

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.

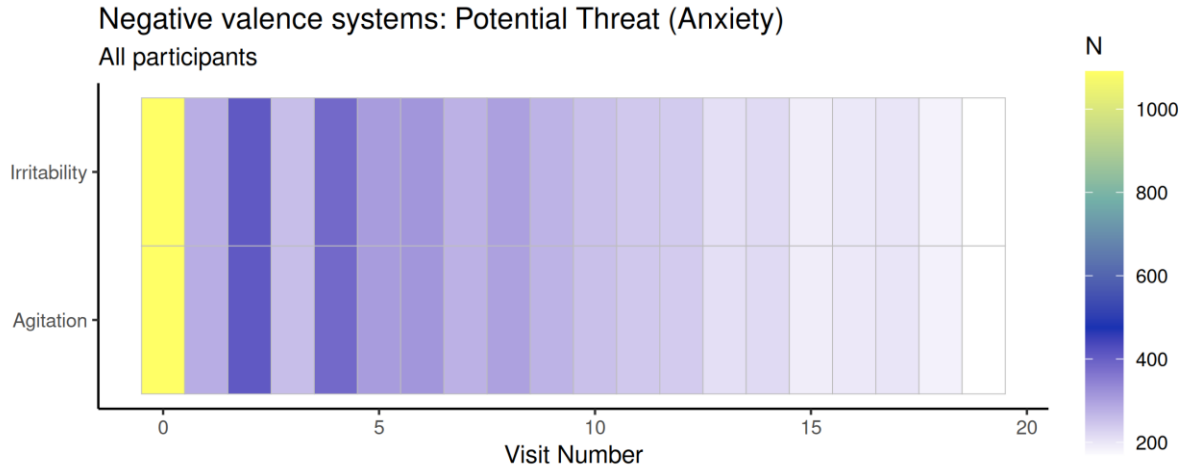


Figure 1: Heatmap showing the number of participants with each Negative valence systems: Potential Threat (Anxiety) variable measured by visit number for the first 10 years after enrollment in NNTC.

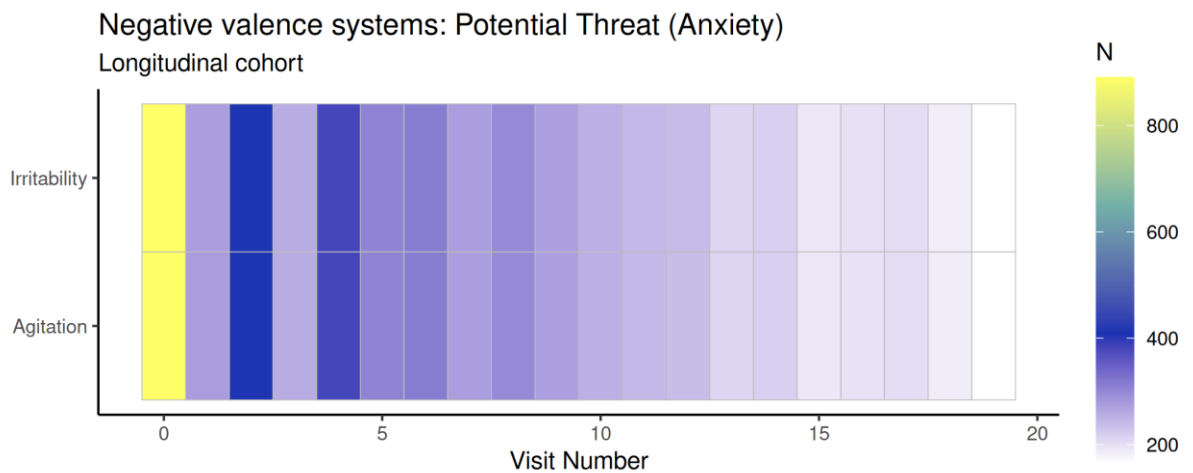


Figure 2: Heatmap showing the number of participants in the longitudinal cohort with each Negative valence systems: Potential Threat (Anxiety) variable measured, by visit number, for the first 10 years.

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.

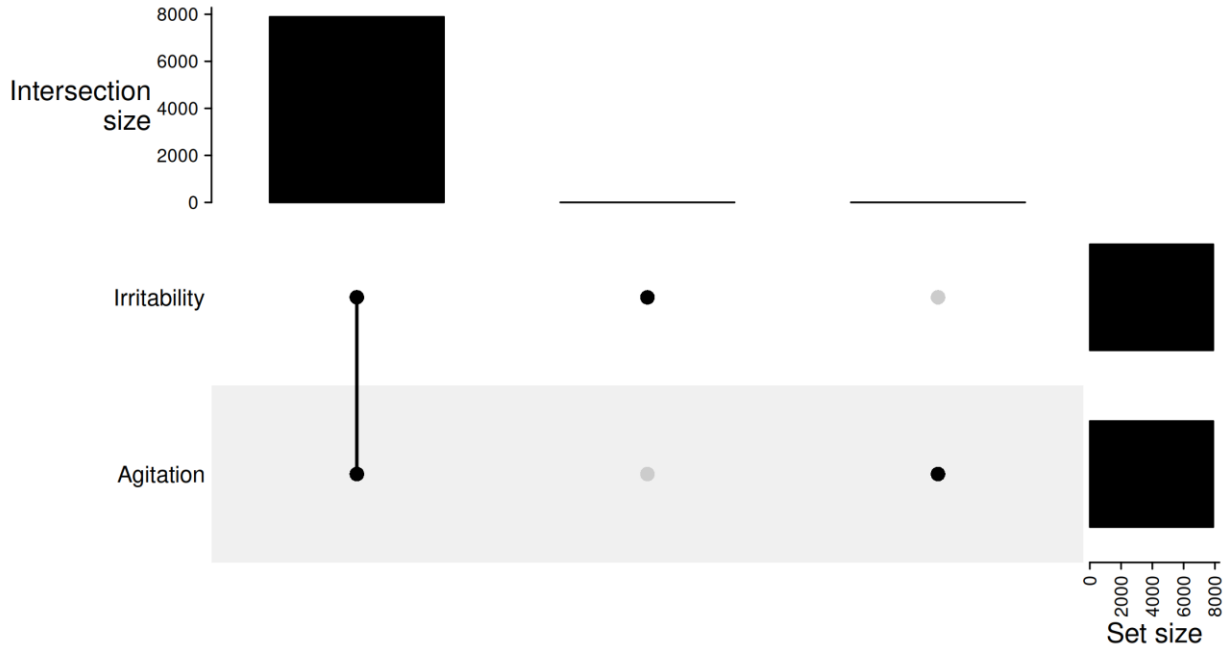


Figure 3: UpSet plot summarizing the joint availability of measures among individuals with one or more visits for the Negative valence systems: Potential Threat (Anxiety) variables across the first 20 visits. The bottom right horizontal barplot shows the number observations for each variable. The filled 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.

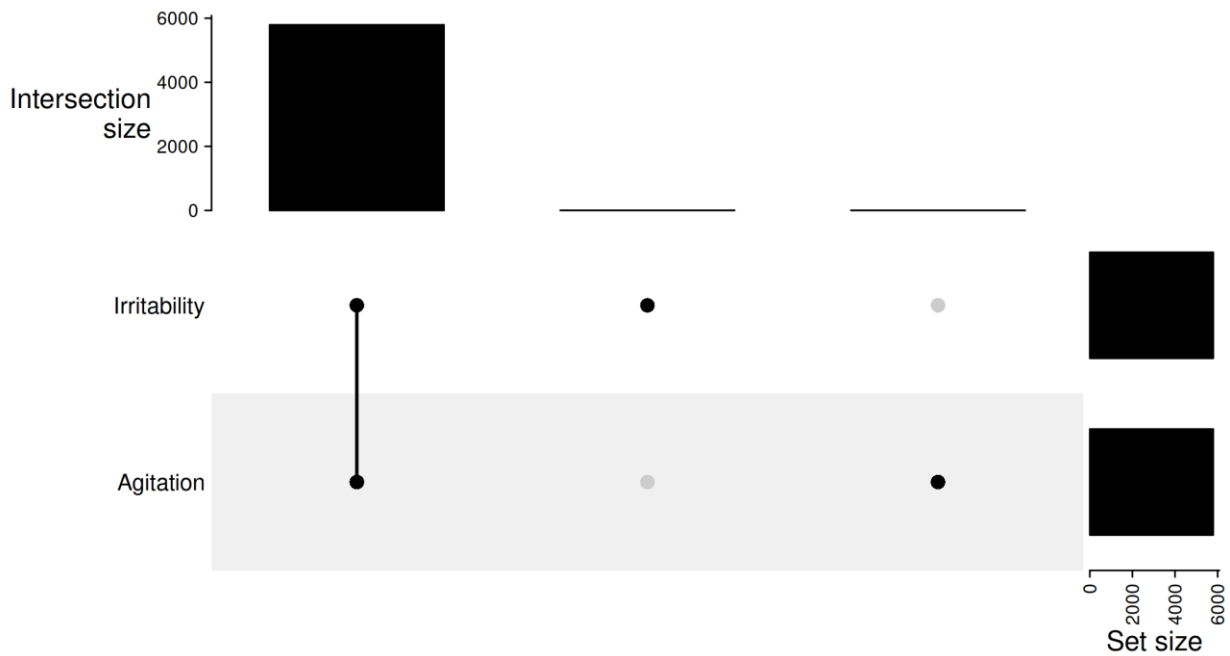


Figure 4: UpSet plot summarizing the joint availability of measures among individuals in the longitudinal cohort for the Negative valence systems: Potential Threat (Anxiety) variables across the first 20 visits. The bottom right horizontal barplot shows the number observations for each variable. The 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.

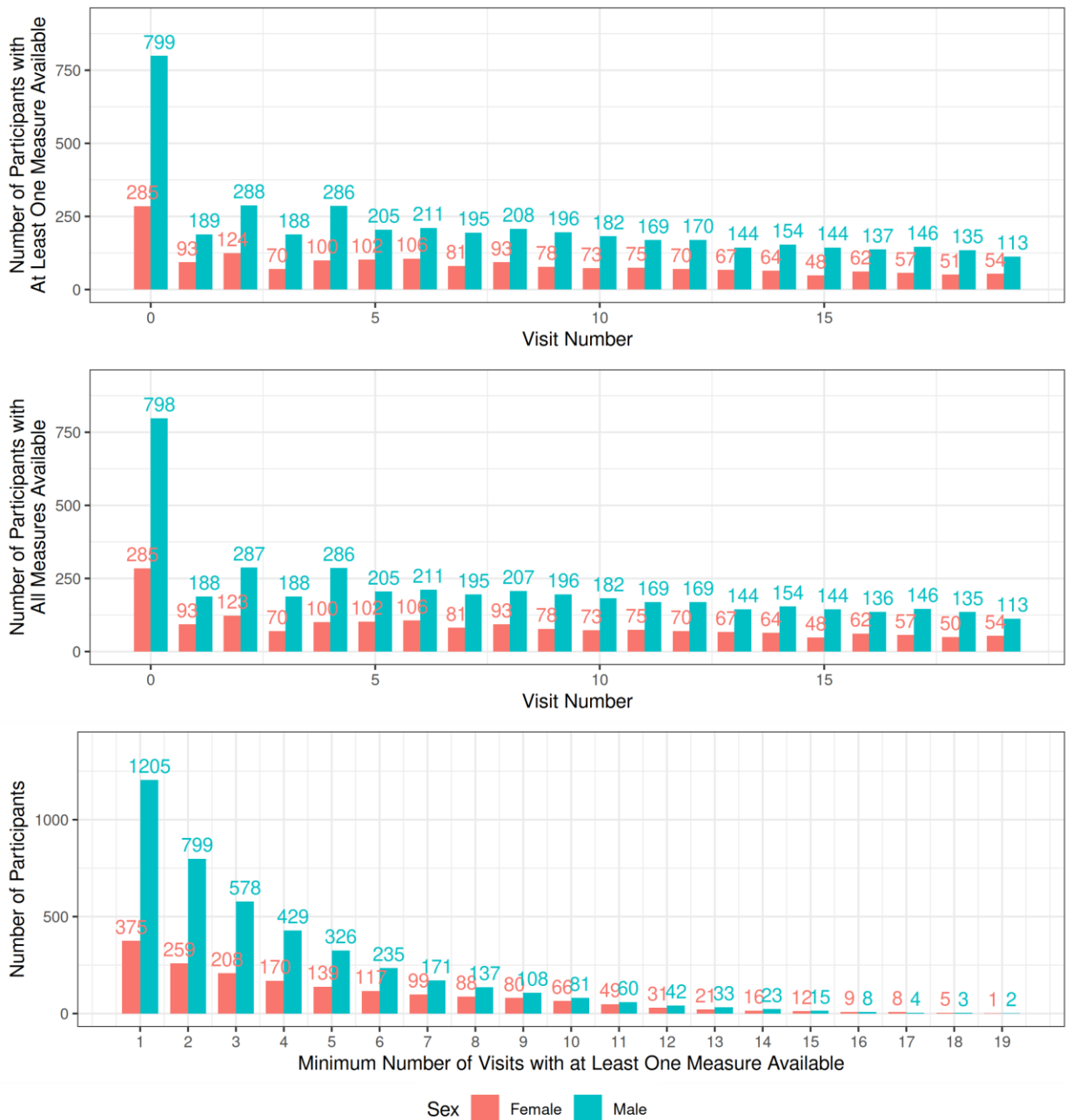


Figure 5: Data availability of participants for Negative valence systems: Potential Threat (Anxiety) variables by sex summarized by the number of participants with at least one measure available at each visit number (top), the number of participants with all measures available at each visit number (middle),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

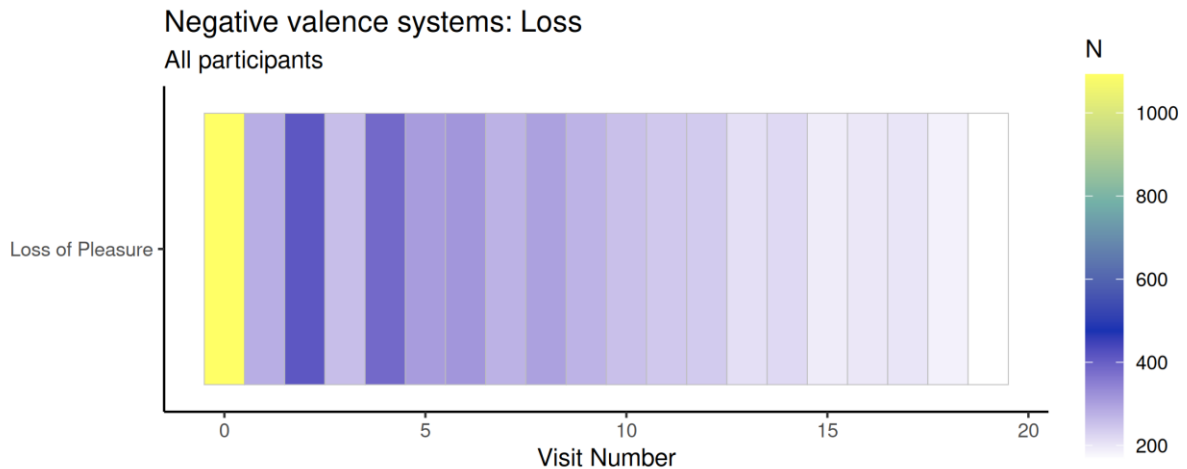


Figure 6: Heatmap showing the number of participants with each Negative valence systems: Loss variable measured by visit number for the first 10 years after enrollment in NNTC.

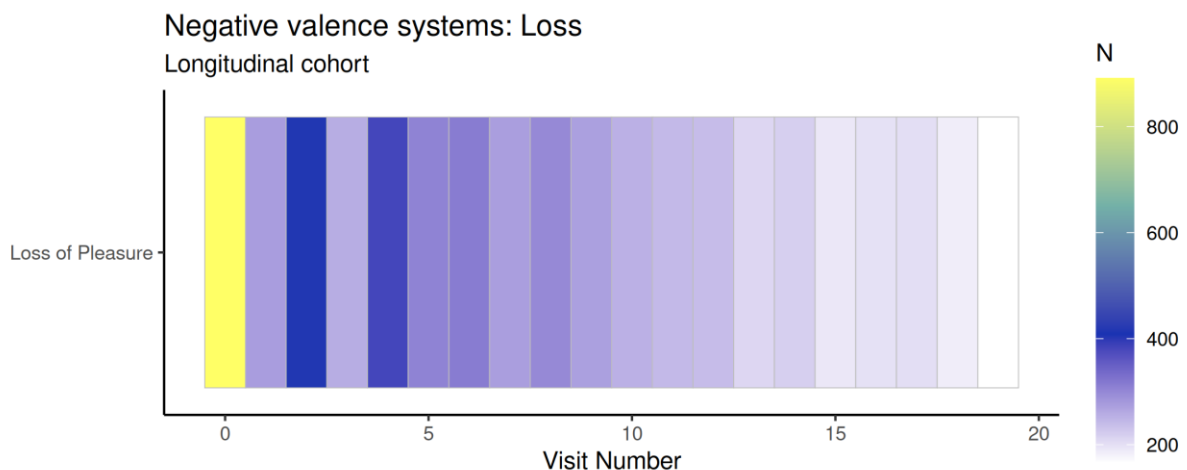


Figure 7: Heatmap showing the number of participants in the longitudinal cohort with each Negative valence systems: Loss variable measured, by visit number, for the first 10 years.

