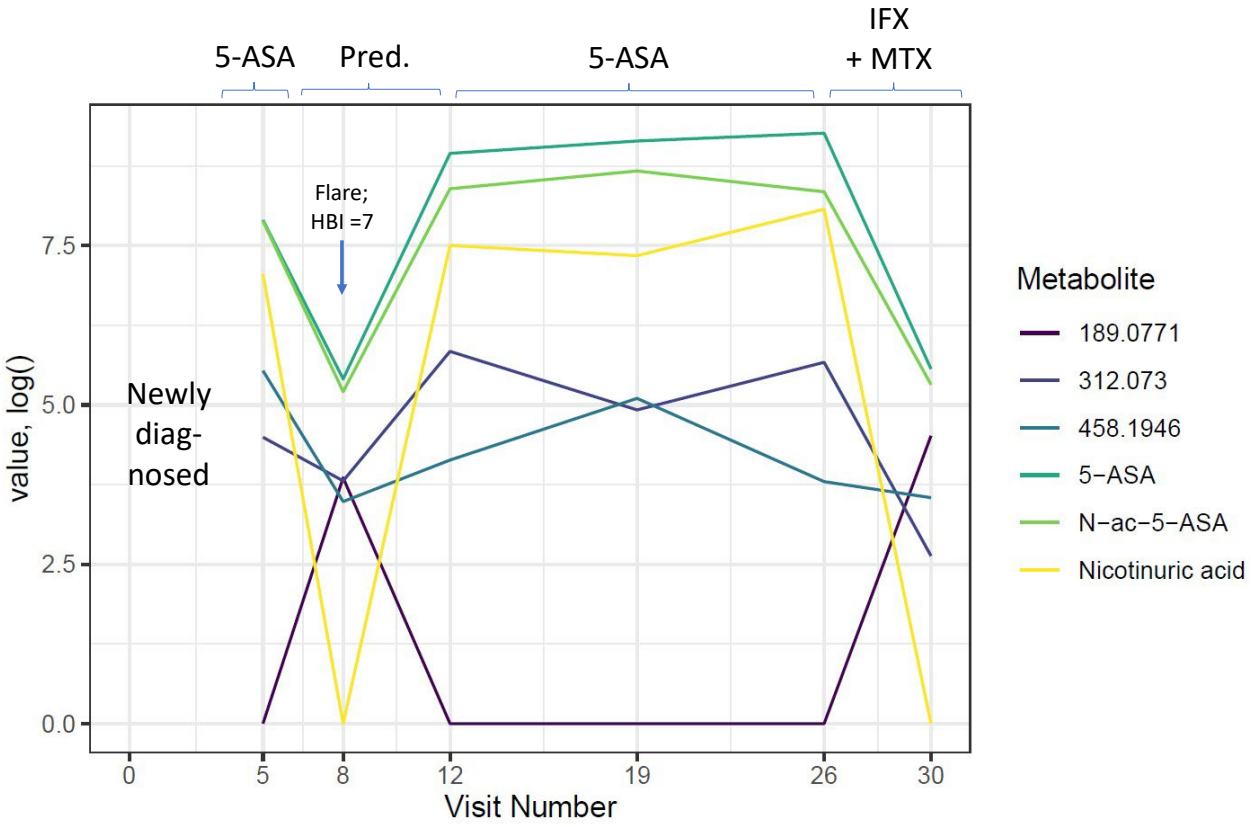
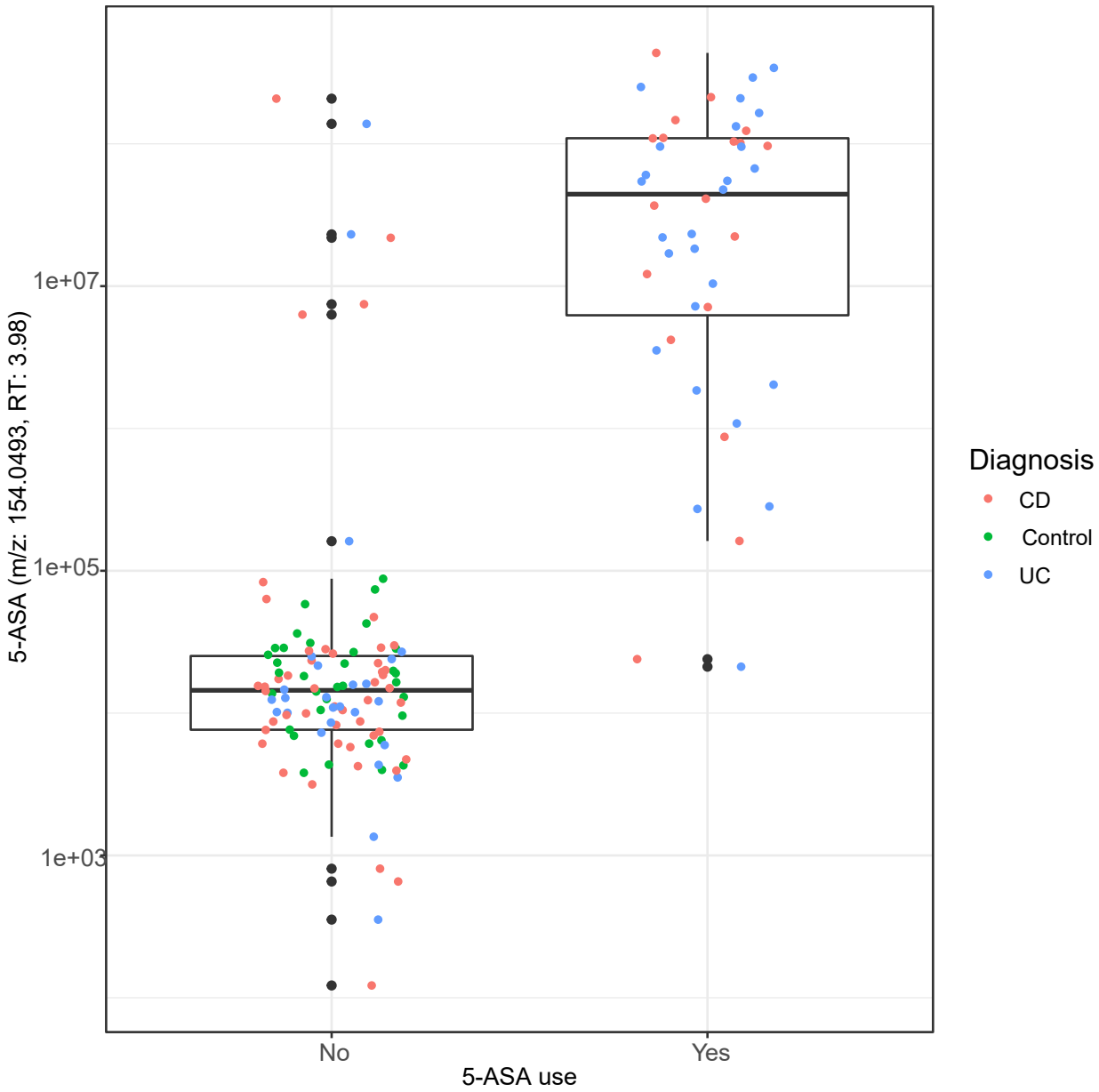
Supplemental figures

