



Supplemental material

Enhanced performance of newborn screening for congenital hypothyroidism by integrating covariate-adjusted results of different tests into CLIR customized interpretive tools

Alexander D. Rowe, Stephanie D. Stoway, et al

Table S1. Unadjusted reference percentiles of measured markers

Marker	Unit	1%ile	10%ile	50%ile	90%ile	99%ile
TRECs	copies/ μ L	99	157	382	1869	3111
GALT	U/g[Hb]	152	187	262	309	356
GALT %	%	65	80	101	116	126
BIOT F%	%	70	81	100	122	137
Tyr	nmol/mL	40	53	82	130	174
BIOT A	ERU	27	34	47	61	71
IRT	μ g/dL	9.8	13	22	39	56
T4	μ g/dL	9.4	12	17	22	25
Cit	nmol/mL	6.3	8.4	13	21	26
17OHP	ng/dL	2.4	3.7	7.3	15	22
TSH	m[UI]/L	1.8	2.7	5.5	11.0	14
GALC	nmol/mL/hr	1.4	2.1	4.0	7.5	11
C16	nmol/mL	1.4	1.9	2.9	4.3	5.3
C3	nmol/mL	0.83	1.1	1.8	2.8	3.8

Legend: Markers are sorted in descending order of the median. Values are shown to include at least two significant figures. Abbreviations (in alphabetical order): 17OHP, 17-hydroxy progesterone; BIOT, Biotinidase activity; C3, propionylcarnitine; CIT, citrulline; C16, palmitoylcarnitine; ERU, enzyme response unit; GALC, galactocerebrosidase activity; GALT, galactose-1-phosphate uridyl transferase activity; IRT, immunoreactive trypsinogen; T4, total thyroxine; TRECS, T-cell receptor excision circles; TSH, thyroid stimulating hormone; TYR, tyrosine.

Table S2. Unadjusted reference percentiles of calculated **TSH** ratios.

Ratio	1%ile	10%ile	50%ile	90%ile	99%ile
17OHP/TSH	0.350	0.600	1.360	3.240	6.230
GALC/TSH	0.150	0.280	0.680	1.810	4.100
C16/TSH	0.140	0.230	0.510	1.230	2.100
TSH/T4	0.130	0.240	0.490	0.820	1.140
C3/TSH	0.098	0.170	0.370	0.820	1.320
TSH/Cit	0.083	0.140	0.310	0.740	1.350
TSH/IRT	0.056	0.110	0.260	0.590	1.000
TSH/BIOT A	0.032	0.054	0.120	0.250	0.380
TSH/Tyr	0.016	0.028	0.064	0.140	0.240
TSH/GALT %	0.023	0.027	0.043	0.081	0.120
TSH/BIOT F%	0.022	0.027	0.042	0.080	0.120
TSH/GALT	0.007	0.011	0.024	0.046	0.070
TSH/TRECS	0.002	0.007	0.019	0.047	0.088

Legend: Ratios are sorted in descending order of the median. Values are shown to include three decimal figures. Abbreviations as listed in the legend of supplemental Table 1.

Table S3. Unadjusted reference percentiles of calculated **T4** ratios.

Ratio	1%ile	10%ile	50%ile	90%ile	99%ile
T4/IRT	0.260	0.400	0.740	1.280	1.840
Cit/T4	0.310	0.430	0.700	1.210	2.000
TSH/T4	0.130	0.240	0.490	0.820	1.140
17OHP/T4	0.150	0.230	0.430	0.840	1.540
T4/BIOT A	0.160	0.250	0.360	0.520	0.700
GALC/T4	0.077	0.120	0.240	0.460	0.790
T4/Tyr	0.077	0.120	0.210	0.360	0.500
C16/T4	0.077	0.110	0.170	0.270	0.370
C3/T4	0.045	0.064	0.110	0.180	0.270
T4/GALT	0.033	0.045	0.066	0.098	0.130
T4/TRECS	0.004	0.006	0.013	0.033	0.069

Legend: Ratios are sorted in descending order of the median. Values are shown to include three decimal figures. Abbreviations as listed in the legend of supplemental Table 1.

Table S4. Unadjusted extended percentiles of disease ranges for conditions **CH TSH** and **FP TSH**.