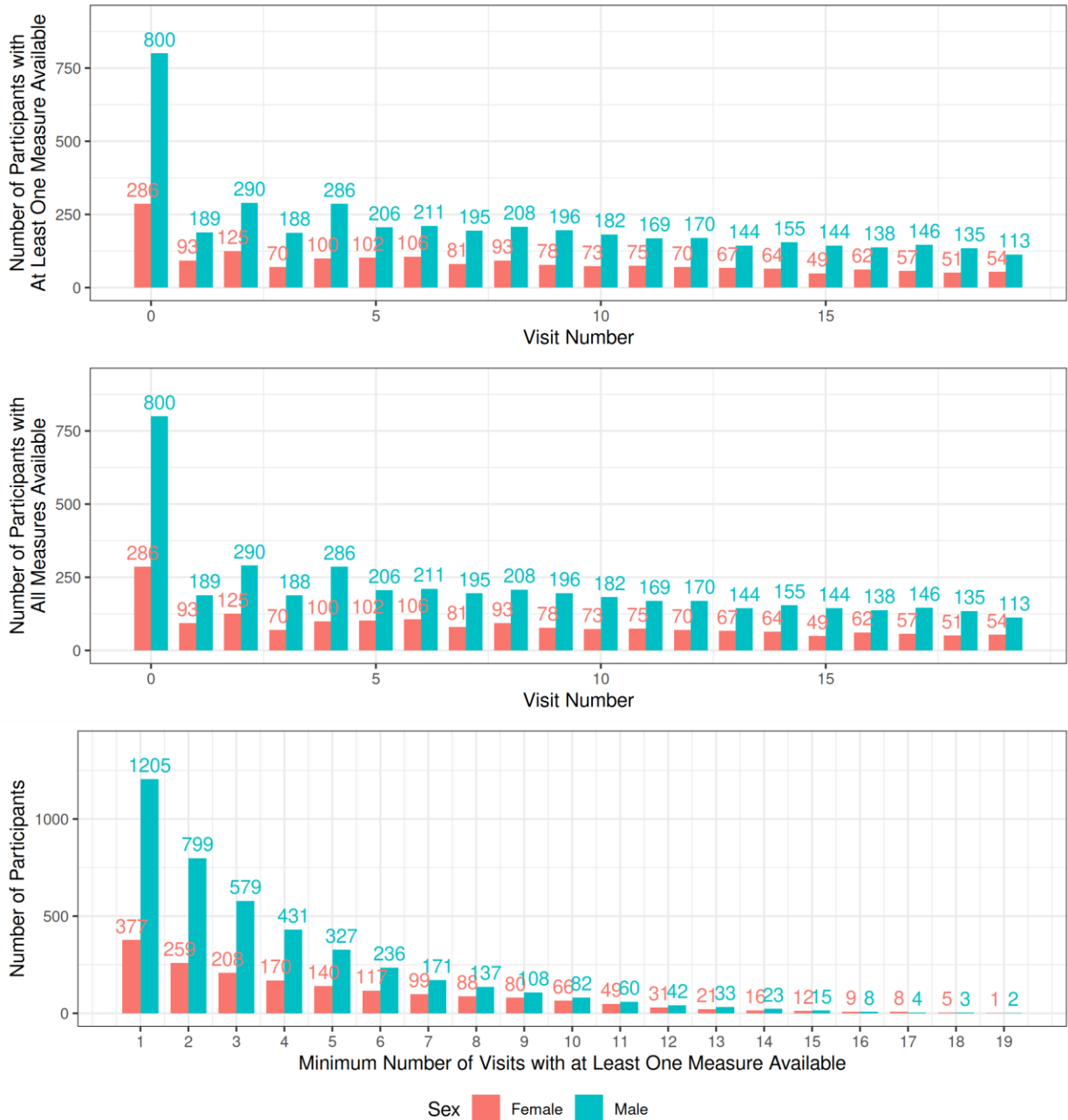


Figure 8: Data availability of participants for Negative valence systems: Loss variables by sex summarized by the number of participants with at least one measure available at each visit number (top), the number of participants with all measures available at each visit number (middle), and the total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

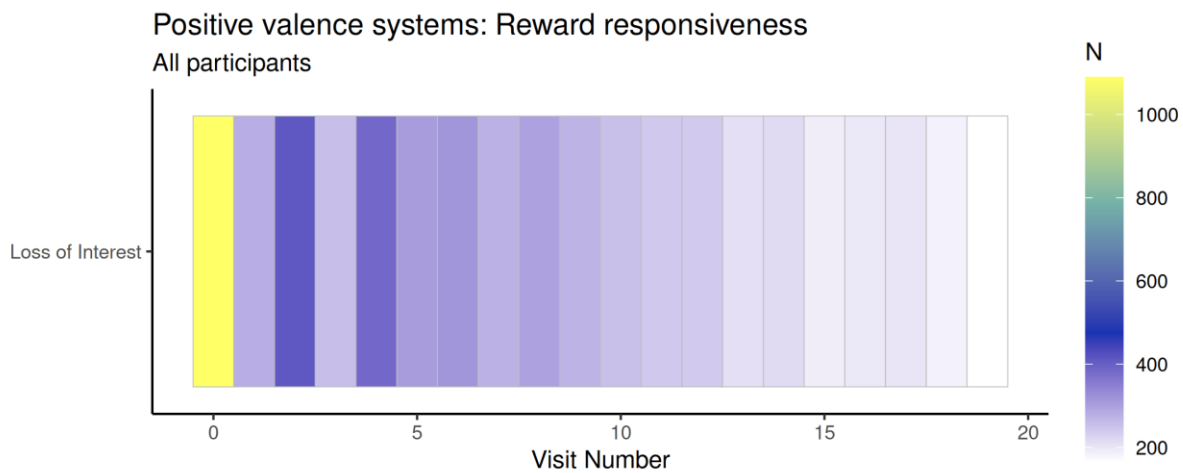


Figure 9: Heatmap showing the number of participants with each Positive valence systems: Reward responsiveness variable measured by visit number for the first 10 years after enrollment in NNTC.

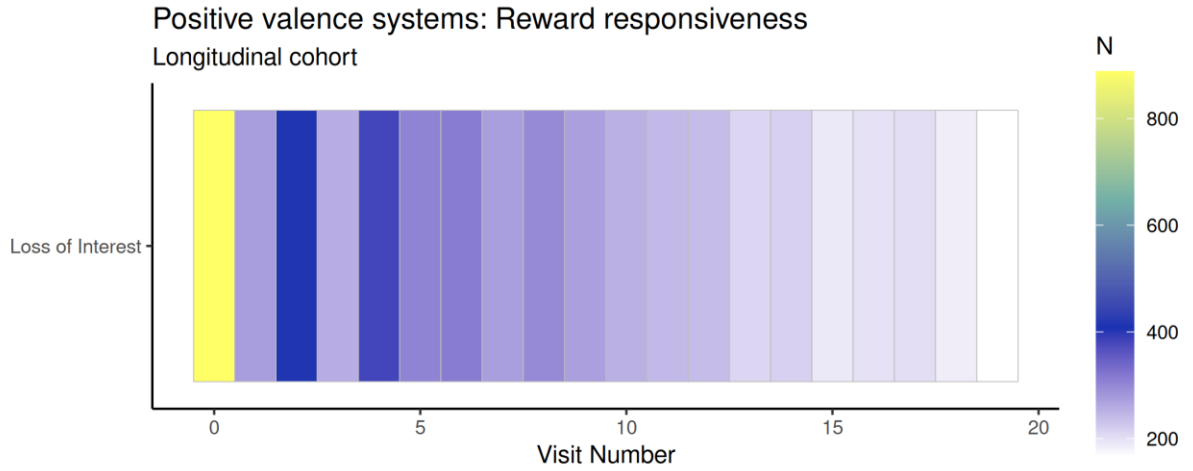


Figure 10: Heatmap showing the number of participants in the longitudinal cohort with each Positive valence systems: Reward responsiveness variable measured, by visit number, for the first 10 years.

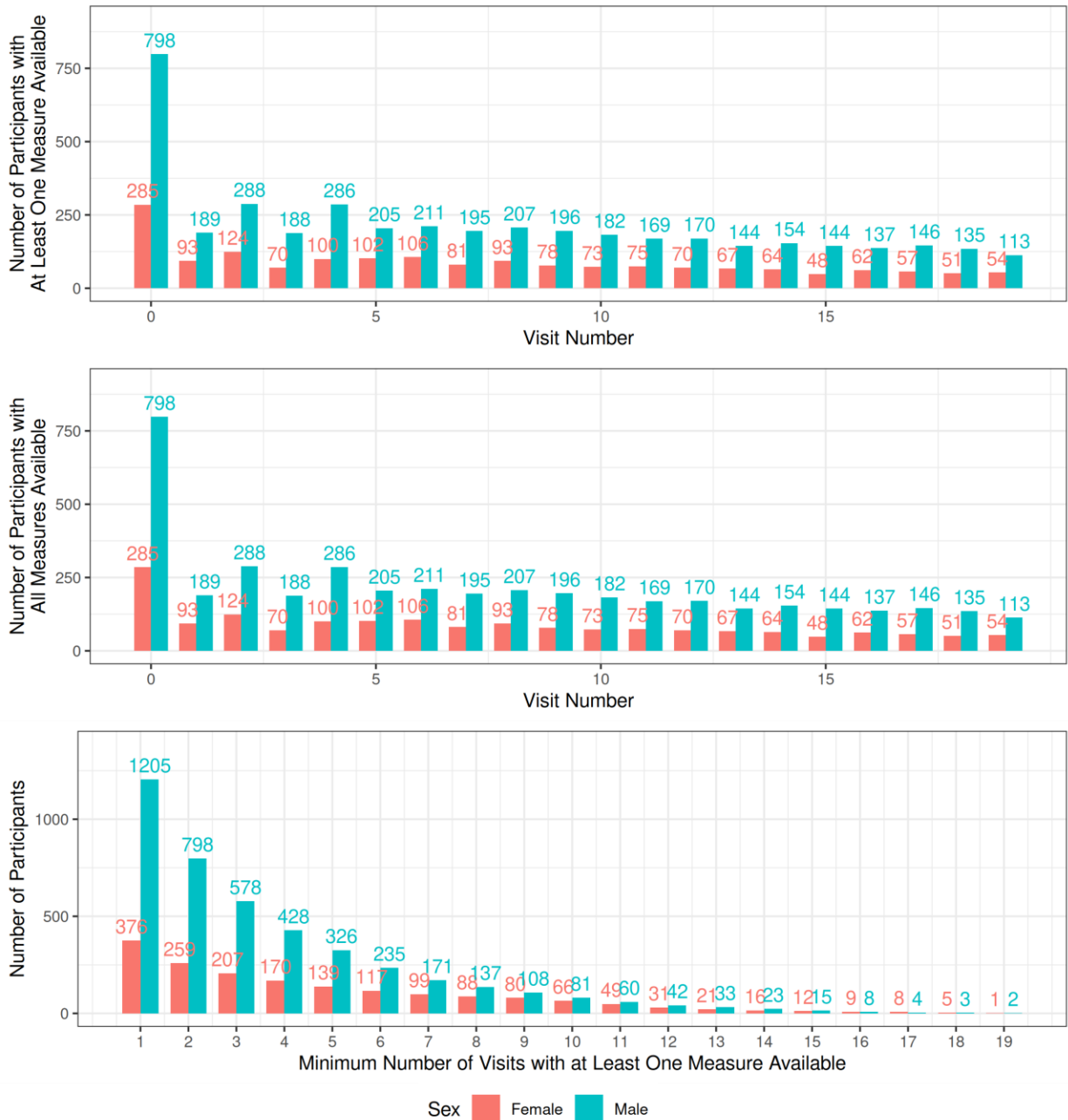


Figure 11: Data availability of participants for Positive valence systems: Reward responsiveness variables by sex summarized by the number of participants with at least one measure available at each visit number (top), the number of participants with all measures available at each visit number (middle),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

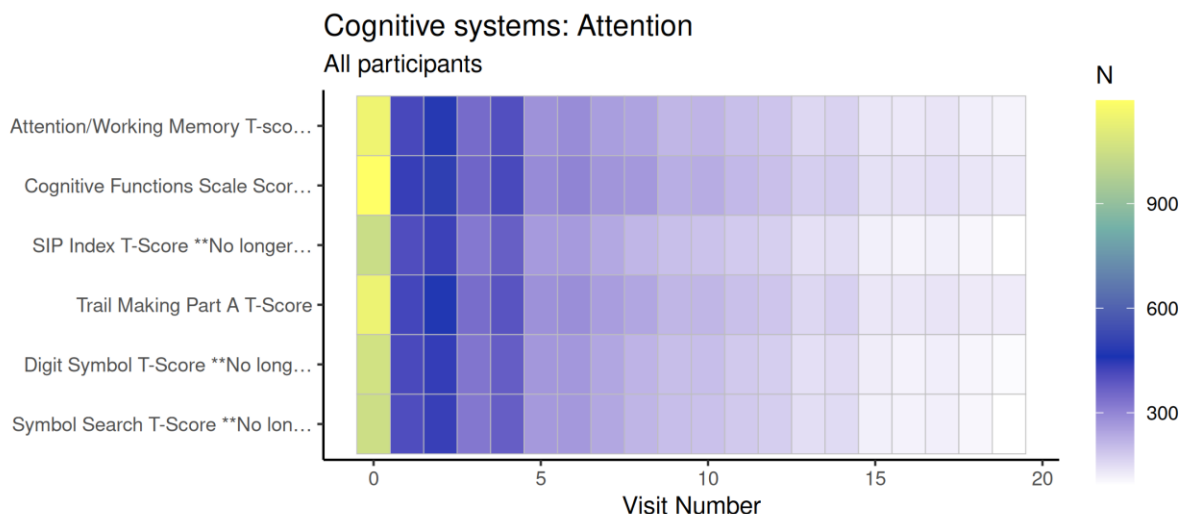


Figure 12: Heatmap showing the number of participants with each Cognitive systems: Attention variable measured by visit number for the first 10 years after enrollment in NNTC.

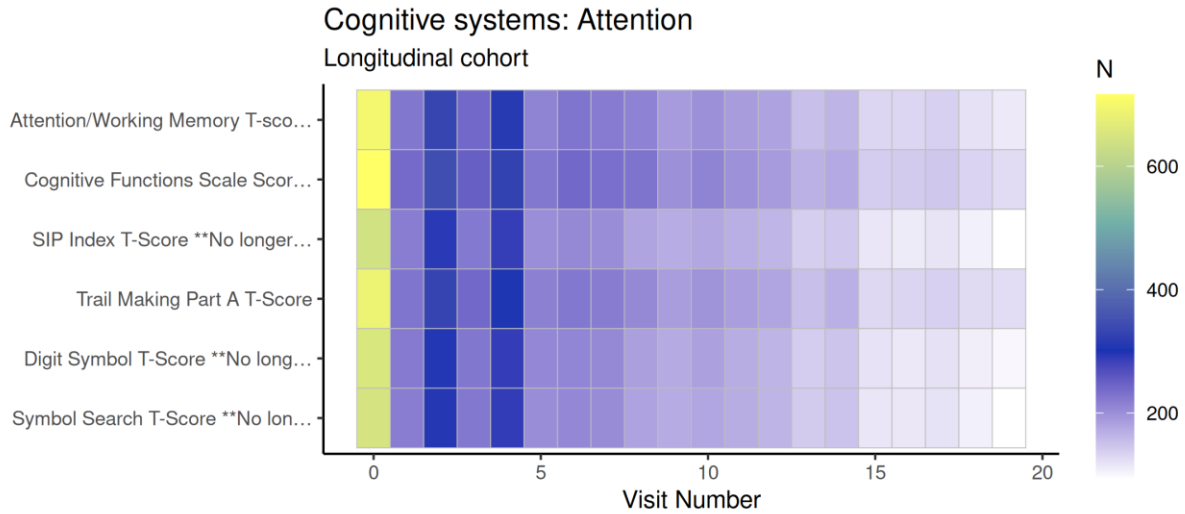


Figure 13: Heatmap showing the number of participants in the longitudinal cohort with each Cognitive systems: Attention variable measured, by visit number, for the first 10 years.

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.

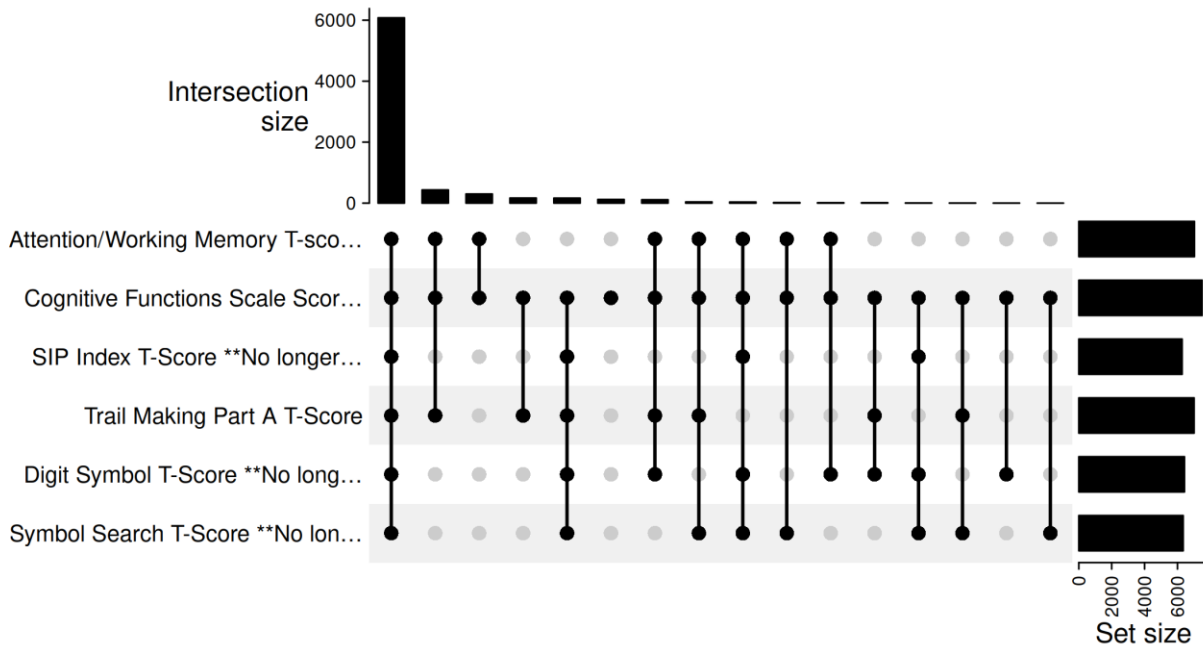


Figure 14: UpSet plot summarizing the joint availability of measures among individuals with one or more visits for the Cognitive systems: Attention variables across the first 20 visits. The bottom right horizontal barplot shows the number observations for each variable. The filled circles in the matrix 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.

