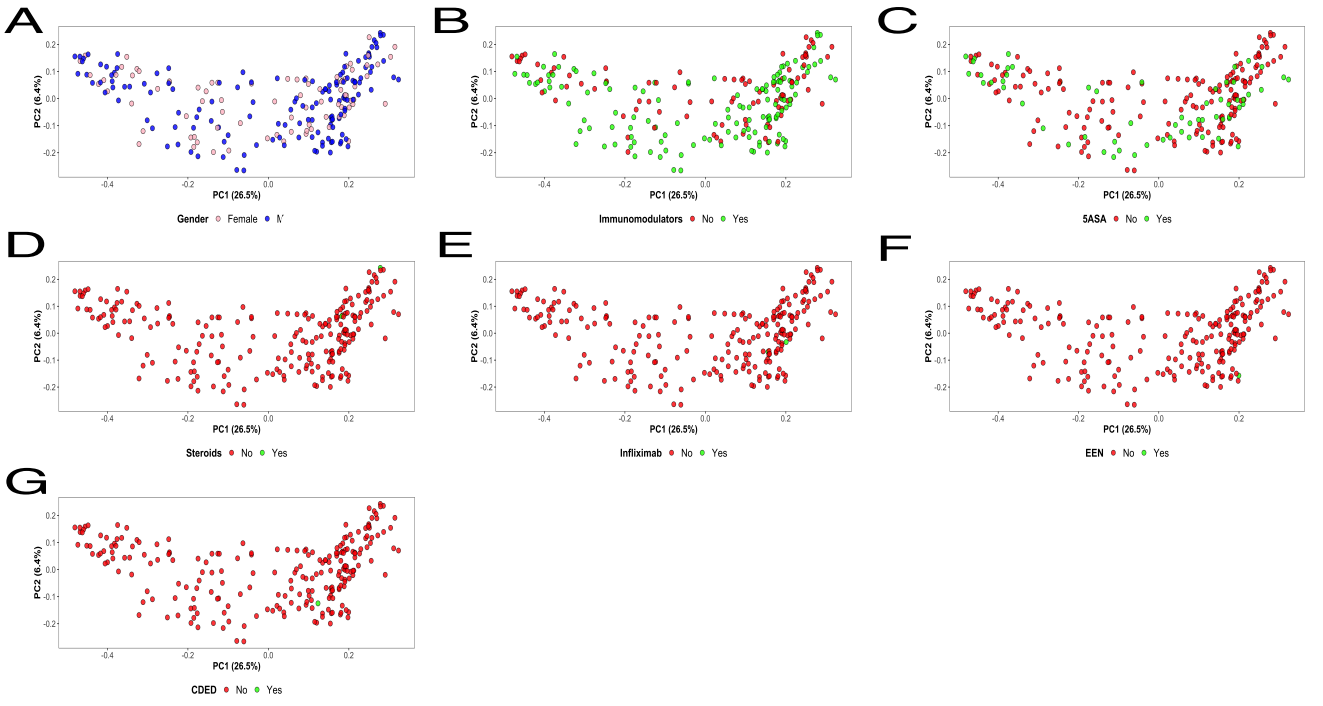

A
MET
MET+AZ
MET/MET+AZ
0.00058
0.65
0.0046
5.8e-05
0.83
3.2e-05
0.023
1
0.023
CRP
15
10
5
0
0
4
8
Week
B
MET
MET+AZ
MET/MET+AZ
0.064
0.89
0.097
0.26
0.93
0.23
0.78
1
0.78
ESR
150
100
50
0
0
4
8
Week
C
MET
MET+AZ
MET/MET+AZ
0.18
0.0093
0.0074
Calprotectin
9000
6000
3000
0
0
8
Week