	Marker	1%ile	5%ile	10%ile	25%ile	50%ile	75%ile	90%ile	99%ile
CH TSH									
HIGH	TSH	23.5	26.2	28.8	35.5	76	243	400	777
	TSH/BIOT A	0.43	0.51	0.63	0.83	1.68	4.96	7.63	13.63
	TSH/BIOT F%	0.27	0.33	0.39	0.55	1.97	4.33	6.17	10.12
	TSH/IRT	0.46	0.7	0.96	1.47	3.08	10.25	20.27	44.9
	TSH/CIT	1.26	1.49	1.81	2.54	5.29	15.14	24.72	72.5
	TSH/TYR	0.18	0.27	0.32	0.47	0.99	2.6	4.49	9.75
	TSH/GALT	0.065	0.086	0.11	0.14	0.35	0.96	1.38	2.31
	TSH/GALT%	0.26	0.31	0.32	0.46	1.54	4.56	6.61	12.51
	TSH/TRECs	0.01	0.016	0.027	0.14	0.45	1.29	2.39	5.58
LOW	17OHP/TSH	0.0075	0.015	0.022	0.046	0.1	0.23	0.39	0.87
	C3/TSH	0.0019	0.0028	0.0038	0.0069	0.02	0.043	0.068	0.13
	C16/TSH	0.0026	0.0042	0.0059	0.011	0.034	0.075	0.11	0.19
	GALC/TSH	0.011	0.016	0.018	0.043	0.1	0.15	0.26	0.36
FP TSH									
HIGH	TSH	24.69	25.4	25.8	27.7	31.7	42.3	66.7	113
	TSH/BIOT A	0.36	0.43	0.47	0.56	0.71	1.07	1.62	3.00
	TSH/BIOT F%	0.19	0.22	0.23	0.27	0.34	0.39	0.51	0.67
	TSH/IRT	0.29	0.48	0.59	0.84	1.26	1.93	2.8	6.2
	TSH/CIT	0.87	1.18	1.37	1.74	2.37	3.42	4.77	9.62
	TSH/TYR	0.16	0.21	0.25	0.32	0.44	0.67	0.99	1.79
	TSH/GALT	0.059	0.074	0.083	0.1	0.13	0.21	0.33	0.66
	TSH/GALT%	0.25	0.26	0.27	0.31	0.33	0.39	0.47	0.56
	TSH/TRECs	0.0087	0.011	0.013	0.023	0.054	0.11	0.23	0.51
LOW	17OHP/TSH	0.073	0.12	0.15	0.21	0.3	0.44	0.62	1.14
	C3/TSH	0.0096	0.015	0.02	0.03	0.045	0.064	0.085	0.14
	C16/TSH	0.012	0.02	0.026	0.05	0.08	0.11	0.13	0.20
	GALC/TSH	0.025	0.038	0.052	0.076	0.12	0.18	0.27	0.59

Figure S1. Plot by Multiple Conditions comparing disease ranges of conditions **CH TSH** and **FP TSH**.