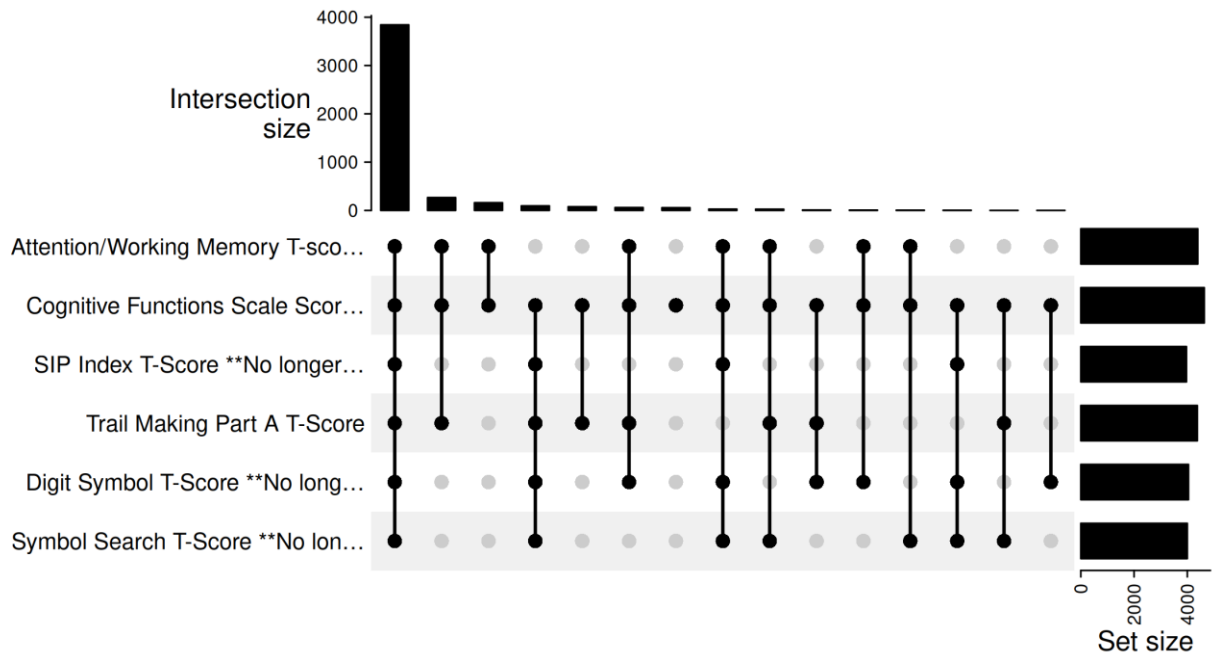


Figure 15: UpSet plot summarizing the joint availability of measures among individuals in the longitudinal cohort for the Cognitive systems: Attention variables across the first 20 visits. The bottom right horizontal barplot shows the number observations for each variable. The filled circles in the matrix 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.

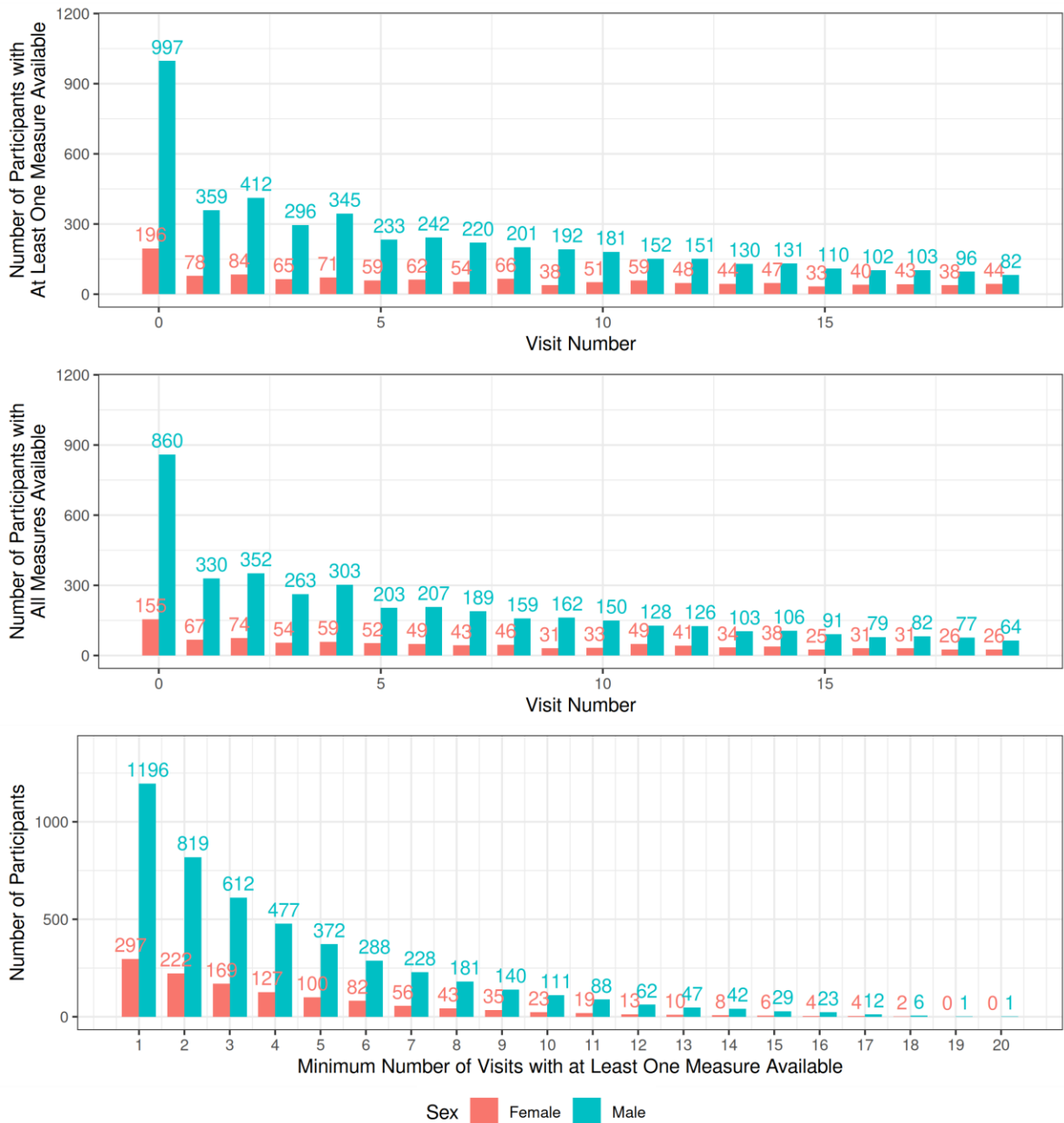


Figure 16: Data availability of participants for Cognitive systems: Attention variables by sex summarized by the number of participants with at least one measure available at each visit number (top), the number of participants with all measures available at each visit number (middle), and the total number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

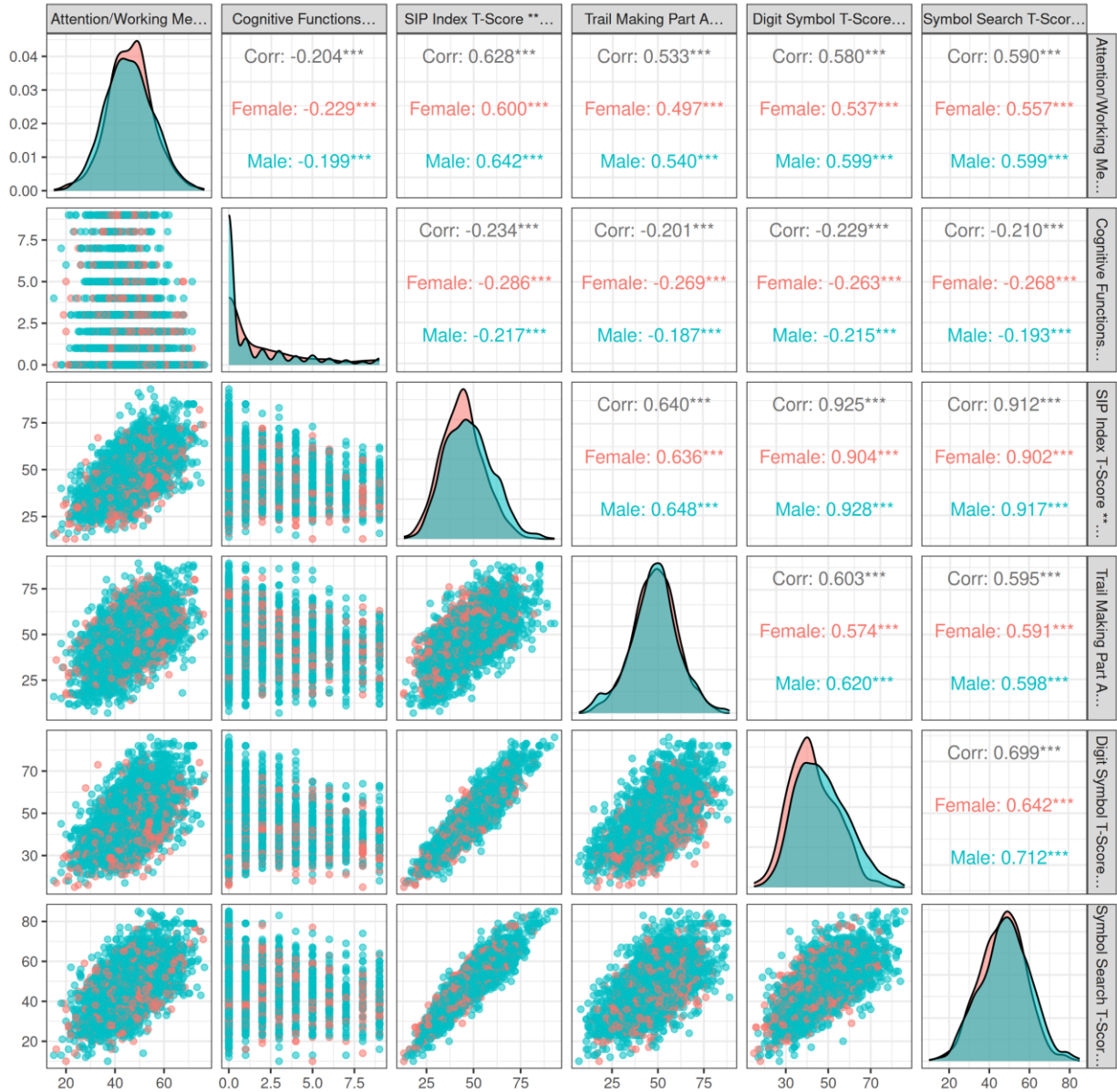


Figure 17: Scatterplot matrix of the Cognitive systems: Attention variables with points colored by sex. The diagonal shows the estimated density curve for each marginal distribution, and the top right cells show the respective estimated pairwise Pearson correlation values overall (in black) and by sex.

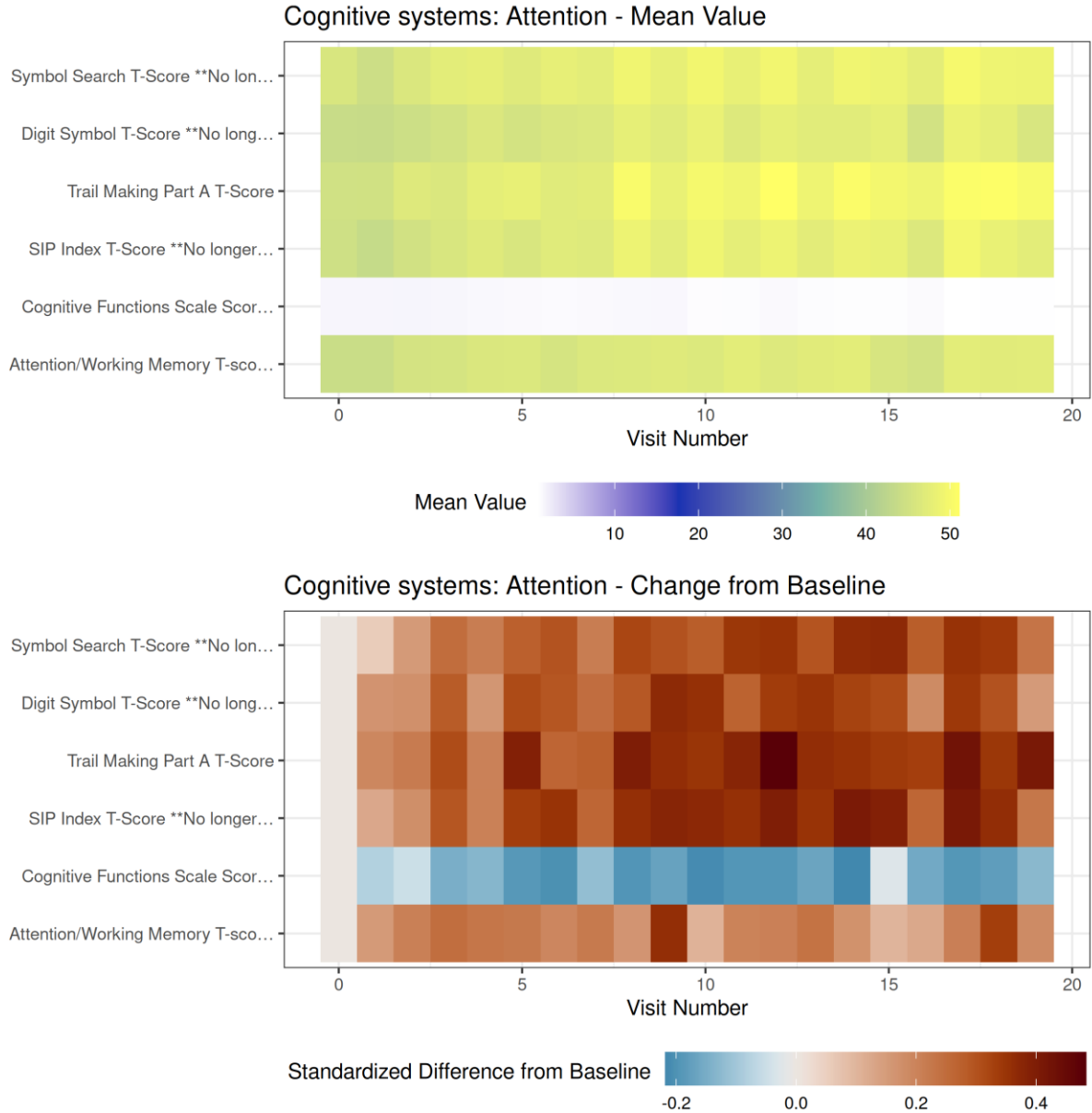


Figure 18: Heatmap of the mean value (top) and standardized mean difference in assessment measurement from baseline (bottom) by visit number for each numeric variable in the Cognitive systems: Attention construct. Standardized mean difference is the mean difference divided by the standard deviation across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

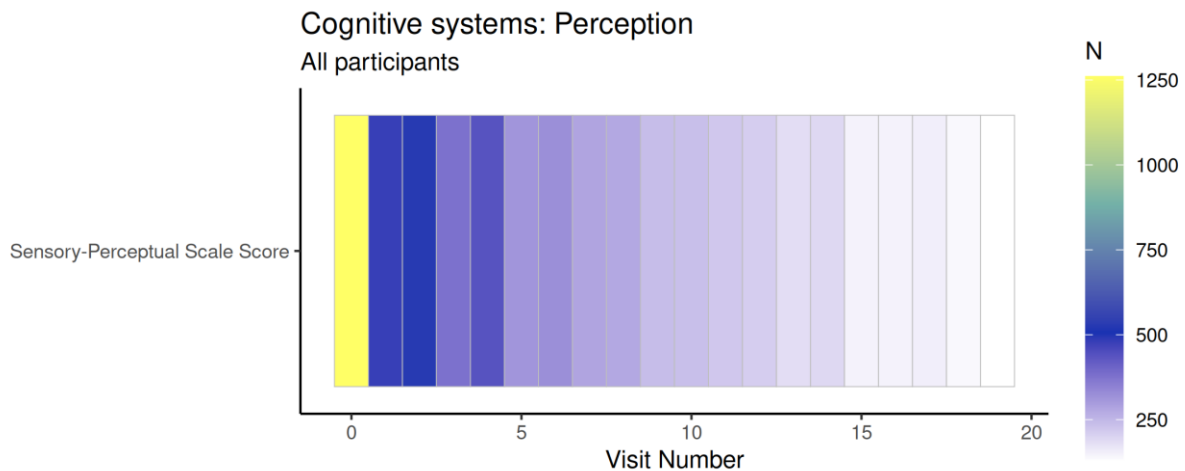


Figure 19: Heatmap showing the number of participants with each Cognitive systems: Perception variable measured by visit number for the first 10 years after enrollment in NNTC.

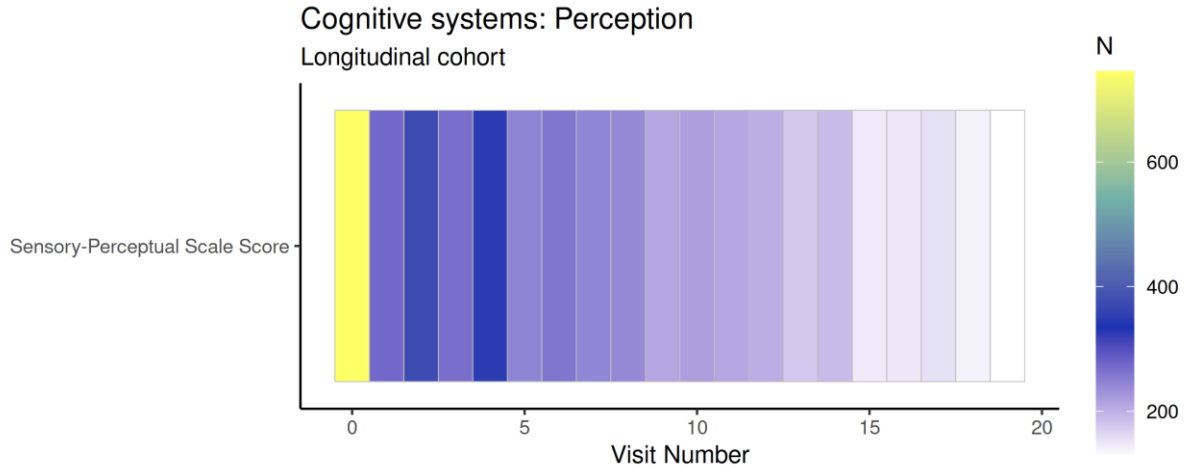


Figure 20: Heatmap showing the number of participants in the longitudinal cohort with each Cognitive systems: Perception variable measured, by visit number, for the first 10 years.