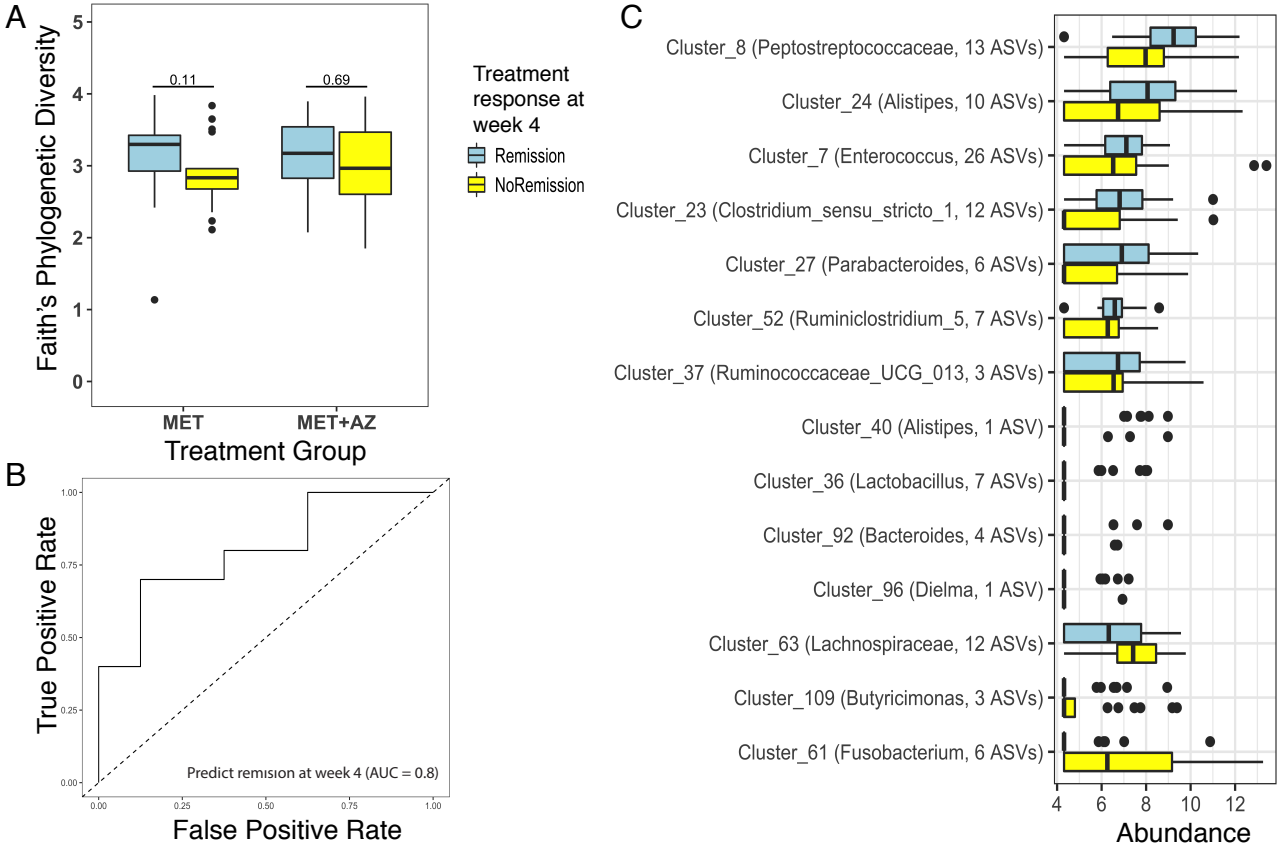
Supplementary Figure 1. Change in markers of inflammation following antibiotic treatment. **A,** C-reactive protein (CRP) levels at weeks 0, 4, and 8, colored by treatment group (MET, red; MET+AZ, blue; MET/MET+AZ, purple). **B,** Fecal calprotectin levels at weeks 0, and 8. **C,** Erythrocyte sedimentation rate (ESR) at weeks 0, 4, and 8. Samples collected during antibiotic administration are darker in color. *P*-values between time points within a treatment group are displayed (Wilcoxon Test).