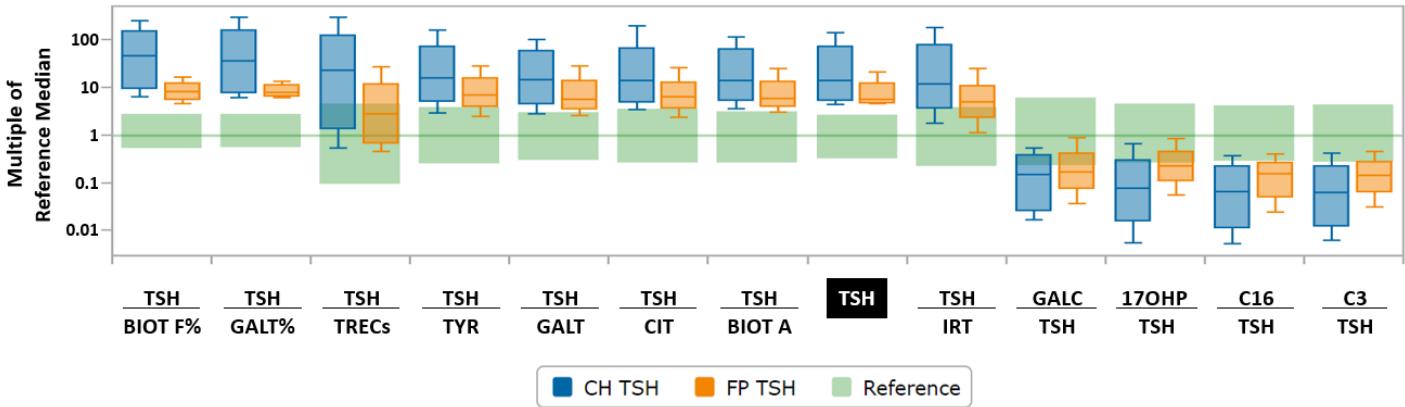


Table S5. Unadjusted extended percentiles of disease ranges for conditions **CH T4** and **FP T4**.

	Marker	1%ile	5%ile	10%ile	25%ile	50%ile	75%ile	90%ile	99%ile
CH T4									
HIGH	TSH/T4	0.30	0.38	0.52	0.74	1.35	2.74	4.74	10.09
	17OHP/T4	0.26	0.30	0.43	1.47	3.84	10.40	20.09	49.6
	C3/T4	0.072	0.094	0.11	0.19	0.38	0.64	1.13	1.55
	C16/T4	0.05	0.08	0.13	0.18	0.33	0.54	0.89	1.51
	CIT/T4	0.99	1.57	2.00	2.81	4.11	6.55	12.47	20.14
	GALC/T4	0.36	0.41	0.51	0.69	1.46	4.18	5.43	8.82
LOW	T4	1.07	1.14	1.58	2.21	3.98	5.22	6.97	8.01
	T4/BIOT A	0.021	0.026	0.029	0.064	0.110	0.130	0.190	0.26
	T4/GALT	0.0038	0.0045	0.0065	0.012	0.020	0.031	0.047	0.077
	T4/IRT	0.011	0.028	0.037	0.083	0.170	0.320	0.410	0.71
	T4/TRECs	0.0011	0.0016	0.0026	0.0034	0.0058	0.011	0.017	0.025
	T4/TYR	0.006	0.008	0.009	0.025	0.047	0.081	0.110	0.25
FP T4									
HIGH	TSH/T4	0.20	0.29	0.34	0.51	0.86	1.5	2.31	4.57
	17OHP/T4	0.24	0.52	0.83	1.73	4.08	9.21	17.29	44.30
	C3/T4	0.053	0.089	0.12	0.19	0.30	0.48	0.73	1.41
	C16/T4	0.054	0.09	0.12	0.18	0.27	0.4	0.56	1.07
	CIT/T4	0.95	1.37	1.63	2.35	3.67	5.58	8.20	17.18
	GALC/T4	0.20	0.35	0.49	0.87	1.89	3.72	6.19	12.88
LOW	T4	1.15	1.69	2.22	3.23	4.29	5.40	7.16	8.12
	T4/BIOT A	0.029	0.047	0.059	0.083	0.12	0.17	0.24	0.41
	T4/GALT	0.0063	0.01	0.013	0.018	0.025	0.036	0.048	0.079
	T4/IRT	0.02	0.037	0.058	0.1	0.19	0.31	0.48	1
	T4/TRECs	0.00068	0.0014	0.0018	0.003	0.0055	0.01	0.019	0.068
	T4/TYR	0.0072	0.014	0.021	0.034	0.053	0.08	0.12	0.23

Supplemental Figure S2. Plot by Multiple Conditions comparing disease ranges of conditions **CH T4** and **FP T4**.