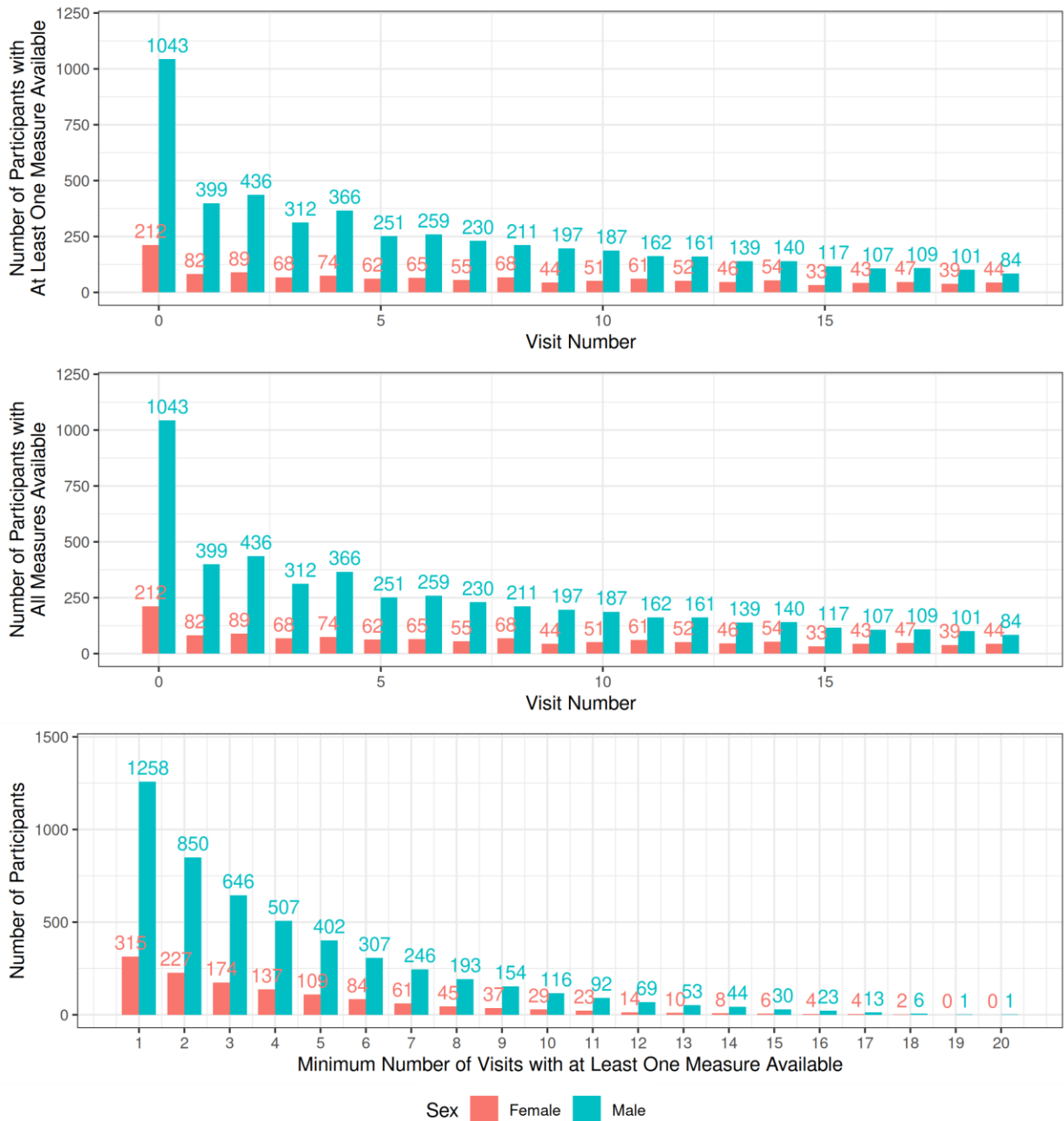


Figure 21: Data availability of participants for Cognitive systems: Perception variables by sex summarized by the number of participants with at least one measure available at each visit number (top), the number of participants with all measures available at each visit number (middle), and the total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

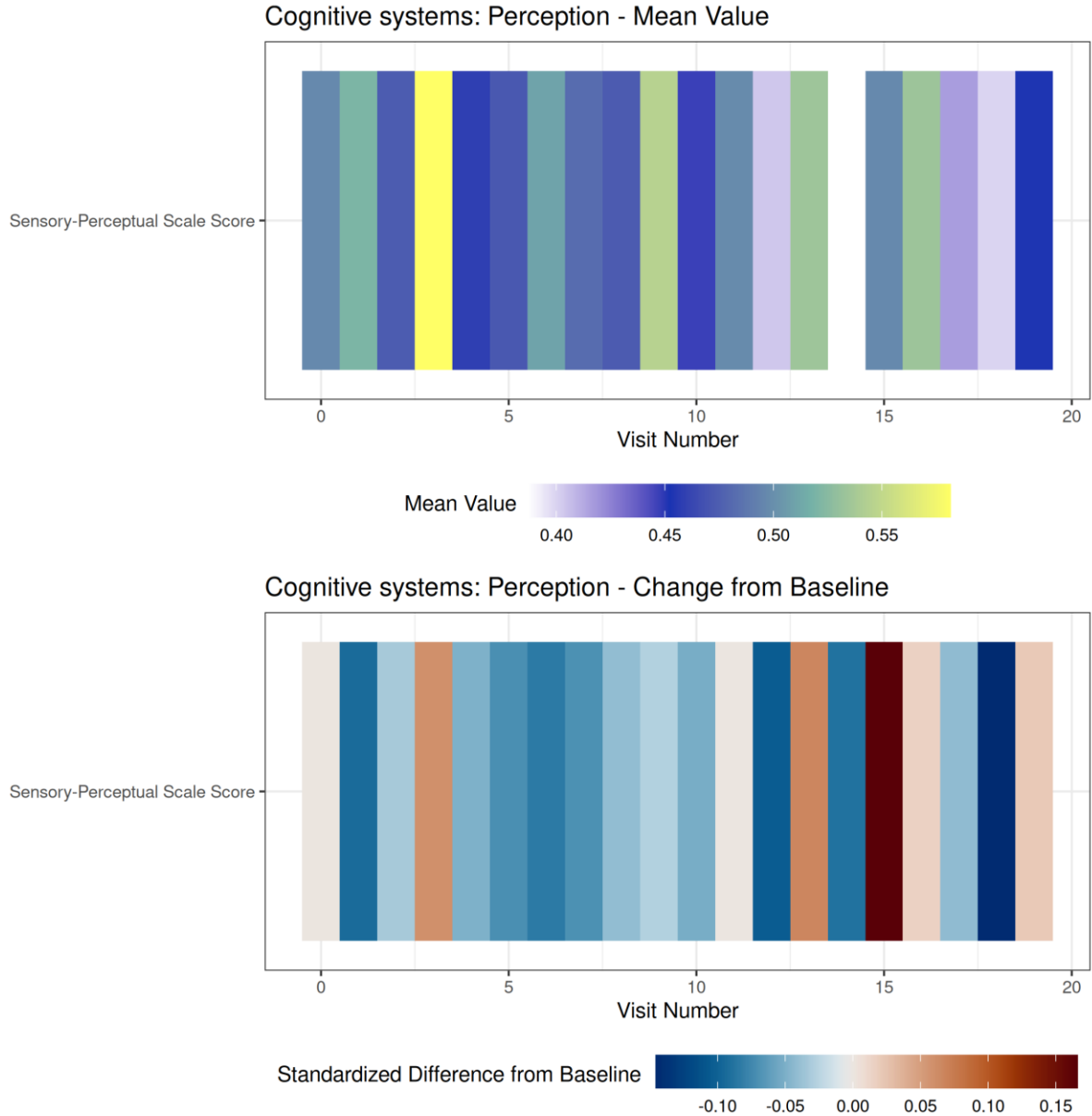


Figure 22: Heatmap of the mean value (top) and standardized mean difference in assessment measurement from baseline (bottom) by visit number for each numeric variable in the Cognitive systems: Perception construct. Standardized mean difference is the mean difference divided by the standard deviation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

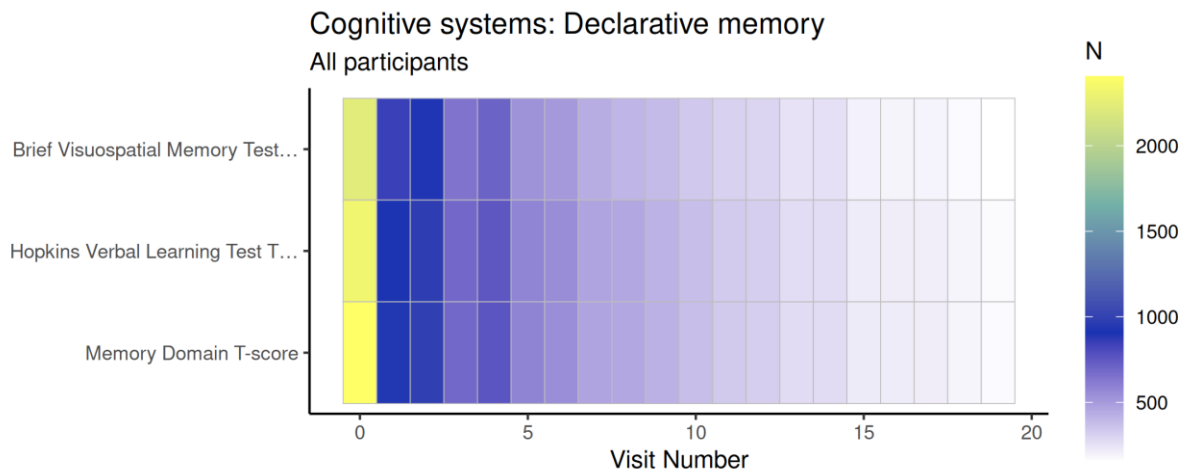


Figure 23: Heatmap showing the number of participants with each Cognitive systems: Declarative memory variable measured by visit number for the first 10 years after enrollment in NNTC.

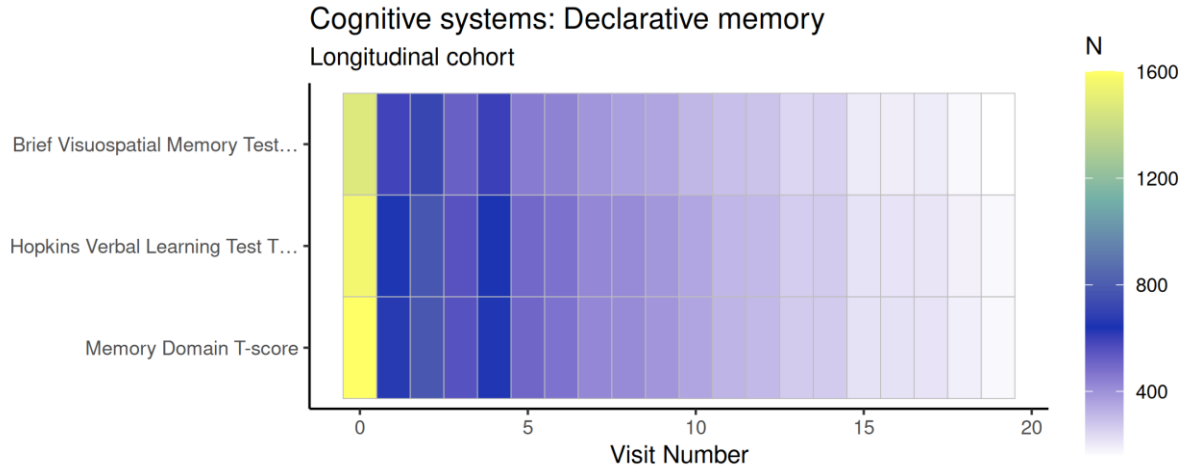


Figure 24: Heatmap showing the number of participants in the longitudinal cohort with each Cognitive systems: Declarative memory variable measured, by visit number, for the first 10 years.

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.

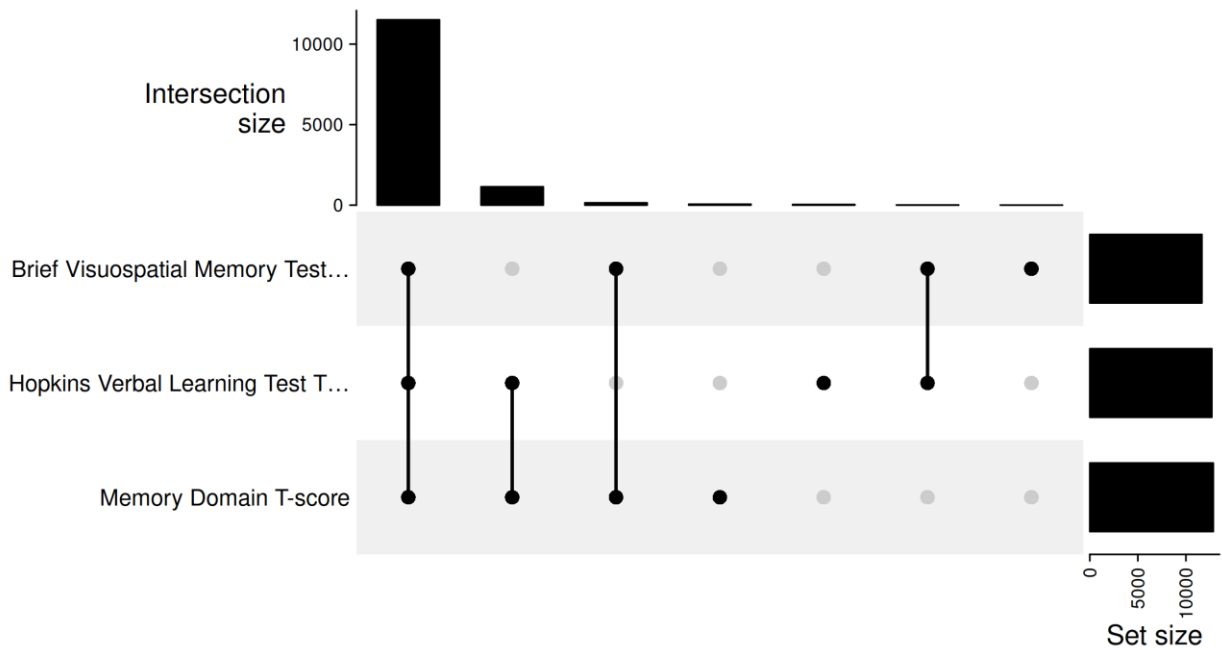


Figure 25: UpSet plot summarizing the joint availability of measures among individuals with one or more visits for the Cognitive systems: Declarative memory variables across the first 20 visits. The bottom right horizontal barplot shows the number observations for each variable. The filled circles in 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.

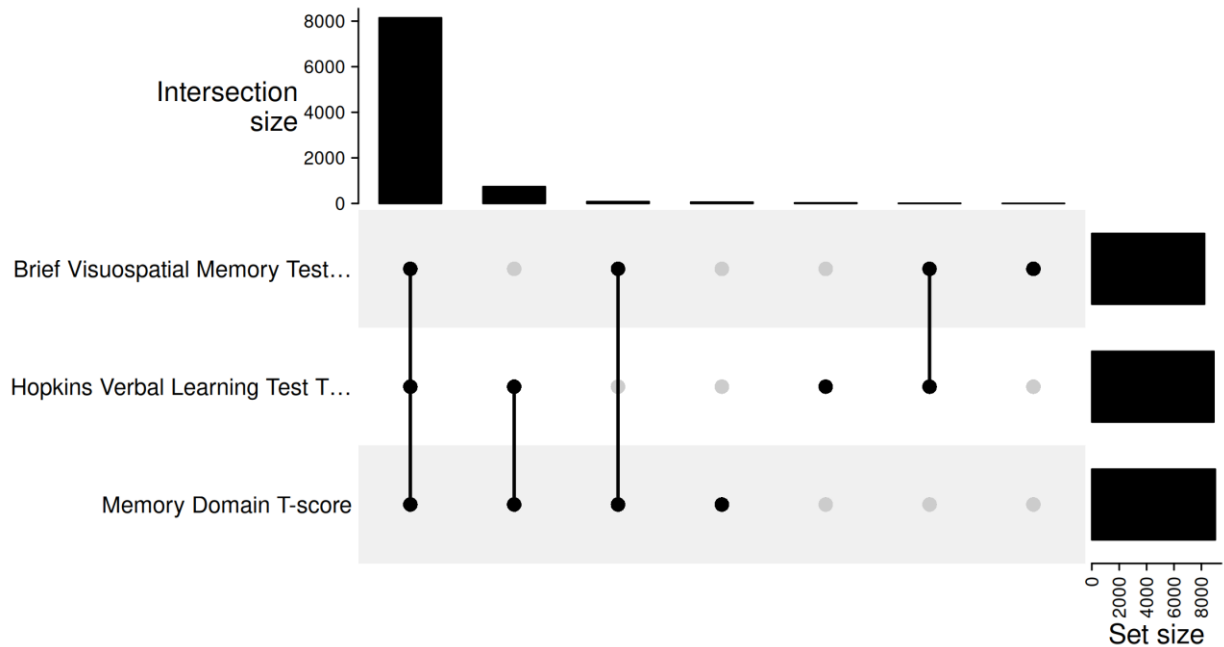


Figure 26: UpSet plot summarizing the joint availability of measures among individuals in the longitudinal cohort for the Cognitive systems: Declarative memory variables across the first 20 visits. The bottom right horizontal barplot shows the number observations for each variable. The filled circles 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.

