Data Availability and Bias Assessment Report

03 February 2026

The NNTC Quarterly Reports and Data Quality Reports provide a broad summary across cohorts and sites for baseline demographics, available fluid collections, number of ancillary lab measurements, and other assessments. To further characterize the data availability for the purpose of modeling and analysis, we provide this **Data Availability and Bias Assessment Report**. This report summarizes the available data in terms of the NIMH Research Domain Criteria (RDoC) framework. Figures and Tables are included to assess the availability of NNTC data within and across variables, with a breakdown by sex for bias assessment. The report summarizes the NNTC variables available that were identified for each RDoC domain/construct. The figures and tables summarize: the number of participants with complete or partial data available; the demographics of the subgroup of participants with available data to enable an assessment of any potential sampling biases; and a high-level summary of the marginal and pair-wise joint distributions of the NNTC variables.

1 NNTC Data Table Abbreviations

Table	Description
ADL	Activities of Daily Living
BDI	Beck Depression Inventory II
CDI	Neuropsychiatric CIDI
DMS	HIV Motor Scale
FFI	Fried Frailty Index
NPV	Neuropsychological Variables Calculator
PFI	Patient's Assessment of Own Functioning
PSQ	Pittsburgh Sleep Quality Index
PSY	Neuropsychiatric PRISM/CIDI Table

2 Analysis Population

For the purpose of this report, a **longitudinal cohort** is defined to include all participants with two or more visits reported. Summary figures and tables that are restricted to this cohort are indicated in the respective caption.

Visit numbers are defined as 6-month intervals, starting with Visit 0 as any visit during the first 6 months of enrollment, Visit 1 as any visit 6 months to 1 year after enrollment, Visit 2 as any visit 1 to 1.5 years after enrollment, and so on.

An assessment is said to be **missing** for a participant if it was not measured on a visit number where other assessments were taken. An assessment is not considered missing on planned visits that did not occur. To check whether missingness is associated with the value of numeric variables, a regression model is fit using the mean assessment value for each participant across visits to predict the percent of missing assessments for each participant. A cubic B-spline with 2 knots is used to model non-linear relationships, and we check whether the adjusted R-squared for the model is greater than 10% as an indication of possible bias. This model is fit for each numeric variable shown in this report, and model fitting is performed once using all participants and again using only participants in the longitudinal cohort. For any variables where this type of bias is detected, a binned scatterplot would be displayed comparing mean assessment value (x-axis) against the missingness rate (y-axis), however no bias was detected in any of the fitted models, so none of these figures are shown in this report.

All figures and tables in this report use the first 10 years (Visits 0 through 19) of data, with further visits excluded from displays.

3 RDoC Domain: Negative Valence Systems

Negative Valence Systems are primarily responsible for responses to aversive situations or context, such as fear, anxiety, and loss.

3.1 Negative Valence Systems: Potential Threat (Anxiety)

Activation of a brain system in which harm may potentially occur but is distant, ambiguous, or low/uncertain in probability, characterized by a pattern of responses such as enhanced risk assessment (vigilance). These responses to low imminence threats are qualitatively different than the high imminence threat behaviors that characterize fear.

3.1.1 Variable Definitions

- **Irritability** (BDI: BDIIRRIT) Question: Irritability
- **Agitation** (BDI: BDIAGITA) Question: Agitation

3.1.2 Figures

The following two heatmaps show the number of participants with assessments available by variable and visit number. The second heatmap only includes participants in the longitudinal cohort.

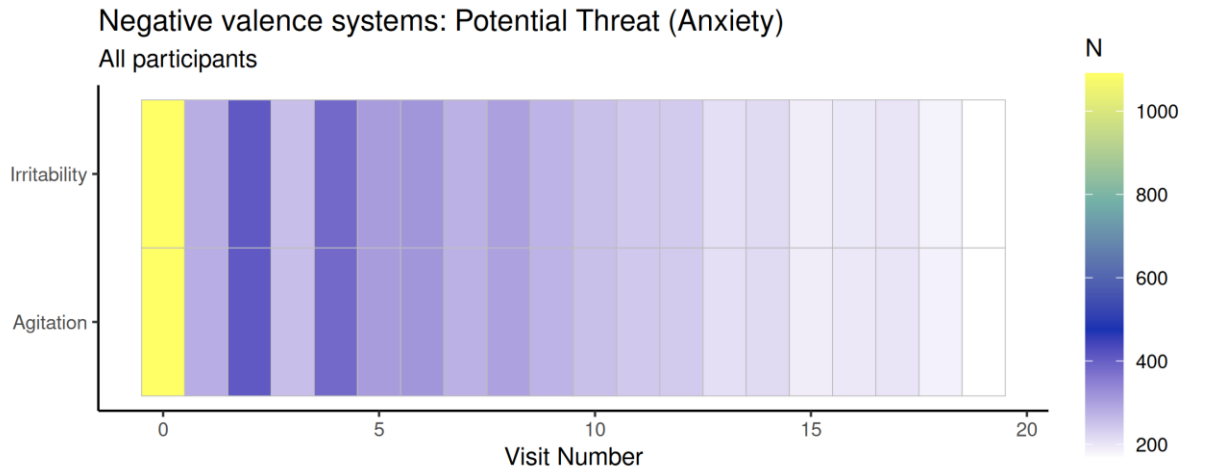

Figure 1: Heatmap showing the number of participants with each Negative valence systems: Potential Threat (Anxiety) variable measured by visit number for the first 10 years after enrollment in NNTC.

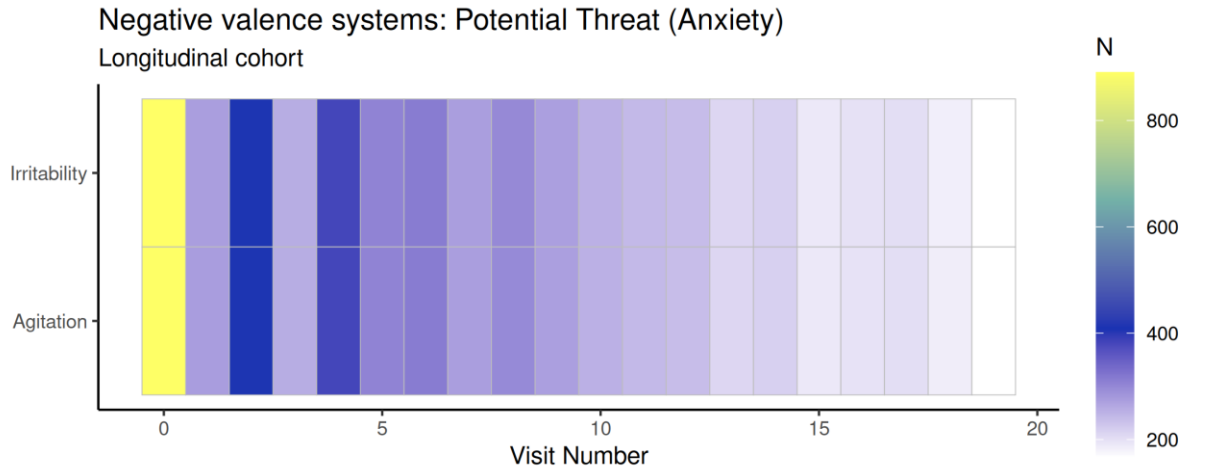

Figure 2: Heatmap showing the number of participants in the longitudinal cohort with each Negative valence systems: Potential Threat (Anxiety) variable measured, by visit number, for the first 10 years.

The following two UpSet plots show the joint availability of assessments across all visits for each subset of variables. The second UpSet plot only includes participants in the longitudinal cohort.

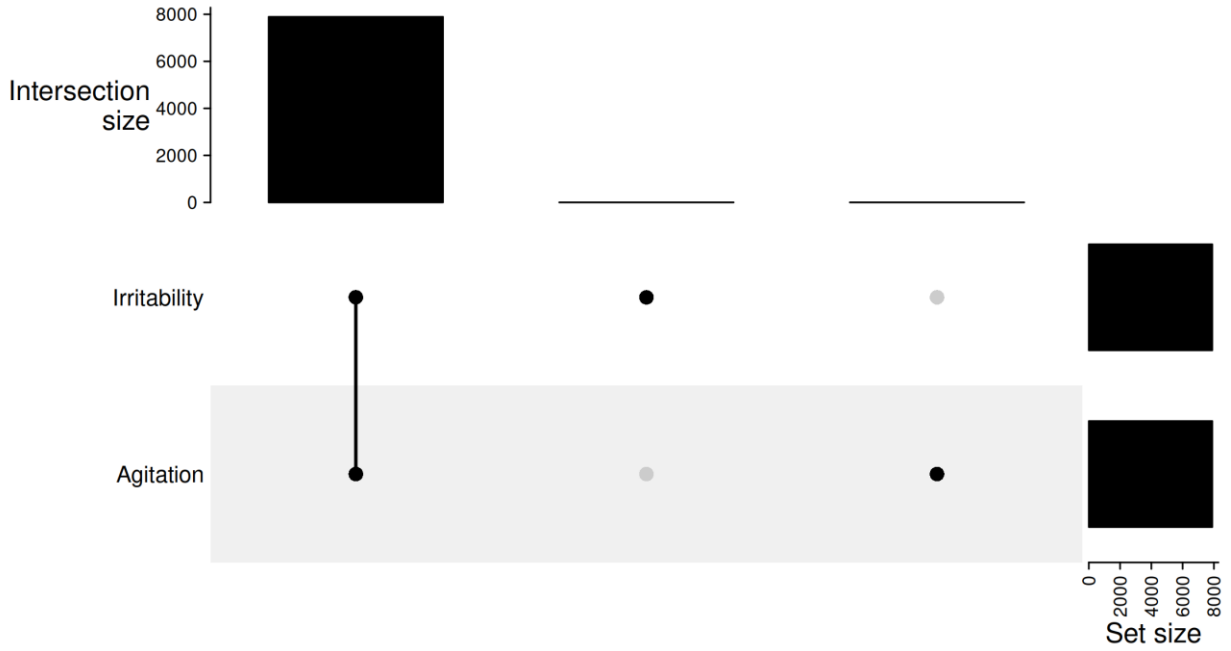

Figure 3: UpSet plot summarizing the joint availability of measures among individuals with one or more visits for the Negative valence systems: Potential Threat (Anxiety) variables across the first 20 visits. The bottom right horizontal barplot shows the number observations for each variable. The filled circles in the matrix represent the different Venn diagram spaces (unique and overlapping sets). Connected filled circles indicate a certain intersection. The barplot along the top shows the number of observations available for each intersection set.

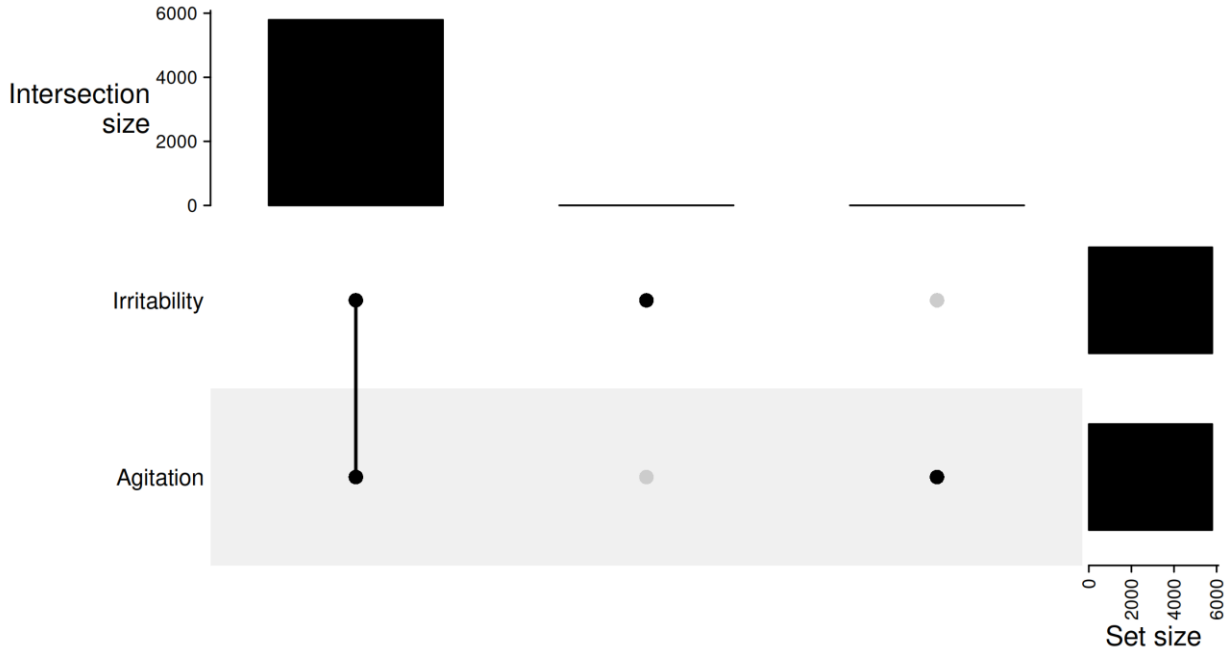

Figure 4: UpSet plot summarizing the joint availability of measures among individuals in the longitudinal cohort for the Negative valence systems: Potential Threat (Anxiety) variables across the first 20 visits. The bottom right horizontal barplot shows the number observations for each variable. The filled circles in the matrix represent the different Venn diagram spaces (unique and overlapping sets). Connected filled circles indicate a certain intersection. The barplot along the top shows the number of observations available for each intersection set.

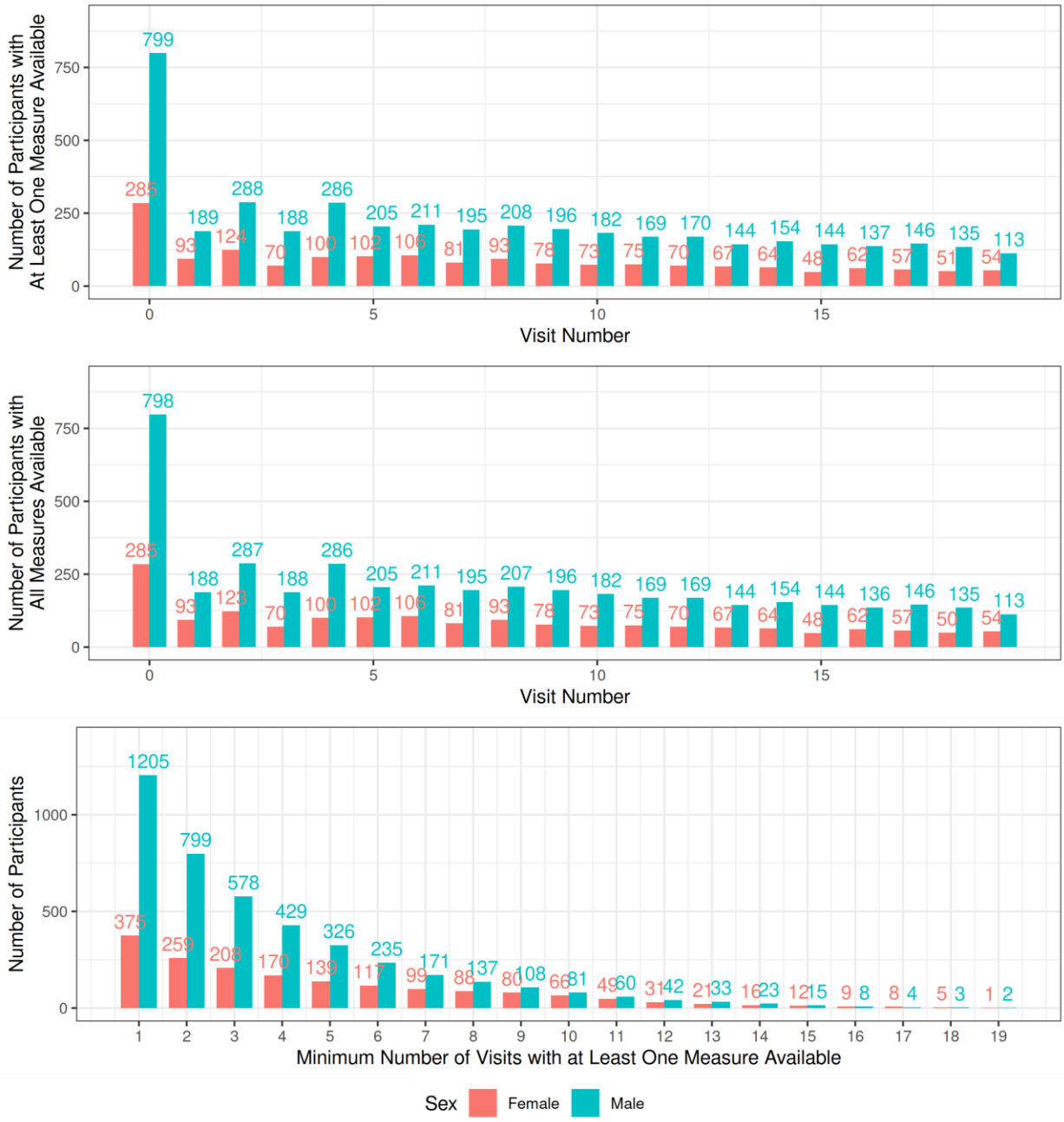

Figure 5: Data availability of participants for Negative valence systems: Potential Threat (Anxiety) variables by sex summarized by the number of participants with at least one measure available at each visit number (top), the number of participants with all measures available at each visit number (middle), and the total number of participants with at least one measurement taken for a given number of visits (bottom).

3.1.3 Tables

Table 1: Number of participants by sex with measures available for the "Negative valence systems: Potential Threat (Anxiety)" variables across the first 10 visits (visit numbers 0 to 9). Total includes 6 additional participants with missing information on sex.

Measure	Visit #:	0	1	2	3	4	5	6	7	8	9
Irritability	Female	285	93	123	70	100	102	106	81	93	78
	Male	799	188	288	188	286	205	211	195	208	196
	Total	1,090	281	411	258	386	307	317	276	301	274
Agitation	Female	285	93	124	70	100	102	106	81	93	78
	Male	798	189	287	188	286	205	211	195	207	196
	Total	1,089	282	411	258	386	307	317	276	300	274

Table 2: Number of participants by sex with measures available for the "Negative valence systems: Potential Threat (Anxiety)" variables across visit numbers 10 to 19.

Measure	Visit #:	10	11	12	13	14	15	16	17	18	19
Irritability	Female	73	75	70	67	64	48	62	57	50	54
	Male	182	169	170	144	154	144	137	146	135	113
	Total	255	244	240	211	218	192	199	203	185	167
Agitation	Female	73	75	70	67	64	48	62	57	51	54
	Male	182	169	169	144	154	144	136	146	135	113
	Total	255	244	239	211	218	192	198	203	186	167

3.2 Negative Valence Systems: Loss

A state of deprivation of a motivationally significant con-specific, object, or situation. Loss may be social or non-social and may include permanent or sustained loss of shelter, behavioral control, status, loved ones, or relationships. The response to loss may be episodic (e.g., grief) or sustained.

3.2.1 Variable Definitions

- **Loss of Pleasure** (BDI: BDILPLEA) Question: Loss of Pleasure

3.2.2 Figures

The following two heatmaps show the number of participants with assessments available by variable and visit number. The second heatmap only includes participants in the longitudinal cohort.

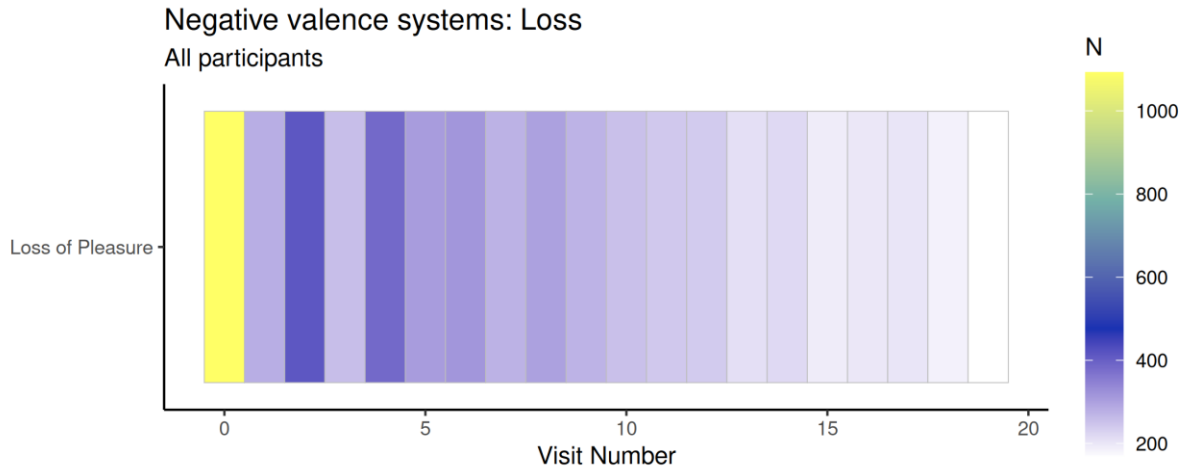

Figure 6: Heatmap showing the number of participants with each Negative valence systems: Loss variable measured by visit number for the first 10 years after enrollment in NNTC.

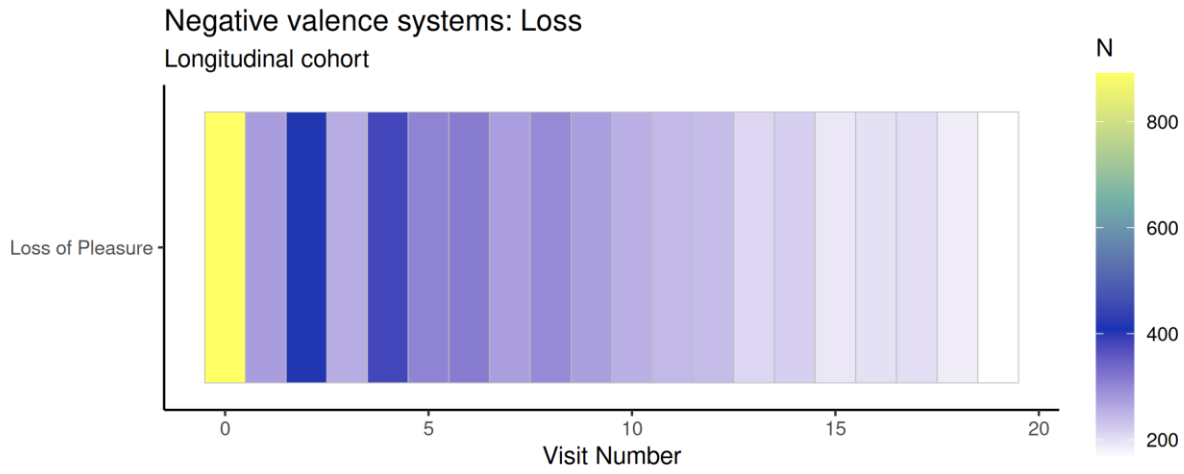

Figure 7: Heatmap showing the number of participants in the longitudinal cohort with each Negative valence systems: Loss variable measured, by visit number, for the first 10 years.

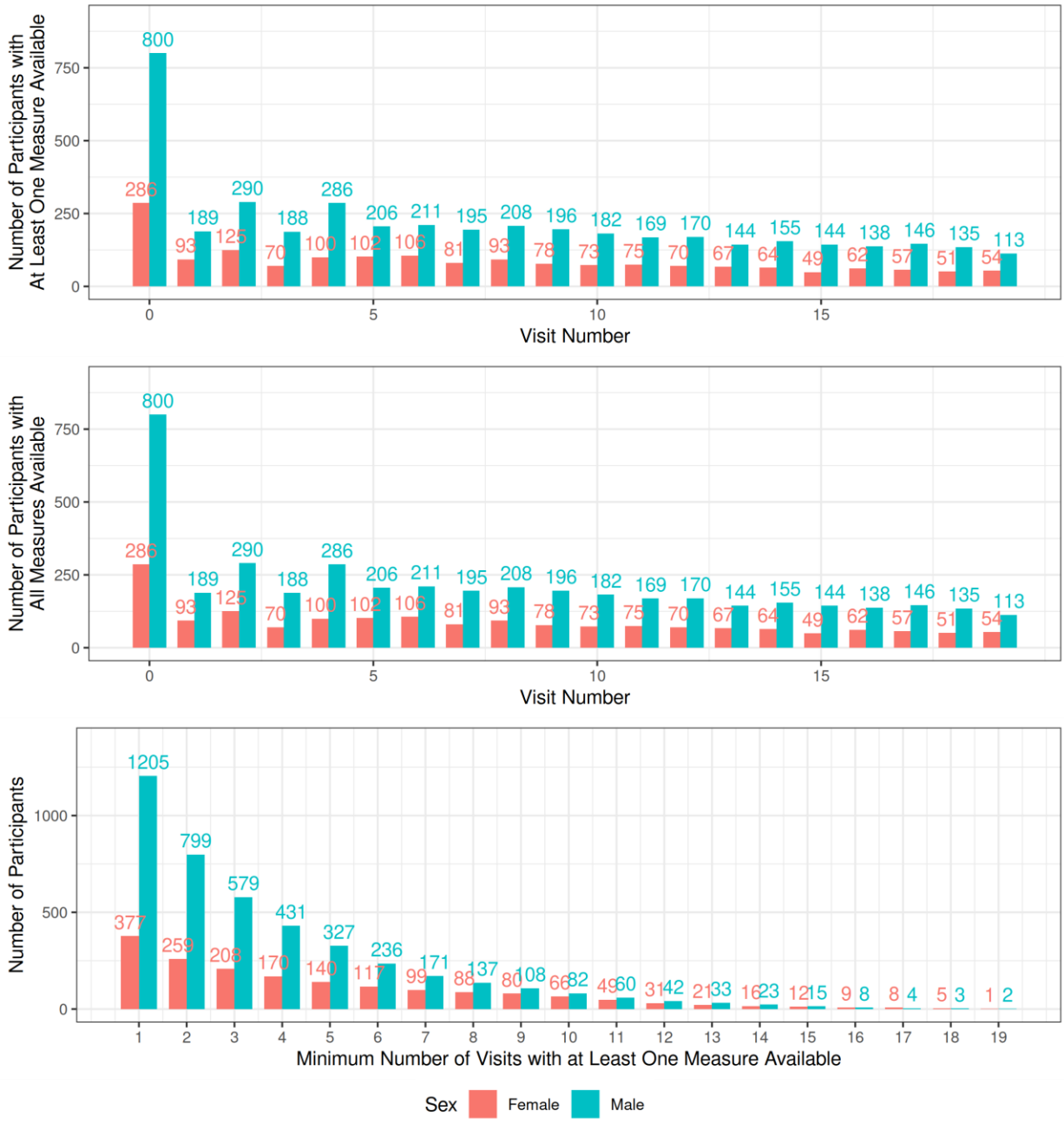

Figure 8: Data availability of participants for Negative valence systems: Loss variables by sex summarized by the number of participants with at least one measure available at each visit number (top), the number of participants with all measures available at each visit number (middle), and the total number of participants with at least one measurement taken for a given number of visits (bottom).

3.2.3 Tables

Table 3: Number of participants by sex with measures available for the "Negative valence systems: Loss" variables across the first 10 visits (visit numbers 0 to 9). Total includes 6 additional participants with missing information on sex.

Measure	Visit #:	0	1	2	3	4	5	6	7	8	9
Loss of Pleasure	Female	286	93	125	70	100	102	106	81	93	78
	Male	800	189	290	188	286	206	211	195	208	196
	Total	1,092	282	415	258	386	308	317	276	301	274

Table 4: Number of participants by sex with measures available for the "Negative valence systems: Loss" variables across visit numbers 10 to 19.

Measure	Visit #:	10	11	12	13	14	15	16	17	18	19
Loss of Pleasure	Female	73	75	70	67	64	49	62	57	51	54
	Male	182	169	170	144	155	144	138	146	135	113
	Total	255	244	240	211	219	193	200	203	186	167

4 RDoC Domain: Positive Valence Systems

Positive Valence Systems are primarily responsible for responses to positive motivational situations or contexts, such as reward seeking, consummatory behavior, and reward/habit learning.

4.1 Positive Valence Systems: Reward Responsiveness

Processes that govern an organism's hedonic response to impending or possible reward (as reflected in reward anticipation), the receipt of reward (as reflected in initial response to reward) and following repeated receipt of reward (as in reward satiation); across these subdomains, reward responsiveness primarily reflects neural activity to receipt of reward and reward cues and can also be measured in terms of subjective and behavioral responses.

4.1.1 Variable Definitions

- **Loss of Interest** (BDI: BDILINTE) Question: Loss of Interest

4.1.2 Figures

The following two heatmaps show the number of participants with assessments available by variable and visit number. The second heatmap only includes participants in the longitudinal cohort.

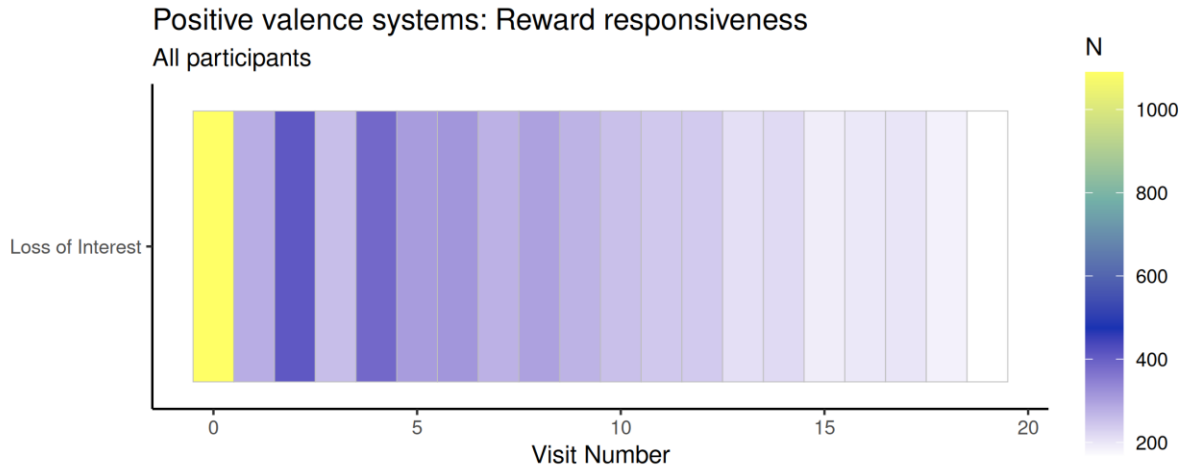

Figure 9: Heatmap showing the number of participants with each Positive valence systems: Reward responsiveness variable measured by visit number for the first 10 years after enrollment in NNTC.

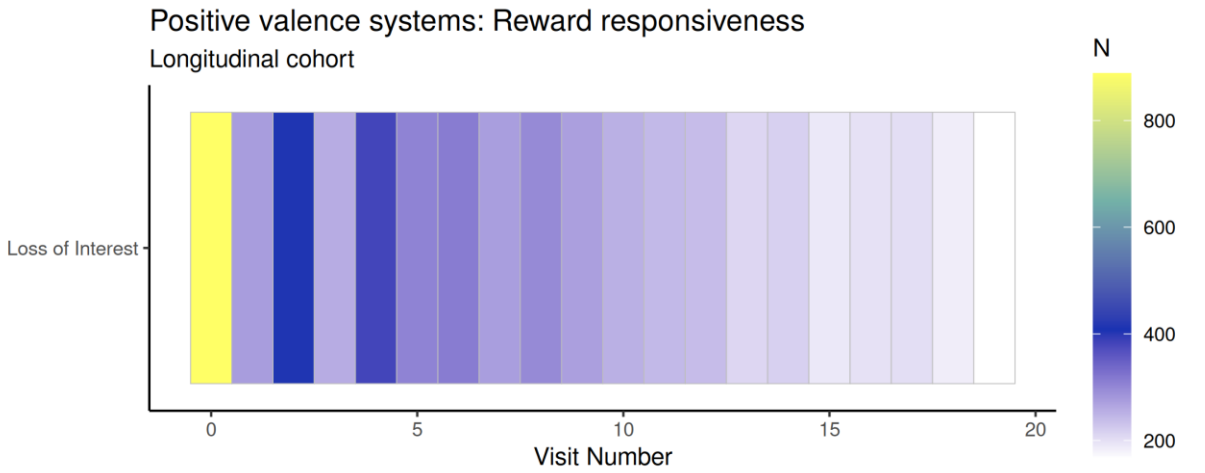

Figure 10: Heatmap showing the number of participants in the longitudinal cohort with each Positive valence systems: Reward responsiveness variable measured, by visit number, for the first 10 years.