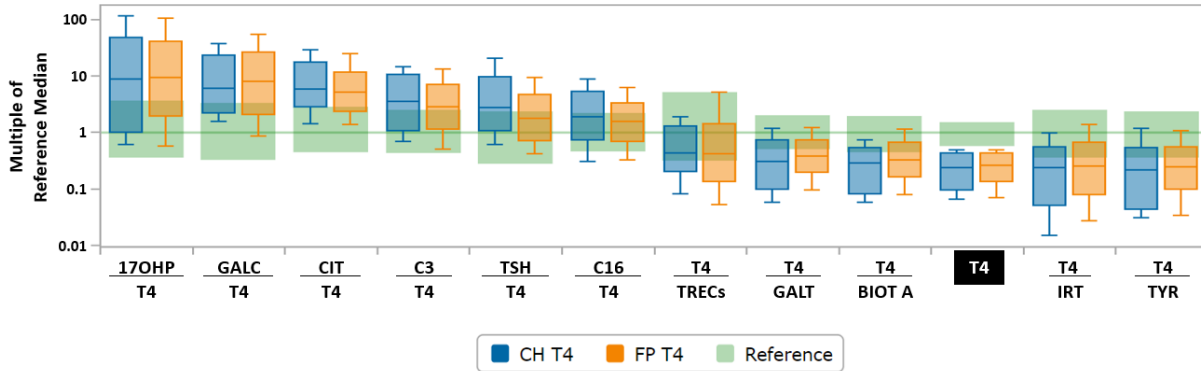


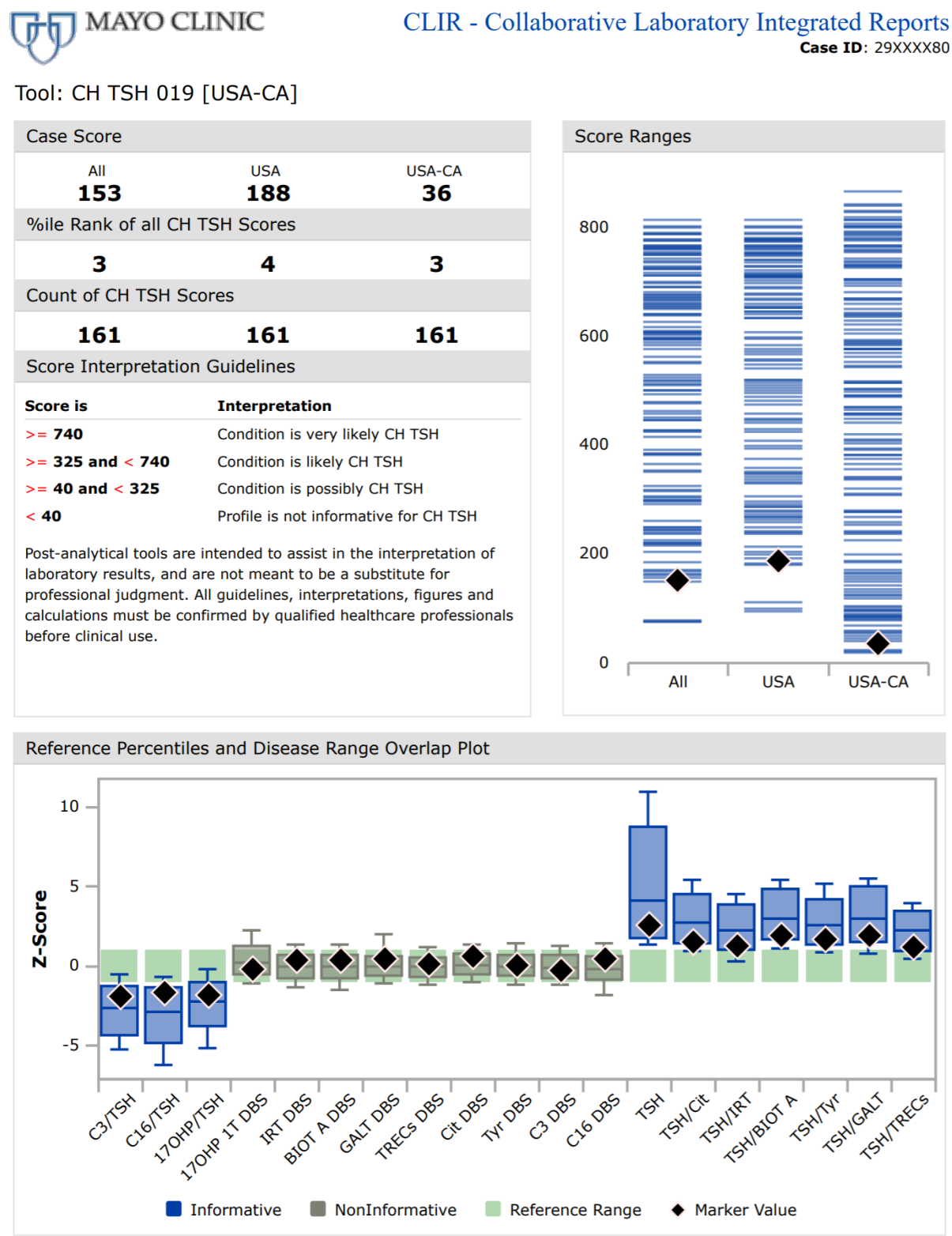
Table S6. Unadjusted extended percentiles of disease ranges for conditions **CH TSH T4** and **FP TSH T4**

