Stool microbiome composition reflects post-menstrual age in preterm infants and differs between infants with and without typical development

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COI disclosure

I am a paid scientific consultant for Astarte Medical

Study design

3024 samples collected from **267 babies** across **3 sites**

- shotgun metagenomics on every sample
- generated ~12M paired-end reads/sample
- taxonomic and functional profiling

- ~ 10 samples/baby
- ~36% have growth failure (≤ -1.2 Z-score from birth to discharge)

- WashU St. Louis (Misty Good)
- Brigham and Women's (Kate Gregory)
- Newcastle University (Nicholas Embleton)

**Analysis is a work-in-progress.
Completed for ~ 900 samples from 86 babies.**

Objective

Can the preterm infant gut microbiome be used to predict gut health and identify infants at risk for growth failure?

Random forest <u>classifier</u>

Typically developing (TD) vs non-typically developing (NTD)

Train RF model on 70% of data.
Test on full dataset

		Predicted	
		NTD	**TD**
Actual	**NTD**	358 (true +)	13 (false -)
	TD	14 (false +)	448 (true -)

97% accuracy

Open questions

How robust is this model?

How early can accurate predictions be made?

Could key taxa be useful as a biomarker panel?

| Species	Mean decrease in accuracy
Bifidobacterium_bifidum	0.067498595
Escherichia_coli	0.045797017
Lactobacillus_acidophilus	0.027465074
Bifidobacterium_longum	0.020643724
Staphylococcus_haemolyticus	0.019453886
Escherichia_unclassified	0.018946799
Propionibacterium_avidum	0.016515139
Bifidobacterium_animalis	0.015575921
Enterobacter_cloacae	0.012367224
Enterococcus_durans	0.009400138
Bifidobacterium_breve	0.009173547
Veillonella_unclassified	0.00897734
Veillonella_parvula	0.007807973
Klebsiella_oxytoca	0.007379208
Enterococcus_faecalis	0.00660995
Actinomyces_urogenitalis	0.006561894
Staphylococcus_lugdunensis	0.006337833
Klebsiella_pneumoniae	0.005498788
Streptococcus_thermophilus	0.005469943
Lactococcus_garvieae	0.004944994
Enterococcus_faecium	0.004306466
Citrobacter_koseri	0.004274305
Lactococcus_lactis	0.003944025
Pseudomonas_aeruginosa	0.003194776
Streptococcus_vestibularis	0.003104751

Increasing important to classifier ⟶
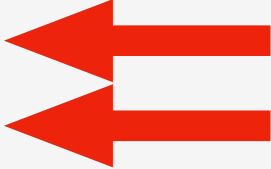
Random forest <u>regression</u>

Microbiome as predictor of post-menstrual age (PMA)

R = 0.77, p < 2e^{-16}

Actual PMA (days)