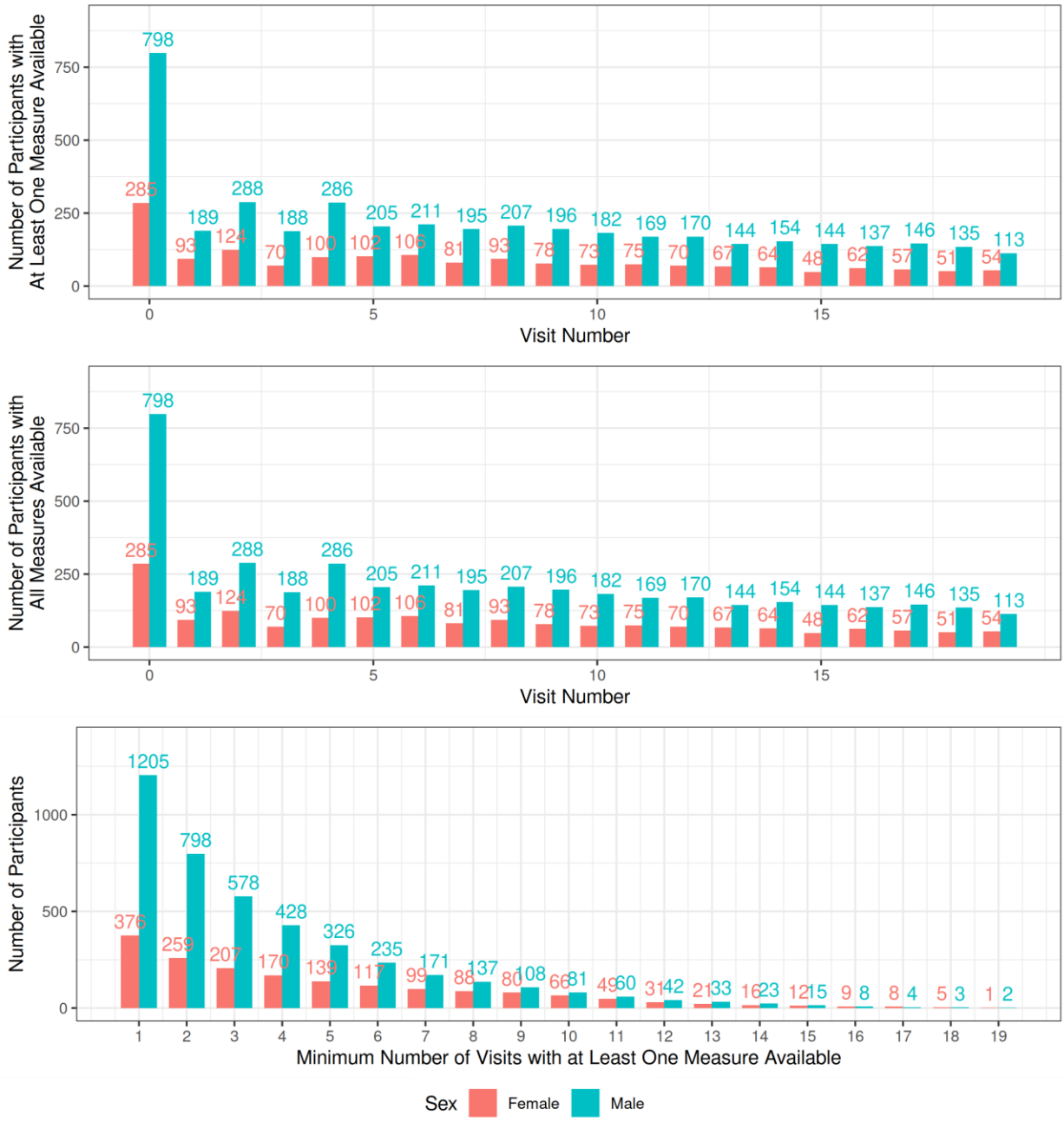

Figure 11: Data availability of participants for Positive valence systems: Reward responsiveness variables by sex summarized by the number of participants with at least one measure available at each visit number (top), the number of participants with all measures available at each visit number (middle), and the total number of participants with at least one measurement taken for a given number of visits (bottom).

4.1.3 Tables

Table 5: Number of participants by sex with measures available for the "Positive valence systems: Reward responsiveness" variables across the first 10 visits (visit numbers 0 to 9). Total includes 6 additional participants with missing information on sex.

Measure	Visit #:	0	1	2	3	4	5	6	7	8	9
Loss of Interest	Female	285	93	124	70	100	102	106	81	93	78
	Male	798	189	288	188	286	205	211	195	207	196
	Total	1,089	282	412	258	386	307	317	276	300	274

Table 6: Number of participants by sex with measures available for the "Positive valence systems: Reward responsiveness" variables across visit numbers 10 to 19.

Measure	Visit #:	10	11	12	13	14	15	16	17	18	19
Loss of Interest	Female	73	75	70	67	64	48	62	57	51	54
	Male	182	169	170	144	154	144	137	146	135	113
	Total	255	244	240	211	218	192	199	203	186	167

5 RDoC Domain: Cognitive Systems

Cognitive Systems are responsible for various cognitive processes.

5.1 Cognitive Systems: Attention

Attention refers to a range of processes that regulate access to capacity-limited systems, such as awareness, higher perceptual processes, and motor action. The concepts of capacity limitation and competition are inherent to the concepts of selective and divided attention.

5.1.1 Variable Definitions

- **Attention/Working Memory T-score** (NPV: CATTNTS)
- **Cognitive Functions Scale Score** (PFI: PFICOGSS) Calculation: PFICOGSS is calculated from the sum of the following scored fields: PFITCI, PFIDST, PFICNL, PFIDFL, PFICLC, PFIPLN, PFISLV, PFIDIR, and PFIINS.
- **SIP Index T-Score** **Discontinued October 2024** (NPV: NPVSIPIT)
- **Trail Making Part A T-Score** (NPV: NPVTMATS)
- **Digit Symbol T-Score** **Discontinued October 2024** (NPV: NPVSYDTS)
- **Symbol Search T-Score** **Discontinued October 2024** (NPV: NPVSYSTS)

5.1.2 Figures

The following two heatmaps show the number of participants with assessments available by variable and visit number. The second heatmap only includes participants in the longitudinal cohort.

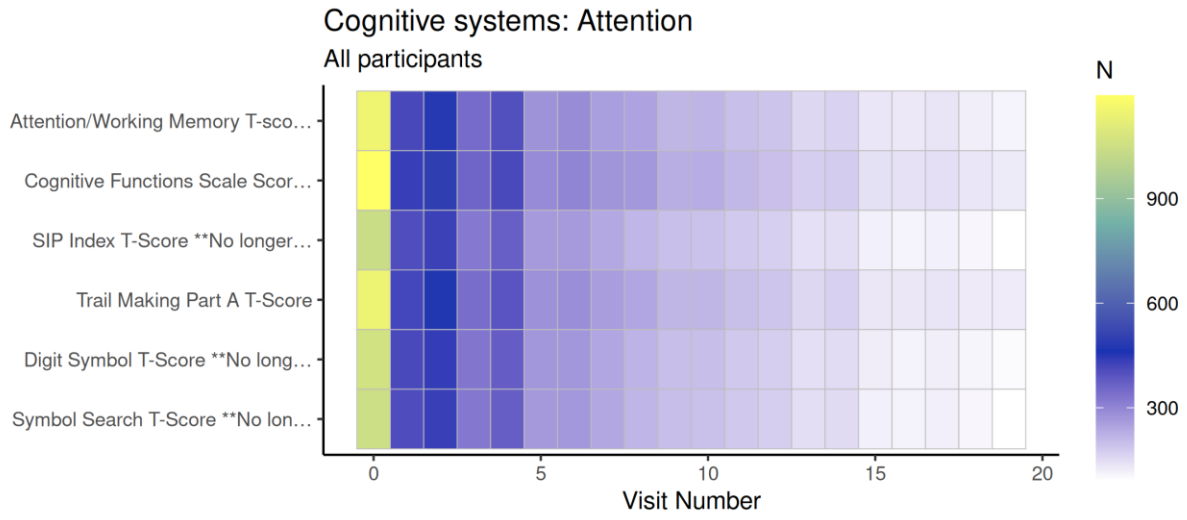

Figure 12: Heatmap showing the number of participants with each Cognitive systems: Attention variable measured by visit number for the first 10 years after enrollment in NNTC.

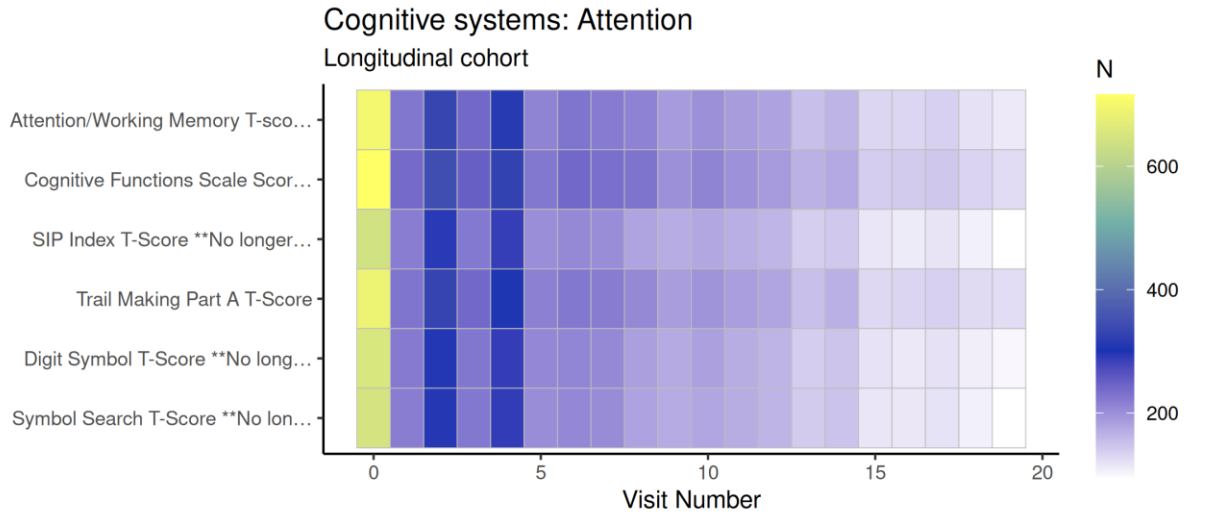

Figure 13: Heatmap showing the number of participants in the longitudinal cohort with each Cognitive systems: Attention variable measured, by visit number, for the first 10 years.

The following two UpSet plots show the joint availability of assessments across all visits for each subset of variables. The second UpSet plot only includes participants in the longitudinal cohort.

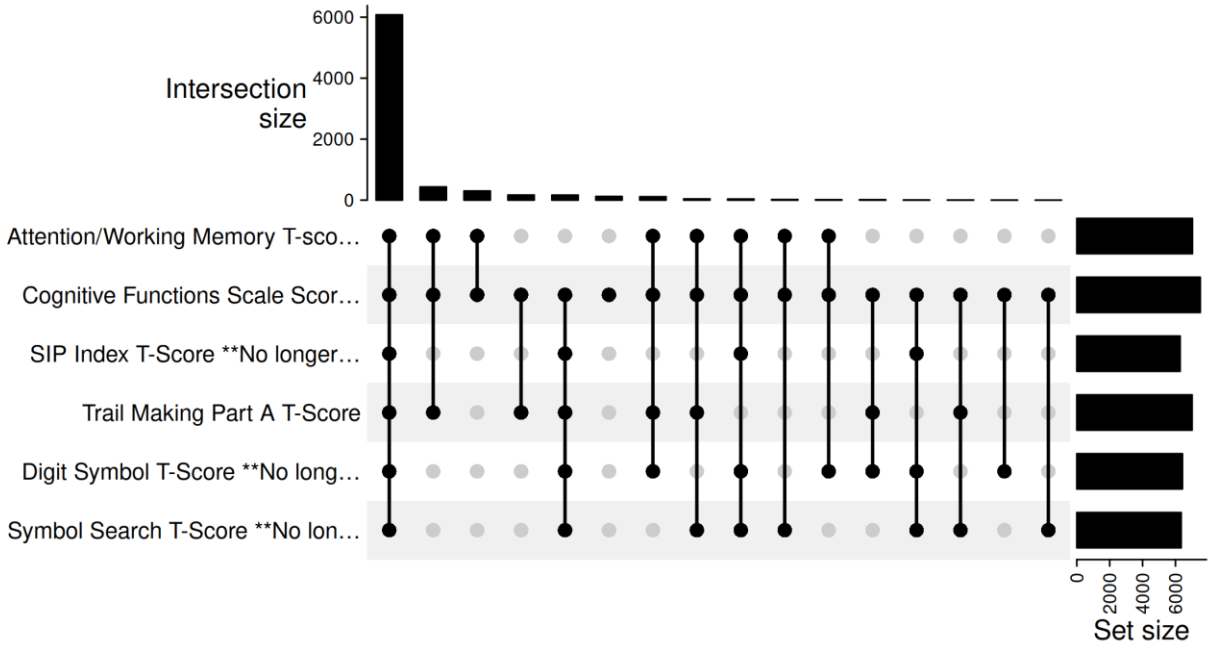

Figure 14: UpSet plot summarizing the joint availability of measures among individuals with one or more visits for the Cognitive systems: Attention variables across the first 20 visits. The bottom right horizontal barplot shows the number observations for each variable. The filled circles in the matrix represent the different Venn diagram spaces (unique and overlapping sets). Connected filled circles indicate a certain intersection. The barplot along the top shows the number of observations available for each intersection set.

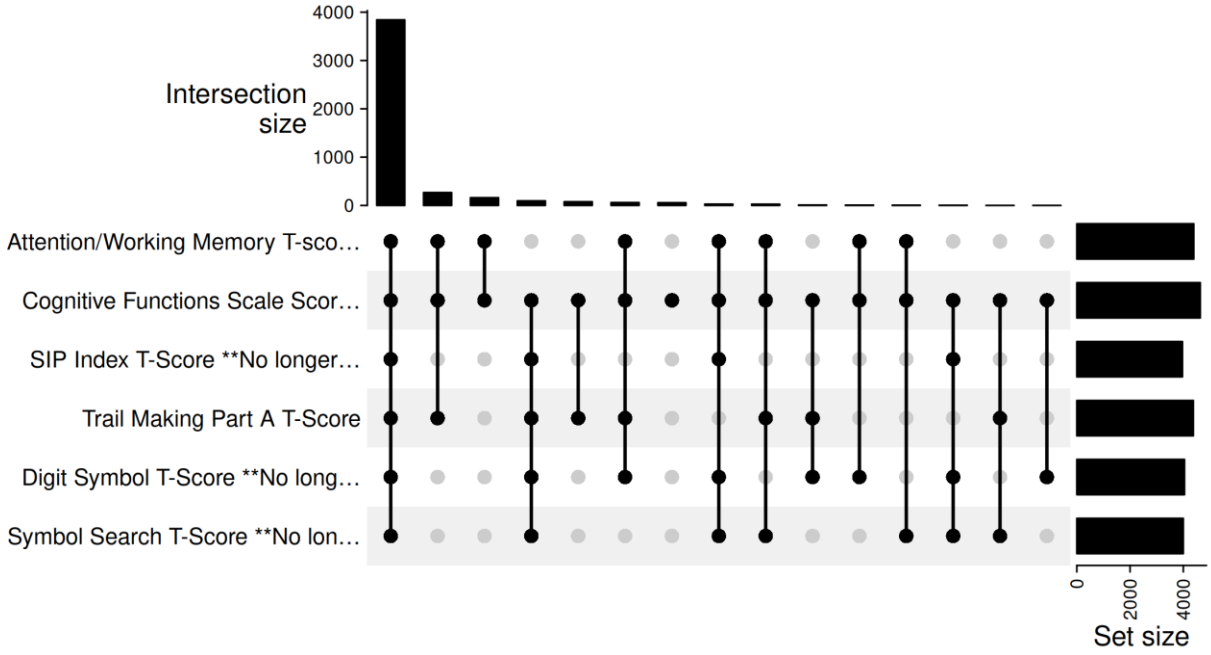

Figure 15: UpSet plot summarizing the joint availability of measures among individuals in the longitudinal cohort for the Cognitive systems: Attention variables across the first 20 visits. The bottom right horizontal barplot shows the number observations for each variable. The filled circles in the matrix represent the different Venn diagram spaces (unique and overlapping sets). Connected filled circles indicate a certain intersection. The barplot along the top shows the number of observations available for each intersection set.

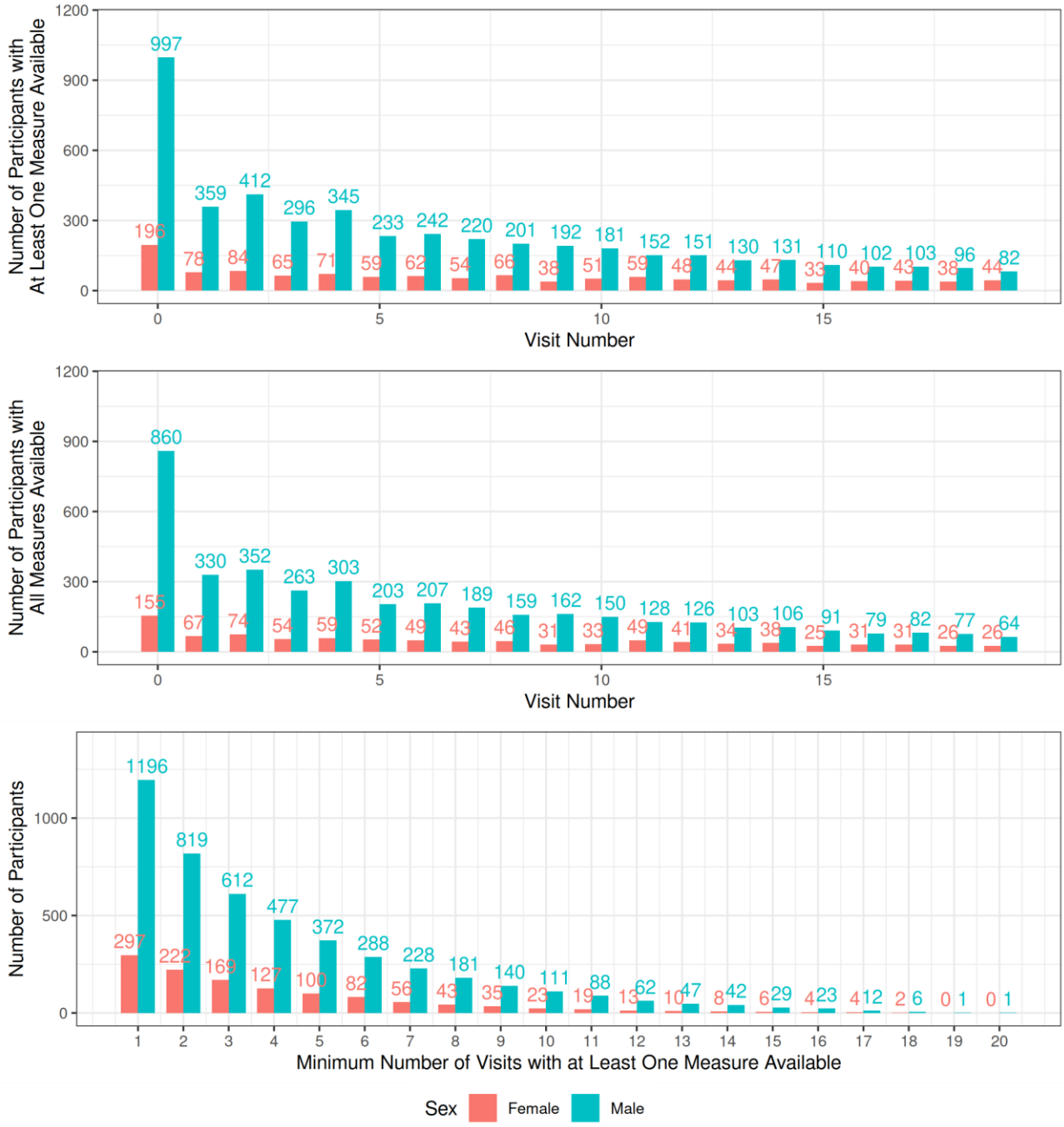

Figure 16: Data availability of participants for Cognitive systems: Attention variables by sex summarized by the number of participants with at least one measure available at each visit number (top), the number of participants with all measures available at each visit number (middle), and the total number of participants with at least one measurement taken for a given number of visits (bottom).

Figure 17: Scatterplot matrix of the Cognitive systems: Attention variables with points colored by sex. The diagonal shows the estimated density curve for each marginal distribution, and the top right cells show the respective estimated pairwise Pearson correlation values overall (in black) and by sex.

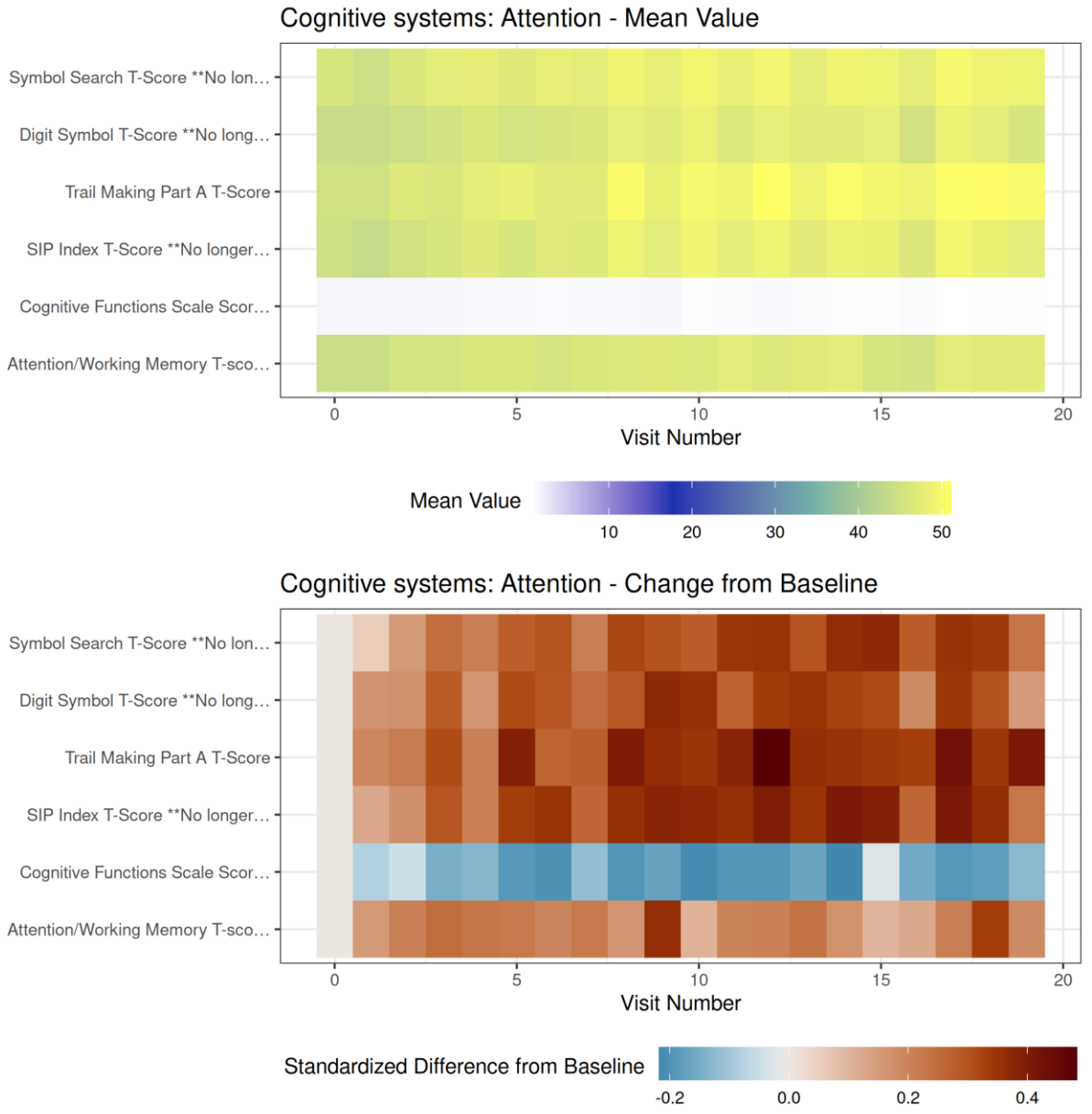

Figure 18: Heatmap of the mean value (top) and standardized mean difference in assessment measurement from baseline (bottom) by visit number for each numeric variable in the Cognitive systems: Attention construct. Standardized mean difference is the mean difference divided by the standard deviation across participants at baseline.

5.1.3 Tables

Table 7: Number of participants by sex with measures available for the "Cognitive systems: Attention" variables across the first 10 visits (visit numbers 0 to 9). Total includes 2 additional participants with missing information on sex.

Measure	Visit #:	0	1	2	3	4	5	6	7	8	9
Attention/Working Memory T-score	Female	181	71	82	62	70	58	58	48	59	34
	Male	966	347	397	288	334	221	232	210	190	182
	Total	1,147	418	479	350	404	279	290	258	249	216
Cognitive Functions Scale Score	Female	196	78	84	65	71	59	62	54	66	38
	Male	997	359	412	296	345	233	242	220	201	192
	Total	1,195	437	496	361	416	292	304	274	267	230
SIP Index T-Score **Discontinued October 2024**	Female	160	72	75	57	61	54	52	47	52	34
	Male	877	335	357	268	312	210	212	193	163	166
	Total	1,037	407	432	325	373	264	264	240	215	200
Trail Making Part A T-Score	Female	188	76	81	63	68	58	57	50	59	36
	Male	953	346	390	283	326	223	229	209	184	180
	Total	1,141	422	471	346	394	281	286	259	243	216
Digit Symbol T-Score **Discontinued October 2024**	Female	166	74	75	59	62	56	52	47	55	34
	Male	894	341	365	272	314	214	217	197	165	168
	Total	1,060	415	440	331	376	270	269	244	220	202
Symbol Search T-Score **Discontinued October 2024**	Female	161	72	75	57	62	55	52	47	54	34
	Male	885	336	361	271	313	211	215	195	163	167
	Total	1,046	408	436	328	375	266	267	242	217	201

Table 8: Number of participants by sex with measures available for the "Cognitive systems: Attention" variables across visit numbers 10 to 19.

Measure	Visit #:	10	11	12	13	14	15	16	17	18	19
Attention/Working Memory T-score	Female	48	55	45	39	42	31	37	38	31	38
	Male	170	145	146	120	125	103	94	99	90	75
	Total	218	200	191	159	167	134	131	137	121	113
Cognitive Functions Scale Score	Female	51	59	48	44	47	33	40	43	38	44
	Male	181	152	151	130	131	110	102	103	96	82
	Total	232	211	199	174	178	143	142	146	134	126
SIP Index T-Score **Discontinued October 2024**	Female	36	50	43	36	40	25	32	34	28	27
	Male	158	131	130	108	108	93	80	84	79	66
	Total	194	181	173	144	148	118	112	118	107	93
Trail Making Part A T-Score	Female	46	57	46	41	47	31	39	39	37	44
	Male	170	141	143	118	124	101	93	98	90	81
	Total	216	198	189	159	171	132	132	137	127	125
Digit Symbol T-Score **Discontinued October 2024**	Female	41	50	44	37	42	28	33	35	29	32
	Male	160	133	130	108	110	94	81	86	80	68
	Total	201	183	174	145	152	122	114	121	109	100
Symbol Search T-Score **Discontinued October 2024**	Female	37	52	43	37	41	25	34	34	28	27
	Male	159	131	131	110	112	93	81	85	79	66
	Total	196	183	174	147	153	118	115	119	107	93

5.2 Cognitive Systems: Perception

Perception refers to the process(es) that perform computations on sensory data to construct and transform representations of the external environment, acquire information from, and make predictions about, the external world, and guide action.

5.2.1 Variable Definitions

- **Sensory-Perceptual Scale Score** (PFI: PFISPSS) Calculation: PFISPSS is calculated from the sum of the following scored fields: PFIFTR, PFIFTL, and PFIVLC.

5.2.2 Figures

The following two heatmaps show the number of participants with assessments available by variable and visit number. The second heatmap only includes participants in the longitudinal cohort.

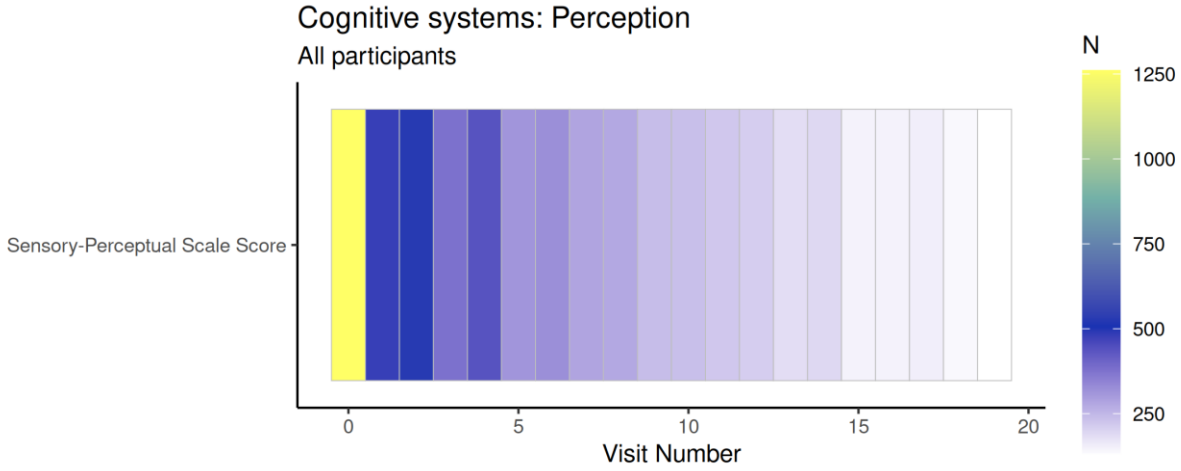

Figure 19: Heatmap showing the number of participants with each Cognitive systems: Perception variable measured by visit number for the first 10 years after enrollment in NNTC.

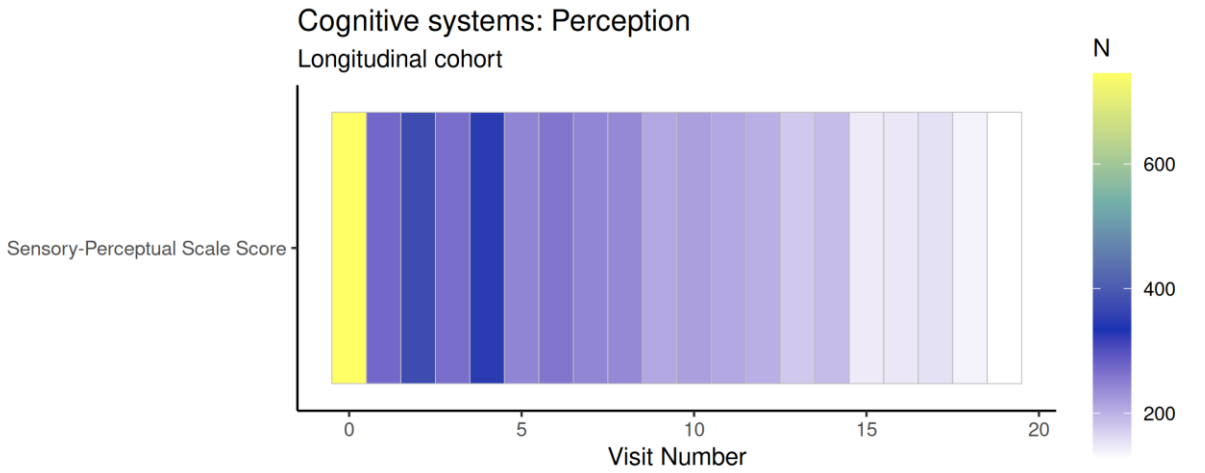

Figure 20: Heatmap showing the number of participants in the longitudinal cohort with each Cognitive systems: Perception variable measured, by visit number, for the first 10 years.

