TPHE	subjects	samples
3 timepoints	78	234
2 timepoints	82	164
1 timepoint	16	16
total	**176**	**414**

TPHE	samples	pre-term	full-term
birth	147	65	82
discharge	163	87	76
12-month	104	58	46
total	**414**	*210*	*204*

ICS	subjects	samples
3 timepoints	69	207
2 timepoints	89	178
1 timepoint	19	19
total	**177**	**404**

ICS	samples	pre-term	full-term
birth	147	64	83
discharge	155	84	71
12-month	102	55	47
total	**404**	*203*	*201*

TPHE_ICS	subjects	samples
3 timepoints	67	201
2 timepoints	83	166
1 timepoint	18	18
total	**168**	**385**

TPHE_ICS	samples	pre-term	full-term
birth	141	63	78
discharge	150	81	69
12-month	94	51	43
total	**385**	*195*	*190*

Supplementary Table 1: Subject numbers for immunophenotyping

Figure Description	Site	Samples	Subjects
Microbiome CGA & CST PCoA plots	Both NAS	1748	149
	Both REC	1899	143
Microbiome CST Occurrence Over CGA	NAS	1748	149
	REC	1899	143
Microbiome Composition Heatmaps	NAS	1748	149
	REC	1899	143
Immuno IST Composition Heatmaps	TPHE	414	176
	ICS	404	177
Immuno IST Occurrence Over CGA	TPHE	414	176
	ICS	404	177
Immuno IST Avg. Occurrence GAB/CGA	TPHE	414	176
	ICS	404	177
NAS 8 Occurrence vs TPHE ISTs	Birth	68	68
	Discharge	95	95
CST-Immuno Association Networks	NAS	1589	109
	REC	1697	117

Supplementary Table 2: Subject numbers microbiome and combined analyses

Cytometer: BDLSRII (URMC FlowCore - Animal)

Tphe Functional Panel (RPRC 12-0012)