Predicted PMA (based on microbi...
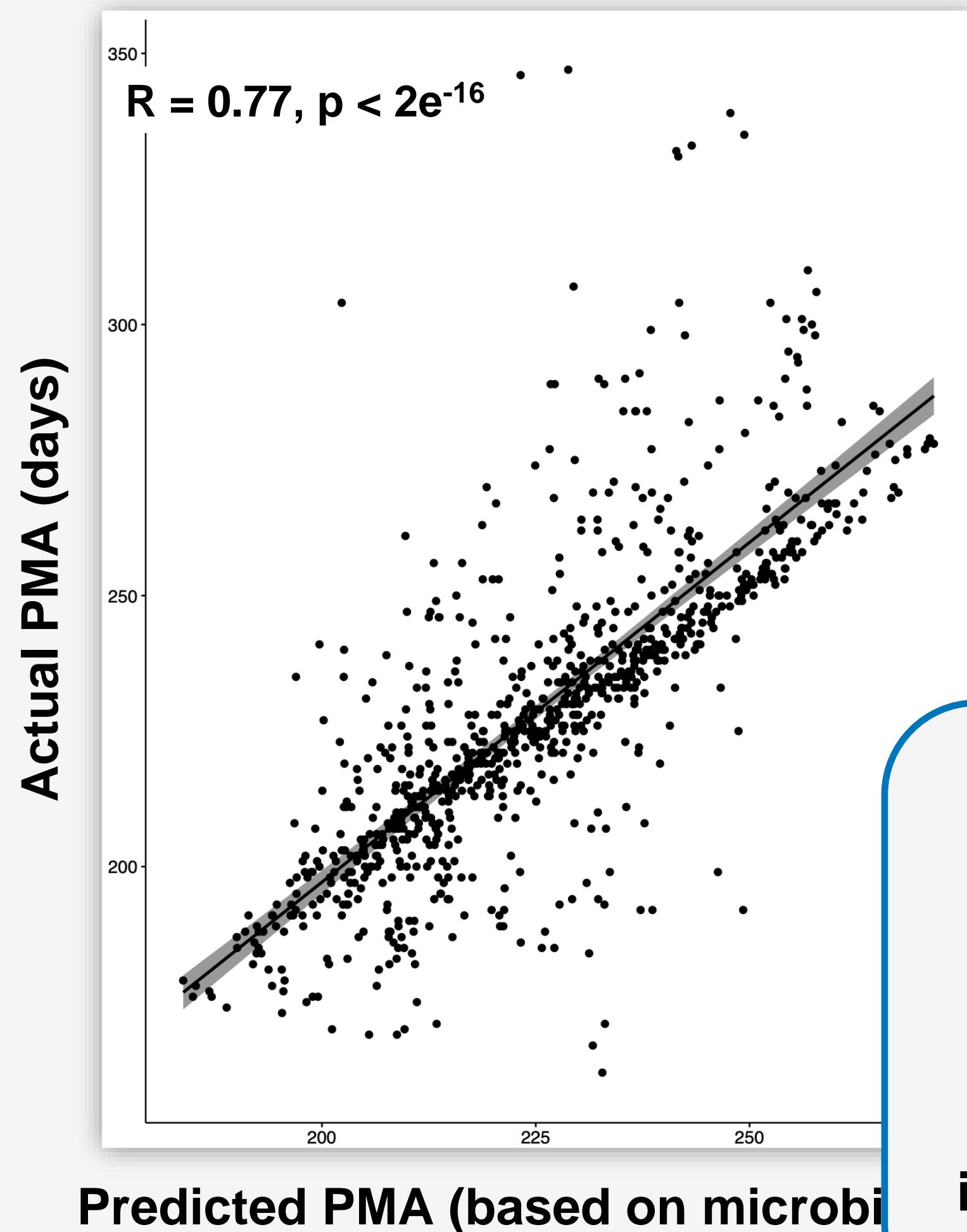
Species	Mean decrease in accuracy
Finegoldia_magna	0.067498595
Escherichia_unclassified	0.045797017
Veillonella_parvula	0.027465074
Enterococcus_faecalis	0.020643724
Propionibacterium_avidum	0.019453886
Veillonella_unclassified	0.018946799
Staphylococcus_aureus	0.016515139
Rothia_mucilaginosa	0.015575921
Clostridium_difficile	0.012367224
Staphylococcus_epidermidis	0.009400138
Bifidobacterium_breve	0.009173547
Lactobacillus_rhamnosus	0.00897734
Veillonella_atypica	0.007807973
Streptococcus_salivarius	0.007379208

...portant to classifier ⟶
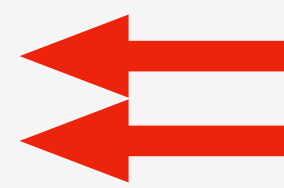
Open questions

Could a microbiota-by-age Z score be a useful predictor of at-risk infants?

What are the key age-discriminatory taxa for preterm infants, and could these be the basis for better probiotics?

microbiomeDB: large-scale integration of maternal and infant microbiome studies

> 6000 samples from children during early life development (0-5yo)

MicrobiomeDB.org

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Preterm Infant Microbiome

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