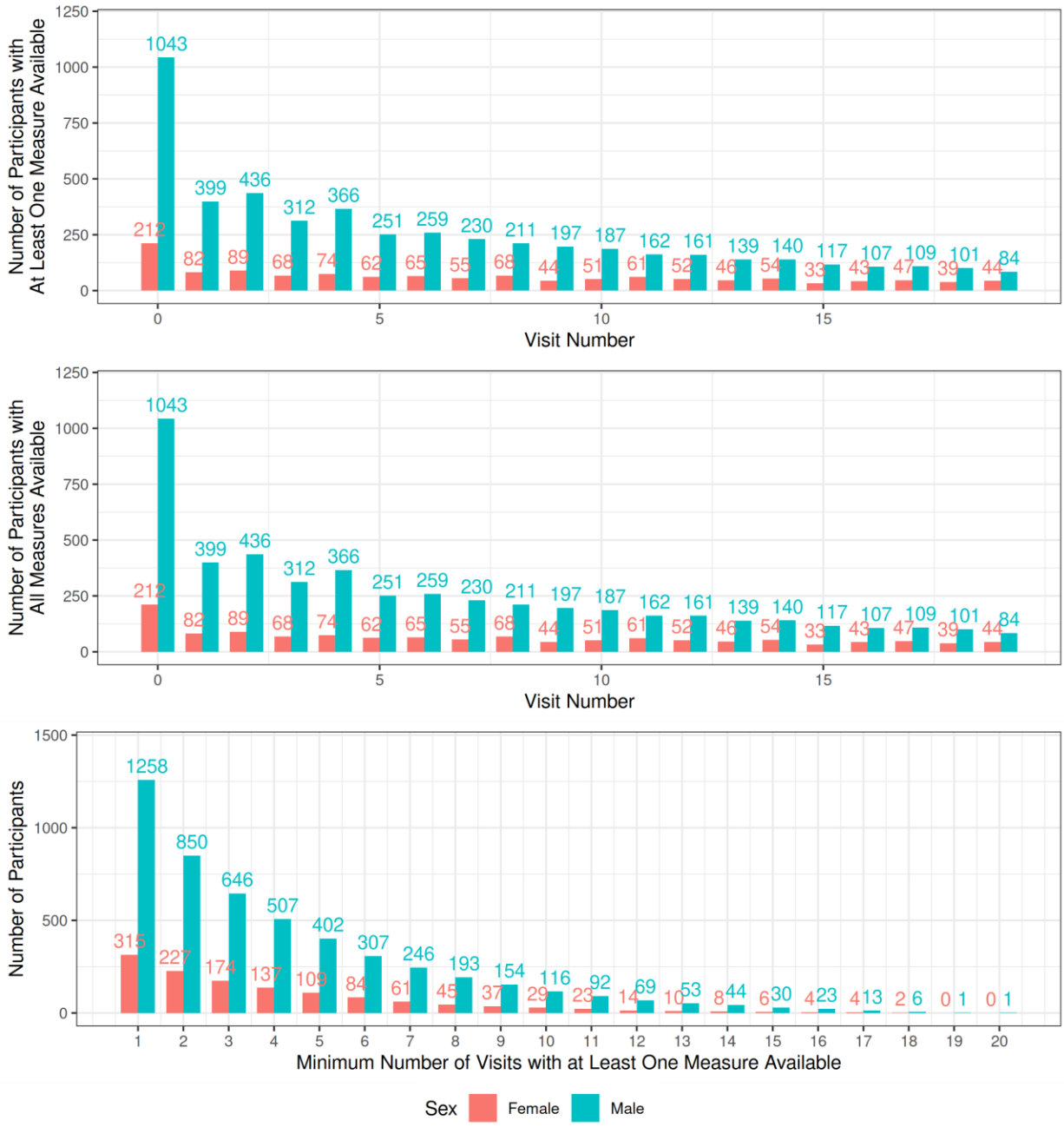

Figure 21: Data availability of participants for Cognitive systems: Perception variables by sex summarized by the number of participants with at least one measure available at each visit number (top), the number of participants with all measures available at each visit number (middle), and the total number of participants with at least one measurement taken for a given number of visits (bottom).

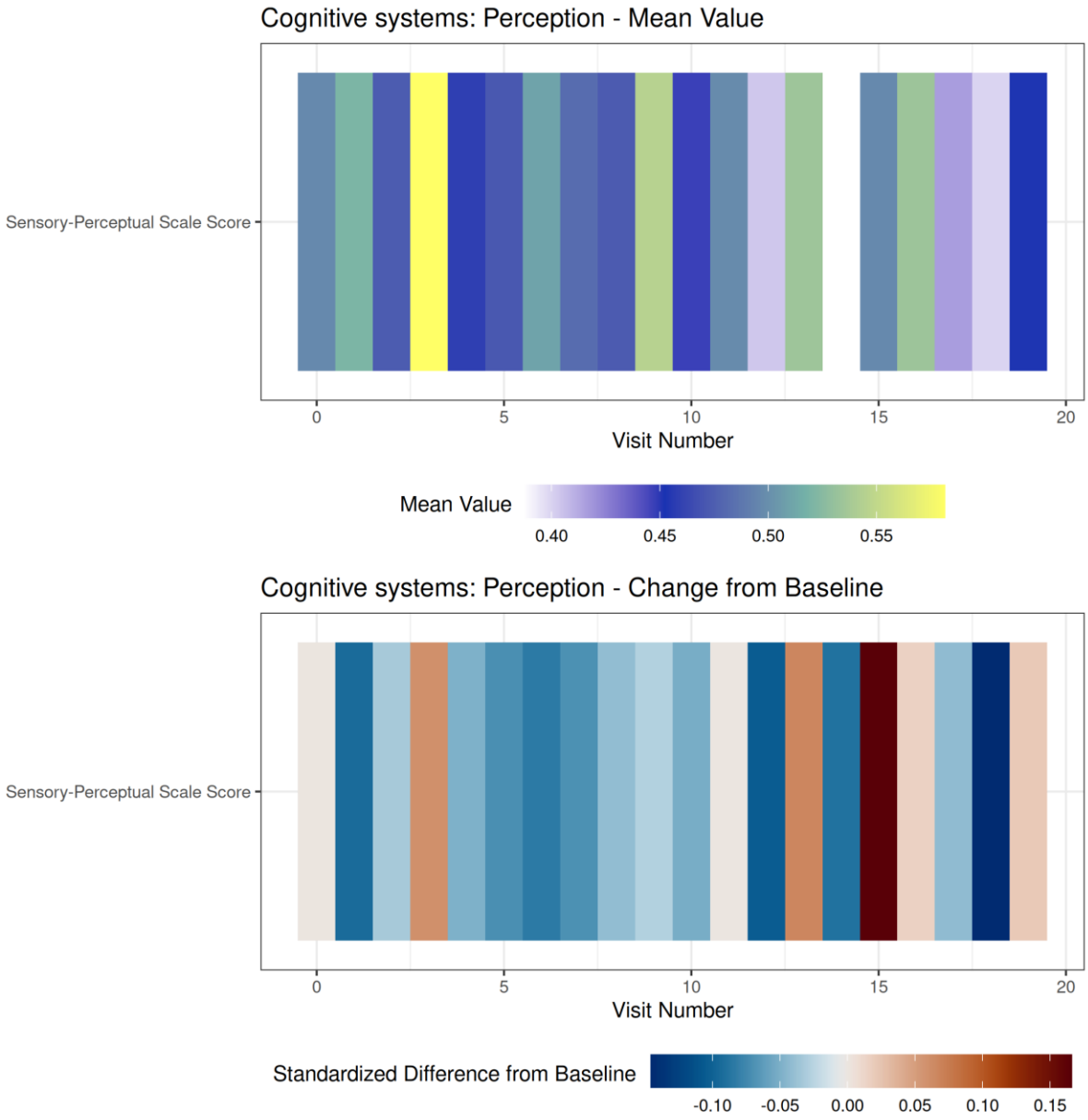

Figure 22: Heatmap of the mean value (top) and standardized mean difference in assessment measurement from baseline (bottom) by visit number for each numeric variable in the Cognitive systems: Perception construct. Standardized mean difference is the mean difference divided by the standard deviation across participants at baseline.

5.2.3 Tables

Table 9: Number of participants by sex with measures available for the "Cognitive systems: Perception" variables across the first 10 visits (visit numbers 0 to 9). Total includes 5 additional participants with missing information on sex.

Measure	Visit #:	0	1	2	3	4	5	6	7	8	9
Sensory-Perceptual Scale Score	Female	212	82	89	68	74	62	65	55	68	44
	Male	1,043	399	436	312	366	251	259	230	211	197
	Total	1,260	481	525	380	440	313	324	285	279	241

Table 10: Number of participants by sex with measures available for the "Cognitive systems: Perception" variables across visit numbers 10 to 19.

Measure	Visit #:	10	11	12	13	14	15	16	17	18	19
Sensory-Perceptual Scale Score	Female	51	61	52	46	54	33	43	47	39	44
	Male	187	162	161	139	140	117	107	109	101	84
	Total	238	223	213	185	194	150	150	156	140	128

5.3 Cognitive Systems: Declarative Memory

Declarative memory is the acquisition or encoding, storage and consolidation, and retrieval of representations of facts and events. Declarative memory provides the critical substrate for relational representations–i.e., for spatial, temporal, and other contextual relations among items, contributing to representations of events (episodic memory) and the integration and organization of factual knowledge (semantic memory). These representations facilitate the inferential and flexible extraction of new information from these relationships.

5.3.1 Variable Definitions

- **Brief Visuospatial Memory Test - Revised Total T-Score** (NPV: NPVBVTTS)
- **Hopkins Verbal Learning Test Total T-Score** (NPV: NPVHVTTS)
- **Memory Domain T-score** (NPV: CMEMTS)

5.3.2 Figures

The following two heatmaps show the number of participants with assessments available by variable and visit number. The second heatmap only includes participants in the longitudinal cohort.

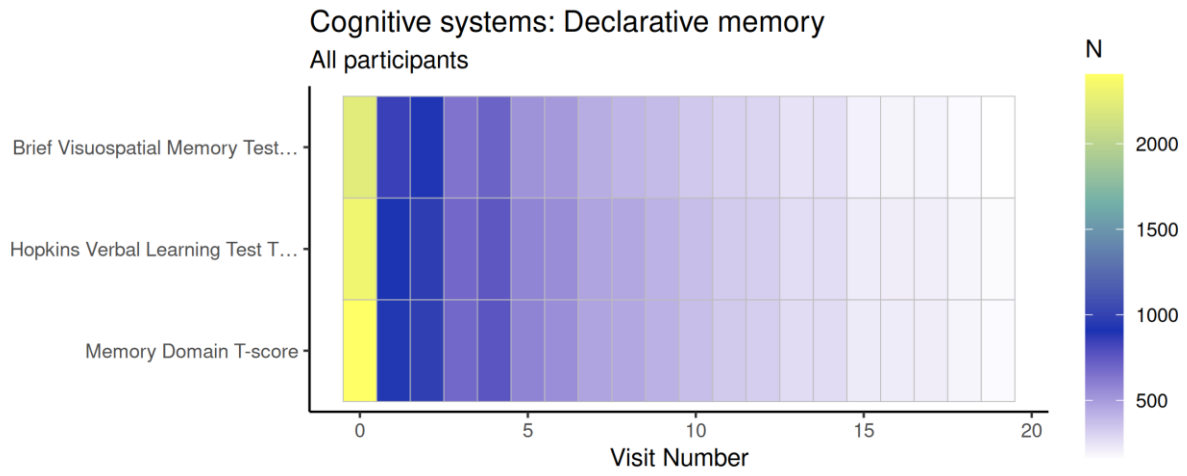

Figure 23: Heatmap showing the number of participants with each Cognitive systems: Declarative memory variable measured by visit number for the first 10 years after enrollment in NNTC.

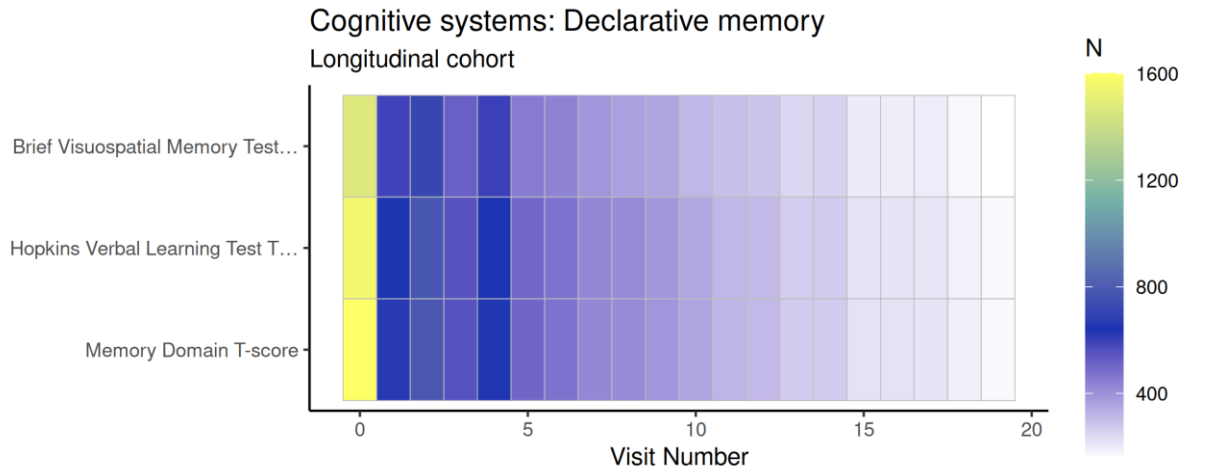

Figure 24: Heatmap showing the number of participants in the longitudinal cohort with each Cognitive systems: Declarative memory variable measured, by visit number, for the first 10 years.

The following two UpSet plots show the joint availability of assessments across all visits for each subset of variables. The second UpSet plot only includes participants in the longitudinal cohort.

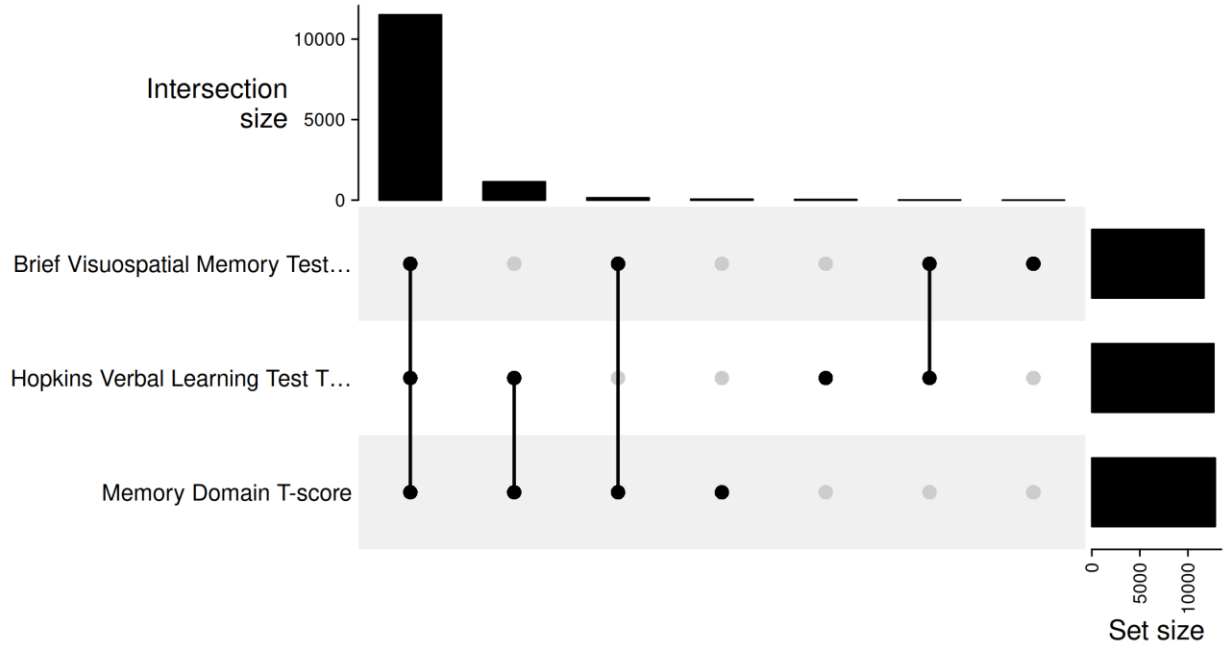

Figure 25: UpSet plot summarizing the joint availability of measures among individuals with one or more visits for the Cognitive systems: Declarative memory variables across the first 20 visits. The bottom right horizontal barplot shows the number observations for each variable. The filled circles in the matrix represent the different Venn diagram spaces (unique and overlapping sets). Connected filled circles indicate a certain intersection. The barplot along the top shows the number of observations available for each intersection set.

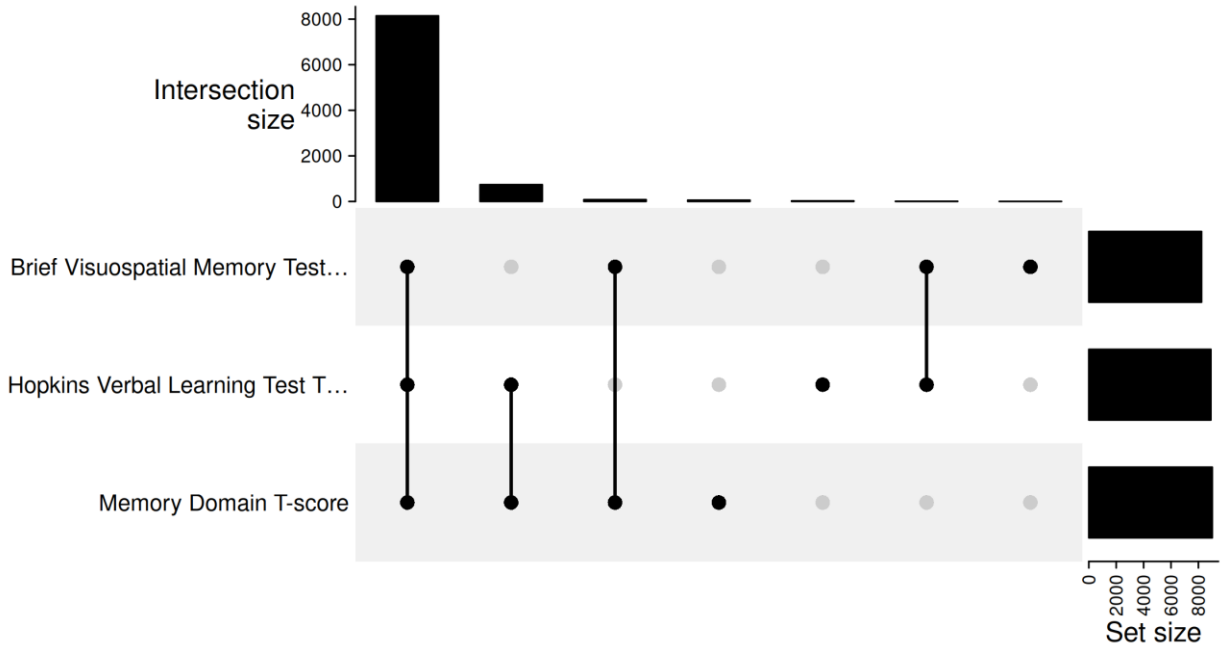

Figure 26: UpSet plot summarizing the joint availability of measures among individuals in the longitudinal cohort for the Cognitive systems: Declarative memory variables across the first 20 visits. The bottom right horizontal barplot shows the number observations for each variable. The filled circles in the matrix represent the different Venn diagram spaces (unique and overlapping sets). Connected filled circles indicate a certain intersection. The barplot along the top shows the number of observations available for each intersection set.

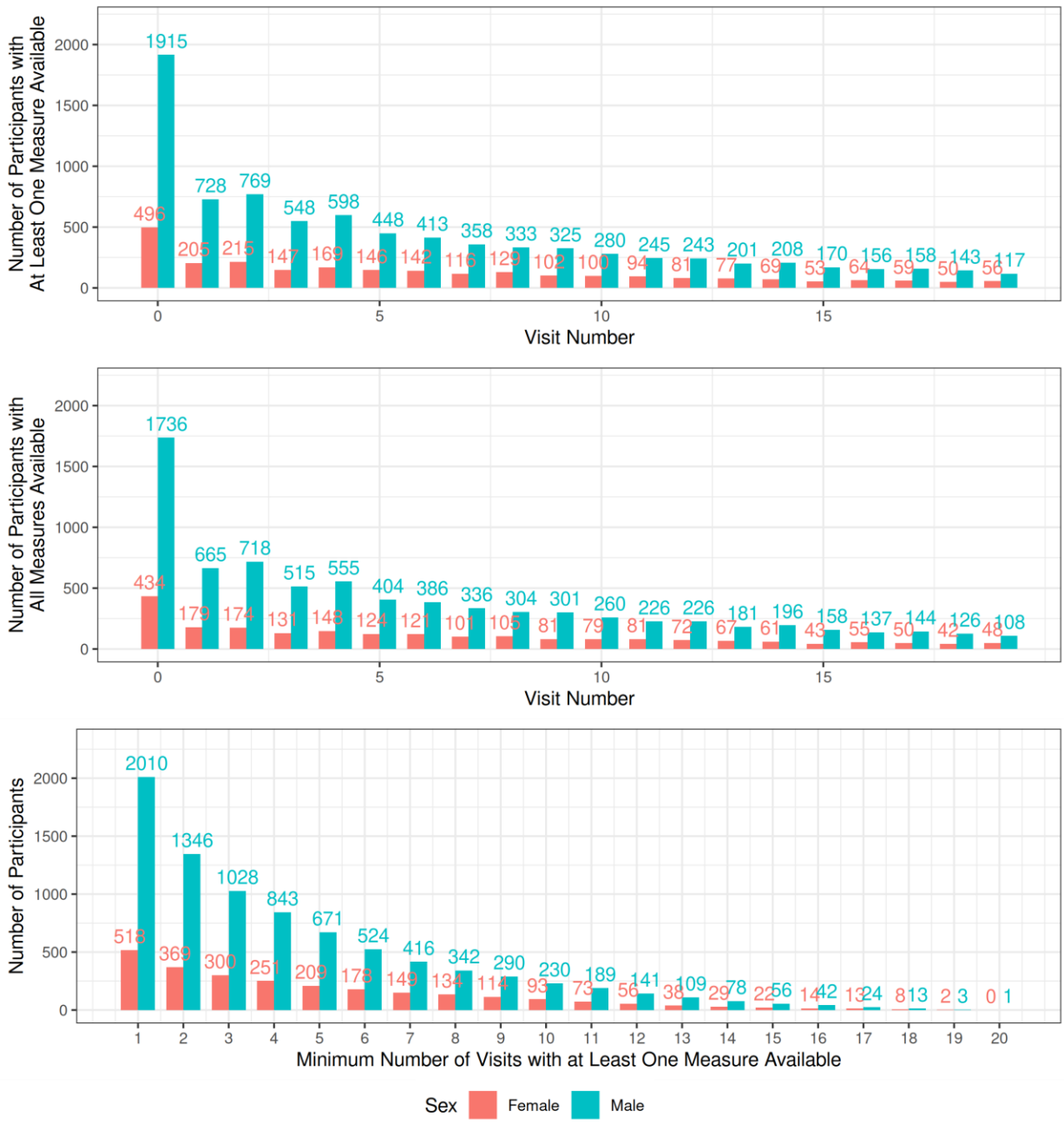

Figure 27: Data availability of participants for Cognitive systems: Declarative memory variables by sex summarized by the number of participants with at least one measure available at each visit number (top), the number of participants with all measures available at each visit number (middle), and the total number of participants with at least one measurement taken for a given number of visits (bottom).

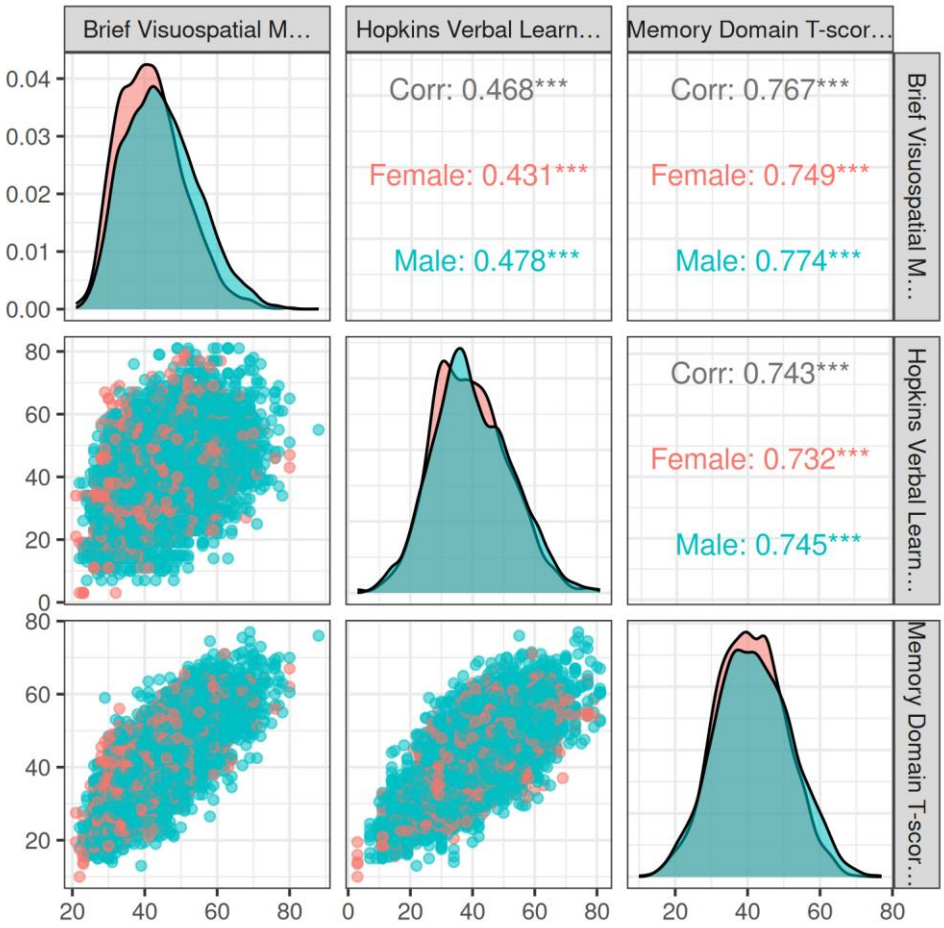

Figure 28: Scatterplot matrix of the Cognitive systems: Declarative memory variables with points colored by sex. The diagonal shows the estimated density curve for each marginal distribution, and the top right cells show the respective estimated pairwise Pearson correlation values overall (in black) and by sex.

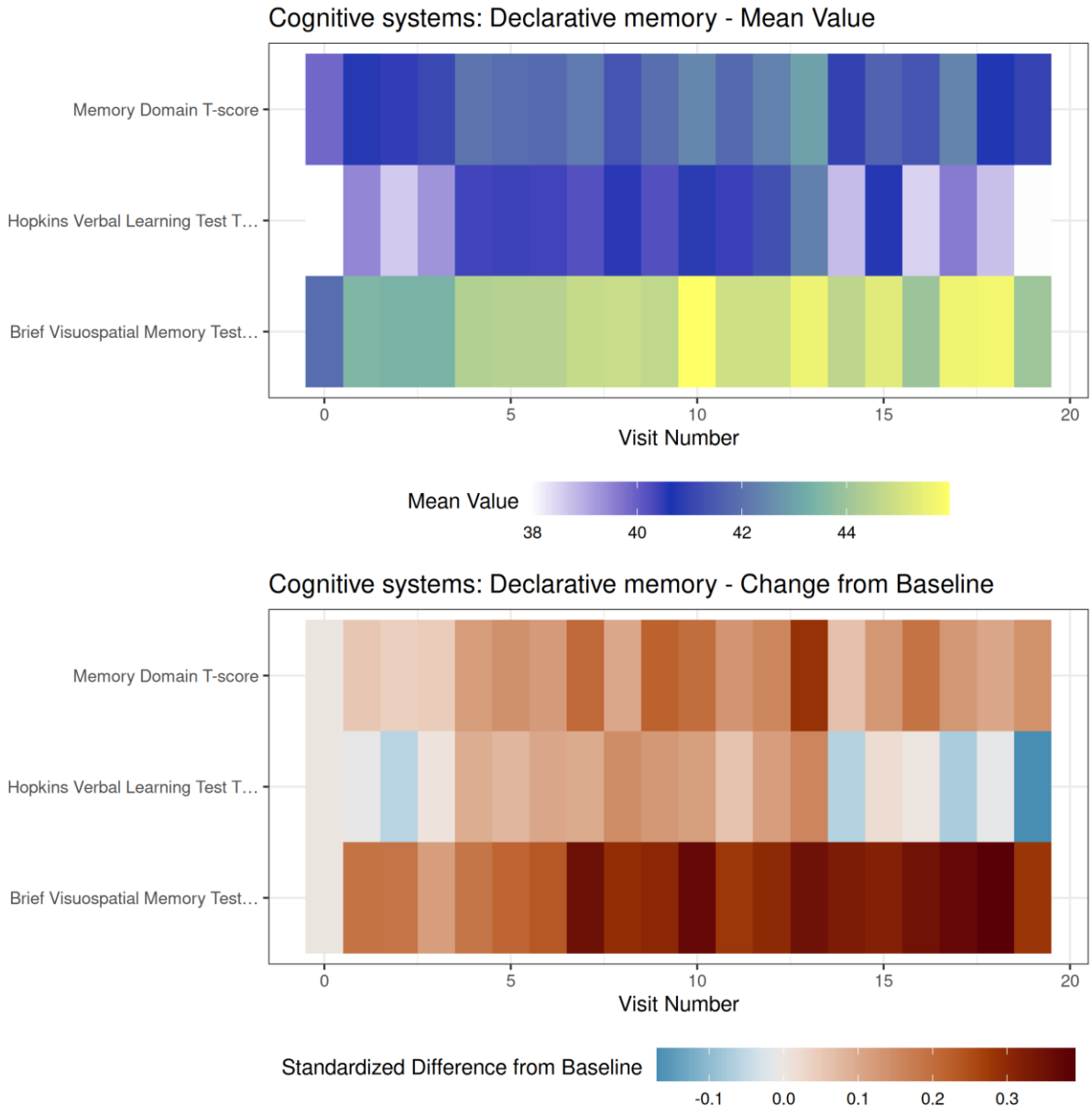

Figure 29: Heatmap of the mean value (top) and standardized mean difference in assessment measurement from baseline (bottom) by visit number for each numeric variable in the Cognitive systems: Declarative memory construct. Standardized mean difference is the mean difference divided by the standard deviation across participants at baseline.

5.3.3 Tables

Table 11: Number of participants by sex with measures available for the "Cognitive systems: Declarative memory" variables across the first 10 visits (visit numbers 0 to 9). Total includes 2 additional participants with missing information on sex.