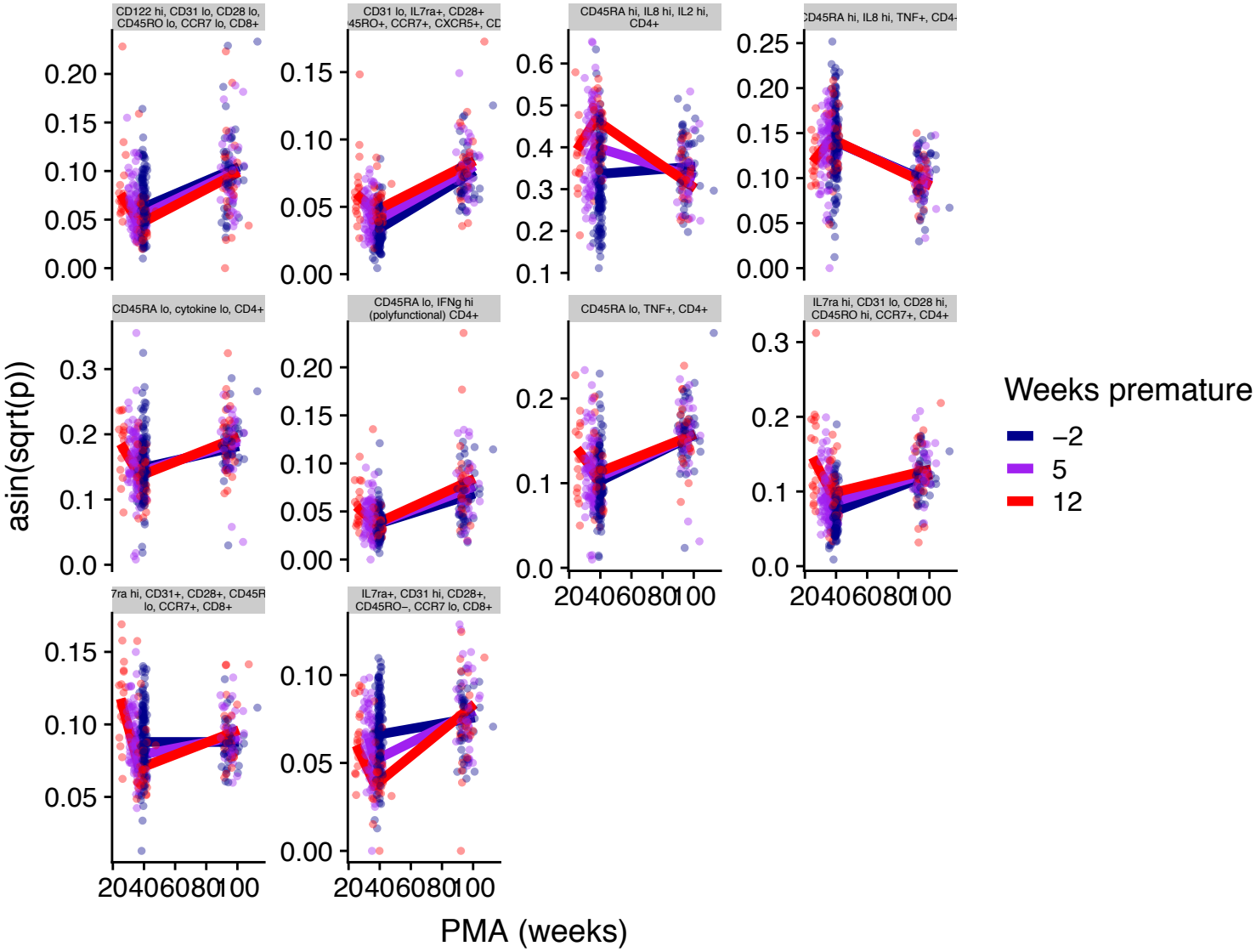
Laser	Long Pass	Band Pass	PMT	Detector	Marker	Color	Clone	Company	Catalog #
488	505	515/20	BB	B515	**CD122**	BB 515	Mik-β	BD Biosciences	564688
488	685	710/50	BA	B710	**Perforin**	PerCP-Cy5.5	dG9	Biolegend	308114
407		450/50	VH	V450	**Granzyme B**	BV 421	GB11	BD Biosciences	563389
407	535	550/40	VG	V550	**Live/Dead**	Aqua		Life Technologies	L34957
407	570	585/42	VE	V585	**CD3**	BV 570	UCHT1	Biolegend	300436
407	595	605/40	VD	V605	**CD31**	BV 605	WM59	BD Biosciences	562855
407	630	660/40	VC	V660	**CD127**	BV 650	HIL-7R-M21	BD Biosciences	563225
407	670	705/70	VB	V705	**CD45RO**	BV 711	UCHL1	BD Biosciences	563722
407	740	780/60	VA	V780	**CD8a**	BV 785	RPA-T8	Biolegend	301045
633		660/20	RC	R660	**KLRG1**	APC	13F12F2	eBioscience	17-9488-42
633	685	710/50	RB	R710	**CD185 (CXCR**	APC-R700	RF8B2	BD Biosciences	565191
633	740	780/60	RA	R780	**CD197 (CCR7**	APC-Cy7	G043H7	Biolegend	353212
532		575/24	GE	G575	**Foxp3**	PE	236A/E7	eBioscience	12-4777-42
532	600	610/20	GD	G610	**CD4**	PE-TR	S3.5	Invitrogen	MHCD0417
532	640	660/40	GC	G660	**CD28**	PE-Cy5	CD28.2	BD Biosciences	561791
532	740	780/40	GA	G780	**CD57**	PE-Cy7	TB01	eBioscience	25-0577-42

ICS Functional Panel (RPRC 12-0012)