	Marker	1%ile	5%ile	10%ile	25%ile	50%ile	75%ile	90%ile	99%ile
CH TSH T4									
HIGH	TSH	15.06	20.66	30.9	75.4	276	534	687	1,180
	TSH/T4	2.38	3.37	4.9	14.03	56.8	159	294	664
	TSH/BIOT A	0.32	0.47	0.55	1.39	4.6	13.51	19.64	37
	TSH/GALT	0.049	0.089	0.13	0.29	1.15	2.36	3.82	8.75
	TSH/CIT	0.84	1.42	2.09	5.44	20.25	39.5	59.6	122
	TSH/TYR	0.12	0.25	0.42	1.12	3.05	6.14	9.08	18.4
	TSH/IRT	0.19	0.76	1.16	3.59	13.54	30.1	45.8	102
	TSH/TRECs	0.0087	0.014	0.021	0.045	0.18	0.4	1	2.5
	17OHP/T4	0.22	0.47	0.66	1.14	2.16	4.4	9.94	36.6
	C3/T4	0.043	0.096	0.13	0.2	0.32	0.6	0.9	1.65
	C16/T4	0.068	0.11	0.16	0.28	0.44	0.72	1.11	2.24
	CIT/T4	0.75	1.01	1.21	1.79	2.93	5.24	8.68	23.72
	GALC/T4	0.21	0.29	0.37	0.59	0.92	2.15	4.17	8.34
LOW	17OHP/TSH	0.0043	0.0095	0.012	0.02	0.037	0.11	0.33	1.53
	C3/TSH	0.0007	0.0014	0.0017	0.0027	0.0055	0.017	0.051	0.11
	C16/TSH	0.0012	0.0017	0.0022	0.004	0.0074	0.022	0.048	0.14
	GALC/TSH	0.0029	0.0035	0.0053	0.01	0.032	0.11	0.28	0.89
	T4	1.02	1.42	1.84	2.83	4.62	6.92	8.26	9.29
	T4/BIOT A	0.024	0.033	0.042	0.064	0.11	0.14	0.2	0.26
	T4/GALT	0.0038	0.0056	0.0075	0.012	0.022	0.034	0.047	0.073
	T4/IRT	0.021	0.049	0.074	0.13	0.22	0.37	0.51	0.94
	T4/TRECs	0.00086	0.0015	0.0018	0.0027	0.0047	0.0075	0.015	0.034
	T4/TYR	0.0095	0.014	0.018	0.03	0.057	0.092	0.13	0.25
FP TSH T4									
HIGH	TSH	14.53	15.94	18.12	26.2	43.9	63.2	81.1	140
	TSH/T4	2.04	2.7	3.17	4.45	6.69	9.11	11.93	22.84
	TSH/BIOT A	0.3	0.4	0.48	0.71	1.17	1.63	2.31	4.6
	TSH/GALT	0.045	0.063	0.081	0.12	0.2	0.29	0.42	0.9
	TSH/CIT	0.69	0.98	1.2	1.91	3.14	4.53	6.2	12.1
	TSH/TYR	0.12	0.17	0.22	0.34	0.61	0.92	1.27	2.25
	TSH/IRT	0.087	0.22	0.35	0.71	1.41	2.77	4.44	9.73
	TSH/TRECs	0.0057	0.011	0.012	0.018	0.026	0.047	0.081	0.5
	17OHP/T4	0.49	0.89	1.2	1.96	3.19	5.2	7.89	18.69
	C3/T4	0.072	0.1	0.12	0.16	0.22	0.32	0.43	0.79
	C16/T4	0.098	0.13	0.15	0.2	0.27	0.38	0.49	0.77
	CIT/T4	0.74	1.05	1.24	1.65	2.14	2.93	3.92	7.43
	GALC/T4	0.23	0.3	0.35	0.58	1.04	2.32	4.13	9.68
LOW	17OHP/TSH	0.066	0.13	0.17	0.27	0.47	0.89	1.5	3.55
	C3/TSH	0.0071	0.011	0.015	0.022	0.034	0.059	0.089	0.17
	C16/TSH	0.0085	0.014	0.019	0.026	0.041	0.067	0.11	0.2
	GALC/TSH	0.026	0.05	0.066	0.14	0.23	0.48	0.94	1.88
	T4	2.36	3.51	4.09	5.33	7.07	8.09	8.89	9.4
	T4/BIOT A	0.071	0.088	0.1	0.13	0.17	0.21	0.25	0.41
	T4/GALT	0.011	0.015	0.017	0.022	0.029	0.037	0.048	0.083
	T4/IRT	0.016	0.035	0.059	0.13	0.23	0.37	0.56	1.06
	T4/TRECs	0.0011	0.0019	0.0024	0.0041	0.006	0.01	0.019	0.05
	T4/TYR	0.026	0.038	0.047	0.068	0.091	0.12	0.14	0.22