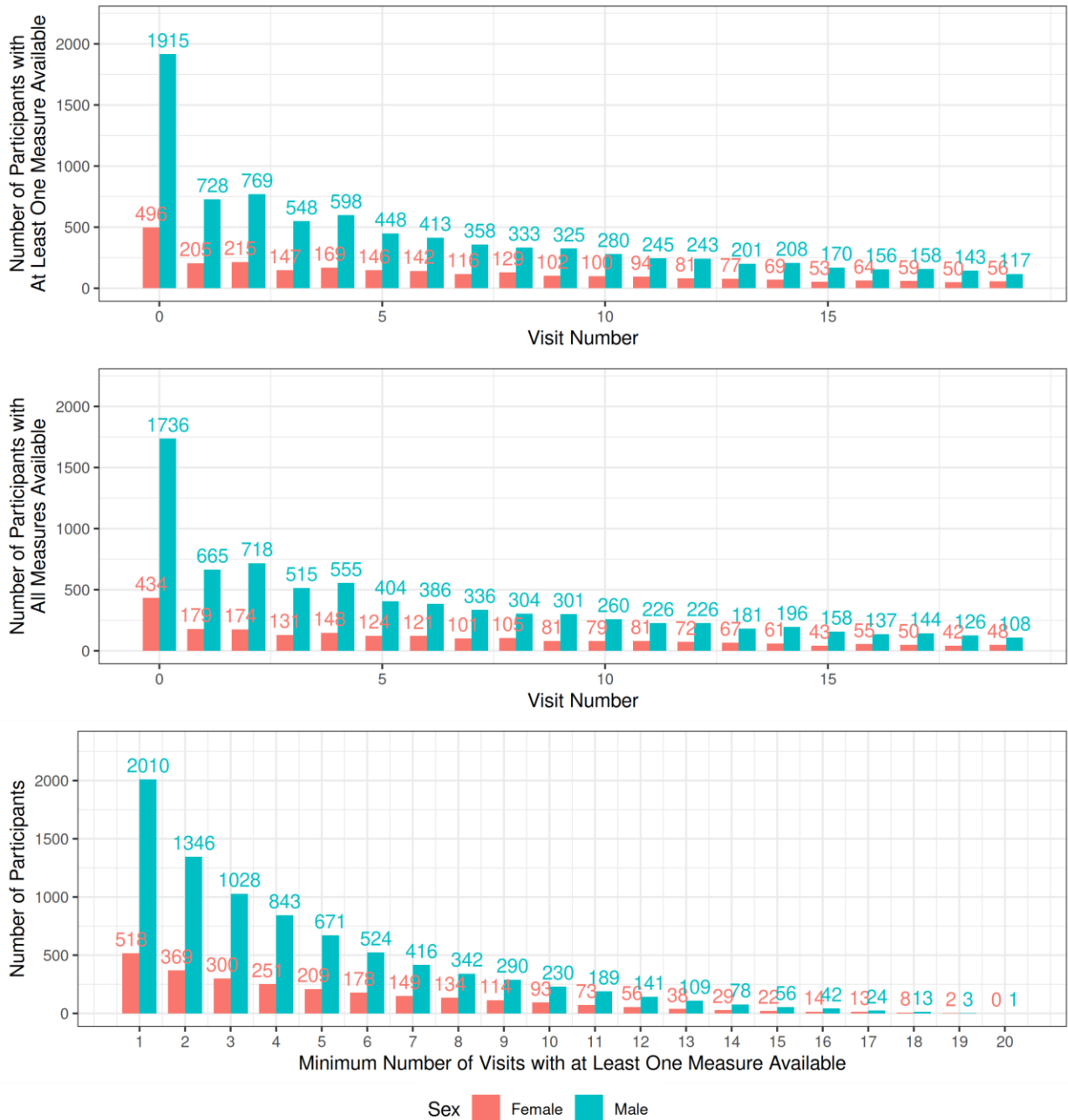


Figure 27: Data availability of participants for Cognitive systems: Declarative memory variables by sex summarized by the number of participants with at least one measure available at each visit number (top), the number of participants with all measures available at each visit number (middle), and the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

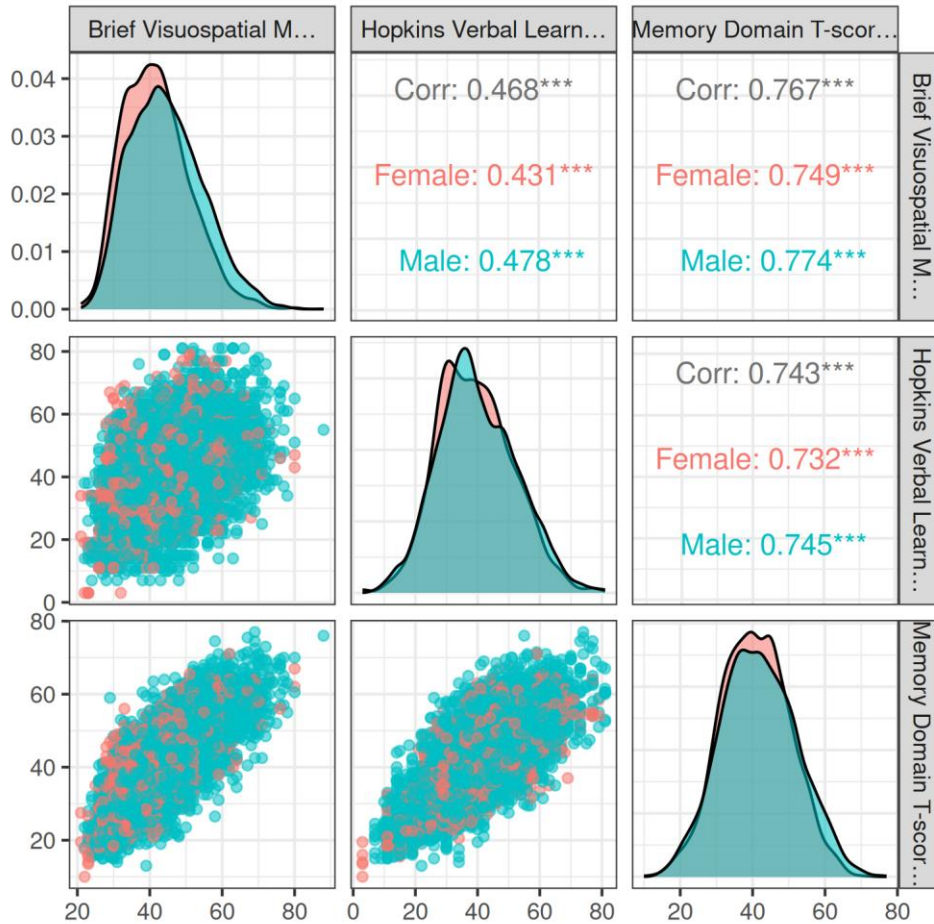


Figure 28: Scatterplot matrix of the Cognitive systems: Declarative memory variables with points colored by sex. The diagonal shows the estimated density curve for each marginal distribution, and the top right cells show the respective estimated pairwise Pearson correlation values overall (in black)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

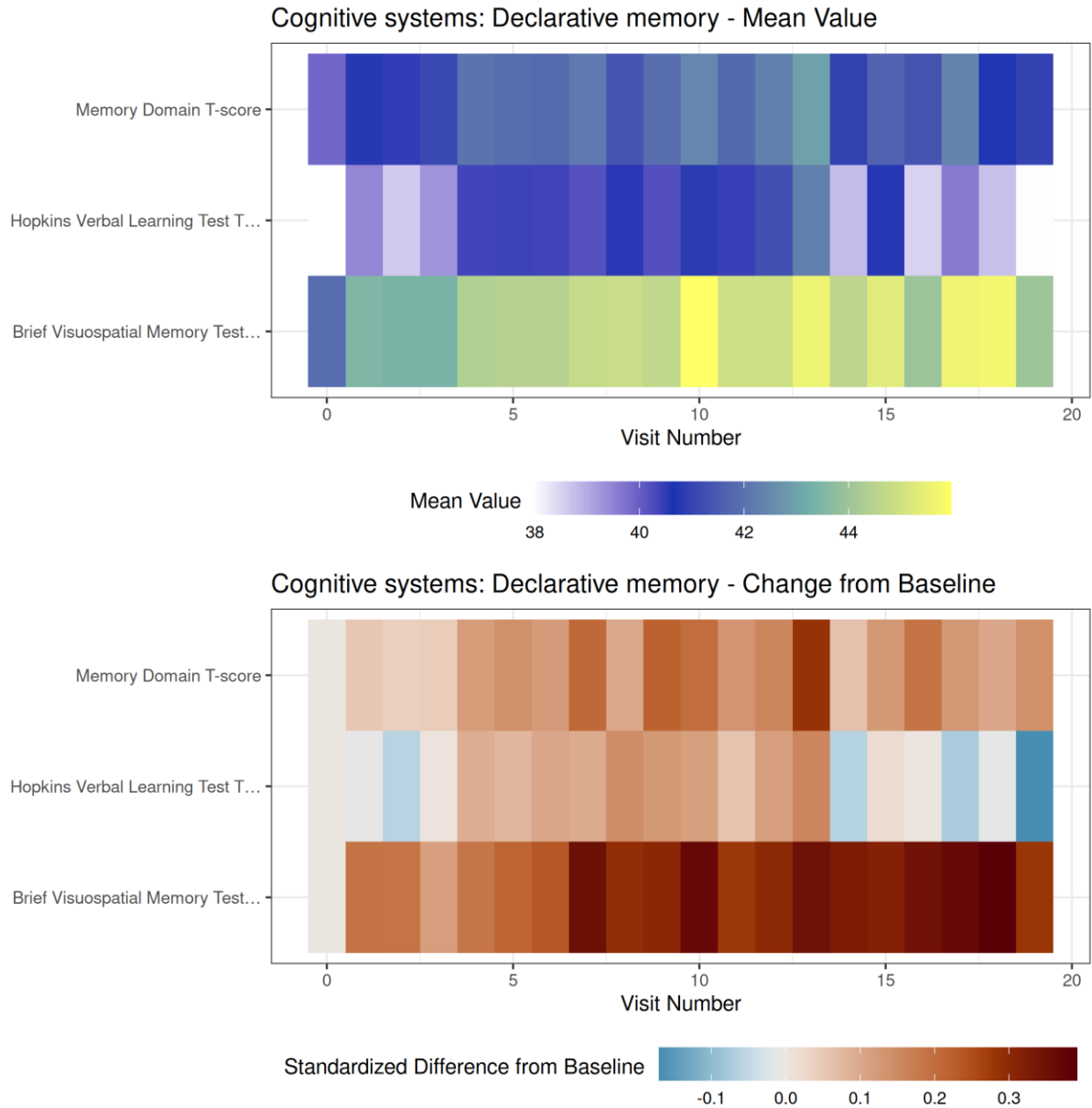


Figure 29: Heatmap of the mean value (top) and standardized mean difference in assessment measurement from baseline (bottom) by visit number for each numeric variable in the Cognitive systems: Declarative memory construct. Standardized mean difference is the mean difference divided by the standard deviation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

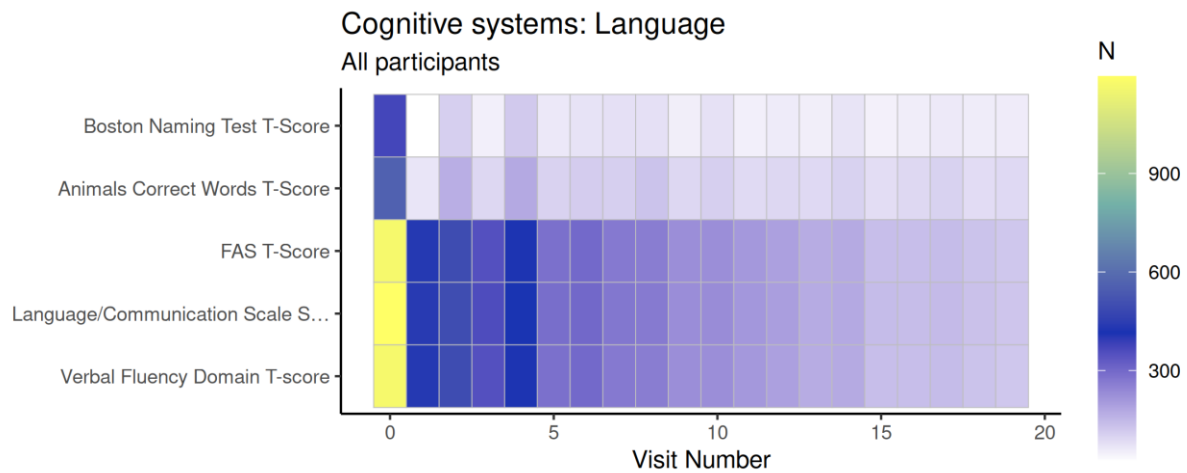


Figure 30: Heatmap showing the number of participants with each Cognitive systems: Language variable measured by visit number for the first 10 years after enrollment in NNTC.

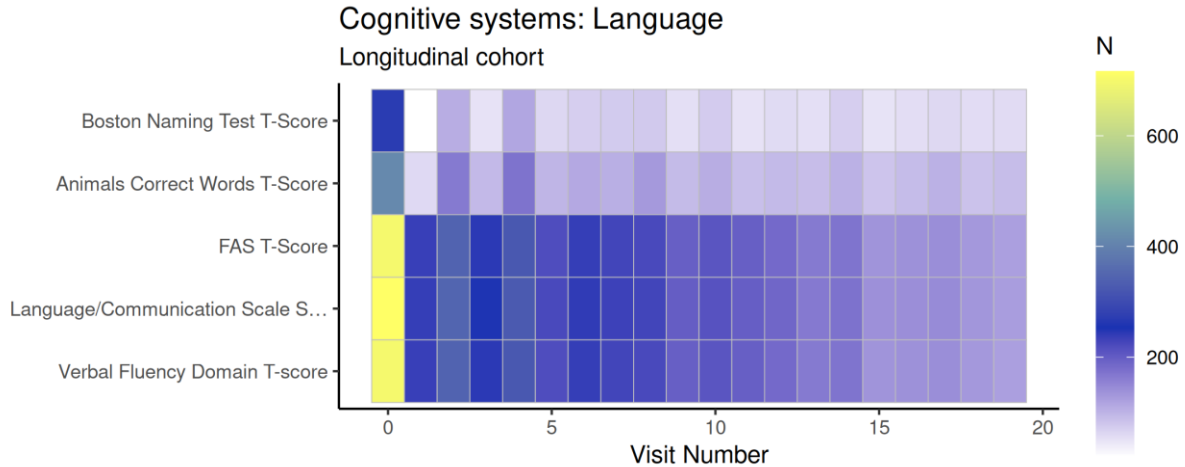


Figure 31: Heatmap showing the number of participants in the longitudinal cohort with each Cognitive systems: Language variable measured, by visit number, for the first 10 years.

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.

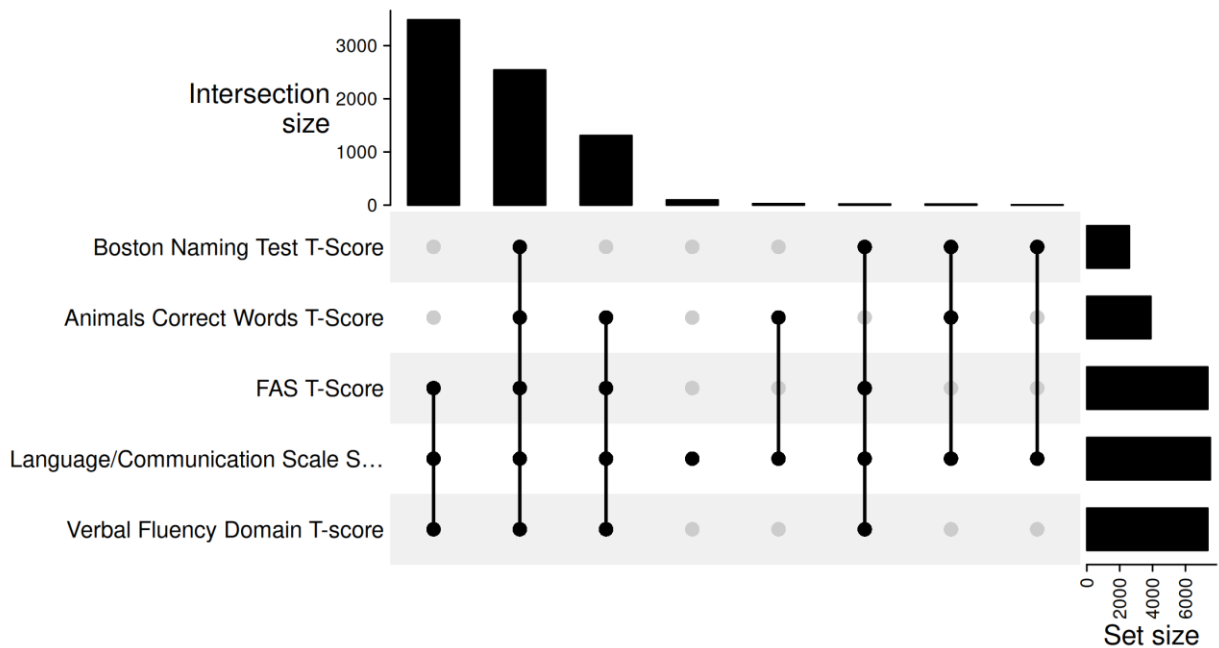


Figure 32: UpSet plot summarizing the joint availability of measures among individuals with one or more visits for the Cognitive systems: Language variables across the first 20 visits. The bottom right horizontal barplot shows the number observations for each variable. The filled circles in the matrix 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.

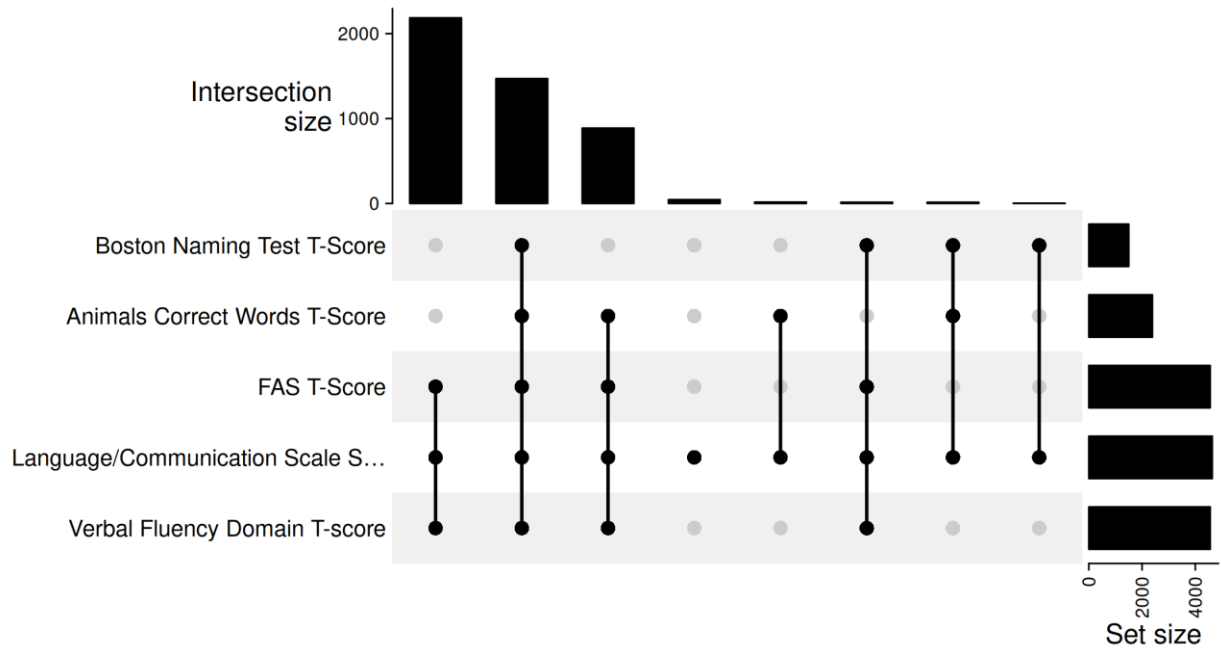


Figure 33: UpSet plot summarizing the joint availability of measures among individuals in the longitudinal cohort for the Cognitive systems: Language variables across the first 20 visits. The bottom right horizontal barplot shows the number observations for each variable. The filled circles in the matrix 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.