Measure	Visit #:	0	1	2	3	4	5	6	7	8	9
Brief Visuospatial Memory Test - Revised Total T-Score	Female	442	181	177	132	150	128	121	102	106	84
	Male	1,781	672	721	518	562	408	390	337	304	305
	Total	2,225	853	898	650	712	536	511	439	410	389
Hopkins Verbal Learning Test Total T-Score	Female	481	202	210	146	167	142	142	116	128	99
	Male	1,838	711	763	545	591	445	411	357	333	321
	Total	2,321	913	973	691	758	587	553	473	461	420
Memory Domain T-score	Female	493	202	214	147	167	145	141	115	128	100
	Male	1,909	727	766	547	598	446	410	358	333	325
	Total	2,404	929	980	694	765	591	551	473	461	425

Table 12: Number of participants by sex with measures available for the "Cognitive systems: Declarative memory" variables across visit numbers 10 to 19.

Measure	Visit #:	10	11	12	13	14	15	16	17	18	19
Brief Visuospatial Memory Test - Revised Total T-Score	Female	80	84	72	68	65	44	55	50	44	48
	Male	260	228	228	185	196	159	140	148	128	109
	Total	340	312	300	253	261	203	195	198	172	157
Hopkins Verbal Learning Test Total T-Score	Female	99	91	81	76	66	52	64	59	48	56
	Male	280	243	241	197	208	169	153	154	141	117
	Total	379	334	322	273	274	221	217	213	189	173
Memory Domain T-score	Female	100	94	79	77	68	53	64	59	49	56
	Male	280	244	243	201	207	170	156	158	143	116
	Total	380	338	322	278	275	223	220	217	192	172

5.4 Cognitive Systems: Language

Language is a system of shared symbolic representations of the world, the self and abstract concepts that supports thought and communication.

5.4.1 Variable Definitions

- **Boston Naming Test T-Score** **Added in 2013** (NPV: NPVBNTTS)
- **Animals Correct Words T-Score** **Added in 2013** (NPV: NPVCFATS)
- **FAS T-Score** (NPV: NPVFASTS)
- **Language/Communication Scale Score** (PFI: PFILANSS) Calculation: PFILANSS is calculated from the sum of the following scored fields: PFIUSW, PFIRPW, PFIURM, PFISVT, PFISWI, PFIODU, PFITHN, PFITHW, PFIWRL, and PFIMDS.
- **Verbal Fluency Domain T-score** (NPV: CVERBTS)

5.4.2 Figures

The following two heatmaps show the number of participants with assessments available by variable and visit number. The second heatmap only includes participants in the longitudinal cohort.

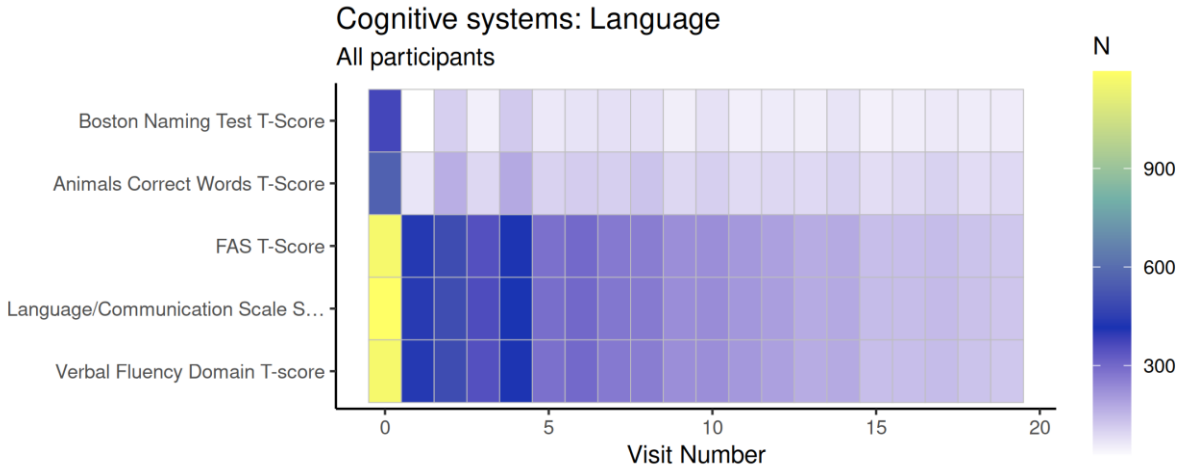

Figure 30: Heatmap showing the number of participants with each Cognitive systems: Language variable measured by visit number for the first 10 years after enrollment in NNTC.

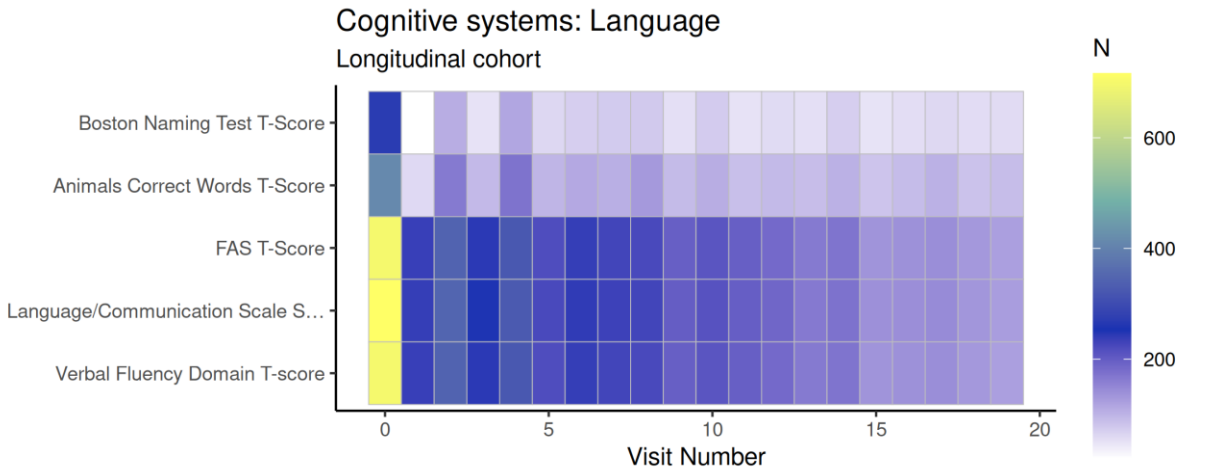

Figure 31: Heatmap showing the number of participants in the longitudinal cohort with each Cognitive systems: Language variable measured, by visit number, for the first 10 years.

The following two UpSet plots show the joint availability of assessments across all visits for each subset of variables. The second UpSet plot only includes participants in the longitudinal cohort.

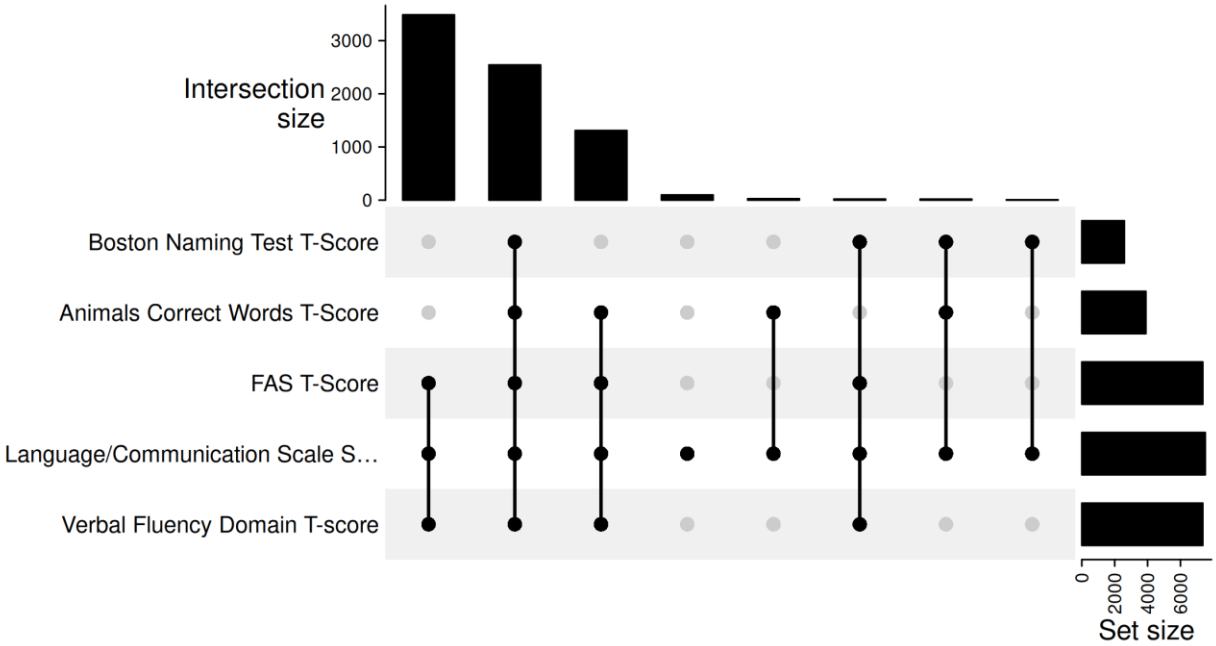

Figure 32: UpSet plot summarizing the joint availability of measures among individuals with one or more visits for the Cognitive systems: Language variables across the first 20 visits. The bottom right horizontal barplot shows the number observations for each variable. The filled circles in the matrix represent the different Venn diagram spaces (unique and overlapping sets). Connected filled circles indicate a certain intersection. The barplot along the top shows the number of observations available for each intersection set.

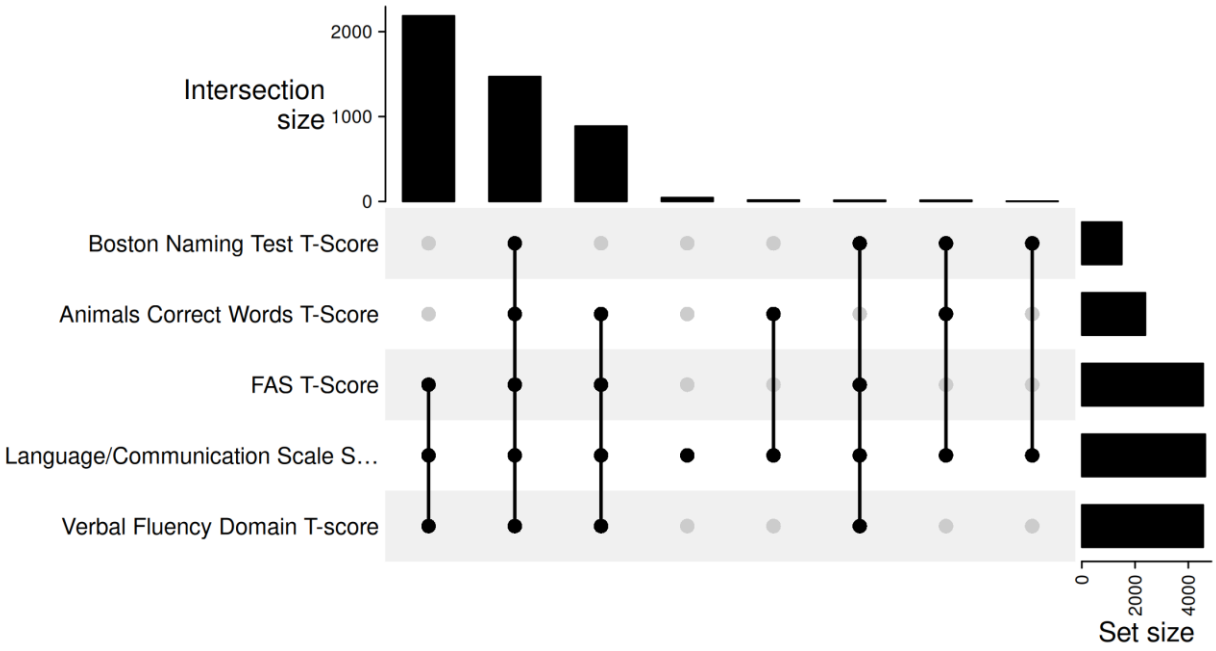

Figure 33: UpSet plot summarizing the joint availability of measures among individuals in the longitudinal cohort for the Cognitive systems: Language variables across the first 20 visits. The bottom right horizontal barplot shows the number observations for each variable. The filled circles in the matrix represent the different Venn diagram spaces (unique and overlapping sets). Connected filled circles indicate a certain intersection. The barplot along the top shows the number of observations available for each intersection set.

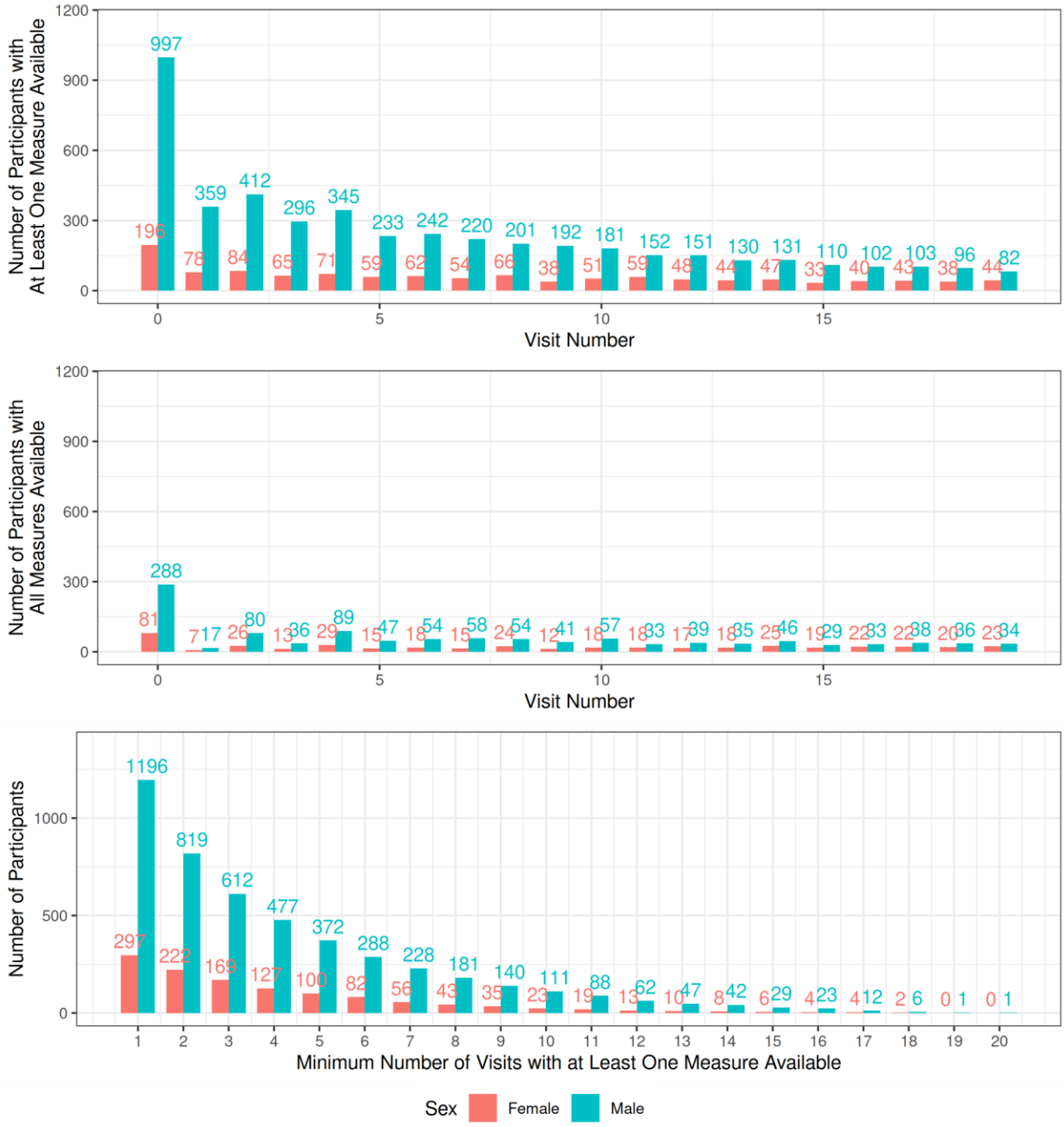

Figure 34: Data availability of participants for Cognitive systems: Language variables by sex summarized by the number of participants with at least one measure available at each visit number (top), the number of participants with all measures available at each visit number (middle), and the total number of participants with at least one measurement taken for a given number of visits (bottom).

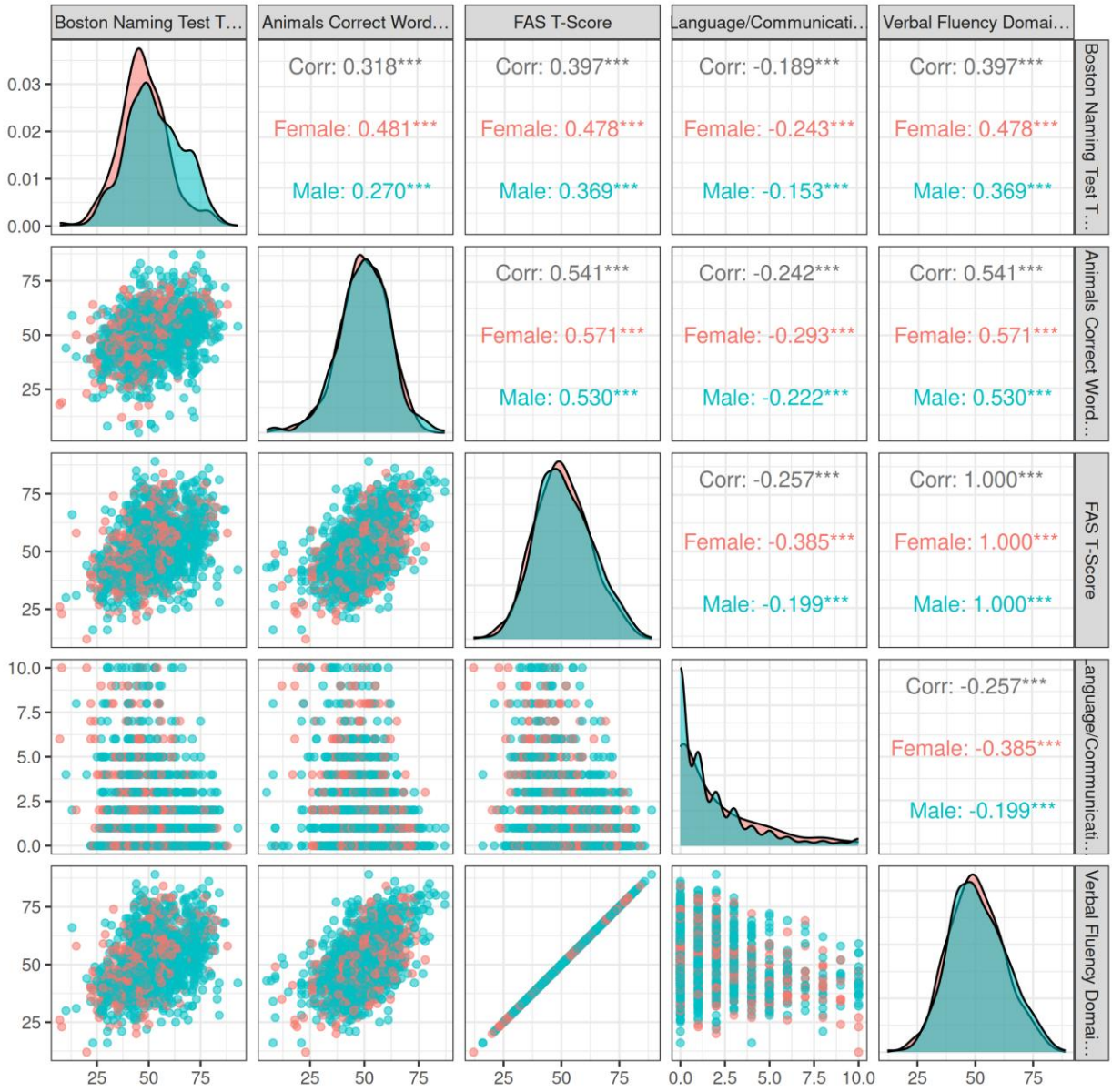

Figure 35: Scatterplot matrix of the Cognitive systems: Language variables with points colored by sex. The diagonal shows the estimated density curve for each marginal distribution, and the top right cells show the respective estimated pairwise Pearson correlation values overall (in black) and by sex.

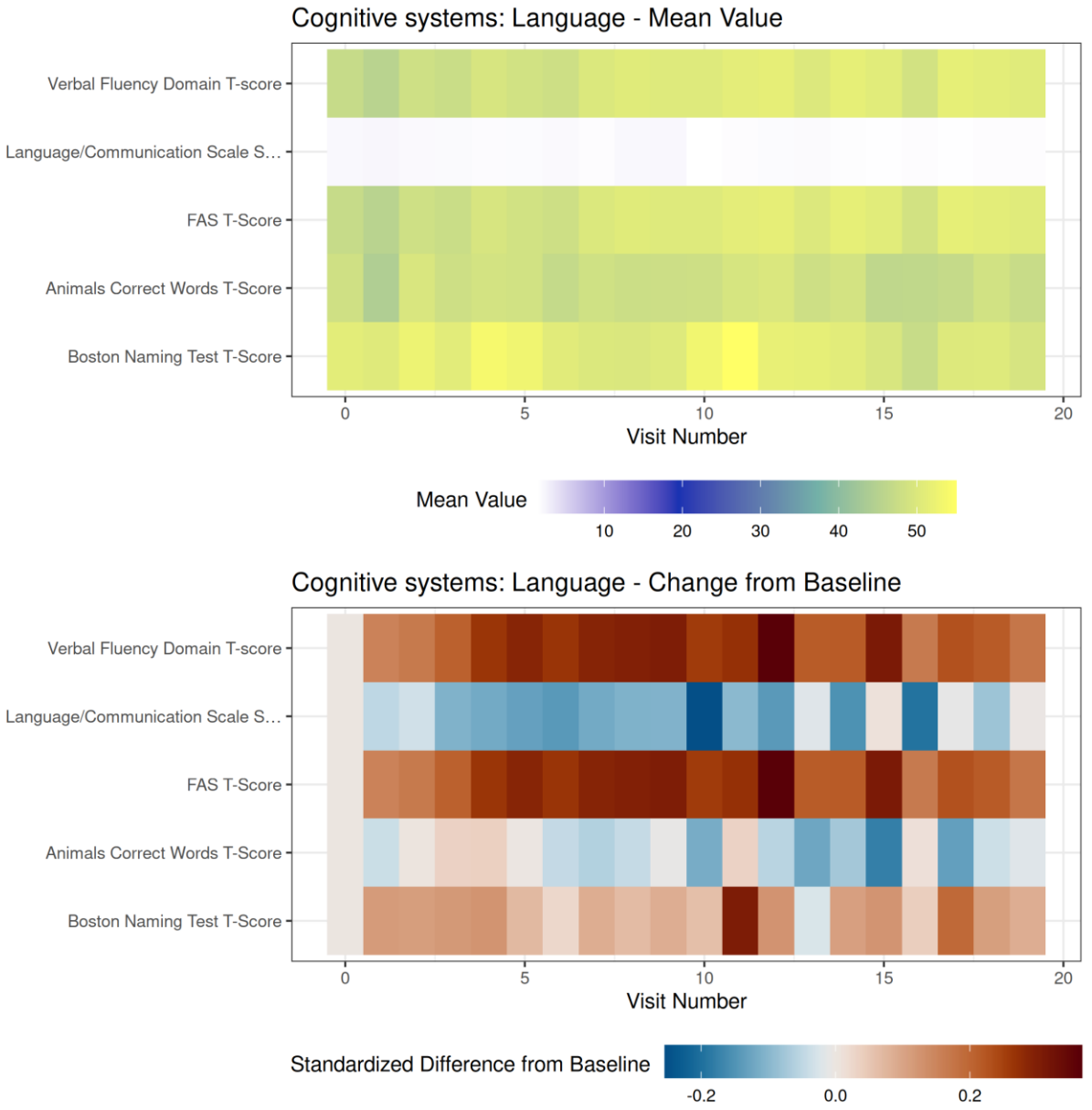

Figure 36: Heatmap of the mean value (top) and standardized mean difference in assessment measurement from baseline (bottom) by visit number for each numeric variable in the Cognitive systems: Language construct. Standardized mean difference is the mean difference divided by the standard deviation across participants at baseline.

5.4.3 Tables

Table 13: Number of participants by sex with measures available for the "Cognitive systems: Language" variables across the first 10 visits (visit numbers 0 to 9). Total includes 2 additional participants with missing information on sex.

Measure	Visit #:	0	1	2	3	4	5	6	7	8	9
Boston Naming Test T-Score **Added in 2013**	Female	84	7	27	14	29	15	18	16	24	12
	Male	290	17	81	37	90	49	55	62	55	42
	Total	374	24	108	51	119	64	73	78	79	54
Animals Correct Words T-Score **Added in 2013**	Female	104	13	36	20	35	24	26	20	38	16
	Male	456	57	133	75	143	79	88	89	93	78
	Total	560	70	169	95	178	103	114	109	131	94
FAS T-Score	Female	191	78	83	63	71	59	61	54	63	38
	Male	976	354	409	289	341	228	240	216	199	190
	Total	1,167	432	492	352	412	287	301	270	262	228
Language/Communication Scale Score	Female	196	78	84	65	71	59	62	54	66	38
	Male	997	359	412	296	345	233	242	220	201	192
	Total	1,195	437	496	361	416	292	304	274	267	230
Verbal Fluency Domain T-score	Female	191	78	83	63	71	59	61	54	63	38
	Male	976	354	409	289	341	228	240	216	199	190
	Total	1,167	432	492	352	412	287	301	270	262	228

Table 14: Number of participants by sex with measures available for the "Cognitive systems: Language" variables across visit numbers 10 to 19.

Measure	Visit #:	10	11	12	13	14	15	16	17	18	19
Boston Naming Test T-Score **Added in 2013**	Female	18	18	18	19	26	19	22	22	20	24
	Male	58	33	41	35	46	31	34	40	37	34
	Total	76	51	59	54	72	50	56	62	57	58
Animals Correct Words T-Score **Added in 2013**	Female	24	24	24	26	31	24	28	30	24	32
	Male	85	65	70	64	73	59	64	74	61	59
	Total	109	89	94	90	104	83	92	104	85	91
FAS T-Score	Female	51	59	46	44	47	33	40	42	36	44
	Male	177	151	149	129	129	106	99	101	95	79
	Total	228	210	195	173	176	139	139	143	131	123
Language/Communication Scale Score	Female	51	59	48	44	47	33	40	43	38	44
	Male	181	152	151	130	131	110	102	103	96	82
	Total	232	211	199	174	178	143	142	146	134	126
Verbal Fluency Domain T-score	Female	51	59	46	44	47	33	40	42	36	44
	Male	177	151	149	129	129	106	99	101	95	79
	Total	228	210	195	173	176	139	139	143	131	123

5.5 Cognitive Systems: Cognitive Control

A system that modulates the operation of other cognitive and emotional systems, in the service of goal-directed behavior, when prepotent modes of responding are not adequate to meet the demands of the current context. Additionally, control processes are engaged in the case of novel contexts, where appropriate responses need to be selected from among competing alternatives.

5.5.1 Variable Definitions

- **Trail Making B T-Score** (NPV: NPVTMBTS)
- **Wisconsin Card Sorting Task - Perseverative Responses T-Score** **Discontinued October 2024** (NPV: NPVWCPTS)

5.5.2 Figures

The following two heatmaps show the number of participants with assessments available by variable and visit number. The second heatmap only includes participants in the longitudinal cohort.

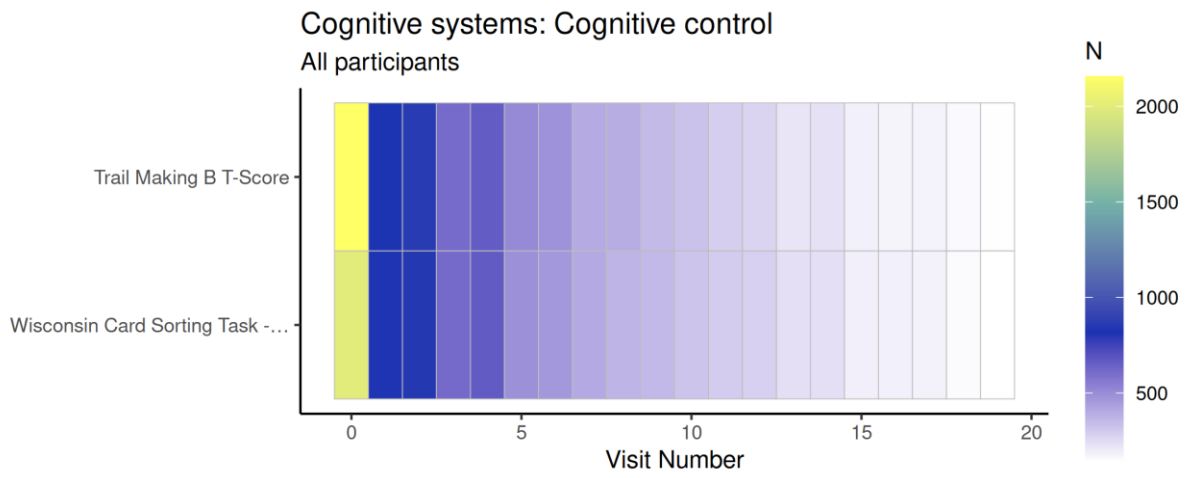

Figure 37: Heatmap showing the number of participants with each Cognitive systems: Cognitive control variable measured by visit number for the first 10 years after enrollment in NNTC.

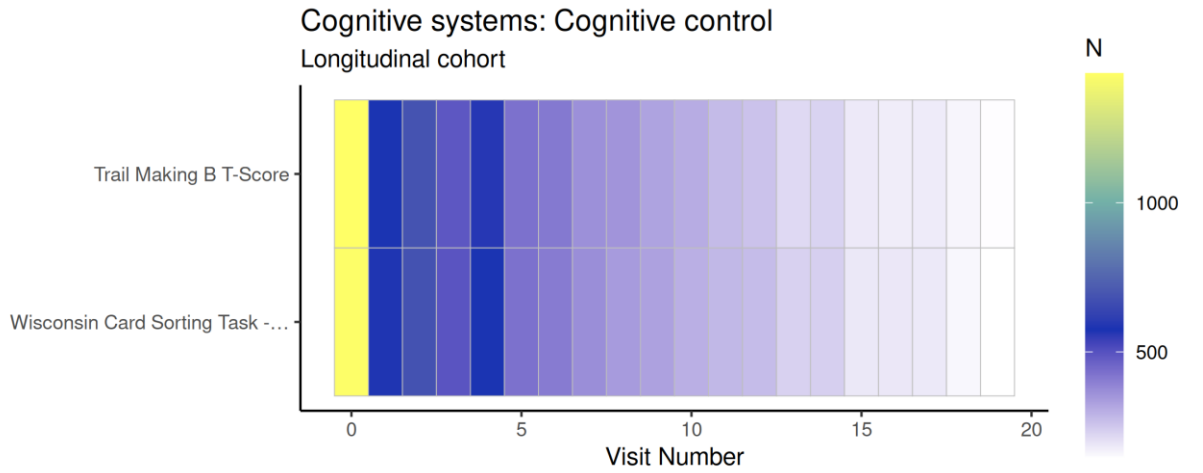

Figure 38: Heatmap showing the number of participants in the longitudinal cohort with each Cognitive systems: Cognitive control variable measured, by visit number, for the first 10 years.

The following two UpSet plots show the joint availability of assessments across all visits for each subset of variables. The second UpSet plot only includes participants in the longitudinal cohort.