Figure S3. Plot by Multiple Conditions comparing disease ranges of conditions **CH** TSH T4 and FP TSH T4.



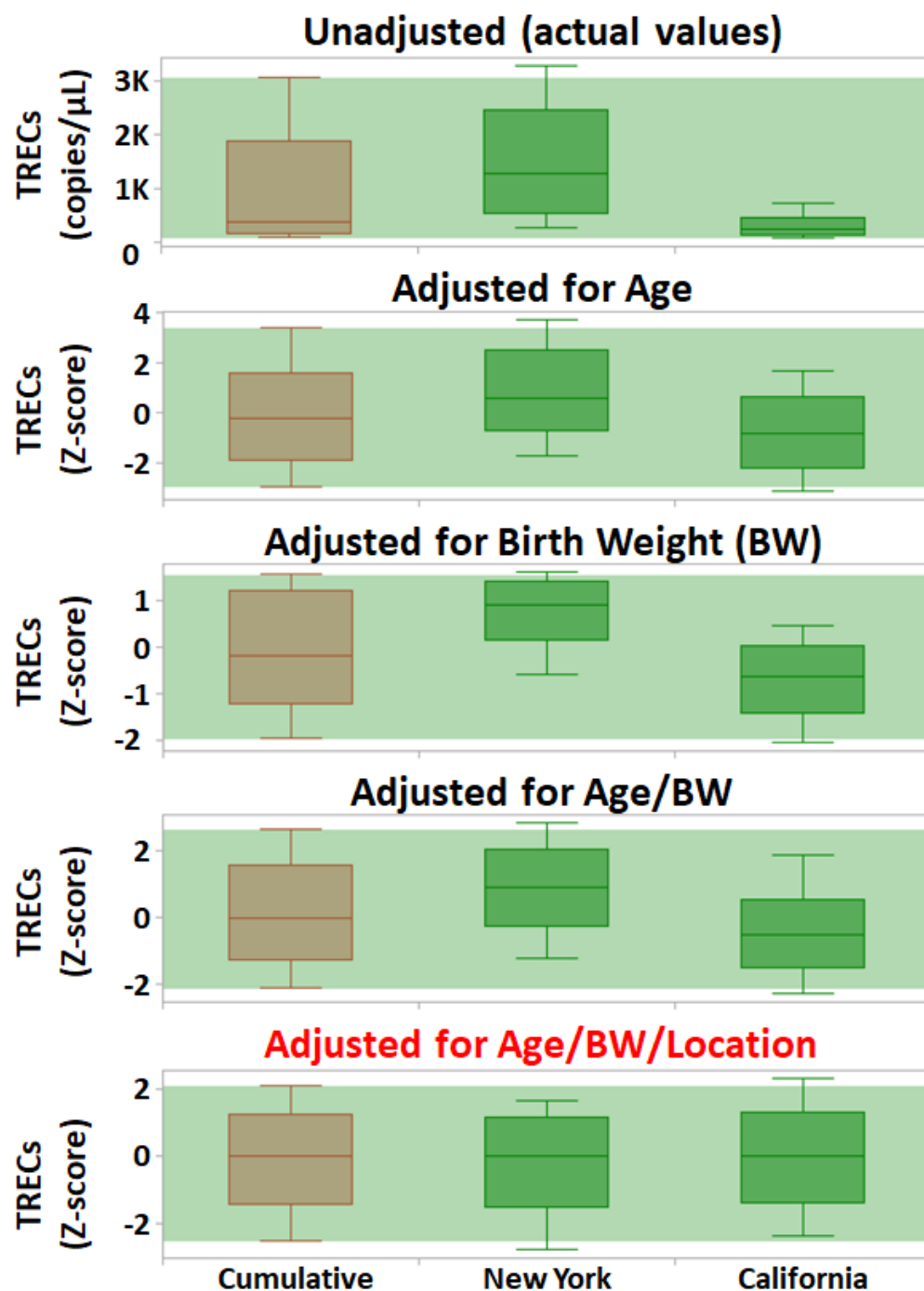
Figure S4. Single Condition Tool for condition CH TSH for location California.