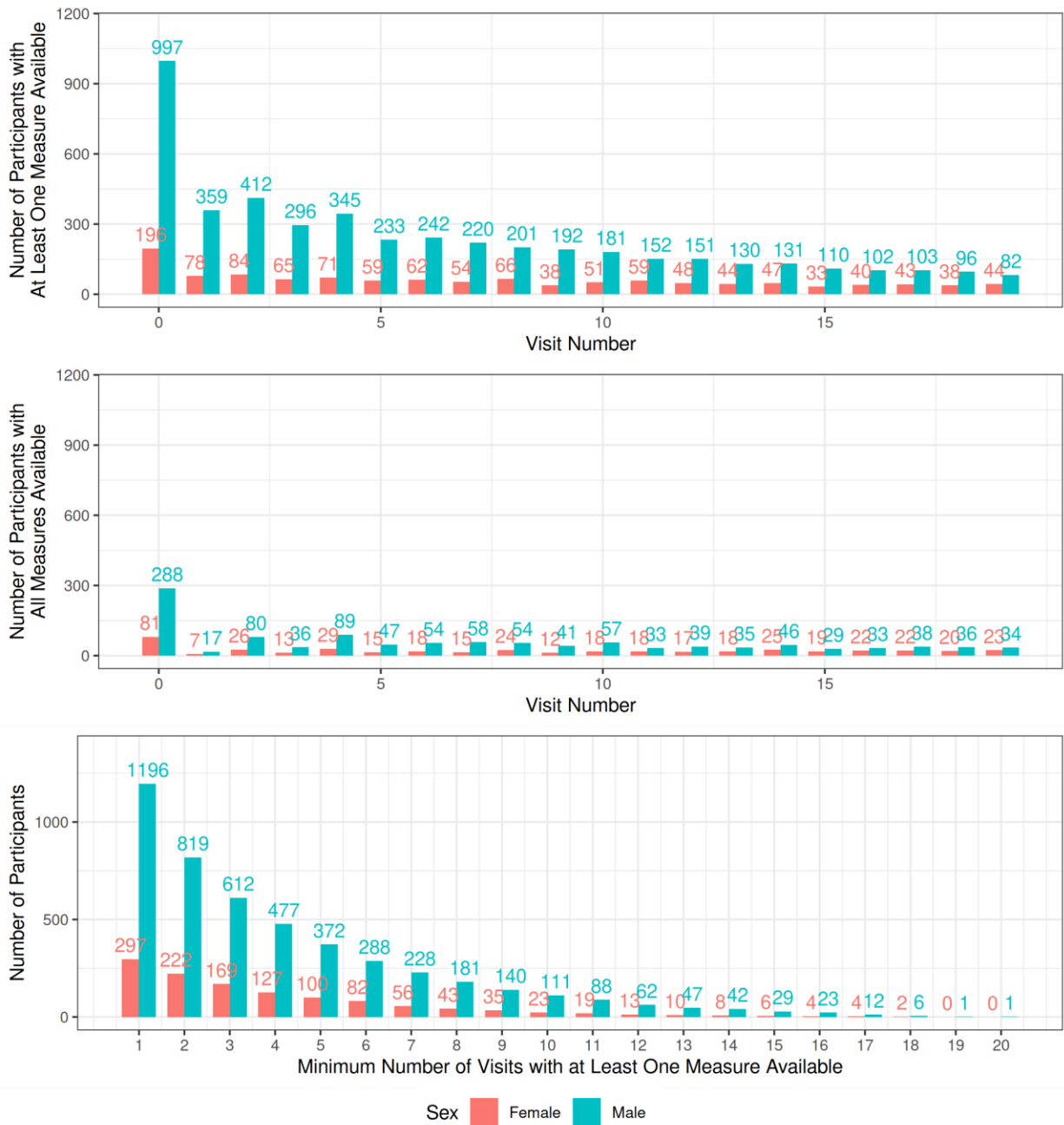


Figure 34: Data availability of participants for Cognitive systems: Language variables by sex summarized by the number of participants with at least one measure available at each visit number (top), the number of participants with all measures available at each visit number (middle), and the total number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

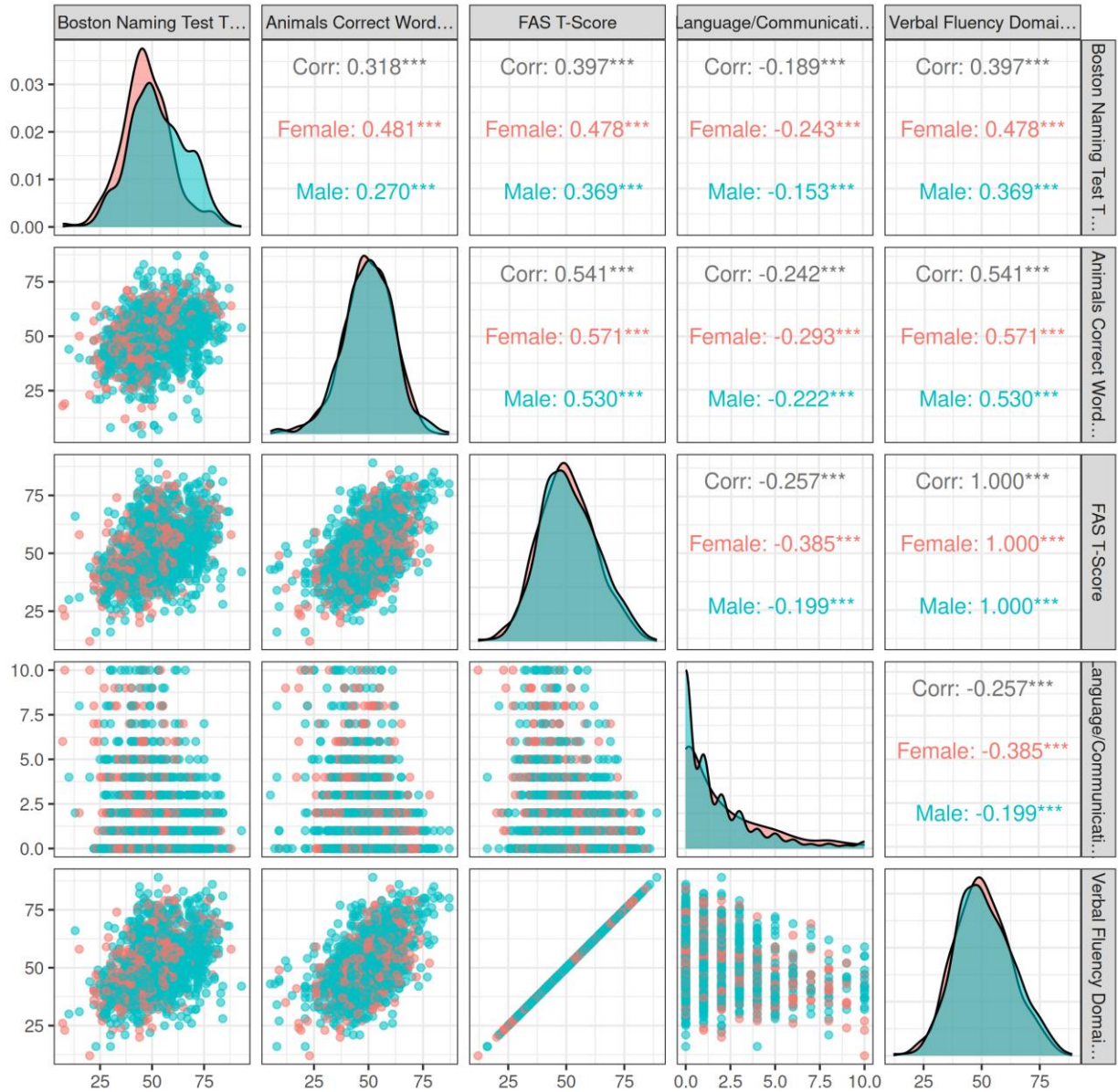


Figure 35: Scatterplot matrix of the Cognitive systems: Language variables with points colored by sex. The diagonal shows the estimated density curve for each marginal distribution, and the top right cells show the respective estimated pairwise Pearson correlation values overall (in black) and by sex.

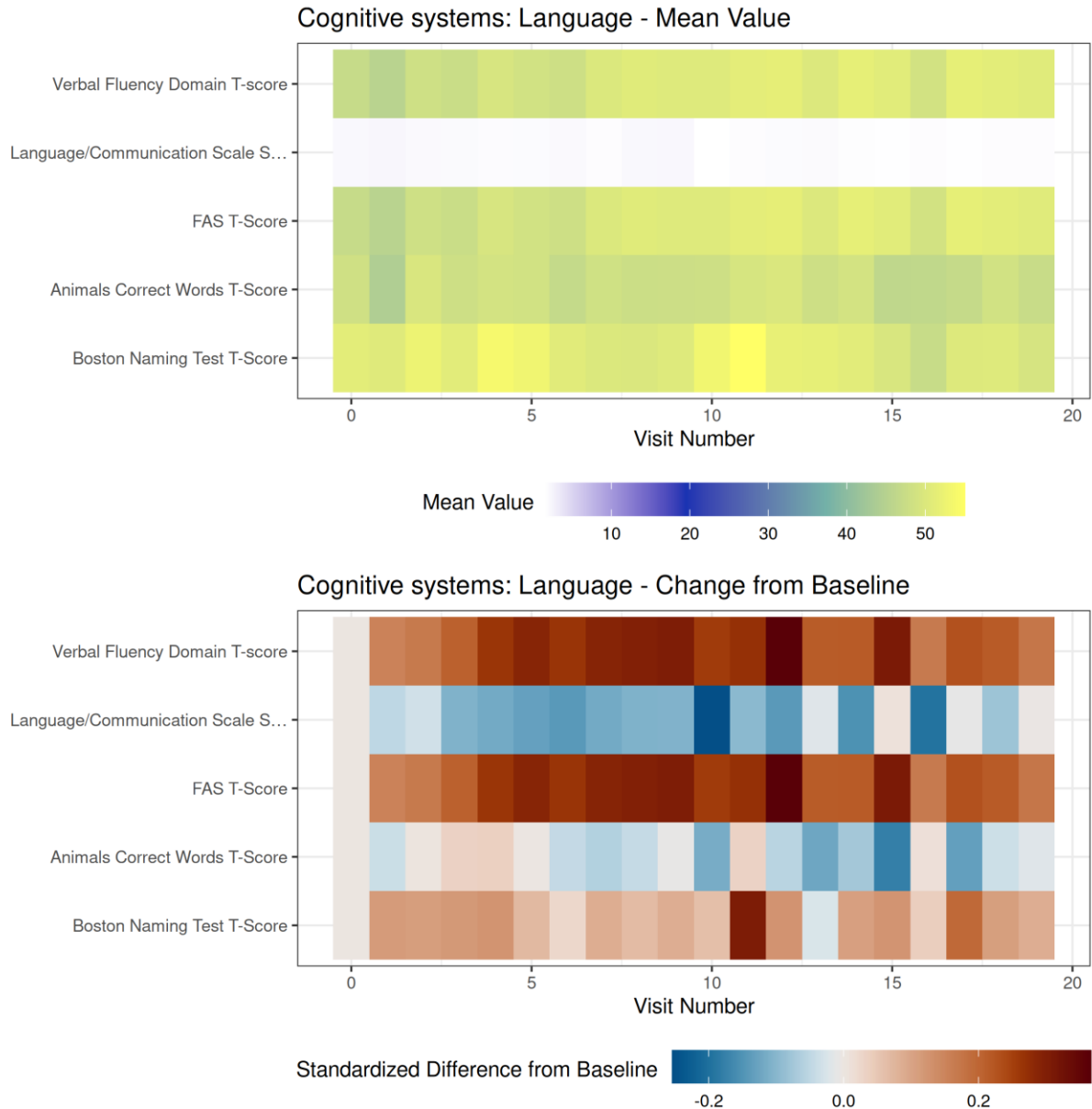


Figure 36: Heatmap of the mean value (top) and standardized mean difference in assessment measurement from baseline (bottom) by visit number for each numeric variable in the Cognitive systems: Language construct. Standardized mean difference is the mean difference divided by the standard deviation across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

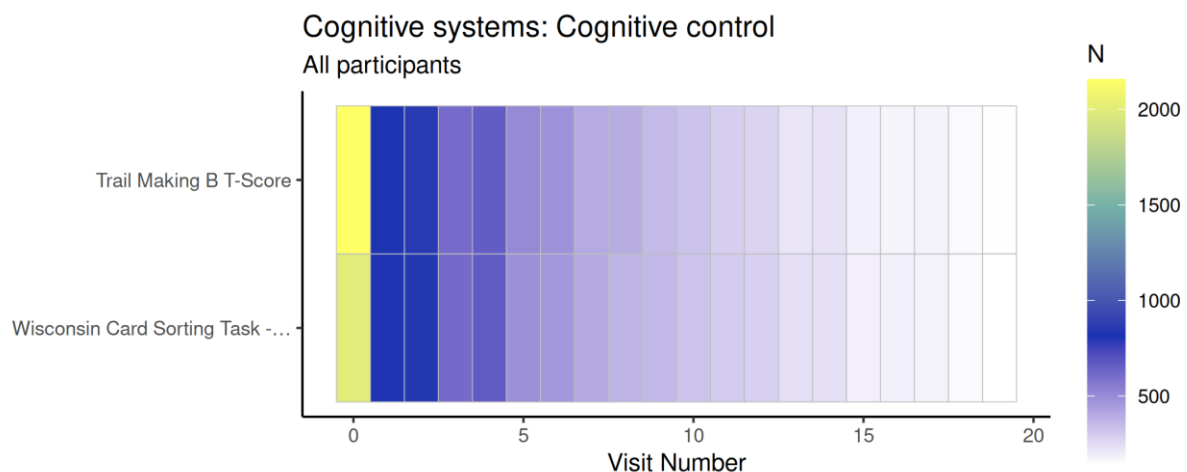


Figure 37: Heatmap showing the number of participants with each Cognitive systems: Cognitive control variable measured by visit number for the first 10 years after enrollment in NNTC.

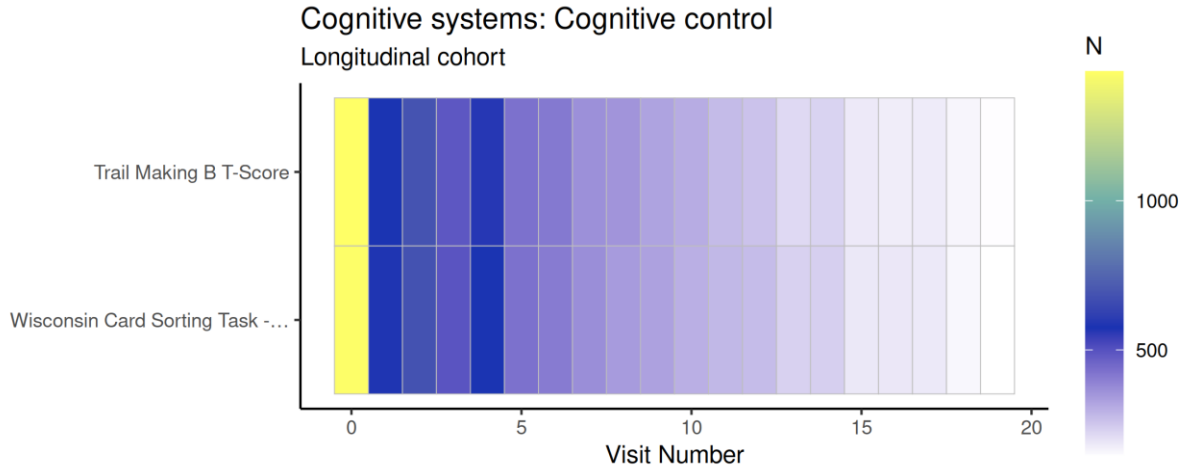


Figure 38: Heatmap showing the number of participants in the longitudinal cohort with each Cognitive systems: Cognitive control variable measured, by visit number, for the first 10 years.

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.

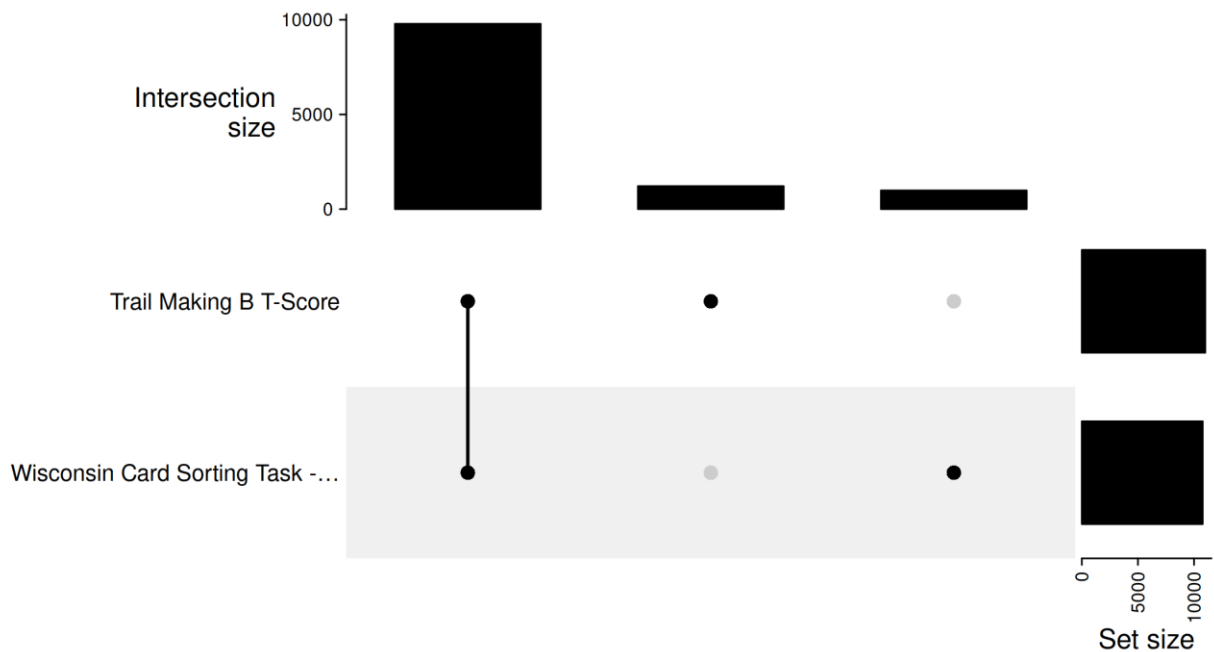


Figure 39: UpSet plot summarizing the joint availability of measures among individuals with one or more visits for the Cognitive systems: Cognitive control variables across the first 20 visits. The bottom right horizontal barplot shows the number observations for each variable. The filled circles in 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.