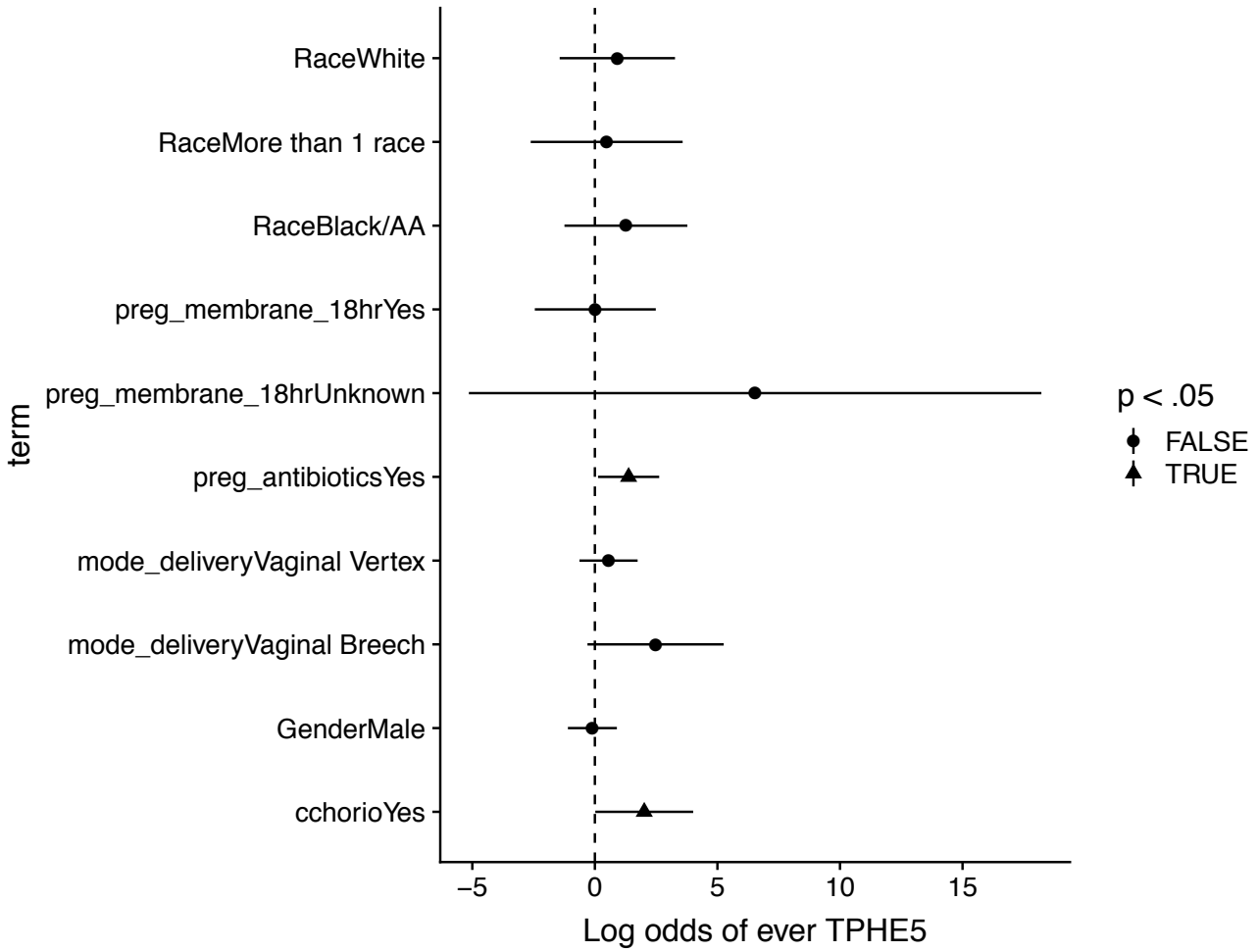
Cytometer: BDLSRII (URMC FlowCore - Animal)

Laser	Long Pass	Band Pass	PMT	Detector	Marker	Color	Clone	Company	Catalog #
488	505	515/20	BB	B515	**IL-8**	FITC	E8N1	BioLegend	511406
407		450/50	VH	V450	**IL-17**	Pacific Blue	BL168	BioLegend	512312
407	535	550/40	VG	V550	**Live/Dead**	Aqua	polyclonal	Life Technologies	L34957
407					**CD14**	BV510	MΦP9	BD Biosciences	563079
407	570	585/42	VE	V585	**CD8a**	BV570	RPA-T8	BioLegend	301037
407	595	605/40	VD	V605	**IL-2**	BV605	MQ1-17H12	BD Biosciences	564165
407	630	660/40	VC	V660	**CD45RA**	BV650	HI100	BD Biosciences	563963
407	670	705/70	VB	V705	**IL-10**	BV711	JES3-9D7	BD Biosciences	564050
407	740	780/60	VA	V780	**TNFa**	BV785	MAb11	BioLegend	502948
633		660/20	RC	R660	**IL-6**	APC	MQ2-13A5	BD Biosciences	561441
633	685	710/50	RB	R710	**CD3**	AF700	UCHT1	BD Biosciences	557943
633	740	780/60	RA	R780	**CD69**	APC-Cy7	FN50	BioLegend	310914
532		575/24	GE	G575	**IL-4**	PE	MP4-25D2		
532	600	610/20	GD	G610	**CD107a**	PE-CF594	H4A3	BD Biosciences	562628
532	690	710/50	GB	G710	**CD4**	PE-Cy5.5	S3.5	ThermoFischer	MHCD0418
532	740	780/40	GA	G780	**IFN-g**	PE-Cy7	B27	BD Biosciences	557643