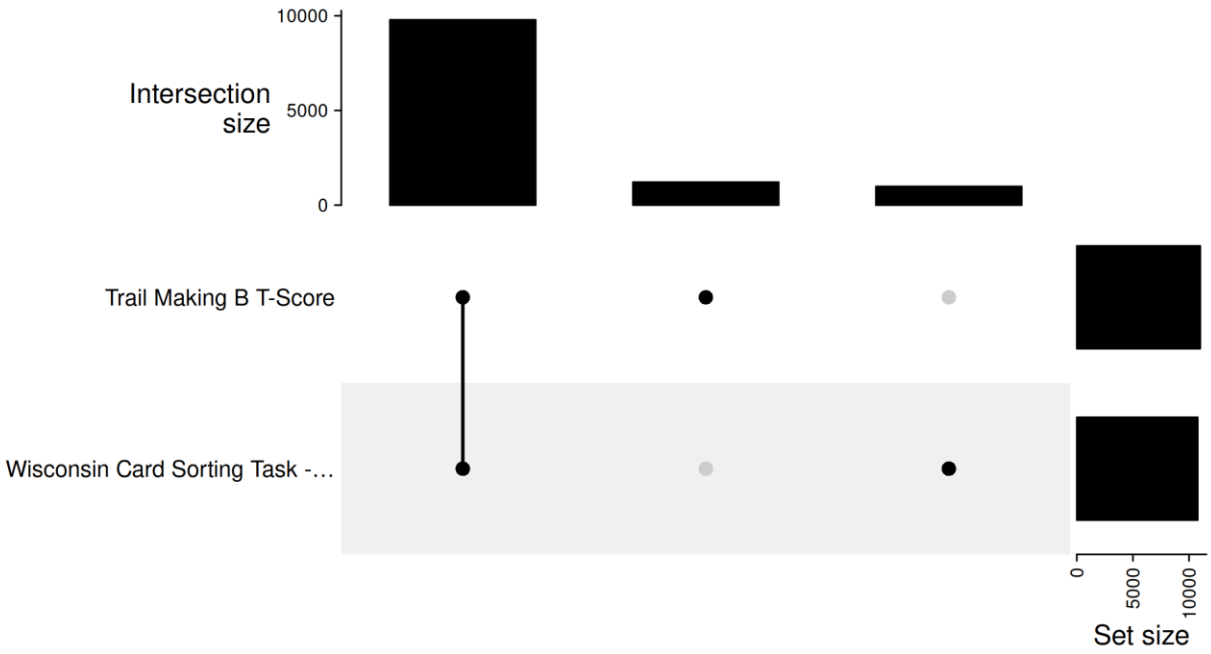

Figure 39: UpSet plot summarizing the joint availability of measures among individuals with one or more visits for the Cognitive systems: Cognitive control variables across the first 20 visits. The bottom right horizontal barplot shows the number observations for each variable. The filled circles in the matrix represent the different Venn diagram spaces (unique and overlapping sets). Connected filled circles indicate a certain intersection. The barplot along the top shows the number of observations available for each intersection set.

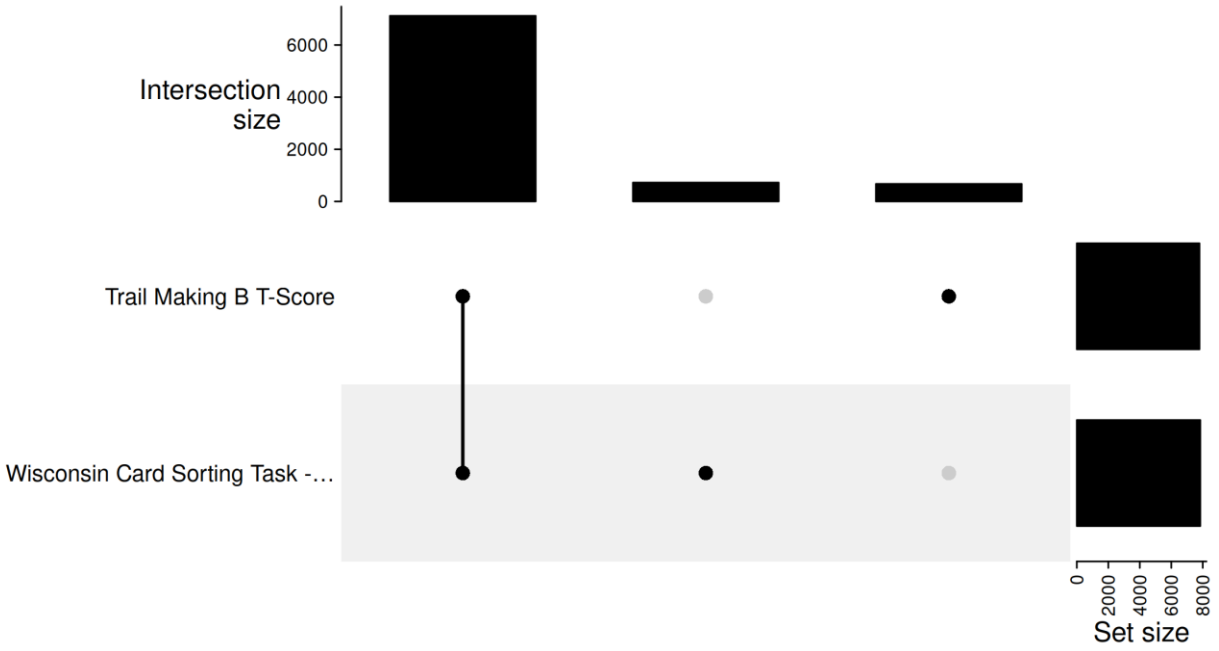

Figure 40: UpSet plot summarizing the joint availability of measures among individuals in the longitudinal cohort for the Cognitive systems: Cognitive control variables across the first 20 visits. The bottom right horizontal barplot shows the number observations for each variable. The filled circles in the matrix represent the different Venn diagram spaces (unique and overlapping sets). Connected filled circles indicate a certain intersection. The barplot along the top shows the number of observations available for each intersection set.

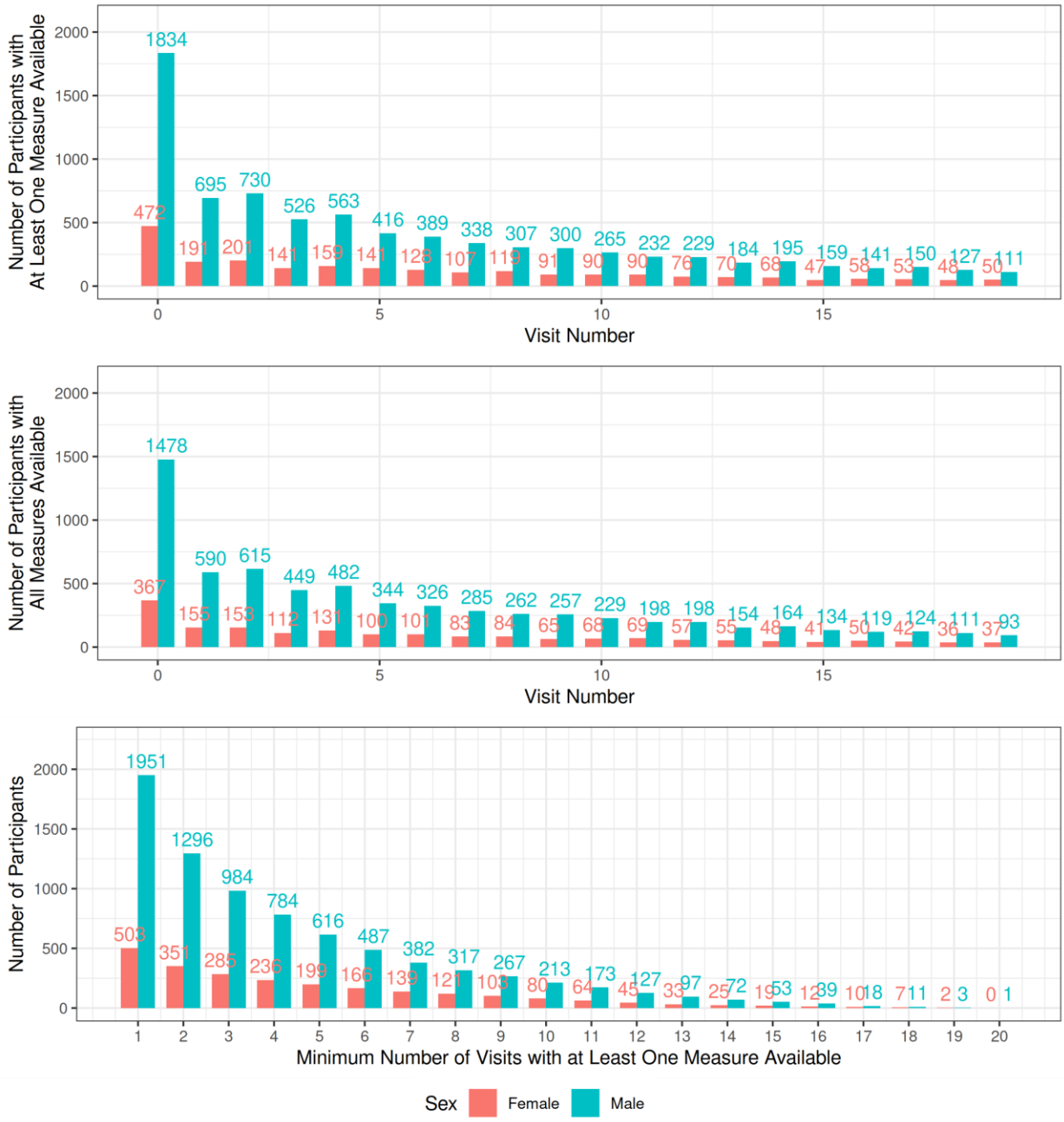

Figure 41: Data availability of participants for Cognitive systems: Cognitive control variables by sex summarized by the number of participants with at least one measure available at each visit number (top), the number of participants with all measures available at each visit number (middle), and the total number of participants with at least one measurement taken for a given number of visits (bottom).

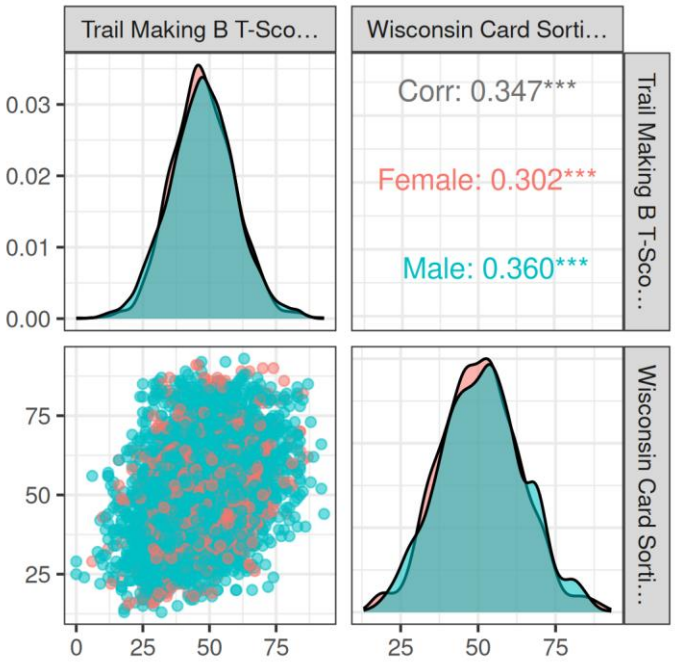

Figure 42: Scatterplot matrix of the Cognitive systems: Cognitive control variables with points colored by sex. The diagonal shows the estimated density curve for each marginal distribution, and the top right cells show the respective estimated pairwise Pearson correlation values overall (in black) and by sex.

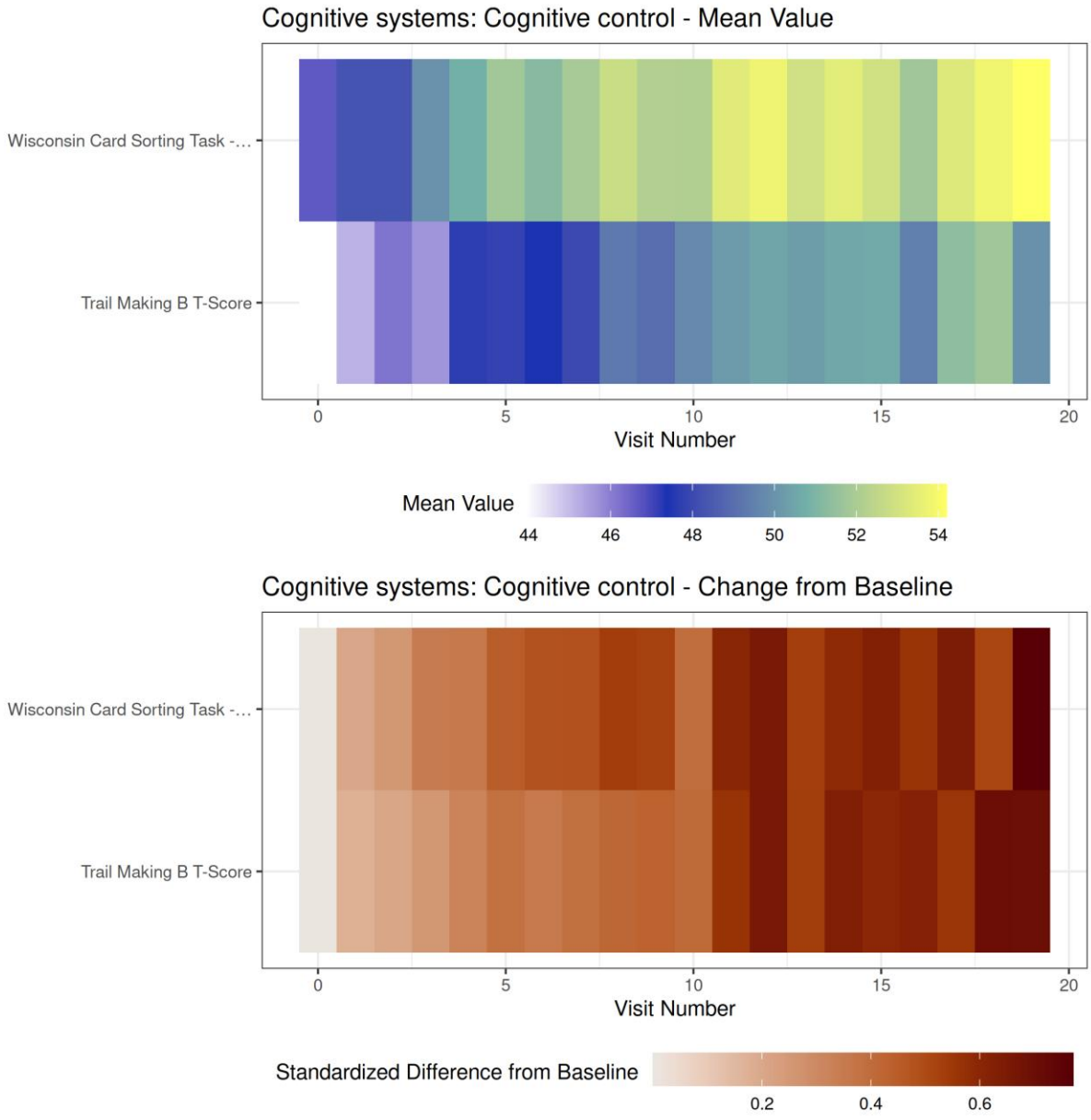

Figure 43: Heatmap of the mean value (top) and standardized mean difference in assessment measurement from baseline (bottom) by visit number for each numeric variable in the Cognitive systems: Cognitive control construct. Standardized mean difference is the mean difference divided by the standard deviation across participants at baseline.

5.5.3 Tables

Table 15: Number of participants by sex with measures available for the "Cognitive systems: Cognitive control" variables across the first 10 visits (visit numbers 0 to 9).

Measure	Visit #:	0	1	2	3	4	5	6	7	8	9
Trail Making B T-Score	Female	440	176	183	127	145	126	119	97	103	79
	Male	1,715	646	675	485	521	385	363	309	294	276
	Total	2,155	822	858	612	666	511	482	406	397	355
Wisconsin Card Sorting Task - Perseverative Responses T-Score **Discontinued October 2024**	Female	399	170	171	126	145	115	110	93	100	77
	Male	1,597	639	670	490	524	375	352	314	275	281
	Total	1,996	809	841	616	669	490	462	407	375	358

Table 16: Number of participants by sex with measures available for the "Cognitive systems: Cognitive control" variables across visit numbers 10 to 19.

Measure	Visit #:	10	11	12	13	14	15	16	17	18	19
Trail Making B T-Score	Female	83	78	65	59	59	45	52	45	43	44
	Male	246	213	209	165	175	144	126	137	120	103
	Total	329	291	274	224	234	189	178	182	163	147
Wisconsin Card Sorting Task - Perseverative Responses T-Score **Discontinued October 2024**	Female	75	81	68	66	57	43	56	50	41	43
	Male	248	217	218	173	184	149	134	137	118	101
	Total	323	298	286	239	241	192	190	187	159	144

5.6 Cognitive Systems: Working Memory

Working Memory is the active maintenance and flexible updating of goal/task relevant information (items, goals, strategies, etc.) in a form that has limited capacity and resists interference. These representations: may involve flexible binding of representations; may be characterized by the absence of external support for the internally maintained representations; and are frequently temporary, though this may be due to ongoing interference. It involves active maintenance, flexible updating, limited capacity, and interference control.

5.6.1 Variable Definitions

- **Memory Scale Score** (PFI: PFIMEMSS) Calculation: PFIMEMSS is calculated from the sum of the following scored fields: PFITLD, PFIEVT, PFIPPD, PFITHI, PFIPPY, PFITME, PFIFWD, PFIFHD, PFILSE, and PFIFIT.
- **PASAT 50 T-Score** **Discontinued October 2024** (NPV: NPVPASTS)
- **WAIS-III Letter Number Sequencing T-Score** (NPV: NPVLNSTS)

5.6.2 Figures

The following two heatmaps show the number of participants with assessments available by variable and visit number. The second heatmap only includes participants in the longitudinal cohort.

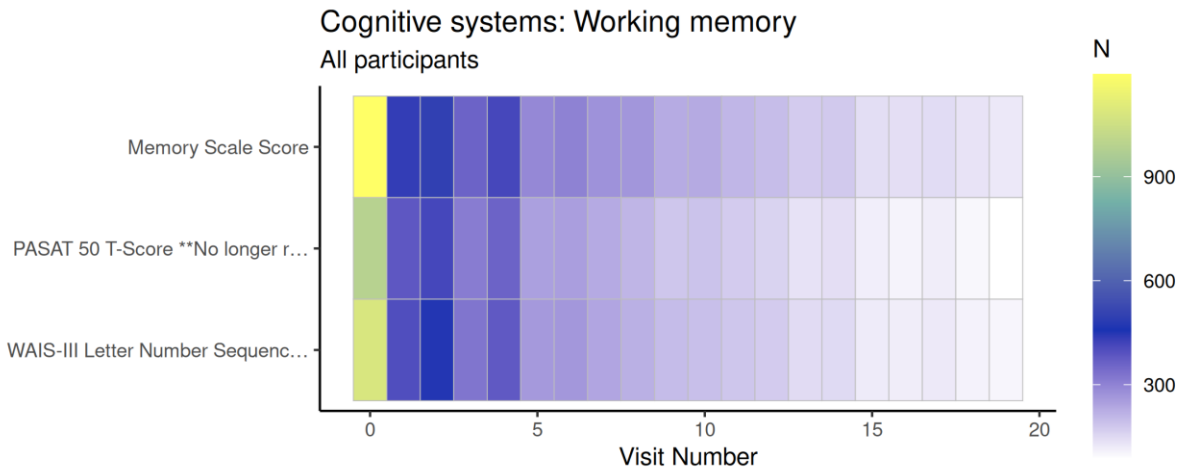

Figure 44: Heatmap showing the number of participants with each Cognitive systems: Working memory variable measured by visit number for the first 10 years after enrollment in NNTC.

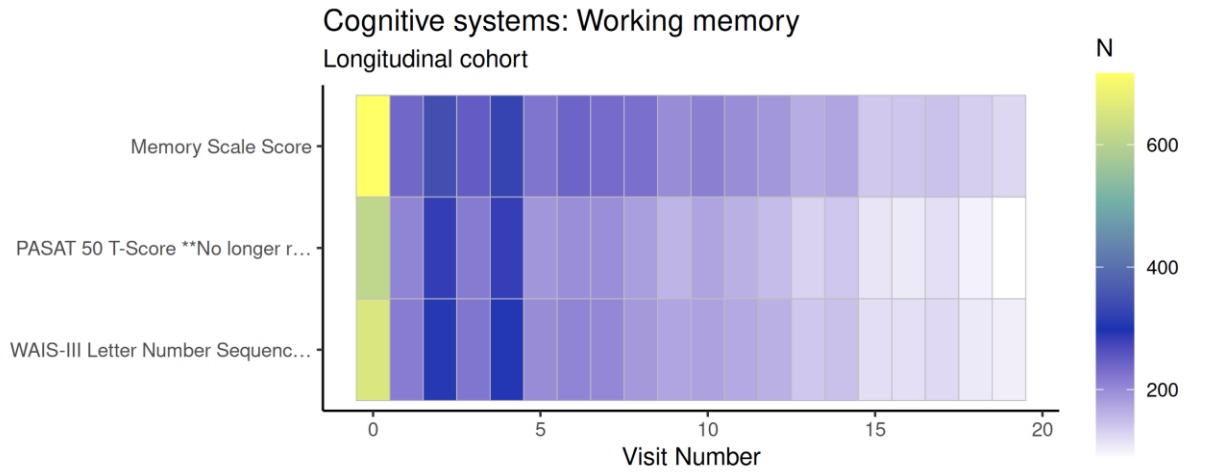

Figure 45: Heatmap showing the number of participants in the longitudinal cohort with each Cognitive systems: Working memory variable measured, by visit number, for the first 10 years.

The following two UpSet plots show the joint availability of assessments across all visits for each subset of variables. The second UpSet plot only includes participants in the longitudinal cohort.

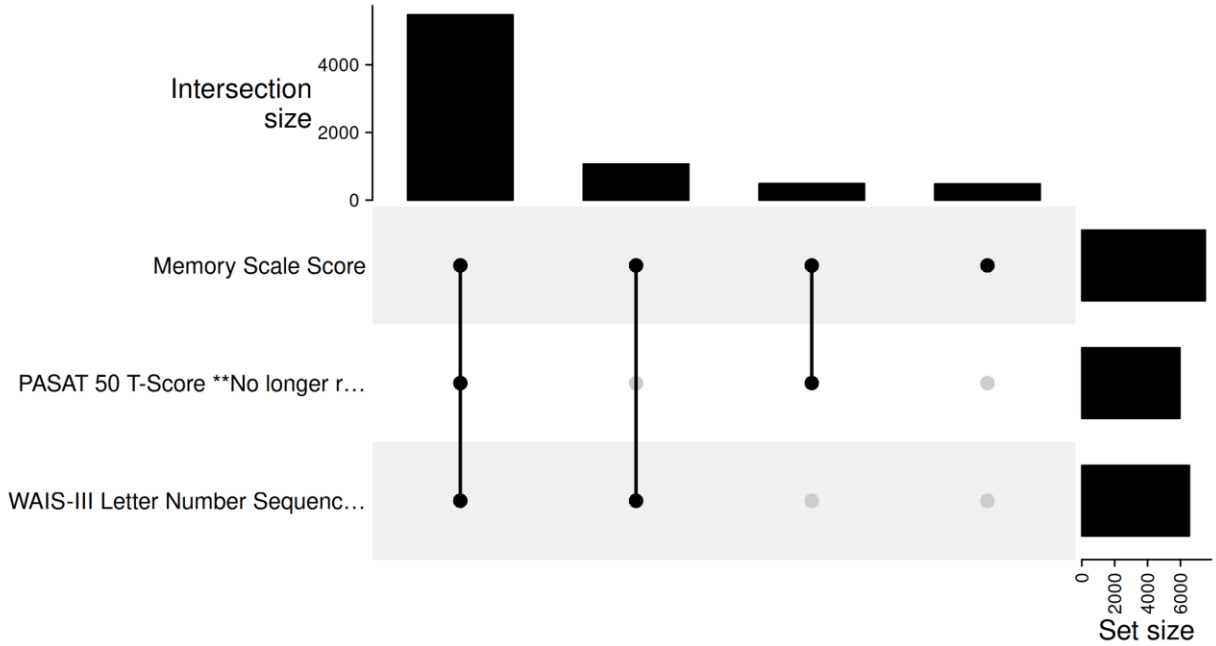

Figure 46: UpSet plot summarizing the joint availability of measures among individuals with one or more visits for the Cognitive systems: Working memory variables across the first 20 visits. The bottom right horizontal barplot shows the number observations for each variable. The filled circles in the matrix represent the different Venn diagram spaces (unique and overlapping sets). Connected filled circles indicate a certain intersection. The barplot along the top shows the number of observations available for each intersection set.

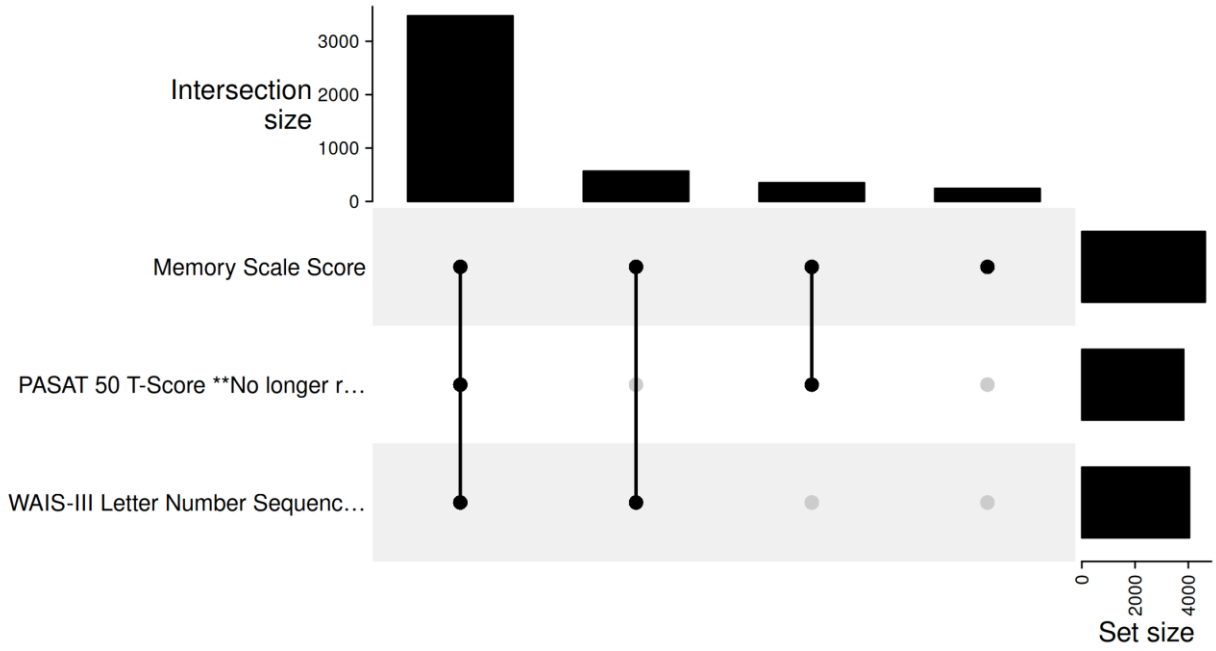

Figure 47: UpSet plot summarizing the joint availability of measures among individuals in the longitudinal cohort for the Cognitive systems: Working memory variables across the first 20 visits. The bottom right horizontal barplot shows the number observations for each variable. The filled circles in the matrix represent the different Venn diagram spaces (unique and overlapping sets). Connected filled circles indicate a certain intersection. The barplot along the top shows the number of observations available for each intersection set.

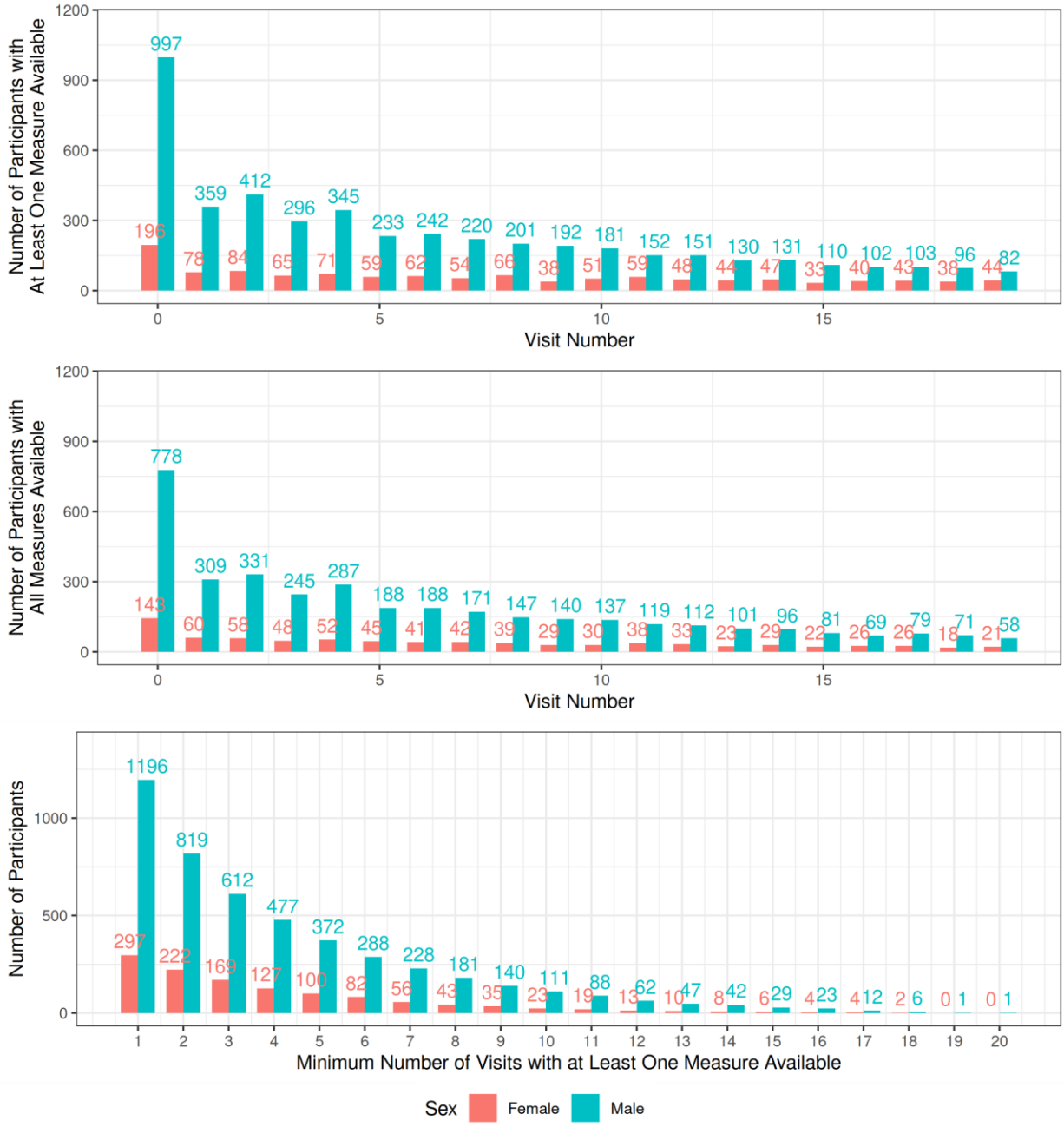

Figure 48: Data availability of participants for Cognitive systems: Working memory variables by sex summarized by the number of participants with at least one measure available at each visit number (top), the number of participants with all measures available at each visit number (middle), and the total number of participants with at least one measurement taken for a given number of visits (bottom).