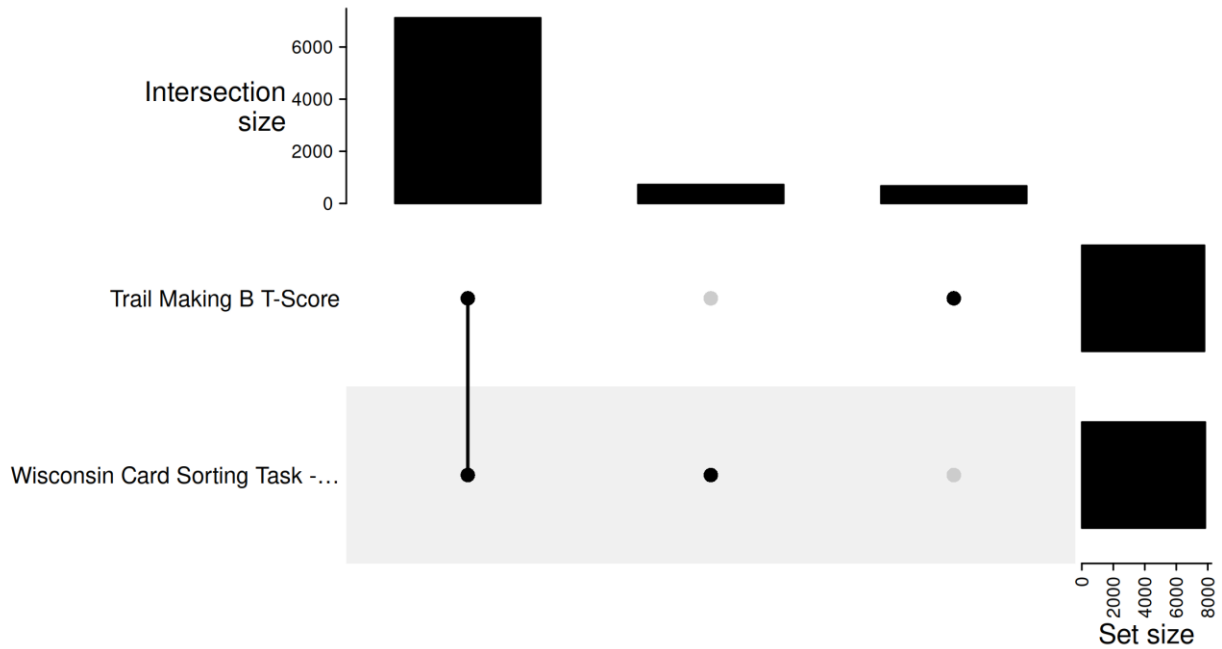


Figure 40: UpSet plot summarizing the joint availability of measures among individuals in the longitudinal cohort for the Cognitive systems: Cognitive control variables across the first 20 visits. The bottom right horizontal barplot shows the number observations for each variable. The filled circles 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.

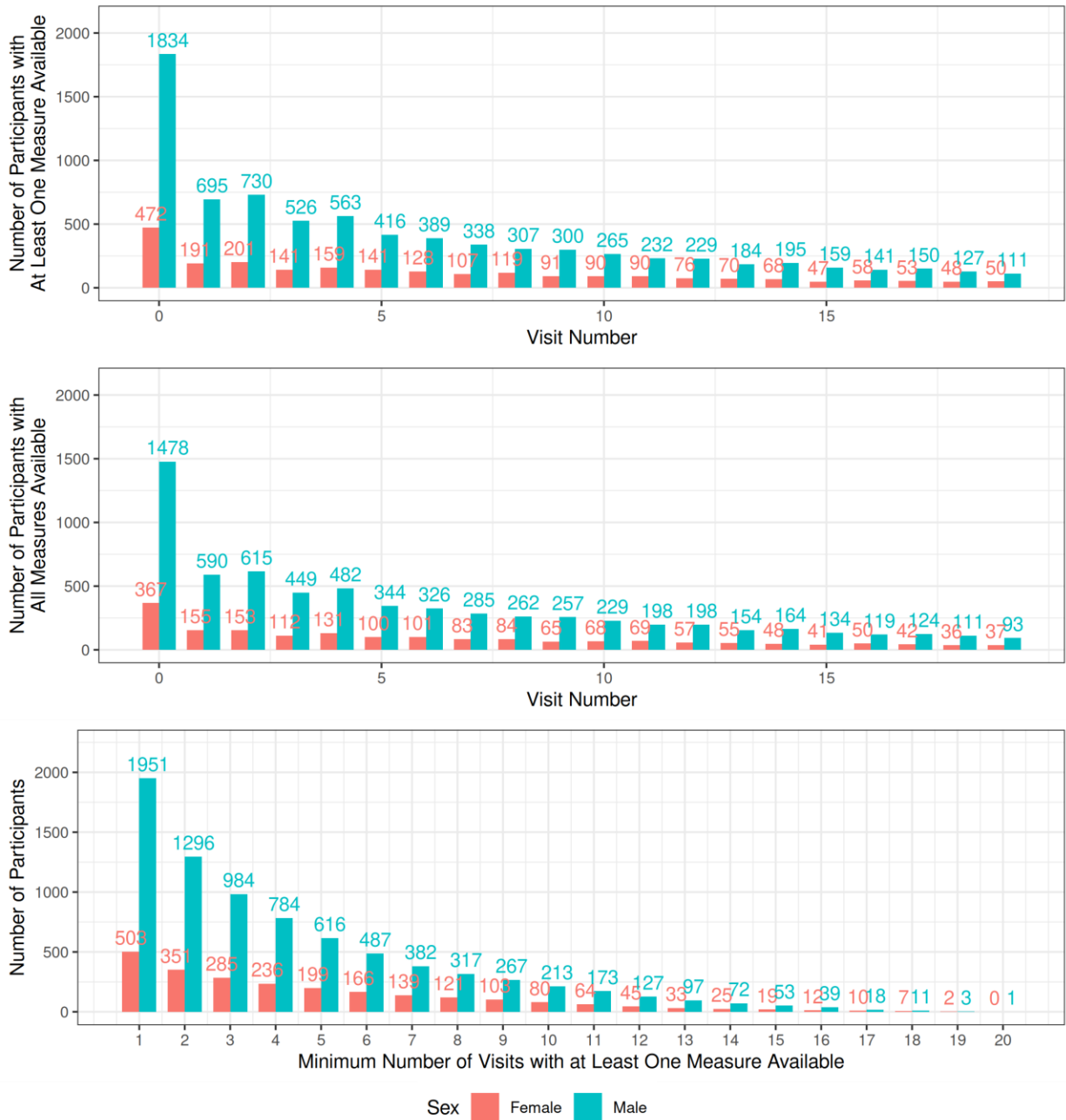


Figure 41: Data availability of participants for Cognitive systems: Cognitive control variables by sex summarized by the number of participants with at least one measure available at each visit number (top), the number of participants with all measures available at each visit number (middle), and the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

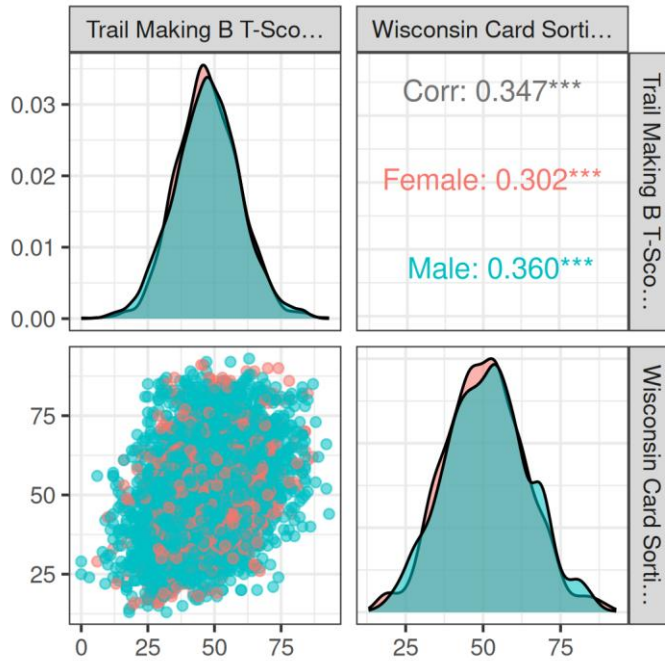


Figure 42: Scatterplot matrix of the Cognitive systems: Cognitive control variables with points colored by sex. The diagonal shows the estimated density curve for each marginal distribution, and the top right cells show the respective estimated pairwise Pearson correlation values overall (in black) and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

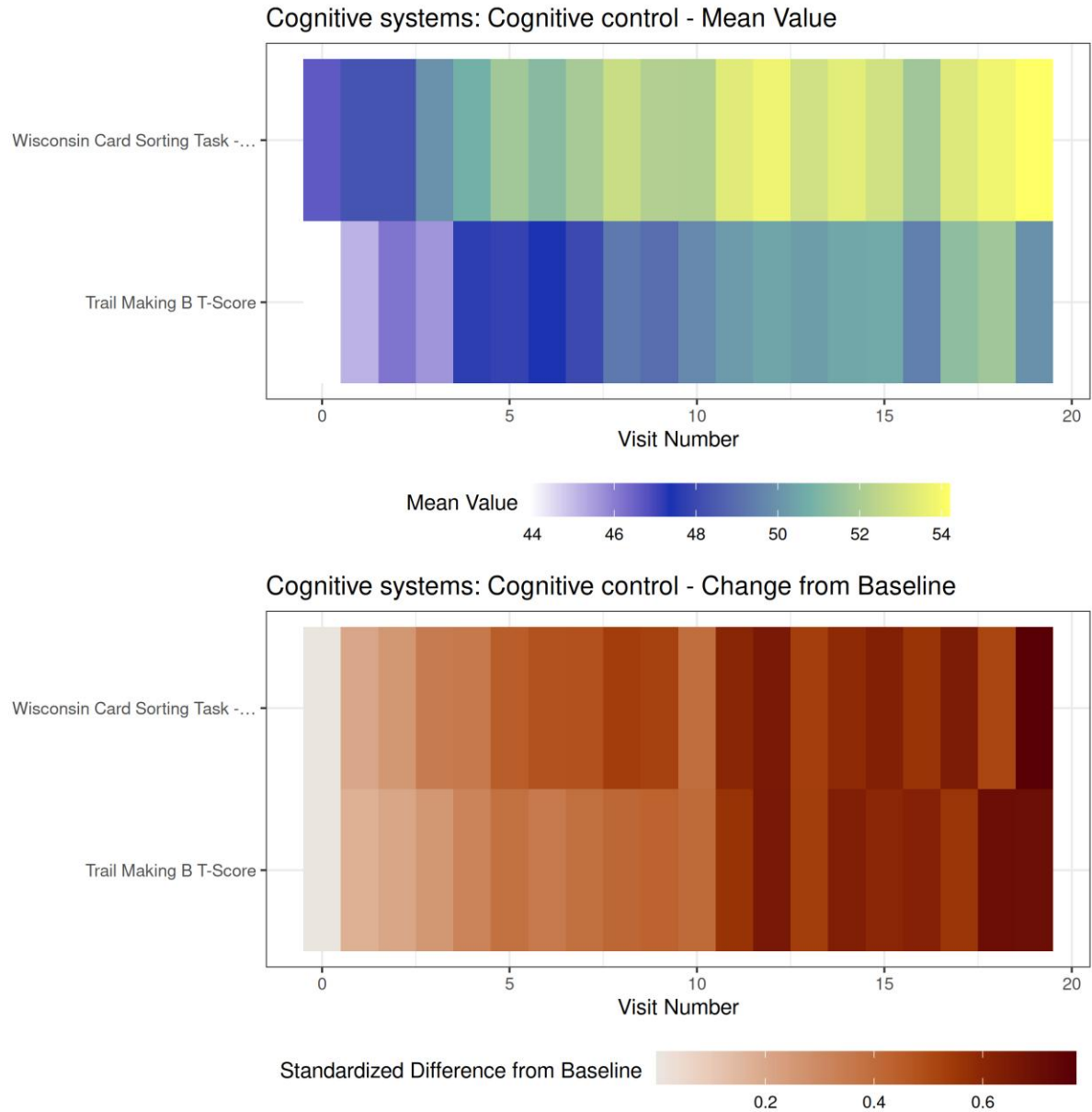


Figure 43: Heatmap of the mean value (top) and standardized mean difference in assessment measurement from baseline (bottom) by visit number for each numeric variable in the Cognitive systems: Cognitive control construct. Standardized mean difference is the mean difference divided by the standard deviation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

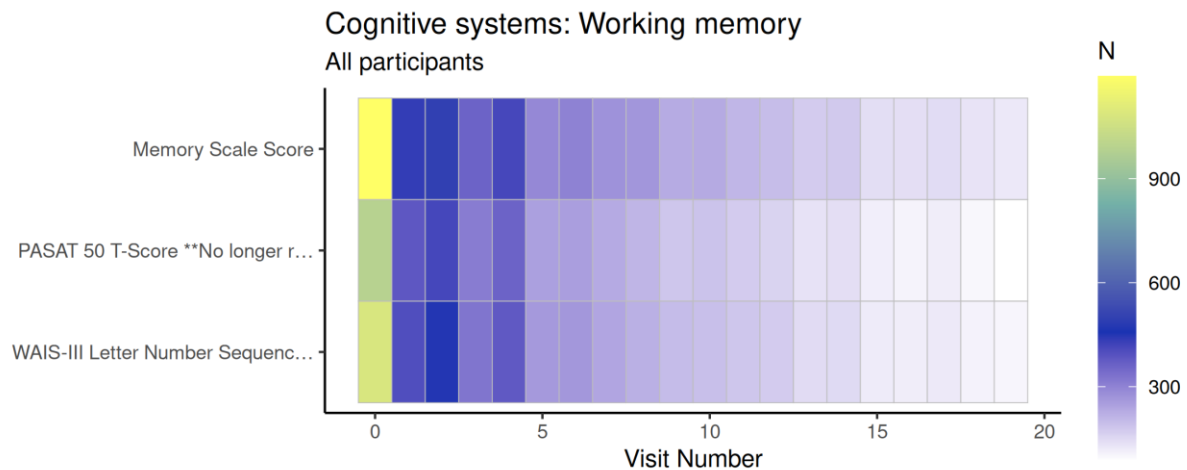


Figure 44: Heatmap showing the number of participants with each Cognitive systems: Working memory variable measured by visit number for the first 10 years after enrollment in NNTC.

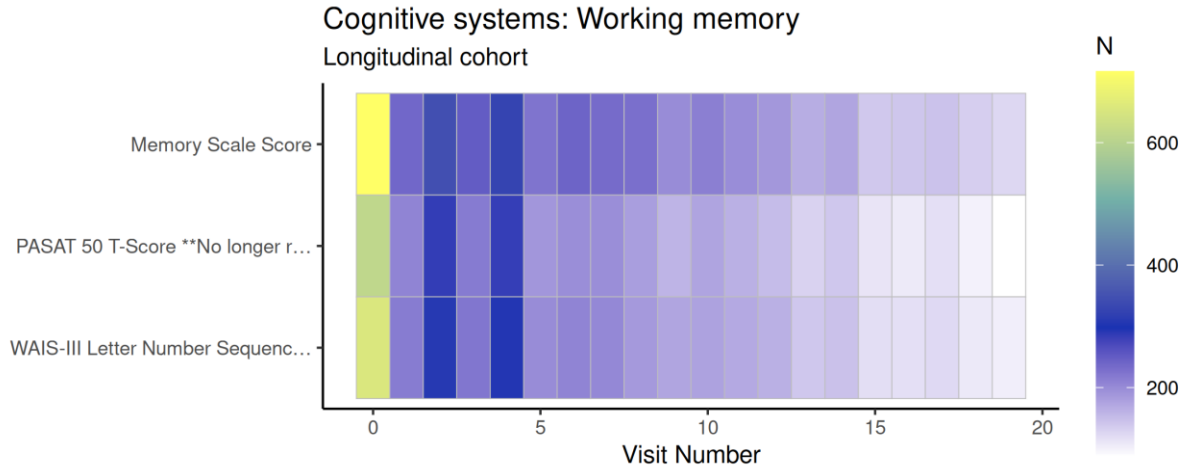


Figure 45: Heatmap showing the number of participants in the longitudinal cohort with each Cognitive systems: Working memory variable measured, by visit number, for the first 10 years.

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.

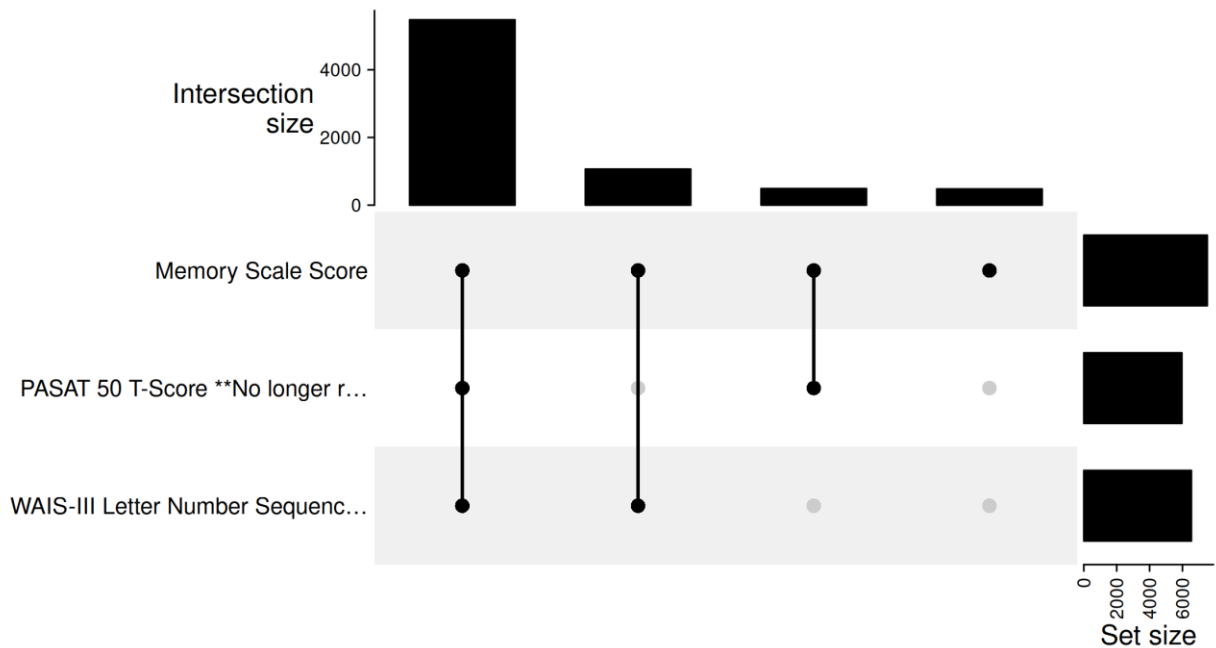


Figure 46: UpSet plot summarizing the joint availability of measures among individuals with one or more visits for the Cognitive systems: Working memory variables across the first 20 visits. The bottom right horizontal barplot shows the number observations for each variable. The filled circles in the 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.