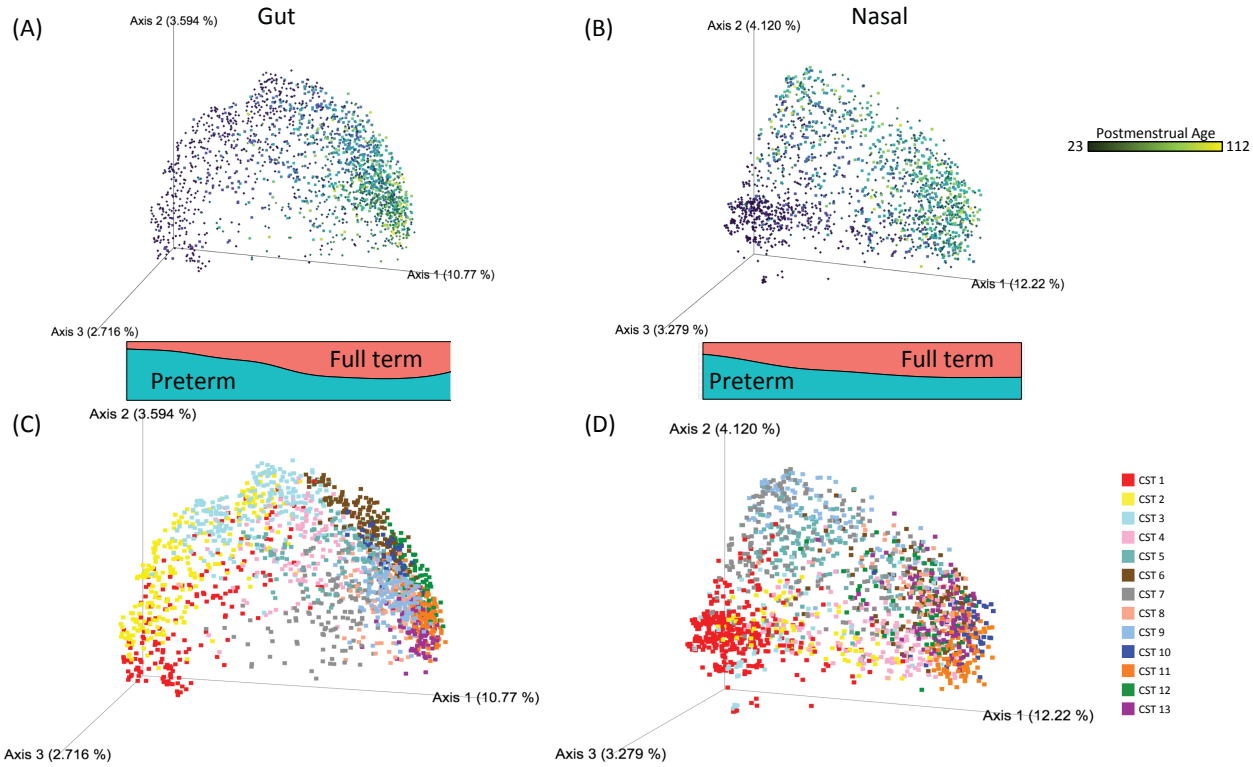
Supplementary Table 3 – Flow Cytometry Panels