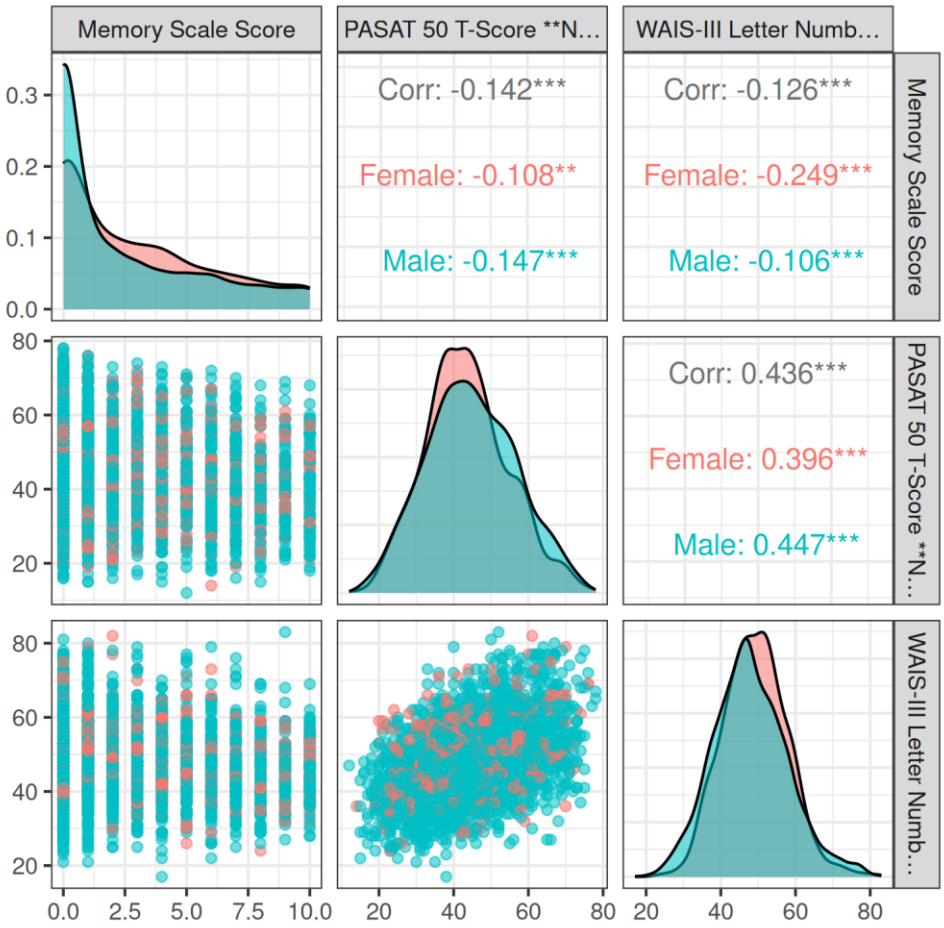

Figure 49: Scatterplot matrix of the Cognitive systems: Working memory variables with points colored by sex. The diagonal shows the estimated density curve for each marginal distribution, and the top right cells show the respective estimated pairwise Pearson correlation values overall (in black) and by sex.

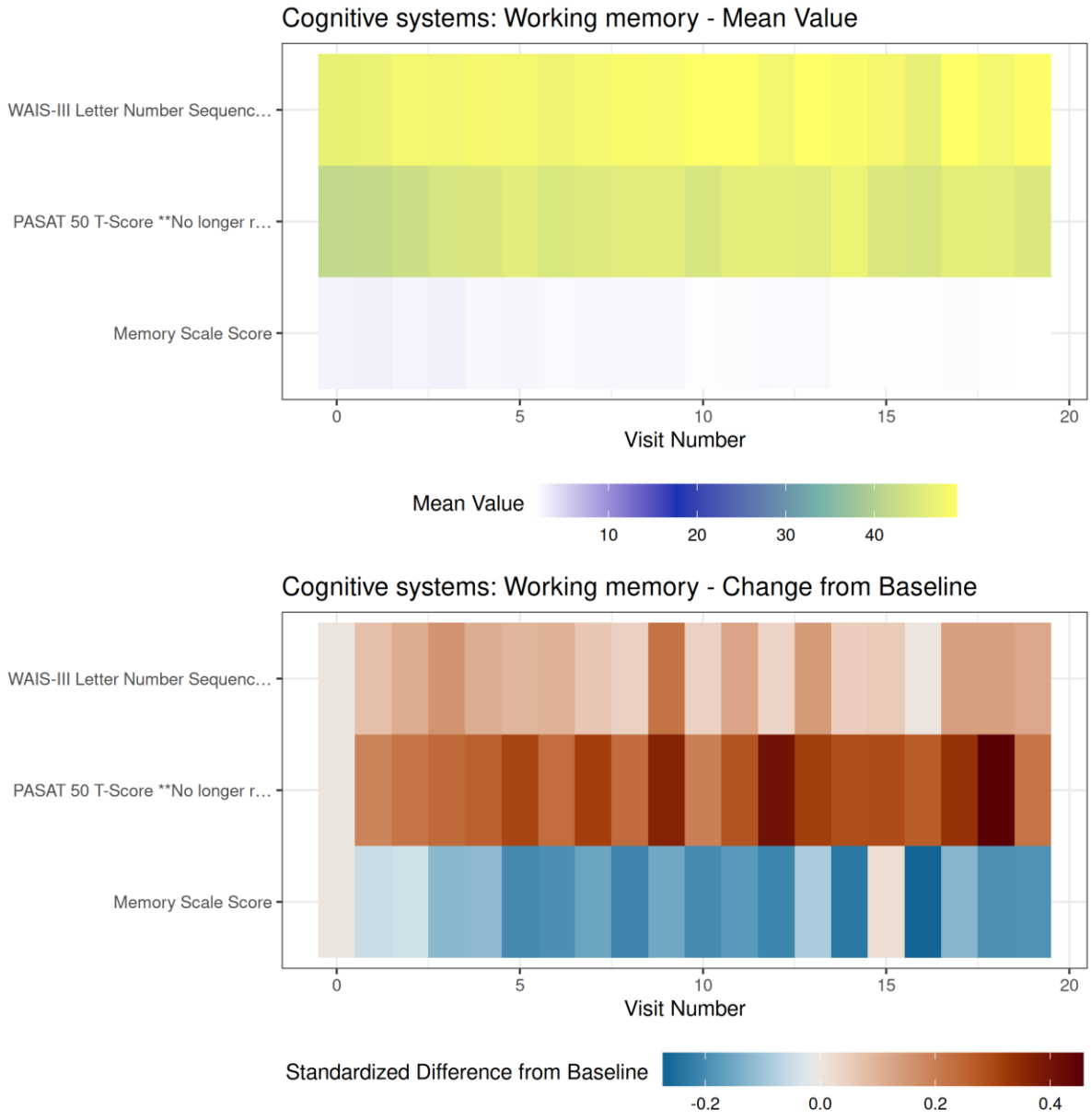

Figure 50: Heatmap of the mean value (top) and standardized mean difference in assessment measurement from baseline (bottom) by visit number for each numeric variable in the Cognitive systems: Working memory construct. Standardized mean difference is the mean difference divided by the standard deviation across participants at baseline.

5.6.3 Tables

Table 17: Number of participants by sex with measures available for the "Cognitive systems: Working memory" variables across the first 10 visits (visit numbers 0 to 9). Total includes 2 additional participants with missing information on sex.

Measure	Visit #:	0	1	2	3	4	5	6	7	8	9
Memory Scale Score	Female	196	78	84	65	71	59	62	54	66	38
	Male	997	359	412	296	345	233	242	220	201	192
	Total	1,195	437	496	361	416	292	304	274	267	230
PASAT 50 T-Score **Discontinued October 2024**	Female	153	62	66	54	59	48	48	44	46	30
	Male	835	322	351	261	303	202	205	187	167	154
	Total	988	384	417	315	362	250	253	231	213	184
WAIS-III Letter Number Sequencing T-Score	Female	171	69	74	56	63	55	51	46	52	33
	Male	909	334	377	272	318	207	215	194	170	168
	Total	1,080	403	451	328	381	262	266	240	222	201

Table 18: Number of participants by sex with measures available for the "Cognitive systems: Working memory" variables across visit numbers 10 to 19.

Measure	Visit #:	10	11	12	13	14	15	16	17	18	19
Memory Scale Score	Female	51	59	48	44	47	33	40	43	38	44
	Male	181	152	151	130	131	110	102	103	96	82
	Total	232	211	199	174	178	143	142	146	134	126
PASAT 50 T-Score **Discontinued October 2024**	Female	36	44	34	26	32	23	29	29	20	23
	Male	153	130	128	110	110	93	79	89	81	65
	Total	189	174	162	136	142	116	108	118	101	88
WAIS-III Letter Number Sequencing T-Score	Female	42	49	44	36	39	30	34	35	29	36
	Male	154	134	130	111	111	91	84	89	80	68
	Total	196	183	174	147	150	121	118	124	109	104

6 RDoC Domain: Arousal/Regulatory Systems

Arousal/Regulatory Systems are responsible for generating activation of neural systems as appropriate for various contexts and providing appropriate homeostatic regulation of such systems as energy balance and sleep.

6.1 Arousal/Regulatory Systems : Sleep and Wakefulness

Sleep and wakefulness are endogenous, recurring, behavioral states that reflect coordinated changes in the dynamic functional organization of the brain and that optimize physiology, behavior, and health. Homeostatic and circadian processes regulate the propensity for wakefulness and sleep. Sleep is reversible, typically characterized by postural recumbence, behavioral quiescence, and reduced responsiveness. Sleep has a complex architecture with predictable cycling of NREM/REM states (or the developmental equivalent of NREM/REM states). NREM and REM sleep have distinct neural substrates (circuitry, transmitters, modulators) and EEG oscillatory properties. The intensity and duration of sleep are affected by homeostatic regulation and experiences during wakefulness. Sleep is evident at cellular, circuit, and system levels and has restorative and transformative effects that optimize neurobehavioral functions during wakefulness

6.1.1 Variable Definitions

- **Minutes to sleep** (PSQ: PSQBEDMN) Question: During the past month, how long (in minutes) has it usually taken you to fall asleep each night?
- **Hours of sleep** (PSQ: PSQSLPHR) Question: During the past month, how many hours of actual sleep did you get at night? (This may be different than the number of hours you spent in bed.)
- **Sleep within thirty** (PSQ: PSQSLP30)
- **Sleep quality** (PSQ: PSQQUAL) Question: During the past month, how would you rate your sleep quality overall?
- **Trouble staying awake** (PSQ: PSQTRAWK) Question: During the past month, how often have you had trouble staying awake while driving, eating meals, or engaging in social activity?
- **Change in Sleep Pattern** (BDI: BDISLEEP) Question: Changes in Sleeping Pattern:
- **Tiredness or Fatigue** (BDI: BDITIRED) Question: Tiredness or Fatigue:

6.1.2 Figures

The following two heatmaps show the number of participants with assessments available by variable and visit number. The second heatmap only includes participants in the longitudinal cohort.

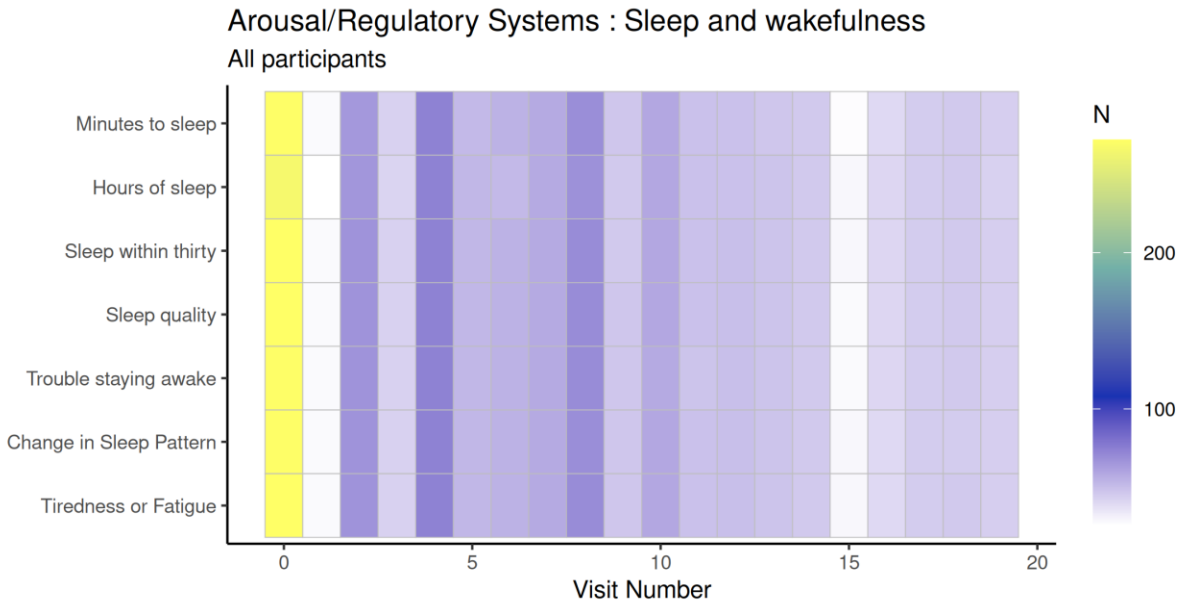

Figure 51: Heatmap showing the number of participants with each Arousal/Regulatory Systems : Sleep and wakefulness variable measured by visit number for the first 10 years after enrollment in NNTC.

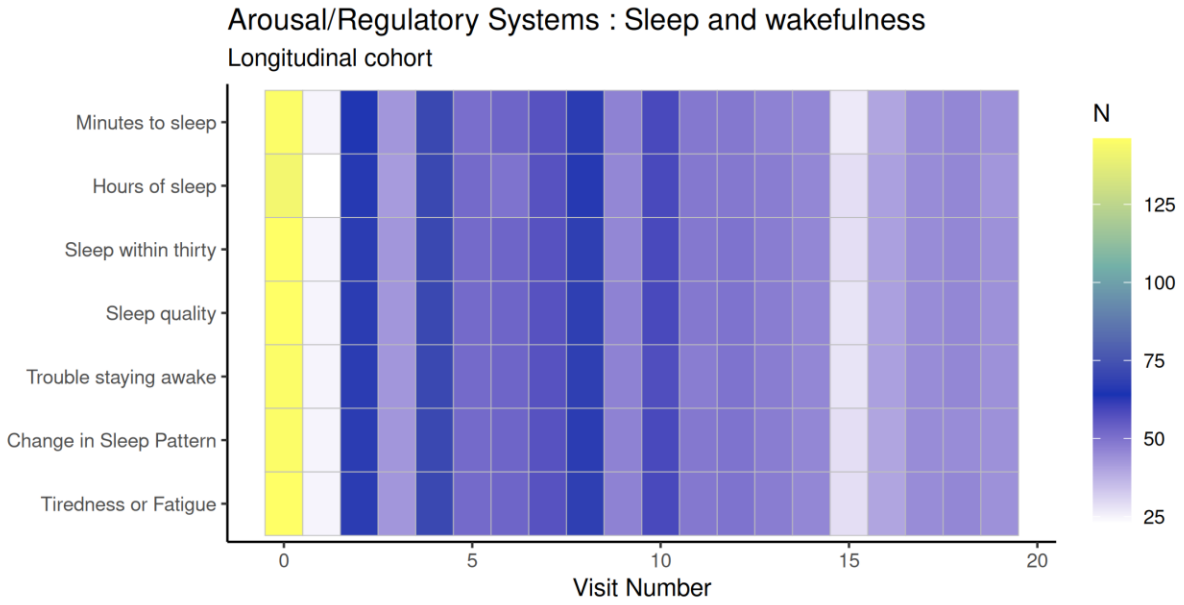

Figure 52: Heatmap showing the number of participants in the longitudinal cohort with each Arousal/Regulatory Systems : Sleep and wakefulness variable measured, by visit number, for the first 10 years.

The following two UpSet plots show the joint availability of assessments across all visits for each subset of variables. The second UpSet plot only includes participants in the longitudinal cohort.

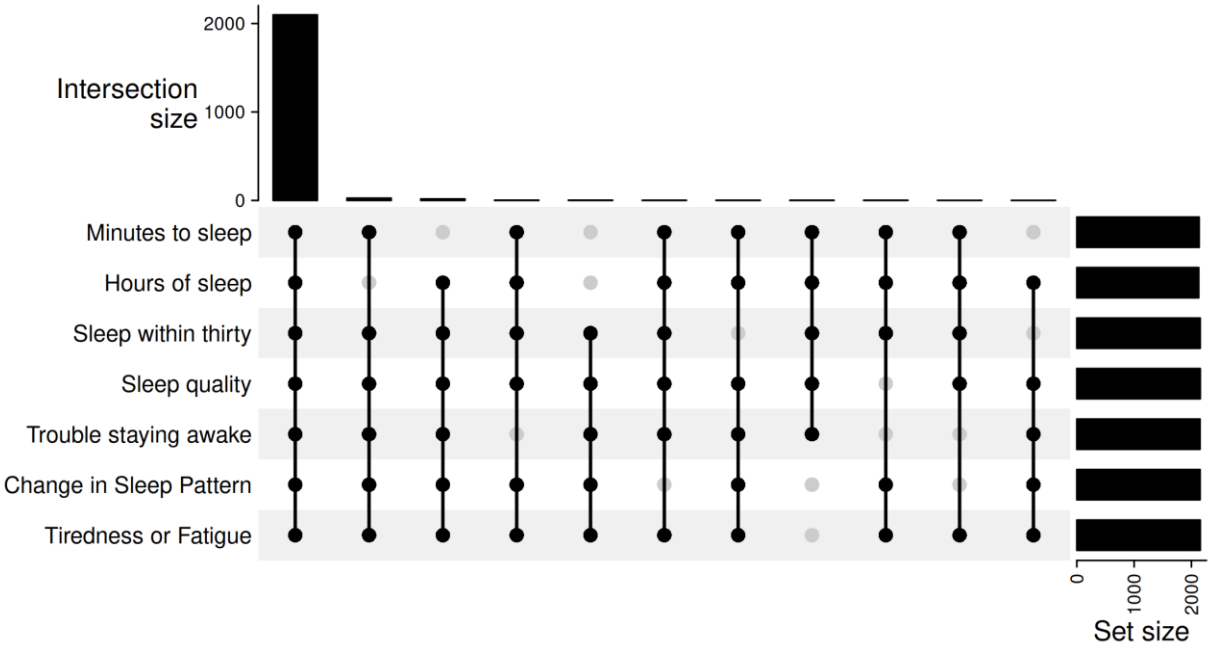

Figure 53: UpSet plot summarizing the joint availability of measures among individuals with one or more visits for the Arousal/Regulatory Systems : Sleep and wakefulness variables across the first 20 visits. The bottom right horizontal barplot shows the number observations for each variable. The filled circles in the matrix represent the different Venn diagram spaces (unique and overlapping sets). Connected filled circles indicate a certain intersection. The barplot along the top shows the number of observations available for each intersection set.

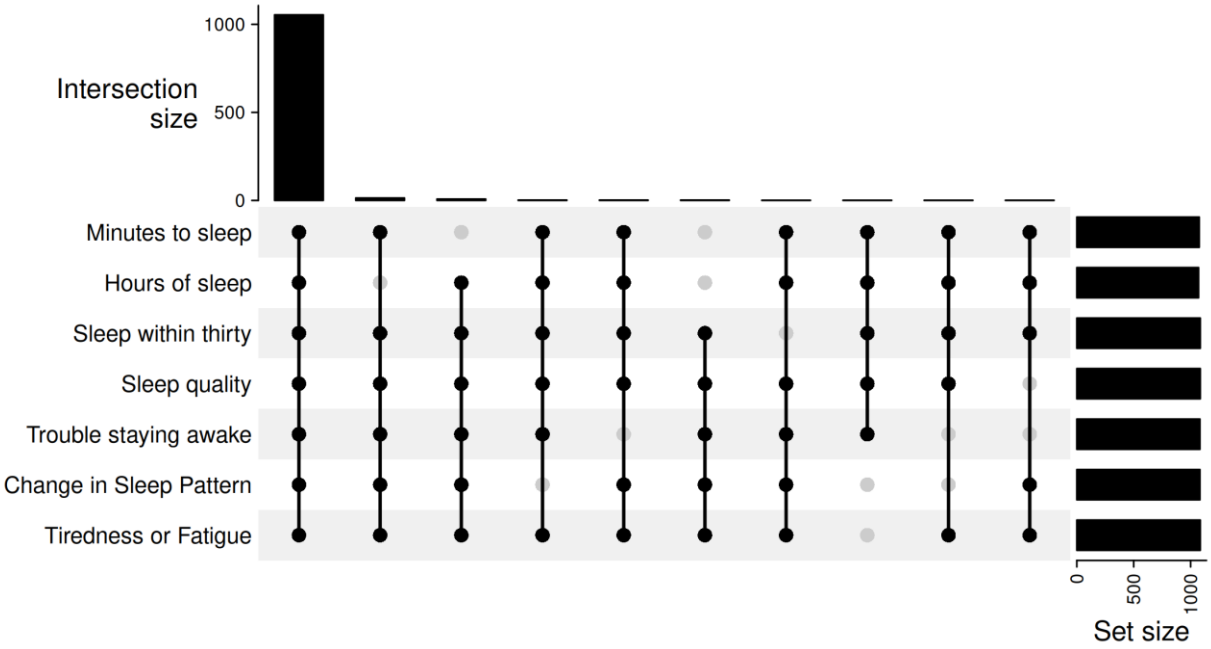

Figure 54: UpSet plot summarizing the joint availability of measures among individuals in the longitudinal cohort for the Arousal/Regulatory Systems : Sleep and wakefulness variables across the first 20 visits. The bottom right horizontal barplot shows the number observations for each variable. The filled circles in the matrix represent the different Venn diagram spaces (unique and overlapping sets). Connected filled circles indicate a certain intersection. The barplot along the top shows the number of observations available for each intersection set.

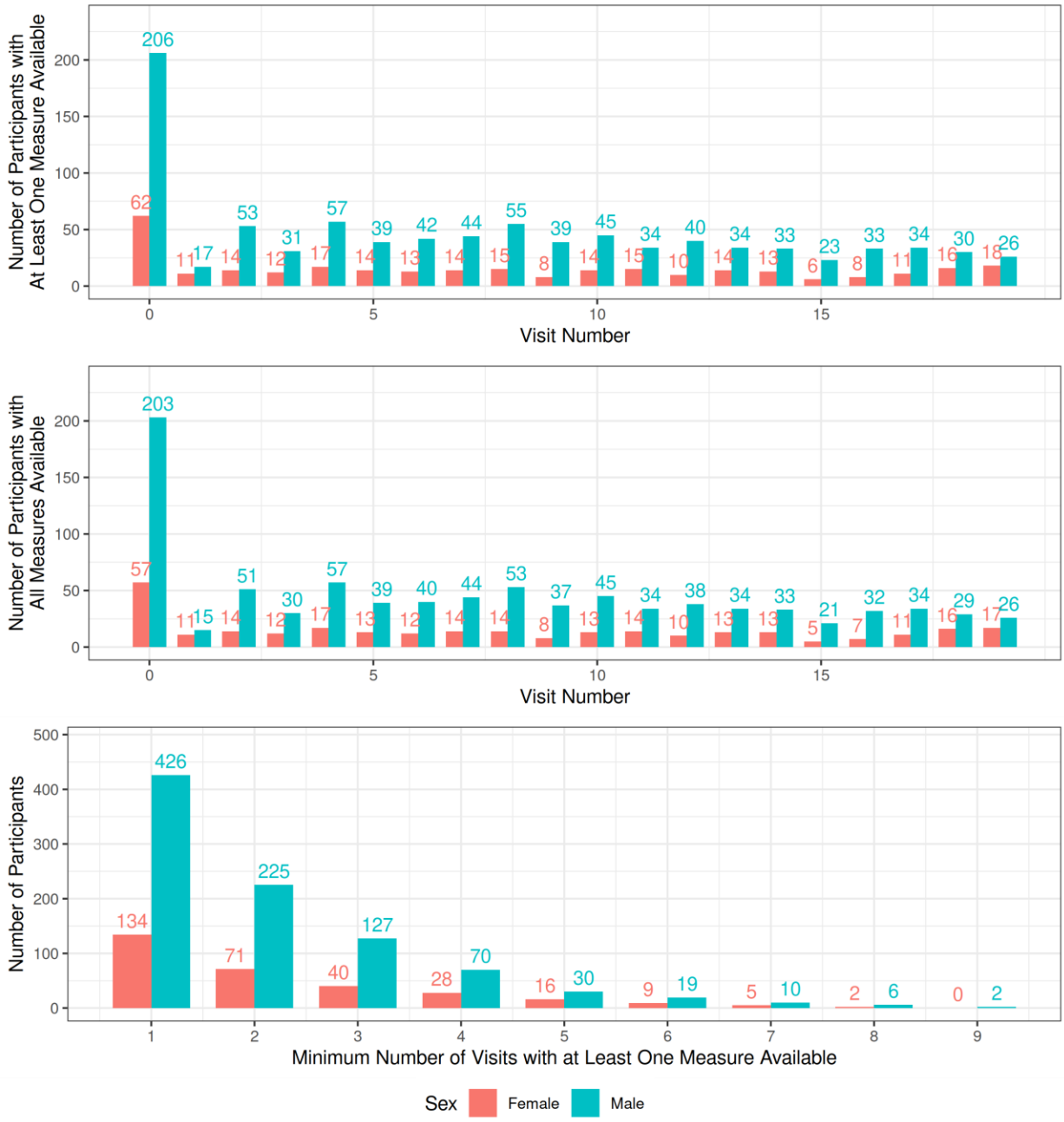

Figure 55: Data availability of participants for Arousal/Regulatory Systems : Sleep and wakefulness variables by sex summarized by the number of participants with at least one measure available at each visit number (top), the number of participants with all measures available at each visit number (middle), and the total number of participants with at least one measurement taken for a given number of visits (bottom).

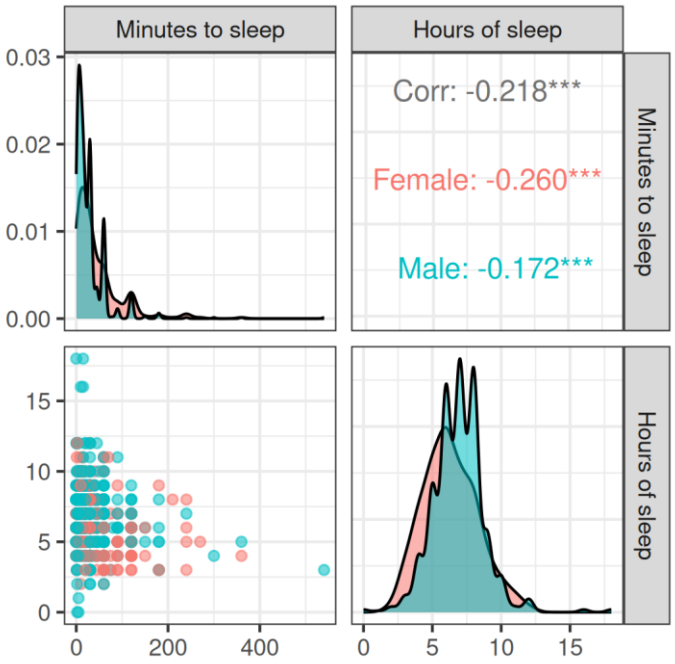

Figure 56: Scatterplot matrix of the Arousal/Regulatory Systems : Sleep and wakefulness variables with points colored by sex. The diagonal shows the estimated density curve for each marginal distribution, and the top right cells show the respective estimated pairwise Pearson correlation values overall (in black) and by sex.

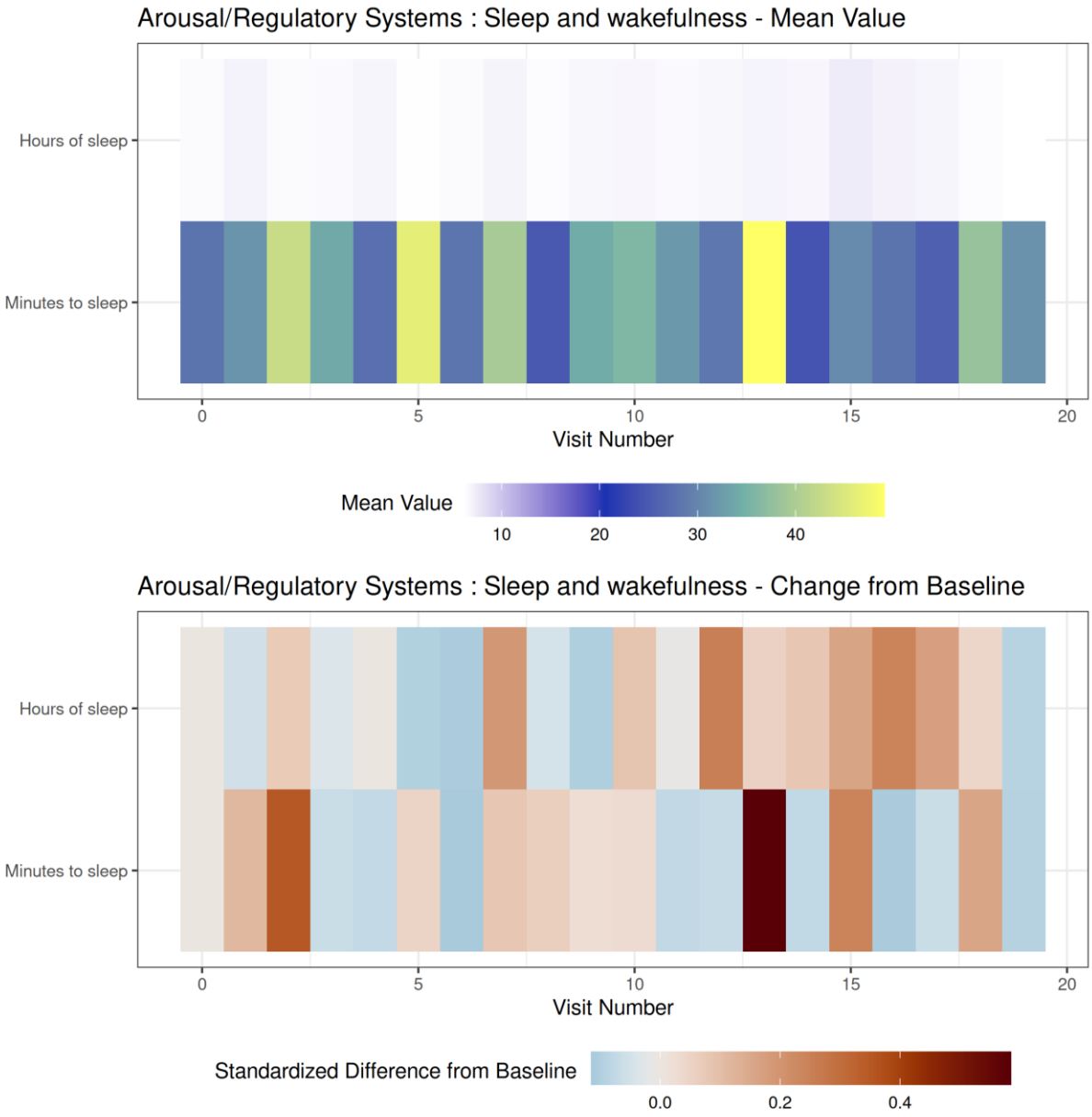

Figure 57: Heatmap of the mean value (top) and standardized mean difference in assessment measurement from baseline (bottom) by visit number for each numeric variable in the Arousal/Regulatory Systems : Sleep and wakefulness construct. Standardized mean difference is the mean difference divided by the standard deviation across participants at baseline.

6.1.3 Tables

Table 19: Number of participants by sex with measures available for the "Arousal/Regulatory Systems : Sleep and wakefulness" variables across the first 10 visits (visit numbers 0 to 9). Total includes 4 additional participants with missing information on sex.

Measure	Visit #:	0	1	2	3	4	5	6	7	8	9
Minutes to sleep	Female	62	11	14	12	17	13	13	14	15	8
	Male	205	17	51	31	57	39	42	44	54	39
	Total	271	28	65	43	74	52	55	58	69	47
Hours of sleep	Female	58	11	14	12	17	14	12	14	14	8
	Male	204	15	52	30	57	39	40	44	54	38
	Total	266	26	66	42	74	53	52	58	68	46
Sleep within thirty	Female	62	11	14	12	17	14	13	14	15	8
	Male	206	17	53	31	57	39	42	44	55	38
	Total	272	28	67	43	74	53	55	58	70	46
Sleep quality	Female	62	11	14	12	17	14	13	14	15	8
	Male	206	17	53	31	57	39	42	44	55	39
	Total	272	28	67	43	74	53	55	58	70	47
Trouble staying awake	Female	61	11	14	12	17	14	13	14	15	8
	Male	206	17	53	31	57	39	42	44	55	39
	Total	271	28	67	43	74	53	55	58	70	47
Change in Sleep Pattern	Female	61	11	14	12	17	14	13	14	15	8
	Male	206	17	53	31	57	39	42	44	54	39
	Total	271	28	67	43	74	53	55	58	69	47
Tiredness or Fatigue	Female	62	11	14	12	17	14	13	14	15	8
	Male	206	17	53	31	57	39	42	44	55	39
	Total	272	28	67	43	74	53	55	58	70	47

Table 20: Number of participants by sex with measures available for the "Arousal/Regulatory Systems : Sleep and wakefulness" variables across visit numbers 10 to 19.