A
0.8
0.89
0.85
Faith's Phylogenetic Diversity
30
20
10
MET
MET+AZ
MET/MET+AZ
Treatment Group
B
PC2 (7%)
PC1 (18.3%)
Treatment Group MET MET+AZ MET/MET+AZ
C
PC2 (7%)
PC1 (18.3%)
Gender Female Male
D
PC2 (7%)
PC1 (18.3%)
Paris L1 No Yes
E
PC2 (7%)
PC1 (18.3%)
Aminosalicylates No Yes
F
PC2 (7%)
PC1 (18.3%)
Immunomodulators No Yes

Supplementary Figure 2. Baseline microbiota diversity and composition. A, Faith's phylogenetic alpha diversity of samples collected at baseline (week 0) was compared between treatment groups (Wilcoxon test). B-F, PCA was performed on the unweighted UniFrac pairwise distances among all stool samples at baseline (B, Treatment Group, $P = 1$; C, Gender, $P = 1$; D, L1 Paris Classification, $P = 0.34$; E, 5-aminosalicylic acid, $P < 0.05$; F, immunomodulators, $P = 0.11$). Significance of group clustering was determined by PERMANOVA (`adonis`) with 1,000 permutations. Bonferroni correction was applied for multiple comparisons.


A
B
C
D
E
F
G
PC2 (6.4%)
PC1 (26.5%)
Gender Female M
Immunomodulators No Yes
5ASA No Yes
Steroids No Yes
Infliximab No Yes
EEN No Yes
CDED No Yes

Supplementary Figure 3. Impact of gender, additional medications and diet regimes on microbiome composition. Principal coordinates analysis (PCoA) on the unweighted UniFrac pairwise distances among all samples and subjects. Samples are colored by A, gender (PERMANOVA, adjusted $P = 0.72$); B, immunomodulators (PERMANOVA, adjusted $P = 0.16$); C, aminosalicylates (PERMANOVA, adjusted $P = 0.09$); D, steroids (PERMANOVA, adjusted $P = 1$); E, infliximab (PERMANOVA, adjusted $P = 1$); F, exclusive enteral nutrition (EEN) (PERMANOVA, adjusted $P = 1$); G, Crohn's disease exclusion diet (CDED) (PERMANOVA, adjusted $P = 1$). Significance of treatment group clustering was determined by PERMANOVA (`adonis`) with 1,000 permutations. Bonferroni correction was applied for multiple comparisons.


A
Faith's Phylogenetic Diversity
0.11
0.69
MET
MET+AZ
Treatment Group
Treatment response at week 4
Remission
NoRemission
B
True Positive Rate
False Positive Rate
Predict remision at week 4 (AUC = 0.8)
C
Cluster_8 (Peptostreptococcaceae, 13 ASVs)
Cluster_24 (Alistipes, 10 ASVs)
Cluster_7 (Enterococcus, 26 ASVs)
Cluster_23 (Clostridium_sensu_stricto_1, 12 ASVs)
Cluster_27 (Parabacteroides, 6 ASVs)
Cluster_52 (Ruminiclostridium_5, 7 ASVs)
Cluster_37 (Ruminococcaceae_UCG_013, 3 ASVs)
Cluster_40 (Alistipes, 1 ASV)
Cluster_36 (Lactobacillus, 7 ASVs)
Cluster_92 (Bacteroides, 4 ASVs)
Cluster_96 (Dielma, 1 ASV)
Cluster_63 (Lachnospiraceae, 12 ASVs)
Cluster_109 (Butyricimonas, 3 ASVs)
Cluster_61 (Fusobacterium, 6 ASVs)
Abundance

Supplementary Figure 4. Pre-treatment microbiota structure predicts treatment outcome. **A,** Alpha-diversity of samples collected at baseline (week 0) grouped by their treatment group and remission status at week 4 (Wilcoxon Test). **B,** The gray ROC curve indicates the accuracy of the random forest classification model built using microbiome data from week 0 as well as gender, age, disease duration, Paris classification, pre-antibiotic immunomodulators, PCDAI and CRP to predict response to treatment at week 4. *AUC* Area under the curve. **C,** Abundances of ASV clusters that are important for the remission-forecasting random forest models. Abundances were transformed using a variance stabilizing transformation (Bioconductor package `vsn`).