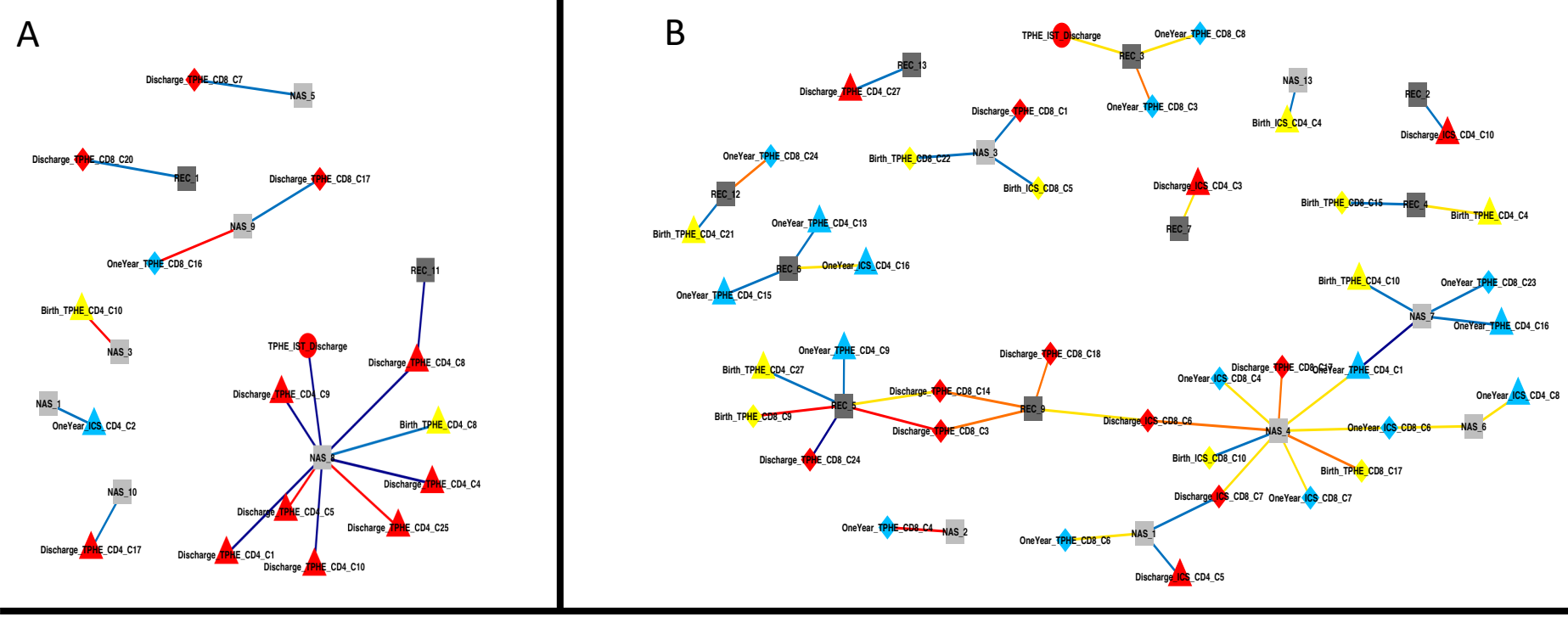
Supplementary fig 1. Meta clusters with non-monotone trajectories as a function of PMA.



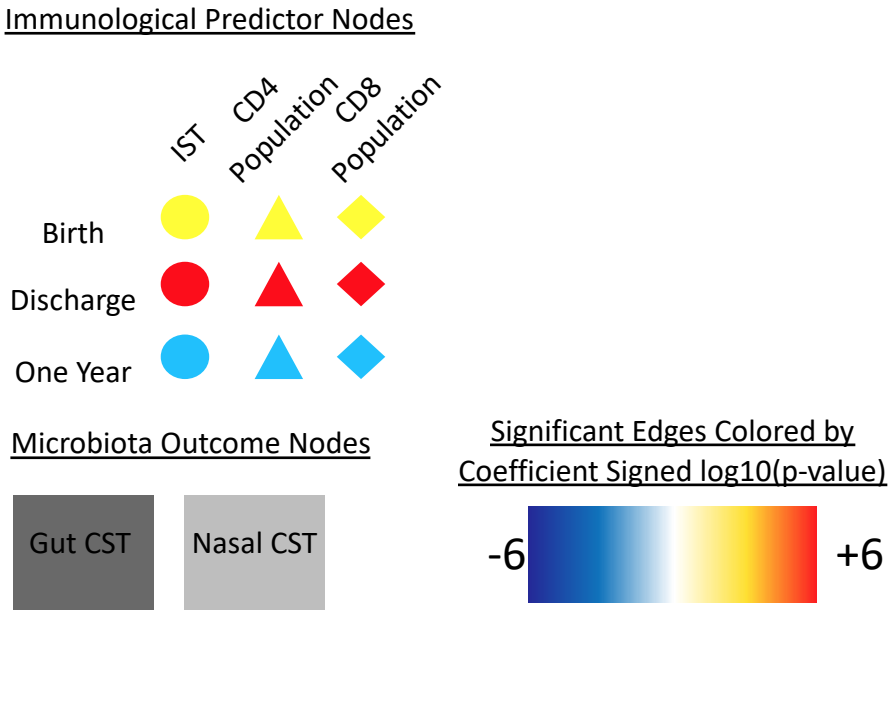
Supplementary fig 2. Risk factors for subjects ever entering IST Tphe5. A joint logistic regression of the form Tphe5 ~ s(gestation_age_birth)+ race + preg_membrane + preg_antibiotics + mode_delivery + gender + cchorio was run using R package mgcv version 1.8.24. The term s(gestational_age_birth) represents an arbitrary, smooth function of gestational age at birth that was simultaneously estimated with the other parametric model terms.