Supplementary Figure 1. 5-ASA associated metabolites predictably rise and fall with initiation and discontinuation of the medication. Time series for a 10-year-old boy with newly diagnosed Crohn's colitis in the IBDMDB who had a stuttering disease course throughout the year-long study. Initially started on Pentasa – an ethylcellulose-coated, controlled-release of oral 5-ASA – he experienced a flare and was switched to prednisone. Ultimately, he resumed 5-ASA -- Lialda, a multimatrix formulation of 5-ASA – but flared again and was escalated to infliximab and methotrexate. With each of these starts and stops, 5-ASA-associated metabolomic features predictably sunk and surged, even with administration of two different formulations. Abbreviations: HBI, Harvey-Bradshaw Index (metric of disease activity).



Supplementary Figure 2. Fecal 5-ASA levels are concordant with self-reported 5-ASA use in PRISM. As in HMP2, there was high accuracy between self-reported use of 5-ASA with detection of fecal 5-ASA. We used the PRISM cohort, an independent cohort of patients with IBD with untargeted fecal metabolomics, to validate our annotation of 5-ASA derivatives beyond N-acetyl 5-ASA. Boxplots show median and lower/upper quartiles; whiskers show inner fences.



Supplementary Figure 3. Comparison of the crystalized *Firmicutes* CAG:176 thiolase (*Fc*THL) with an acetylated thiolase crystal structure in complex with acetyl CoA from the well-characterized gram-negative *Zoogloea ramigera (ZrTHL, PDB ID: 1dm3*) highlights agreement between monomers ([RMSD] 1.652)