Measure	Visit #:	10	11	12	13	14	15	16	17	18	19
Minutes to sleep	Female	14	15	10	13	13	5	7	11	16	18
	Male	45	34	39	34	33	22	33	34	30	26
	Total	59	49	49	47	46	27	40	45	46	44
Hours of sleep	Female	14	15	10	14	13	6	8	11	16	17
	Male	45	34	39	34	33	23	33	34	30	26
	Total	59	49	49	48	46	29	41	45	46	43
Sleep within thirty	Female	14	15	10	14	13	6	8	11	16	18
	Male	45	34	40	34	33	23	33	34	30	26
	Total	59	49	50	48	46	29	41	45	46	44
Sleep quality	Female	14	15	10	14	13	6	8	11	16	18
	Male	45	34	40	34	33	22	33	34	30	26
	Total	59	49	50	48	46	28	41	45	46	44
Trouble staying awake	Female	13	14	10	14	13	6	8	11	16	18
	Male	45	34	40	34	33	22	33	34	30	26
	Total	58	48	50	48	46	28	41	45	46	44
Change in Sleep Pattern	Female	14	15	10	14	13	6	8	11	16	18
	Male	45	34	40	34	33	23	32	34	29	26
	Total	59	49	50	48	46	29	40	45	45	44
Tiredness or Fatigue	Female	14	15	10	14	13	6	8	11	16	18
	Male	45	34	40	34	33	23	32	34	30	26
	Total	59	49	50	48	46	29	40	45	46	44

7 RDoC Domain: Sensorimotor Systems

Sensorimotor systems are primarily responsible for the control and execution of motor behaviors, and their refinement during learning and development.

7.1 Sensorimotor Systems: Motor Actions

A multifaceted construct comprising the processes that must be engaged during the planning and execution of a motor action in a context-appropriate manner. Component processes include action planning and selection, sensorimotor dynamics, initiation, execution, and inhibition and termination. Of note, these processes will often be recruited in conjunction with motivational processes described in other domains, as when appetitive motivations drive approach behaviors. This construct explicitly includes the modulation and refinement of actions during development and learning.

7.1.1 Variable Definitions

- **Weight loss** (FFI: FFIWTLOS) Question: Weight Loss
- **Exhaustion yes or no** (FFI: FFIEXHYN) Question: Exhaustion
- **Physical activity** (FFI: FFIPHYSA) Question: Physical activity
- **Walk time** (FFI: FFIWLKTM) Question: Walk Time
- **Walk time seconds** (FFI: FFITIME) Question: Time:
- **Grip strength** (FFI: FFIGRPST) Question: Grip Strength:
- **Grip strength kilograms** (FFI: FFISTREN) Question: Strength:
- **Pegboard Dom T-Score** (NPV: NPVGPDTS)
- **Peg Non-Dom T-Score** (NPV: NPVGPNTS)
- **Motor Domain T-score** (NPV: CMOTORTS)
- **Motor Scale Score** (PFI: PFIMOTSS) Calculation: PFIMOTSS is calculated from the sum of the following scored fields: PFIPTR and PFIPTL.

7.1.2 Figures

The following two heatmaps show the number of participants with assessments available by variable and visit number. The second heatmap only includes participants in the longitudinal cohort.

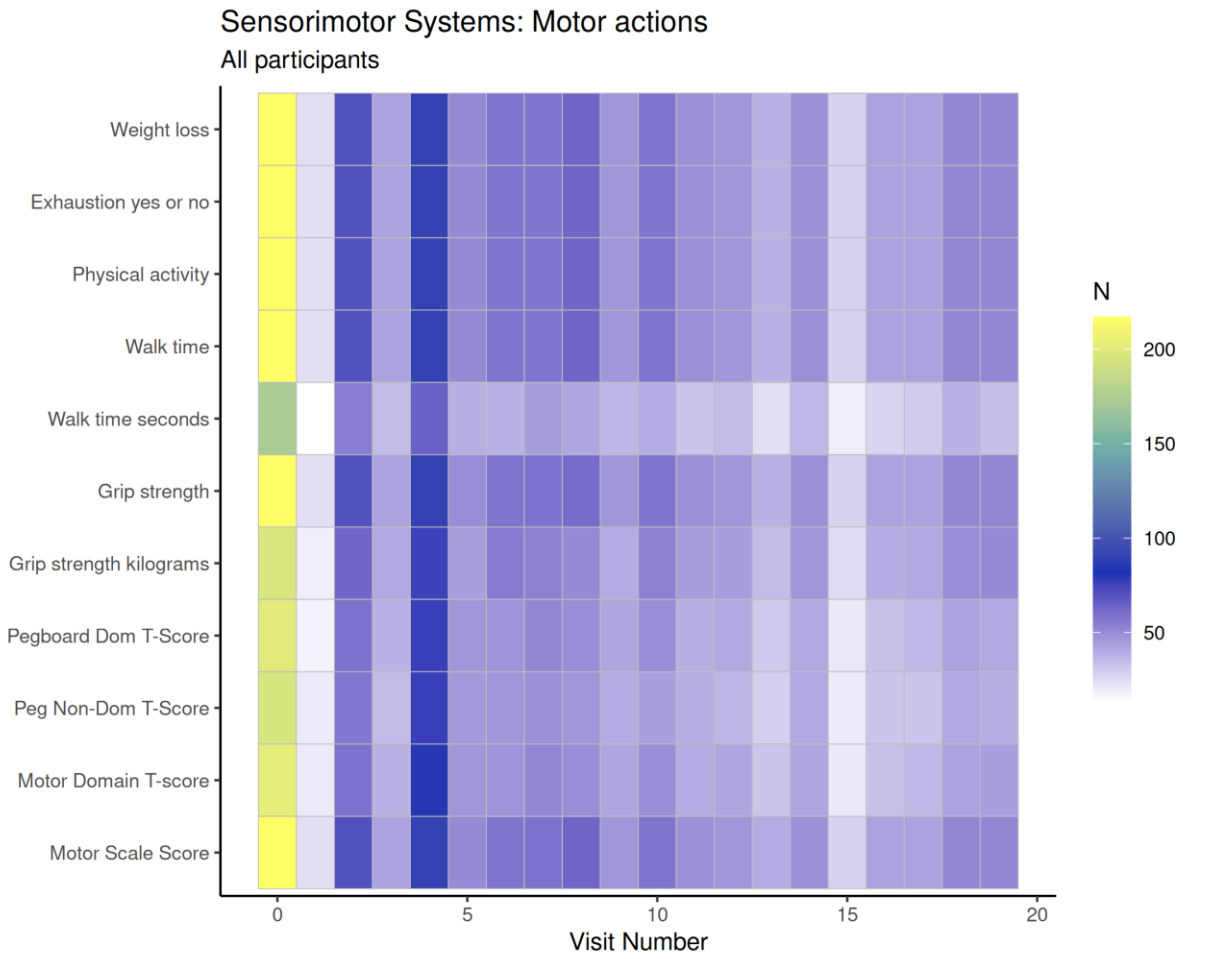

Figure 58: Heatmap showing the number of participants with each Sensorimotor Systems: Motor actions variable measured by visit number for the first 10 years after enrollment in NNTC.

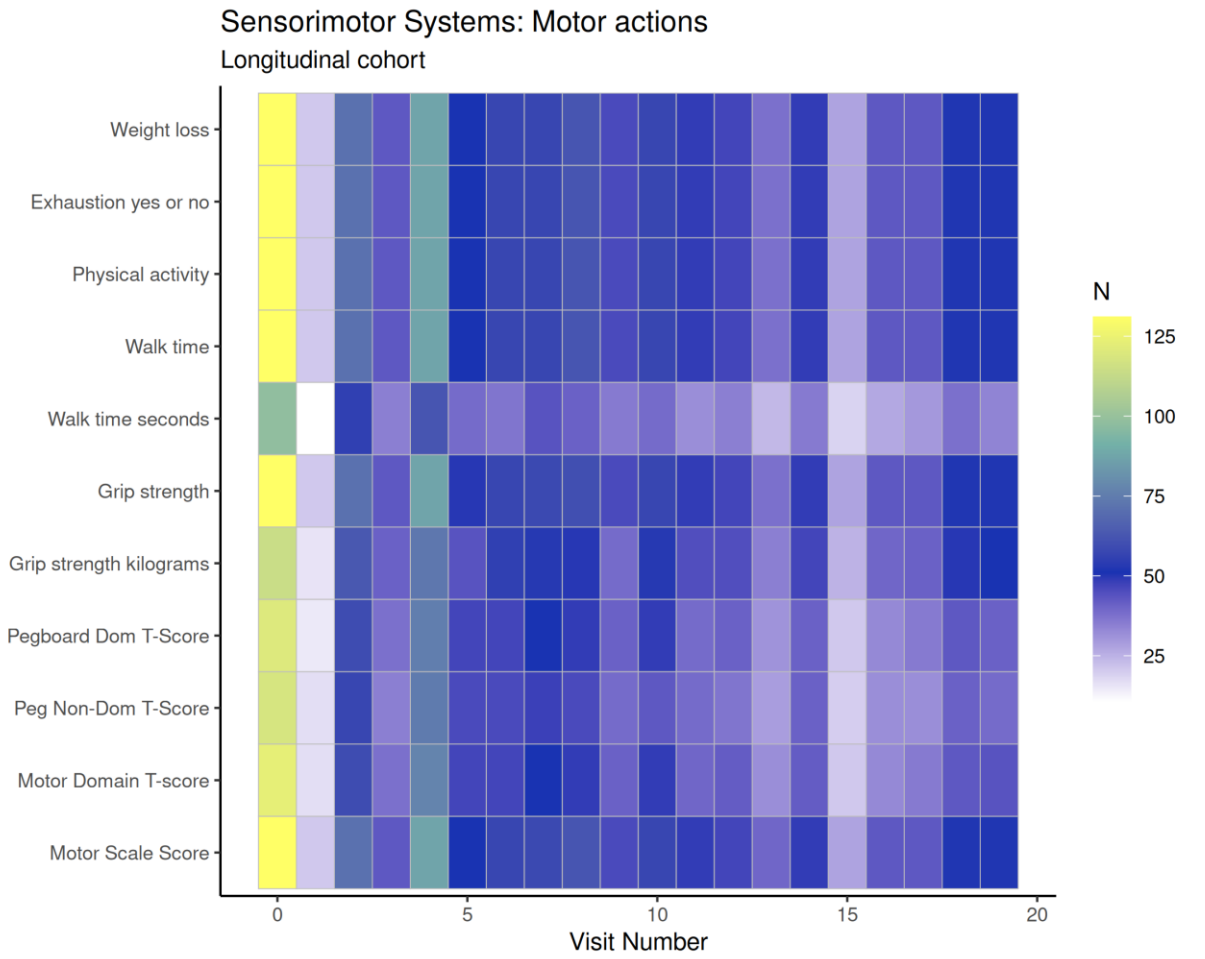

Figure 59: Heatmap showing the number of participants in the longitudinal cohort with each Sensorimotor Systems: Motor actions variable measured, by visit number, for the first 10 years.

The following two UpSet plots show the joint availability of assessments across all visits for each subset of variables. The second UpSet plot only includes participants in the longitudinal cohort.

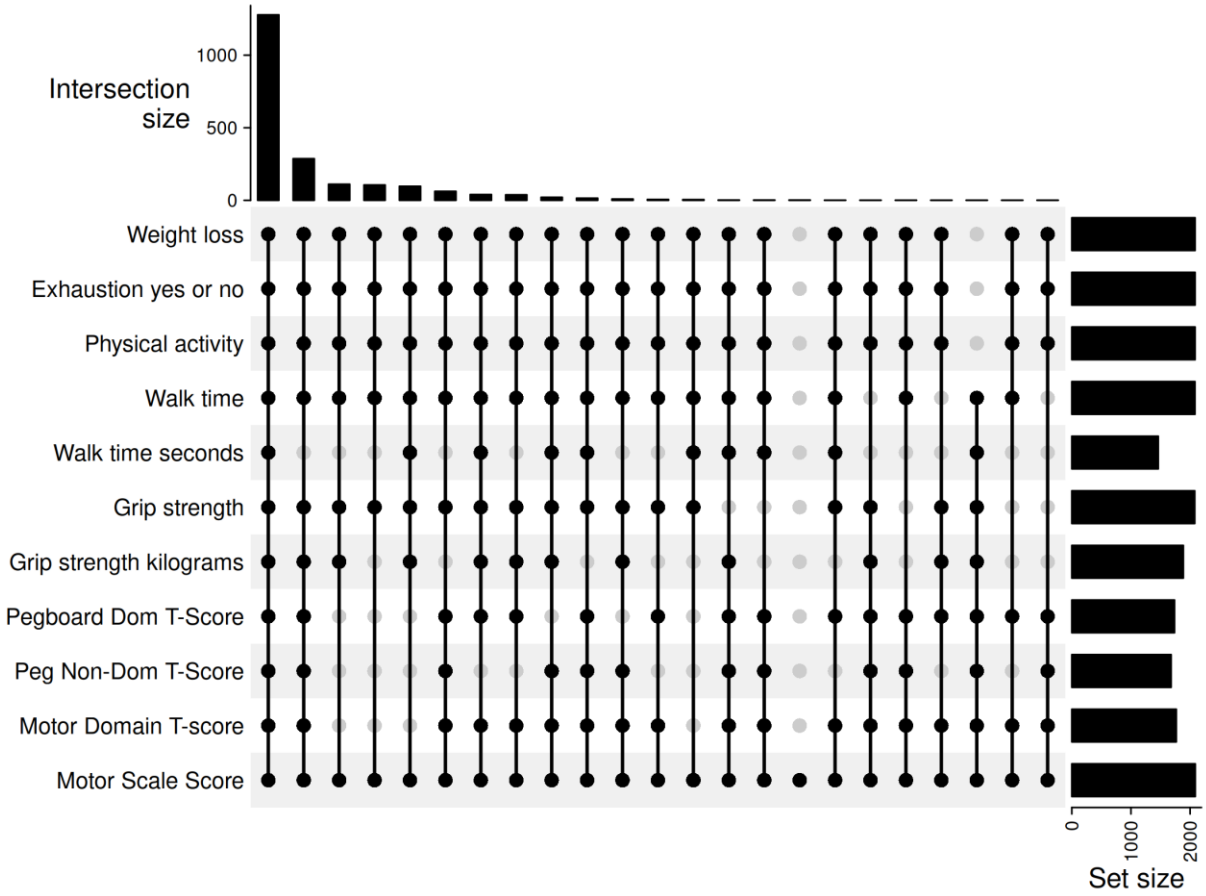

Figure 60: UpSet plot summarizing the joint availability of measures among individuals with one or more visits for the Sensorimotor Systems: Motor actions variables across the first 20 visits. The bottom right horizontal barplot shows the number observations for each variable. The filled circles in the matrix represent the different Venn diagram spaces (unique and overlapping sets). Connected filled circles indicate a certain intersection. The barplot along the top shows the number of observations available for each intersection set.

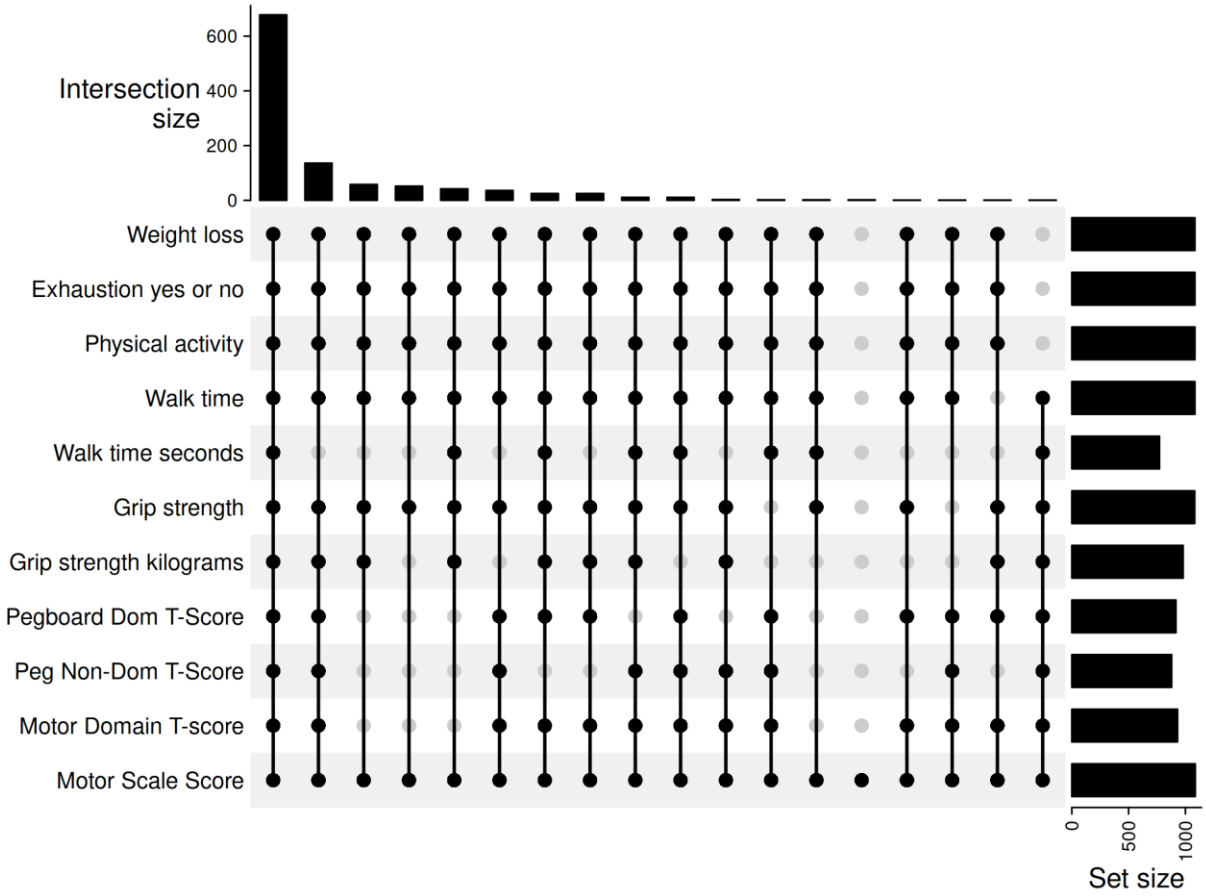

Figure 61: UpSet plot summarizing the joint availability of measures among individuals in the longitudinal cohort for the Sensorimotor Systems: Motor actions variables across the first 20 visits. The bottom right horizontal barplot shows the number observations for each variable. The filled circles in the matrix represent the different Venn diagram spaces (unique and overlapping sets). Connected filled circles indicate a certain intersection. The barplot along the top shows the number of observations available for each intersection set.

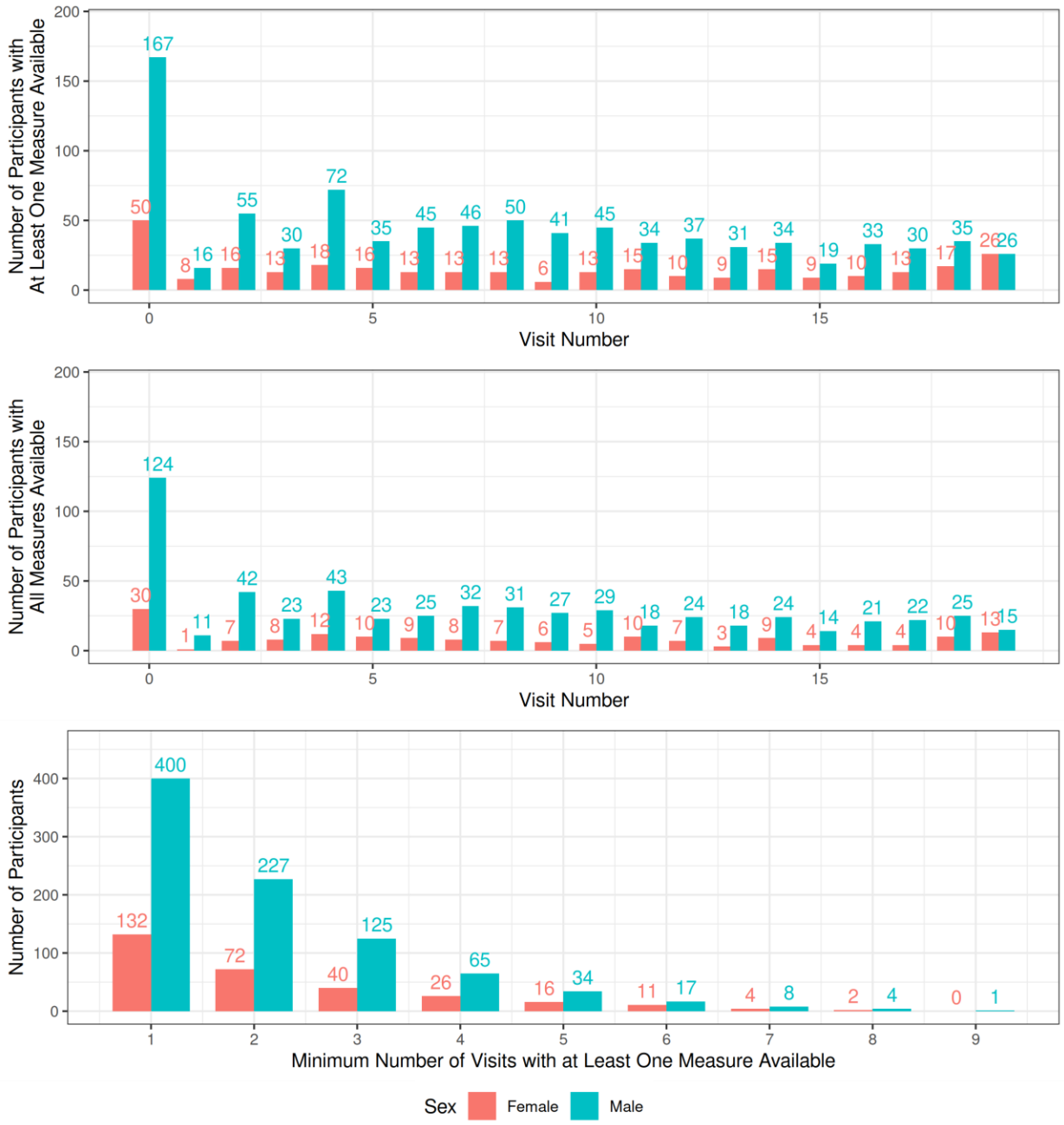

Figure 62: Data availability of participants for Sensorimotor Systems: Motor actions variables by sex summarized by the number of participants with at least one measure available at each visit number (top), the number of participants with all measures available at each visit number (middle), and the total number of participants with at least one measurement taken for a given number of visits (bottom).

Figure 63: Scatterplot matrix of the Sensorimotor Systems: Motor actions variables with points colored by sex. The diagonal shows the estimated density curve for each marginal distribution, and the top right cells show the respective estimated pairwise Pearson correlation values overall (in black) and by sex.

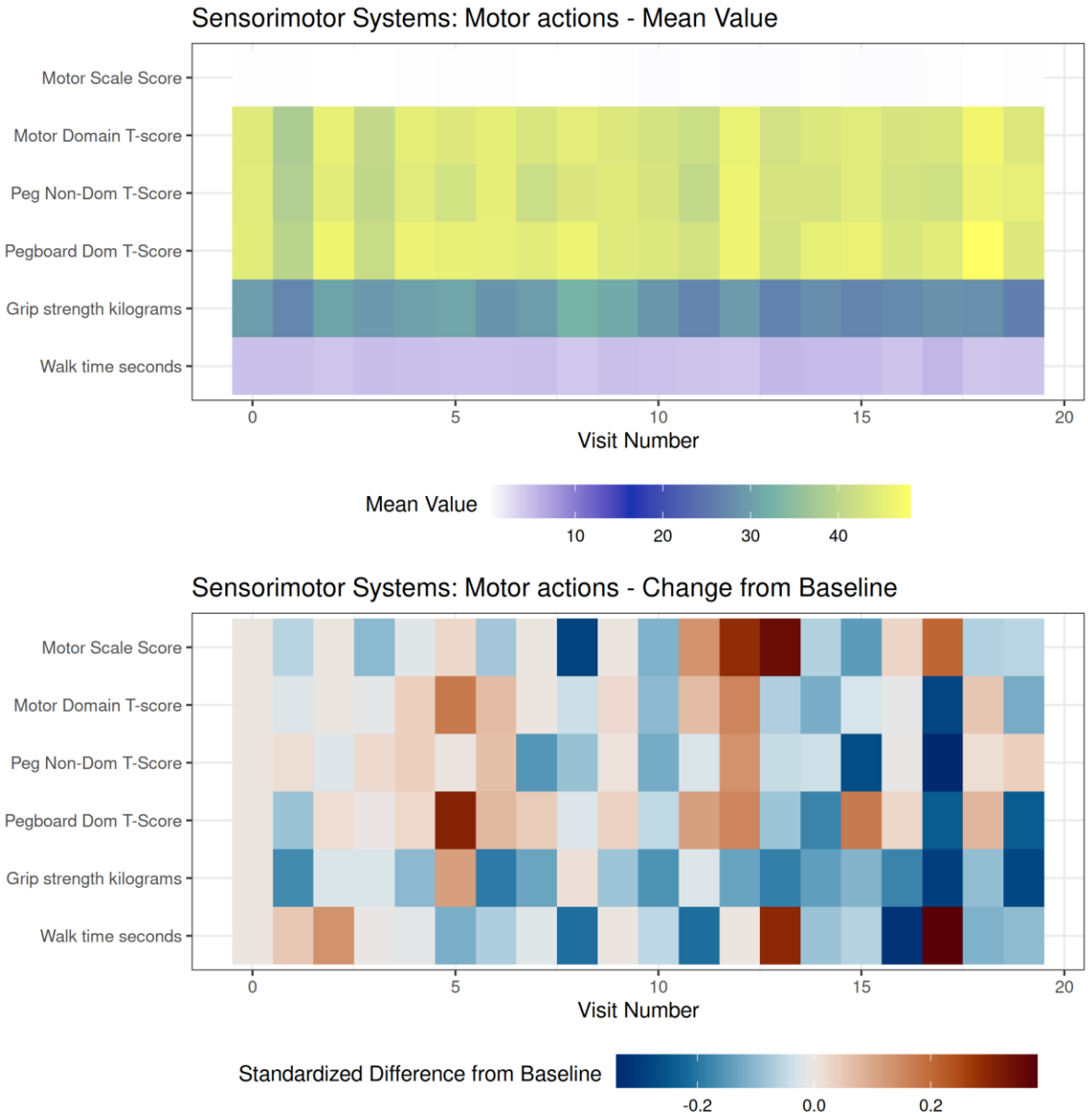

Figure 64: Heatmap of the mean value (top) and standardized mean difference in assessment measurement from baseline (bottom) by visit number for each numeric variable in the Sensorimotor Systems: Motor actions construct. Standardized mean difference is the mean difference divided by the standard deviation across participants at baseline.

7.1.3 Tables

Table 21: Number of participants by sex with measures available for the "Sensorimotor Systems: Motor actions" variables across the first 10 visits (visit numbers 0 to 9).

Measure	Visit #:	0	1	2	3	4	5	6	7	8	9
Weight loss	Female	50	8	16	13	18	16	13	13	13	6
	Male	167	16	55	30	72	35	45	45	50	41
	Total	217	24	71	43	90	51	58	58	63	47
Exhaustion yes or no	Female	50	8	16	13	18	16	13	13	13	6
	Male	167	16	55	30	72	35	45	45	50	41
	Total	217	24	71	43	90	51	58	58	63	47
Physical activity	Female	50	8	16	13	18	16	13	13	13	6
	Male	167	16	55	30	72	35	45	45	50	41
	Total	217	24	71	43	90	51	58	58	63	47
Walk time	Female	50	8	16	13	18	16	13	13	13	6
	Male	167	16	55	30	72	35	45	45	50	41
	Total	217	24	71	43	90	51	58	58	63	47
Walk time seconds	Female	37	3	10	11	15	12	11	9	8	6
	Male	136	11	45	24	50	27	27	36	34	31
	Total	173	14	55	35	65	39	38	45	42	37
Grip strength	Female	50	8	16	13	18	15	13	13	13	6
	Male	167	16	55	30	72	35	45	46	48	41
	Total	217	24	71	43	90	50	58	59	61	47
Grip strength kilograms	Female	45	6	14	12	17	14	13	11	11	6
	Male	152	13	49	29	59	30	43	43	40	34
	Total	197	19	63	41	76	44	56	54	51	40
Pegboard Dom T-Score	Female	42	4	10	9	14	16	10	11	9	6
	Male	158	14	49	29	63	31	38	41	41	36

Measure	Visit #:	0	1	2	3	4	5	6	7	8	9
	Total	200	18	59	38	77	47	48	52	50	42
Peg Non-Dom T-Score	Female	39	5	10	8	14	15	9	10	9	6
	Male	157	15	47	27	63	31	38	39	38	34
	Total	196	20	57	35	77	46	47	49	47	40
Motor Domain T-score	Female	42	5	10	9	15	16	10	11	9	6
	Male	161	15	49	29	65	31	38	41	41	36
	Total	203	20	59	38	80	47	48	52	50	42
Motor Scale Score	Female	50	8	16	13	18	16	13	13	13	6
	Male	167	16	55	30	72	35	45	46	50	41
	Total	217	24	71	43	90	51	58	59	63	47

Table 22: Number of participants by sex with measures available for the "Sensorimotor Systems: Motor actions" variables across visit numbers 10 to 19.

Measure	Visit #:	10	11	12	13	14	15	16	17	18	19
Weight loss	Female	13	15	10	9	15	9	10	13	17	26
	Male	45	34	37	29	34	19	33	30	35	26
	Total	58	49	47	38	49	28	43	43	52	52
Exhaustion yes or no	Female	13	15	10	9	15	9	10	13	17	26
	Male	45	34	37	29	34	19	33	30	35	26
	Total	58	49	47	38	49	28	43	43	52	52
Physical activity	Female	13	15	10	9	15	9	10	13	17	26
	Male	45	34	37	29	34	19	33	30	35	26
	Total	58	49	47	38	49	28	43	43	52	52
Walk time	Female	13	15	10	9	15	9	10	13	17	26
	Male	45	34	37	29	34	19	33	30	35	26
	Total	58	49	47	38	49	28	43	43	52	52

Measure	Visit #:	10	11	12	13	14	15	16	17	18	19
Walk time seconds	Female	9	11	7	4	10	5	4	6	12	16
	Male	31	21	28	20	26	14	23	24	26	18
	Total	40	32	35	24	36	19	27	30	38	34
Grip strength	Female	13	15	10	9	15	9	10	13	17	26
	Male	45	34	37	29	34	19	33	30	35	26
	Total	58	49	47	38	49	28	43	43	52	52
Grip strength kilograms	Female	13	15	10	8	15	8	10	12	17	25
	Male	41	30	35	27	32	17	30	29	33	26
	Total	54	45	45	35	47	25	40	41	50	51
Pegboard Dom T-Score	Female	10	14	10	6	12	6	7	8	14	19
	Male	40	25	31	25	29	15	26	28	29	22
	Total	50	39	41	31	41	21	33	36	43	41
Peg Non-Dom T-Score	Female	7	14	8	7	12	5	7	6	13	17
	Male	37	25	29	22	29	15	25	26	28	22
	Total	44	39	37	29	41	20	32	32	41	39
Motor Domain T-score	Female	10	15	10	7	12	6	7	8	14	20
	Male	40	25	32	25	30	15	26	28	29	24
	Total	50	40	42	32	42	21	33	36	43	44
Motor Scale Score	Female	13	15	10	9	15	9	10	13	17	26
	Male	45	34	37	31	34	19	33	30	35	26
	Total	58	49	47	40	49	28	43	43	52	52

7.2 Sensorimotor Systems: Innate Motor Patterns

Unlearned action plans that may be triggered by internal or external stimuli. This can include such behaviors as stereotyped expressions of affect, orientation to salience, innate approach and withdrawal phenomena, and startle responses.