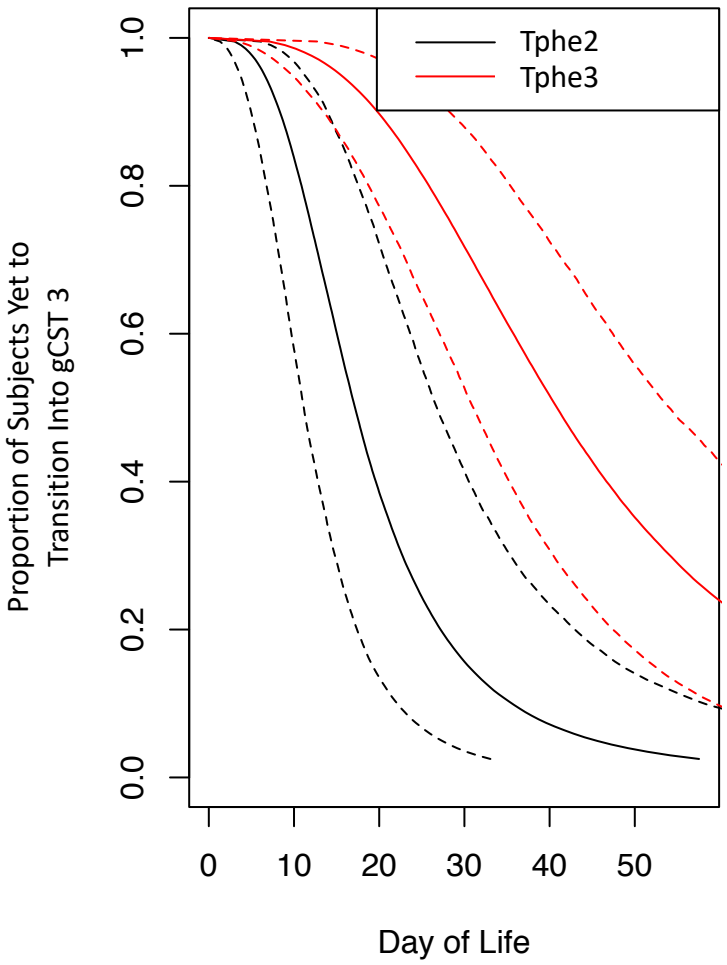


Supplementary Fig 3. Premature birth influences long-term age-related respiratory and gut microbiota community progression. Microbiota community profiling was performed on rectal (A, C) and nasal (B, D) samples obtained from 159 infants during regular surveillance and acute respiratory illness. (A-D) Principal coordinate analysis (PCOA) plots using Unweighted Unifrac distances summarize overall variation and structure. (A-B) Points were colored by postmenstrual age (PMA) at the time the sample was obtained. Colored bands at the base of PCOA plots show the proportion of samples along each point of axis 1 that are from either preterm (teal) or full term (salmon) subjects. (C and D) Microbiota community state types (CST) were defined for each body site, with samples in the PCOA colored according to the CST they represent. CSTs are ordered according to average PMA of occurrence.