(continued, Figure S4)

Reference Percentiles and Disease Range Overlap Values										
Markers		RR	Overlap	Informative Disease Range Scoring %iles					Case	Adjusted
Low	Unit	10%ile	%ile	99	95	90	85	50	Value	Value
C3/TSH	Ratio	-1.3	1.0	-1.3	-2.27	-2.89	-3.2	-5.89	0.05	-4.16
C16/TSH	Ratio	-1.31	0.5	-1.59	-2.48	-3	-3.47	-6.53	0.12	-3.66
17OHP/TSH	Ratio	-1.32	3.1	-0.45	-1.58	-2.44	-2.74	-5.16	0.3	-4.28
High	Unit	90%ile	%ile	1	5	10	15	50	Case	Adjusted
TSH	m[IU]/L	0.99	0.0	2.52	2.96	3.37	3.8	8.38	32.3	5.18
TSH/Cit	Ratio	1.31	0.2	2.09	2.57	3.28	3.53	6.16	1.35	3.55
TSH/IRT	Ratio	1.28	3.7	0.62	1.58	2.13	2.53	4.88	1.01	2.85
TSH/BIOT A	Ratio	1.28	0.0	2.26	2.96	3.5	3.81	6.53	0.56	4.2
TSH/Tyr	Ratio	1.31	0.2	1.92	2.43	3	3.37	5.78	0.34	3.86
TSH/GALT	Ratio	1.3	0.6	1.59	2.56	3.22	3.69	6.55	0.1	4.31
TSH/TRECs	Ratio	1.35	3.0	1.03	1.75	2.09	2.5	5.31	0.11	2.91
		RR	RR	Differentiator Disease Range %iles						
Differentiator	Unit	10%ile	90%ile	1	10	50	90	99	Case	Adjusted
17OHP 1T DBS	ng/mL	-1.3	1.35	-2.37	-1.19	0.54	3.08	5.49	9.55	-0.38
IRT DBS	ug/L	-1.27	1.43	-2.68	-1.58	-0.075	1.61	2.95	31.9	0.93
BIOT A DBS	ERU	-1.44	1.26	-3.62	-1.92	-0.03	1.37	2.62	57.5	0.82
GALT DBS	U/g[Hb]	-1.35	1.27	-2.55	-1.5	-0.083	1.55	4.78	310	1.19
TRECs DBS	copies/uL	-1.44	1.22	-2.94	-1.85	-0.096	1.16	2.48	302	0.36
Cit DBS	nmol/mL	-1.34	1.33	-2.4	-1.25	0.21	1.68	3.08	24	1.51
Tyr DBS	nmol/mL	-1.33	1.39	-2.57	-1.41	-0.031	1.6	3.2	94.2	0.16
C3 DBS	nmol/mL	-1.32	1.37	-2.6	-1.75	-0.18	1.55	2.84	1.6	-0.53
C16 DBS	nmol/mL	-1.38	1.31	-4.24	-2.09	-0.37	1.29	2.95	3.99	1.02
				RR - DR Overlap						
Covariate		Value								
Age hr		28								
BW		4030								
Sex		Male								

Figure S5. Reference range comparison of unadjusted and adjusted values for marker TRECs.



Legend: New York N=353,322; California N=520,539.



© 2021 by the authors. Submitted for possible open access publication under the terms and conditions of the Creative Commons Attribution (CC BY) license (<http://creativecommons.org/licenses/by/4.0/>).