7.2.1 Variable Definitions

- **Right shoulder abduction** (DMS: HDSRSA) Question: Right shoulder abduction
- **Left shoulder abduction** (DMS: HDSLSA) Question: Left shoulder abduction
- **Right grip** (DMS: HDSRGR) Question: Right grip
- **Left grip** (DMS: HDSLGR) Question: Left grip
- **Right hip flexion** (DMS: HDSRHF) Question: Right hip flexion
- **Left hip flexion** (DMS: HDSLHF) Question: Left hip flexion
- **Right foot dorsiflexion** (DMS: HDSRFD) Question: Right foot dorsiflexion
- **Left foot dorsiflexion** (DMS: HDSLFD) Question: Left foot dorsiflexion
- **Right upper extremity** (DMS: HDSRUE) Question: Right upper extremity
- **Left upper extremity** (DMS: HDSLUE) Question: Left upper extremity
- **Right lower extremity** (DMS: HDSRLE) Question: Right lower extremity
- **Left lower extremity** (DMS: HDSLLE) Question: Left lower extremity
- **Right biceps** (DMS: HDSRBI) Question: Right biceps
- **Left biceps** (DMS: HDSLBI) Question: Left biceps
- **Right patellar** (DMS: HDSRPA) Question: Right patellar
- **Left patellar** (DMS: HDSLPA) Question: Left patellar
- **Right plantar response** (DMS: HDSRPR) Question: Right plantar response
- **Left plantar response** (DMS: HDSLPR) Question: Left plantar response
- **Glabellar** (DMS: HDSGLB) Question: Glabellar
- **Snout** (DMS: HDSSNT) Question: Snout
- **Coordination** (DMS: HDSCOR) Question: Coordination
- **Gait** (DMS: HDSGIT) Question: Gait

7.2.2 Figures

The following two heatmaps show the number of participants with assessments available by variable and visit number. The second heatmap only includes participants in the longitudinal cohort.

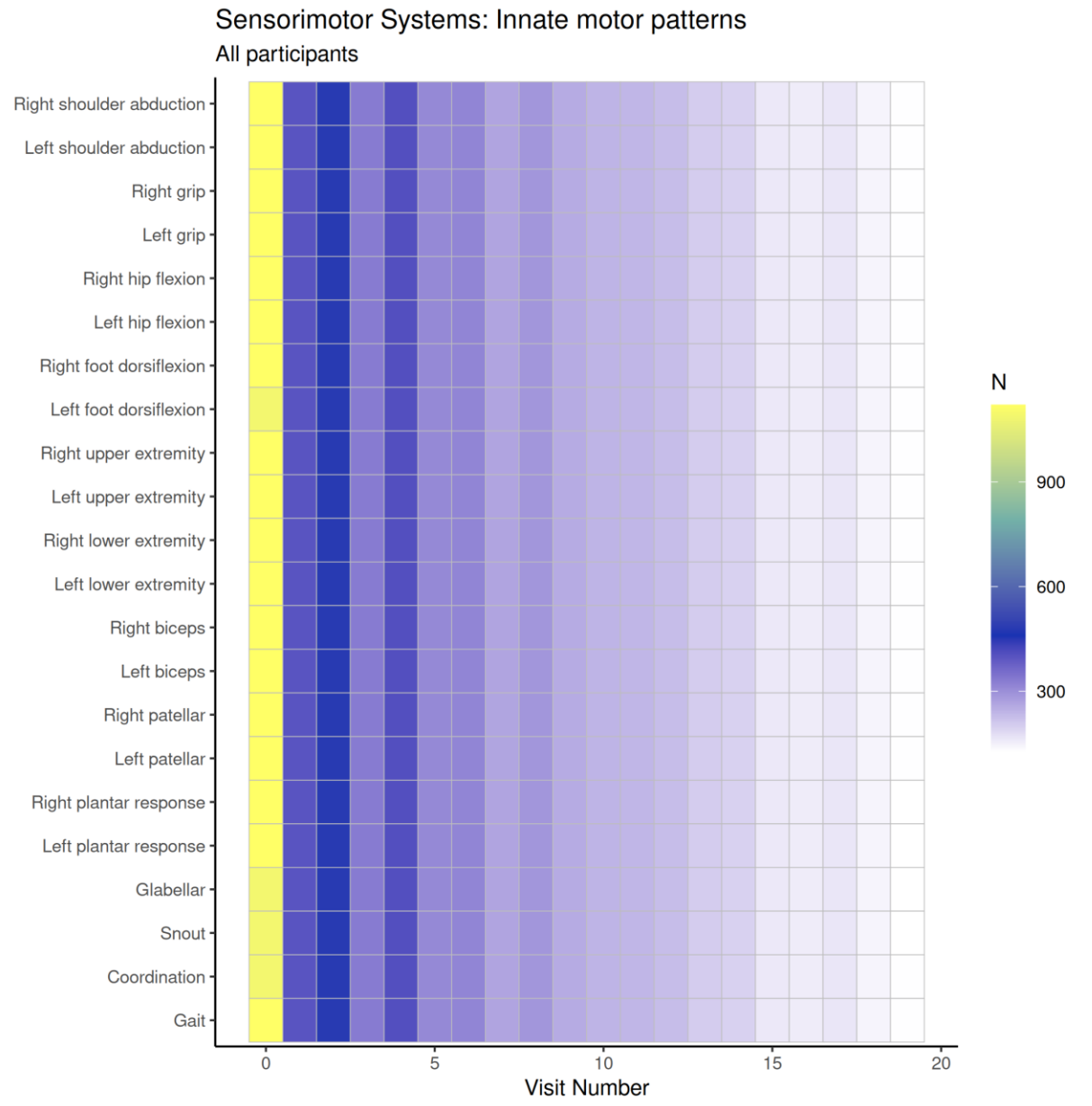

Figure 65: Heatmap showing the number of participants with each Sensorimotor Systems: Innate motor patterns variable measured by visit number for the first 10 years after enrollment in NNTC.

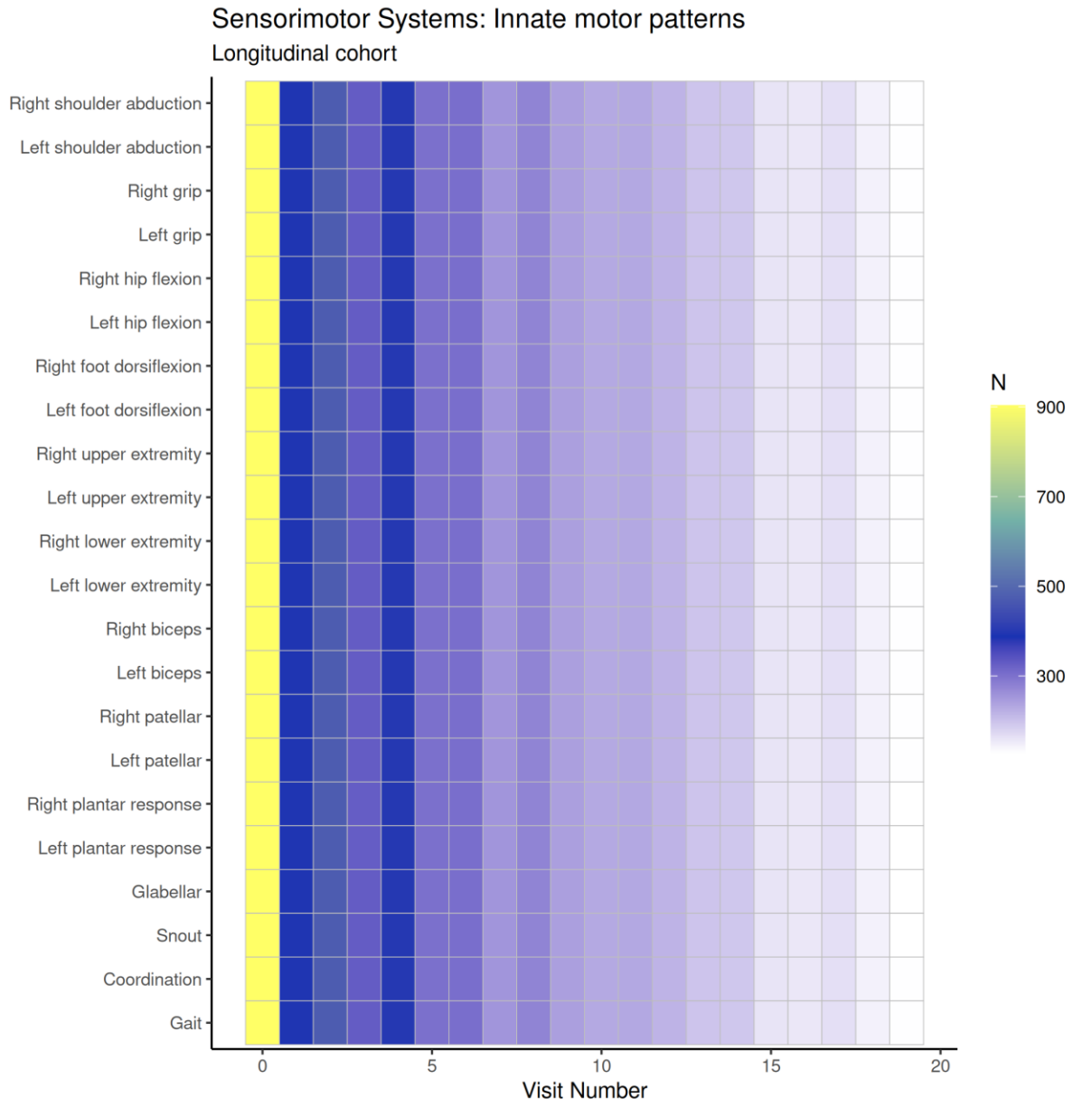

Figure 66: Heatmap showing the number of participants in the longitudinal cohort with each Sensorimotor Systems: Innate motor patterns variable measured, by visit number, for the first 10 years.

The following two UpSet plots show the joint availability of assessments across all visits for each subset of variables. The second UpSet plot only includes participants in the longitudinal cohort.

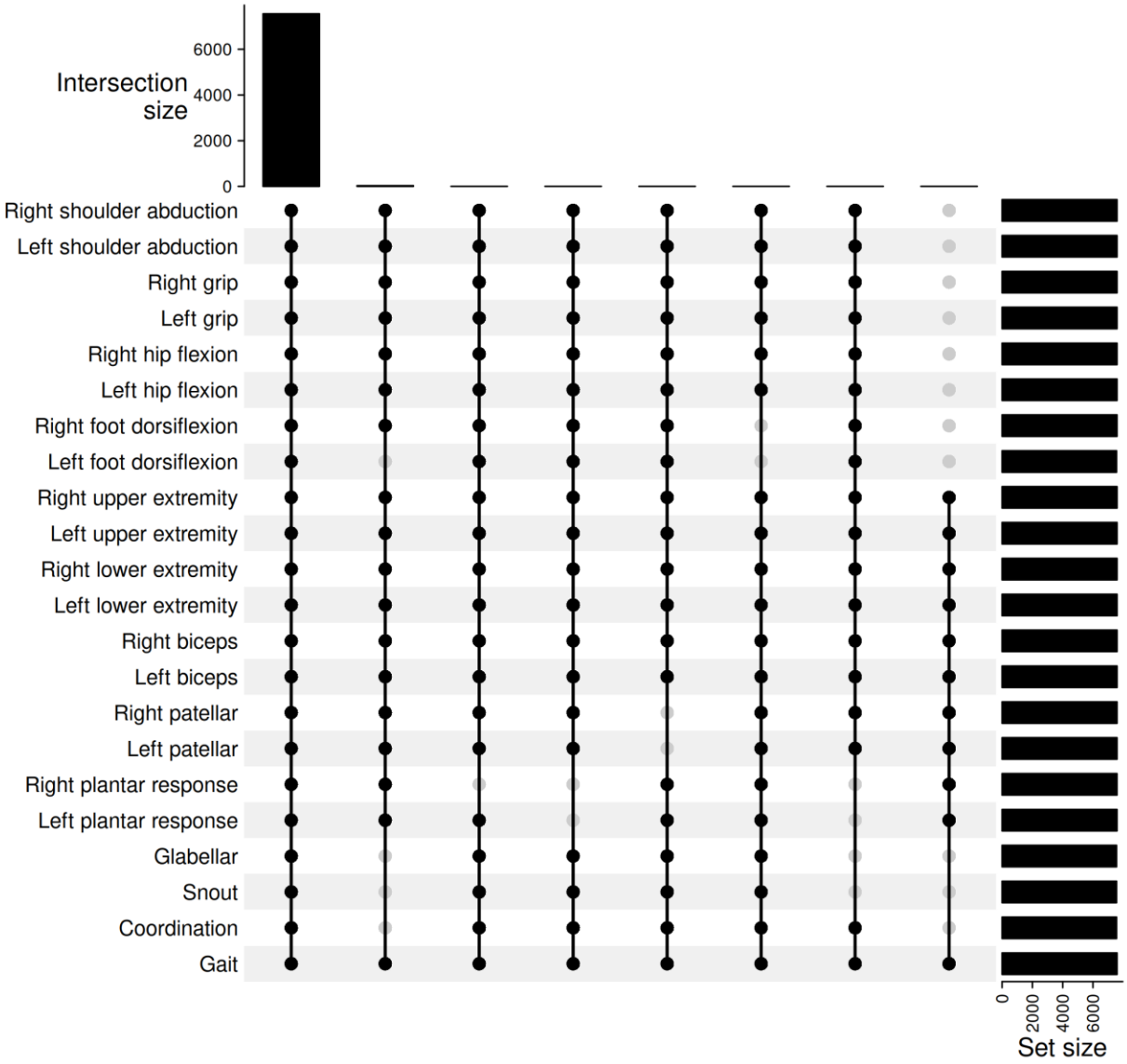

Figure 67: UpSet plot summarizing the joint availability of measures among individuals with one or more visits for the Sensorimotor Systems: Innate motor patterns variables across the first 20 visits. The bottom right horizontal barplot shows the number observations for each variable. The filled circles in the matrix represent the different Venn diagram spaces (unique and overlapping sets). Connected filled circles indicate a certain intersection. The barplot along the top shows the number of observations available for each intersection set.

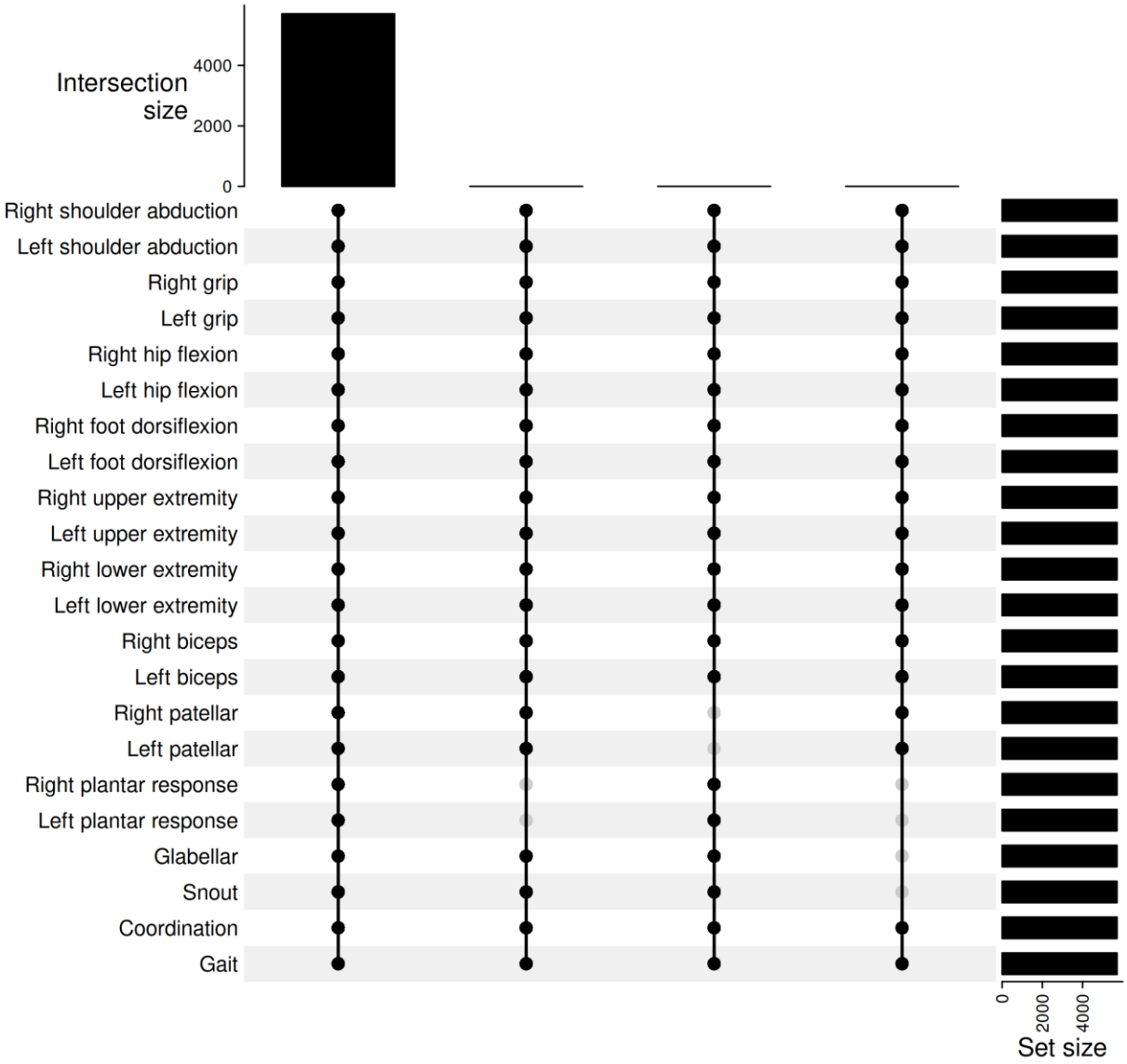

Figure 68: UpSet plot summarizing the joint availability of measures among individuals in the longitudinal cohort for the Sensorimotor Systems: Innate motor patterns variables across the first 20 visits. The bottom right horizontal barplot shows the number observations for each variable. The filled circles in the matrix represent the different Venn diagram spaces (unique and overlapping sets). Connected filled circles indicate a certain intersection. The barplot along the top shows the number of observations available for each intersection set.

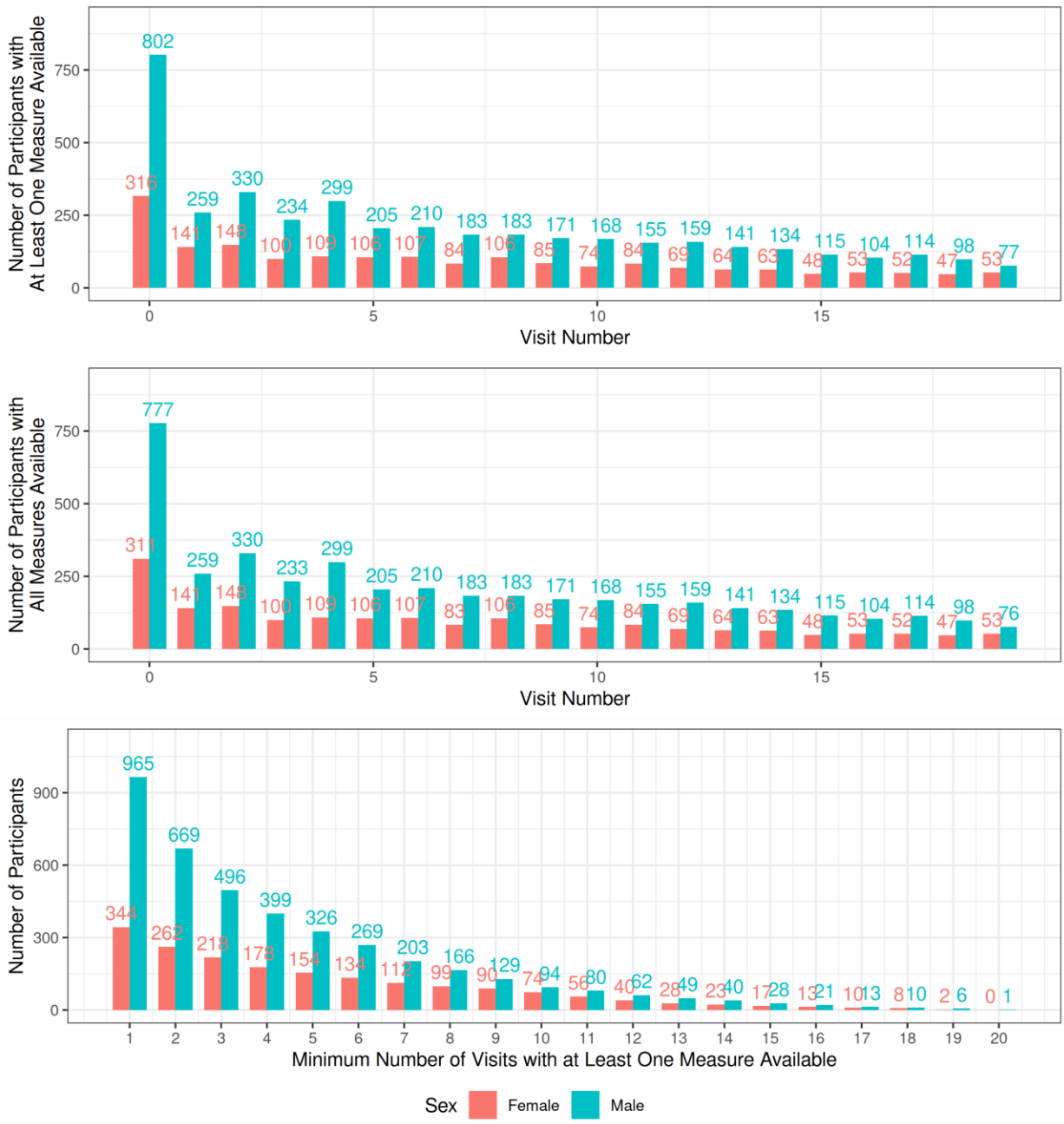

Figure 69: Data availability of participants for Sensorimotor Systems: Innate motor patterns variables by sex summarized by the number of participants with at least one measure available at each visit number (top), the number of participants with all measures available at each visit number (middle), and the total number of participants with at least one measurement taken for a given number of visits (bottom).

7.2.3 Tables

Table 23: Number of participants by sex with measures available for the "Sensorimotor Systems: Innate motor patterns" variables across the first 10 visits (visit numbers 0 to 9). Total includes 2 additional participants with missing information on sex.

Measure	Visit #:	0	1	2	3	4	5	6	7	8	9
Right shoulder abduction	Female	316	141	148	100	109	106	107	84	106	85
	Male	801	259	330	234	299	205	210	183	183	171
	Total	1,119	400	478	334	408	311	317	267	289	256
Left shoulder abduction	Female	316	141	148	100	109	106	107	84	106	85
	Male	801	259	330	234	299	205	210	183	183	171
	Total	1,119	400	478	334	408	311	317	267	289	256
Right grip	Female	316	141	148	100	109	106	107	84	106	85
	Male	801	259	330	234	299	205	210	183	183	171
	Total	1,119	400	478	334	408	311	317	267	289	256
Left grip	Female	316	141	148	100	109	106	107	84	106	85
	Male	801	259	330	234	299	205	210	183	183	171
	Total	1,119	400	478	334	408	311	317	267	289	256
Right hip flexion	Female	316	141	148	100	109	106	107	84	106	85
	Male	801	259	330	234	299	205	210	183	183	171
	Total	1,119	400	478	334	408	311	317	267	289	256
Left hip flexion	Female	316	141	148	100	109	106	107	84	106	85
	Male	801	259	330	234	299	205	210	183	183	171
	Total	1,119	400	478	334	408	311	317	267	289	256
Right foot dorsiflexion	Female	316	141	148	100	109	106	107	84	106	85
	Male	801	259	330	234	299	205	210	183	183	171
	Total	1,119	400	478	334	408	311	317	267	289	256

Measure	Visit #:	0	1	2	3	4	5	6	7	8	9
Left foot dorsiflexion	Female	311	141	148	100	109	106	107	84	106	85
	Male	777	259	330	234	299	205	210	183	183	171
	Total	1,088	400	478	334	408	311	317	267	289	256
Right upper extremity	Female	316	141	148	100	109	106	107	84	106	85
	Male	802	259	330	234	299	205	210	183	183	171
	Total	1,120	400	478	334	408	311	317	267	289	256
Left upper extremity	Female	316	141	148	100	109	106	107	84	106	85
	Male	802	259	330	234	299	205	210	183	183	171
	Total	1,120	400	478	334	408	311	317	267	289	256
Right lower extremity	Female	316	141	148	100	109	106	107	84	106	85
	Male	802	259	330	234	299	205	210	183	183	171
	Total	1,120	400	478	334	408	311	317	267	289	256
Left lower extremity	Female	316	141	148	100	109	106	107	84	106	85
	Male	802	259	330	234	299	205	210	183	183	171
	Total	1,120	400	478	334	408	311	317	267	289	256
Right biceps	Female	316	141	148	100	109	106	107	84	106	85
	Male	802	259	330	234	299	205	210	183	183	171
	Total	1,120	400	478	334	408	311	317	267	289	256
Left biceps	Female	316	141	148	100	109	106	107	84	106	85
	Male	802	259	330	234	299	205	210	183	183	171
	Total	1,120	400	478	334	408	311	317	267	289	256
Right patellar	Female	316	141	148	100	109	106	107	83	106	85
	Male	802	259	330	234	299	205	210	183	183	171
	Total	1,120	400	478	334	408	311	317	266	289	256
Left patellar	Female	316	141	148	100	109	106	107	83	106	85
	Male	802	259	330	234	299	205	210	183	183	171

Measure	Visit #:	0	1	2	3	4	5	6	7	8	9
	Total	1,120	400	478	334	408	311	317	266	289	256
Right plantar response	Female	316	141	148	100	109	106	107	84	106	85
	Male	802	259	330	233	299	205	210	183	183	171
	Total	1,120	400	478	333	408	311	317	267	289	256
Left plantar response	Female	316	141	148	100	109	106	107	84	106	85
	Male	802	259	330	233	299	205	210	183	183	171
	Total	1,120	400	478	333	408	311	317	267	289	256
Glabellar	Female	311	141	148	100	109	106	107	84	106	85
	Male	777	259	330	234	299	205	210	183	183	171
	Total	1,088	400	478	334	408	311	317	267	289	256
Snout	Female	311	141	148	100	109	106	107	84	106	85
	Male	777	259	330	234	299	205	210	183	183	171
	Total	1,088	400	478	334	408	311	317	267	289	256
Coordination	Female	311	141	148	100	109	106	107	84	106	85
	Male	777	259	330	234	299	205	210	183	183	171
	Total	1,088	400	478	334	408	311	317	267	289	256
Gait	Female	316	141	148	100	109	106	107	84	106	85
	Male	802	259	330	234	299	205	210	183	183	171
	Total	1,120	400	478	334	408	311	317	267	289	256

Table 24: Number of participants by sex with measures available for the "Sensorimotor Systems: Innate motor patterns" variables across visit numbers 10 to 19.

Measure	Visit #:	10	11	12	13	14	15	16	17	18	19
Right shoulder abduction	Female	74	84	69	64	63	48	53	52	47	53
	Male	168	155	159	141	134	115	104	114	98	77
	Total	242	239	228	205	197	163	157	166	145	130

Measure	Visit #:	10	11	12	13	14	15	16	17	18	19
Left shoulder abduction	Female	74	84	69	64	63	48	53	52	47	53
	Male	168	155	159	141	134	115	104	114	98	77
	Total	242	239	228	205	197	163	157	166	145	130
Right grip	Female	74	84	69	64	63	48	53	52	47	53
	Male	168	155	159	141	134	115	104	114	98	77
	Total	242	239	228	205	197	163	157	166	145	130
Left grip	Female	74	84	69	64	63	48	53	52	47	53
	Male	168	155	159	141	134	115	104	114	98	77
	Total	242	239	228	205	197	163	157	166	145	130
Right hip flexion	Female	74	84	69	64	63	48	53	52	47	53
	Male	168	155	159	141	134	115	104	114	98	77
	Total	242	239	228	205	197	163	157	166	145	130
Left hip flexion	Female	74	84	69	64	63	48	53	52	47	53
	Male	168	155	159	141	134	115	104	114	98	77
	Total	242	239	228	205	197	163	157	166	145	130
Right foot dorsiflexion	Female	74	84	69	64	63	48	53	52	47	53
	Male	168	155	159	141	134	115	104	114	98	77
	Total	242	239	228	205	197	163	157	166	145	130
Left foot dorsiflexion	Female	74	84	69	64	63	48	53	52	47	53
	Male	168	155	159	141	134	115	104	114	98	77
	Total	242	239	228	205	197	163	157	166	145	130
Right upper extremity	Female	74	84	69	64	63	48	53	52	47	53
	Male	168	155	159	141	134	115	104	114	98	77
	Total	242	239	228	205	197	163	157	166	145	130
Left upper extremity	Female	74	84	69	64	63	48	53	52	47	53
	Male	168	155	159	141	134	115	104	114	98	77

Measure	Visit #:	10	11	12	13	14	15	16	17	18	19
	Total	242	239	228	205	197	163	157	166	145	130
Right lower extremity	Female	74	84	69	64	63	48	53	52	47	53
	Male	168	155	159	141	134	115	104	114	98	77
	Total	242	239	228	205	197	163	157	166	145	130
Left lower extremity	Female	74	84	69	64	63	48	53	52	47	53
	Male	168	155	159	141	134	115	104	114	98	77
	Total	242	239	228	205	197	163	157	166	145	130
Right biceps	Female	74	84	69	64	63	48	53	52	47	53
	Male	168	155	159	141	134	115	104	114	98	77
	Total	242	239	228	205	197	163	157	166	145	130
Left biceps	Female	74	84	69	64	63	48	53	52	47	53
	Male	168	155	159	141	134	115	104	114	98	77
	Total	242	239	228	205	197	163	157	166	145	130
Right patellar	Female	74	84	69	64	63	48	53	52	47	53
	Male	168	155	159	141	134	115	104	114	98	77
	Total	242	239	228	205	197	163	157	166	145	130
Left patellar	Female	74	84	69	64	63	48	53	52	47	53
	Male	168	155	159	141	134	115	104	114	98	77
	Total	242	239	228	205	197	163	157	166	145	130
Right plantar response	Female	74	84	69	64	63	48	53	52	47	53
	Male	168	155	159	141	134	115	104	114	98	76
	Total	242	239	228	205	197	163	157	166	145	129
Left plantar response	Female	74	84	69	64	63	48	53	52	47	53
	Male	168	155	159	141	134	115	104	114	98	76
	Total	242	239	228	205	197	163	157	166	145	129

Measure	Visit #:	10	11	12	13	14	15	16	17	18	19
Glabellar	Female	74	84	69	64	63	48	53	52	47	53
	Male	168	155	159	141	134	115	104	114	98	76
	Total	242	239	228	205	197	163	157	166	145	129
Snout	Female	74	84	69	64	63	48	53	52	47	53
	Male	168	155	159	141	134	115	104	114	98	76
	Total	242	239	228	205	197	163	157	166	145	129
Coordination	Female	74	84	69	64	63	48	53	52	47	53
	Male	168	155	159	141	134	115	104	114	98	77
	Total	242	239	228	205	197	163	157	166	145	130
Gait	Female	74	84	69	64	63	48	53	52	47	53
	Male	168	155	159	141	134	115	104	114	98	77
	Total	242	239	228	205	197	163	157	166	145	130