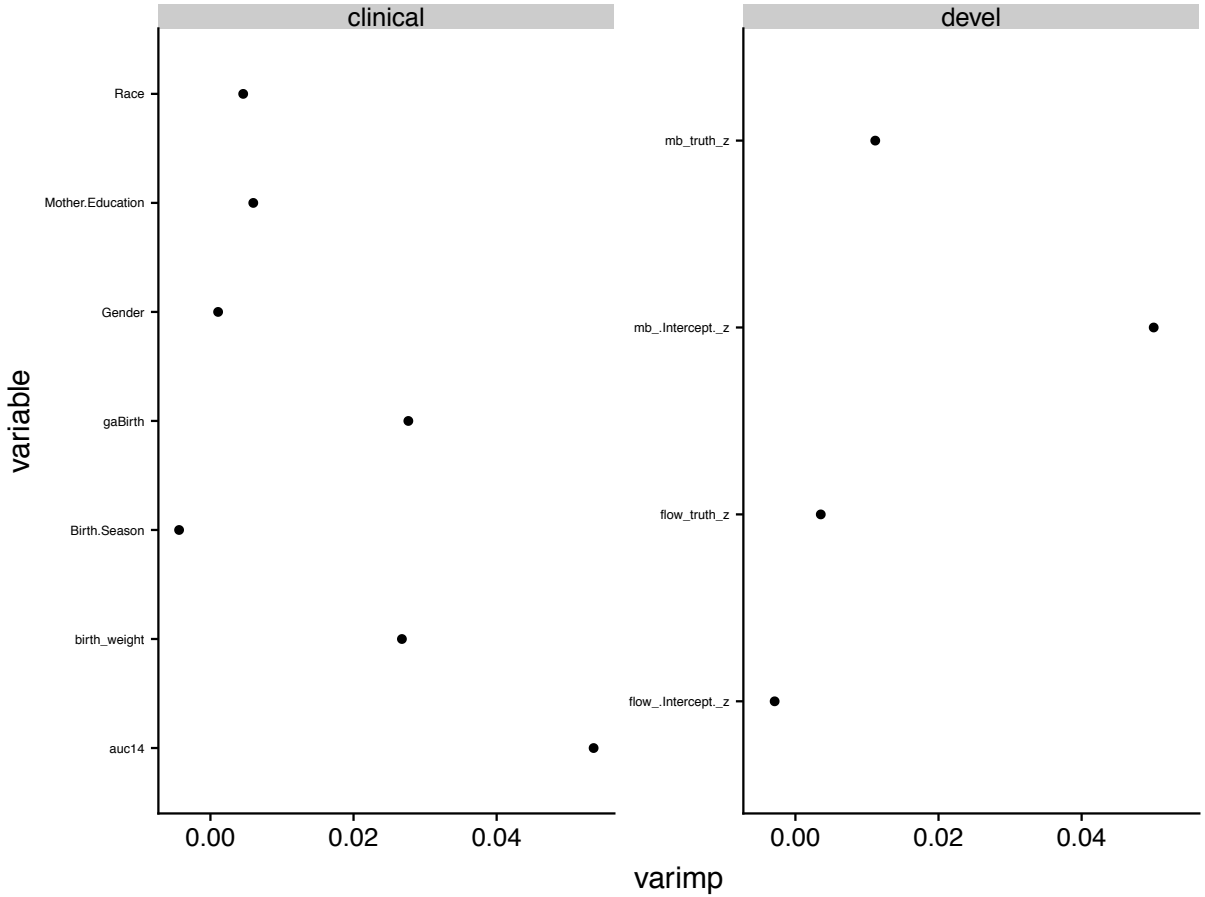


Supplemental fig 4. Networks of associations between CST occurrence and T cell populations and ISTs. (A) Logistic regression was used to assess the relationship between T cell populations or ISTs at birth, discharge, or one year and the probability of ever observing a given CST within a subject. (B) Interval censored survival modeling was used to assess the relationship between T cell populations and ISTs at birth, discharge, or one year and the time to occurrence of a given CST within a subject. Mode of delivery and gestational age at birth were included as covariates in both types of models. All significant associations (after multiple test correction) are plotted, with edges between an immunological parameter and a CST indicating a significant relationship. Edges are colored according to the direction of the relationship and the magnitude of its significance. Nodes are colored to indicate time point or body site and are shaped to distinguish between CSTs, ISTs, and individual T cell populations.





Supplemental fig 5. Time to transition into gCST 3 based on Tphe IST at discharge. Survival analysis using an accelerated failure time model was used to assess the time to initially transition into gCST 3 as a function of Tphe IST at discharge, gestational age at birth, and mode of delivery. Fitted mean probabilities of not having transitioned in gCST 3 are shown for infants born at 30 weeks GA by Cesarean section, with 95% confidence intervals. Tphe3 at discharge significantly delayed initial transition into gCST 3.



Supplementary figure 6. Random forest variable importance plots for clinical and developmental index models. Larger values represent greater decreases in the Gini purity coefficient. Importance was calculated using the default method in R package randomForestSRC version 2.7.0.