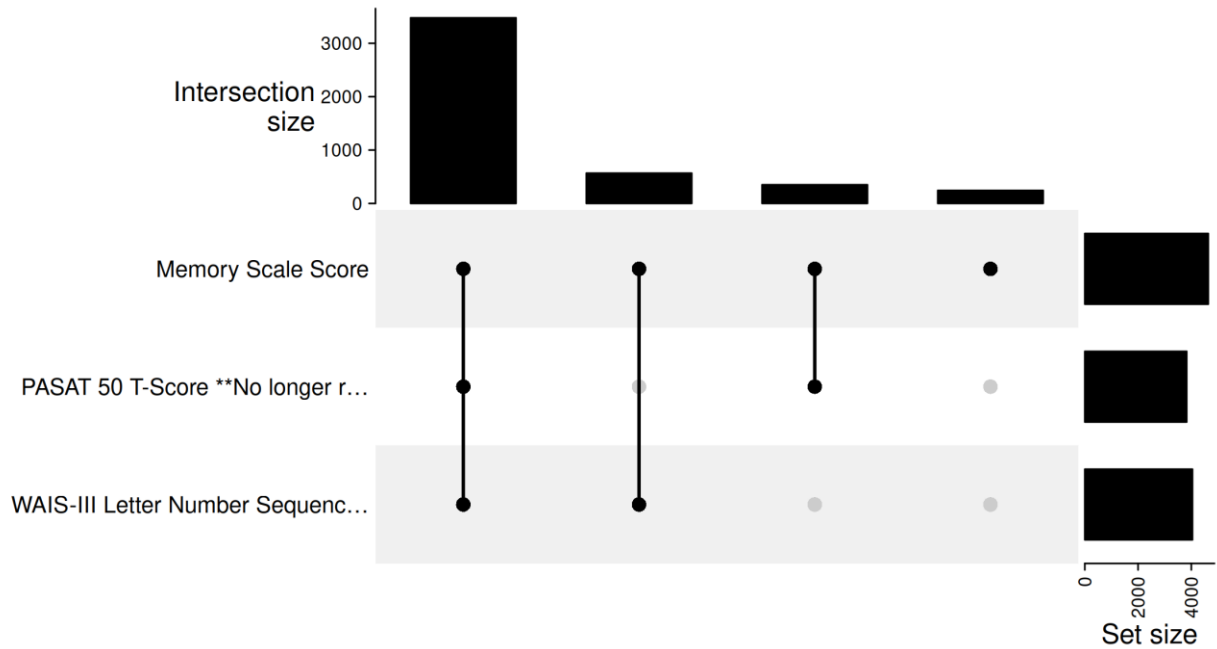


Figure 47: UpSet plot summarizing the joint availability of measures among individuals in the longitudinal cohort for the Cognitive systems: Working memory variables across the first 20 visits. The bottom right horizontal barplot shows the number observations for each variable. The filled circles in 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.

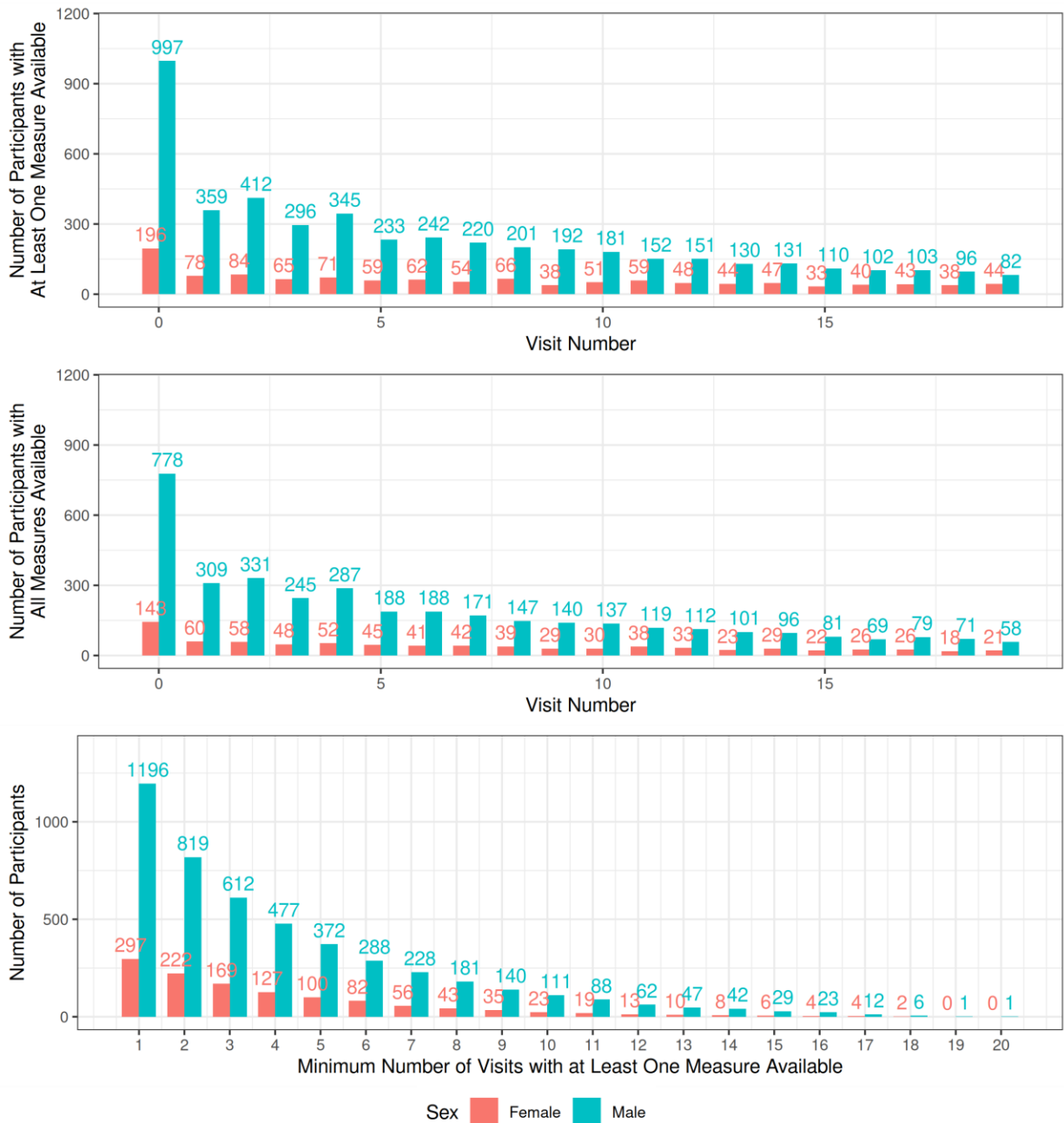


Figure 48: Data availability of participants for Cognitive systems: Working memory variables by sex summarized by the number of participants with at least one measure available at each visit number (top), the number of participants with all measures available at each visit number (middle), and the total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

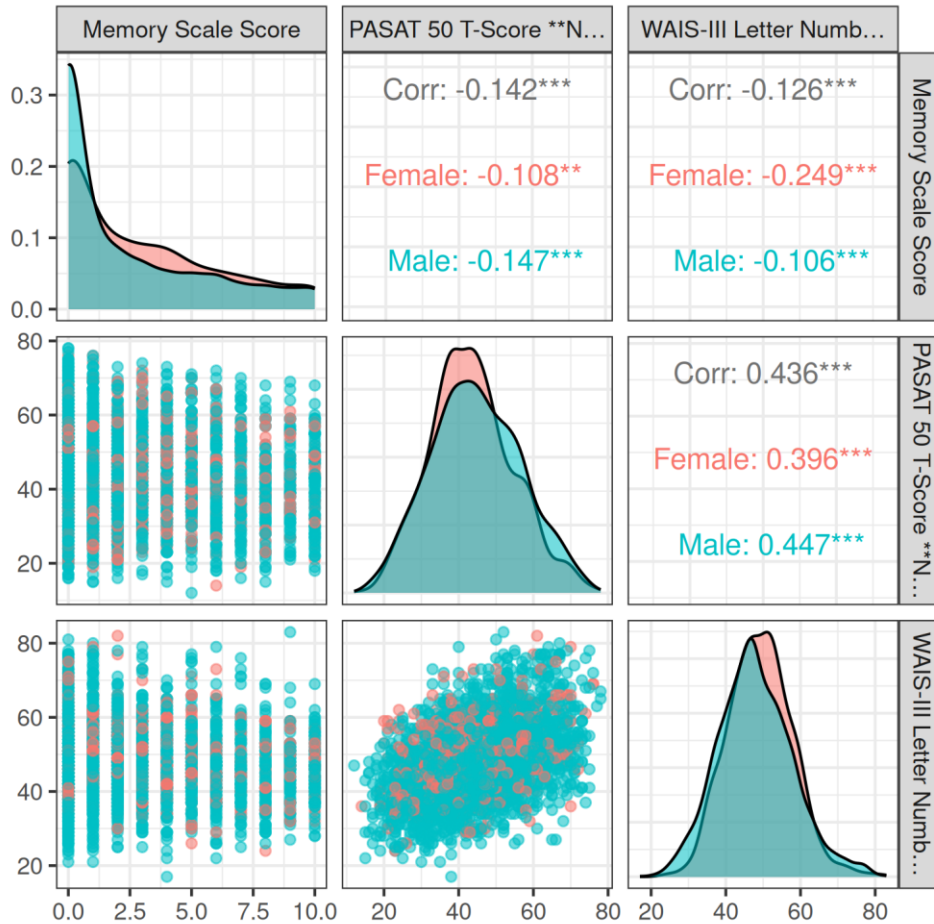
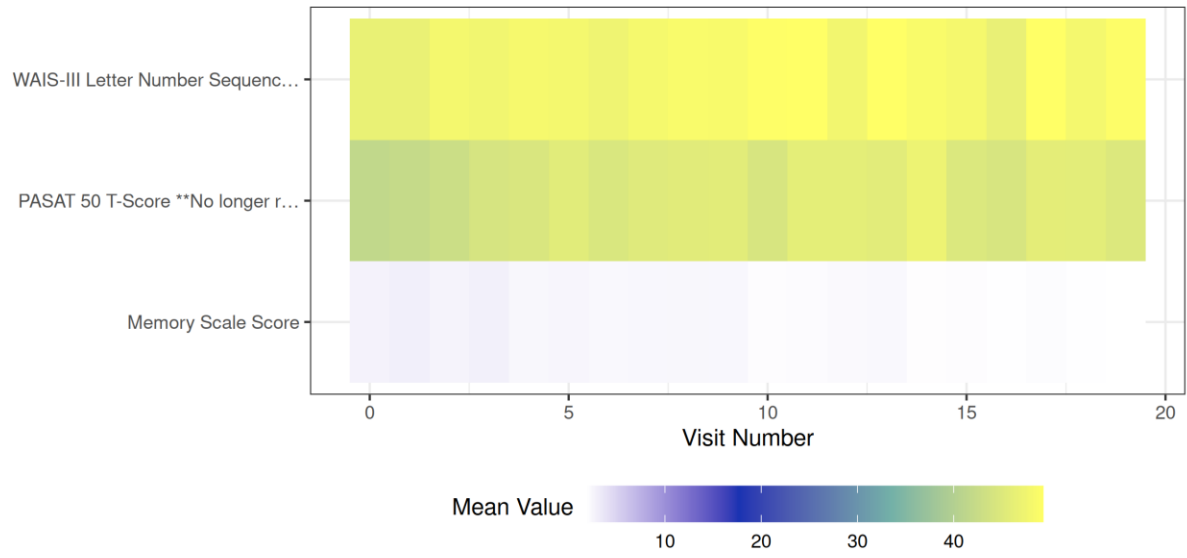


Figure 49: Scatterplot matrix of the Cognitive systems: Working memory variables with points colored by sex. The diagonal shows the estimated density curve for each marginal distribution, and the top right cells show the respective estimated pairwise Pearson correlation values overall (in black) and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

Cognitive systems: Working memory - Mean Value



Cognitive systems: Working memory - Change from Baseline

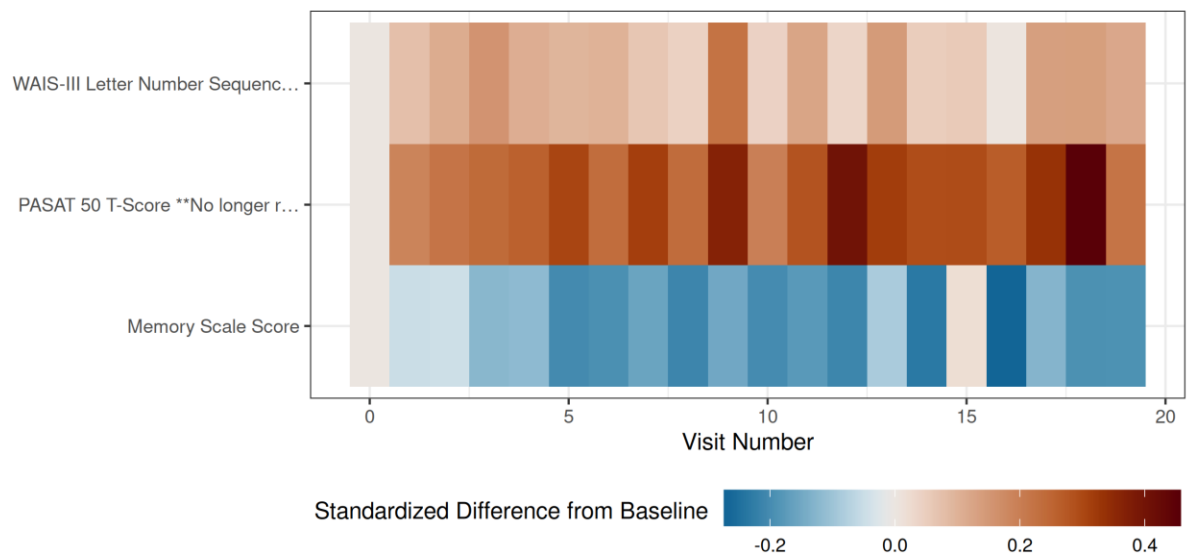


Figure 50: Heatmap of the mean value (top) and standardized mean difference in assessment measurement from baseline (bottom) by visit number for each numeric variable in the Cognitive systems: Working memory construct. Standardized mean difference is the mean difference divided by the standard deviation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

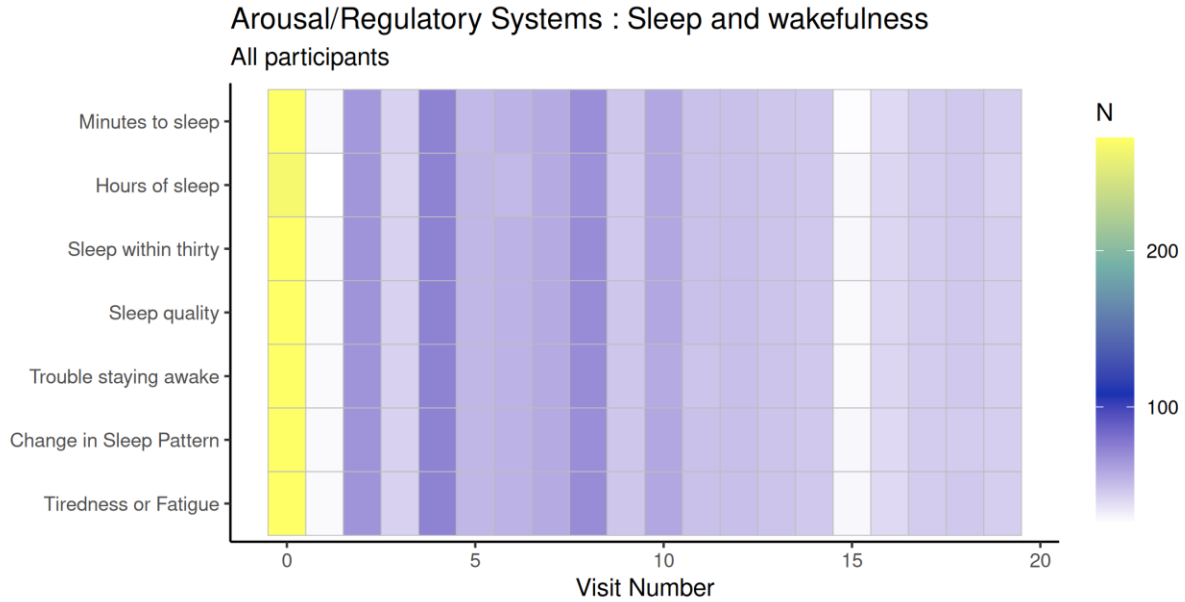


Figure 51: Heatmap showing the number of participants with each Arousal/Regulatory Systems : Sleep and wakefulness variable measured by visit number for the first 10 years after enrollment in NNTC.

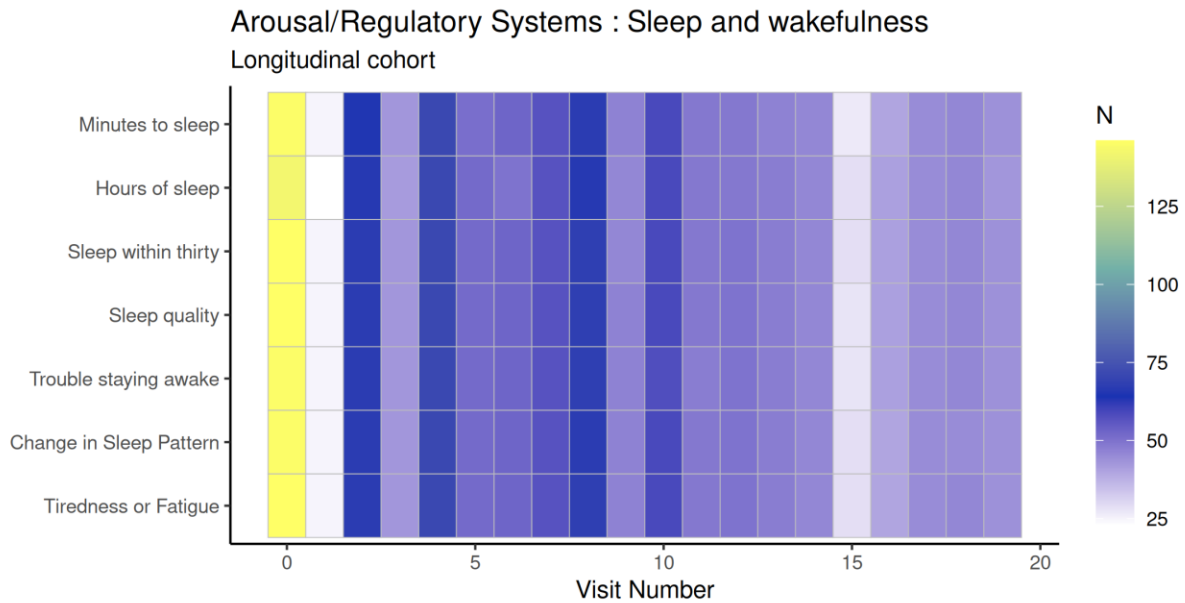


Figure 52: Heatmap showing the number of participants in the longitudinal cohort with each Arousal/Regulatory Systems : Sleep and wakefulness variable measured, by visit number, for the first 10 years.

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.

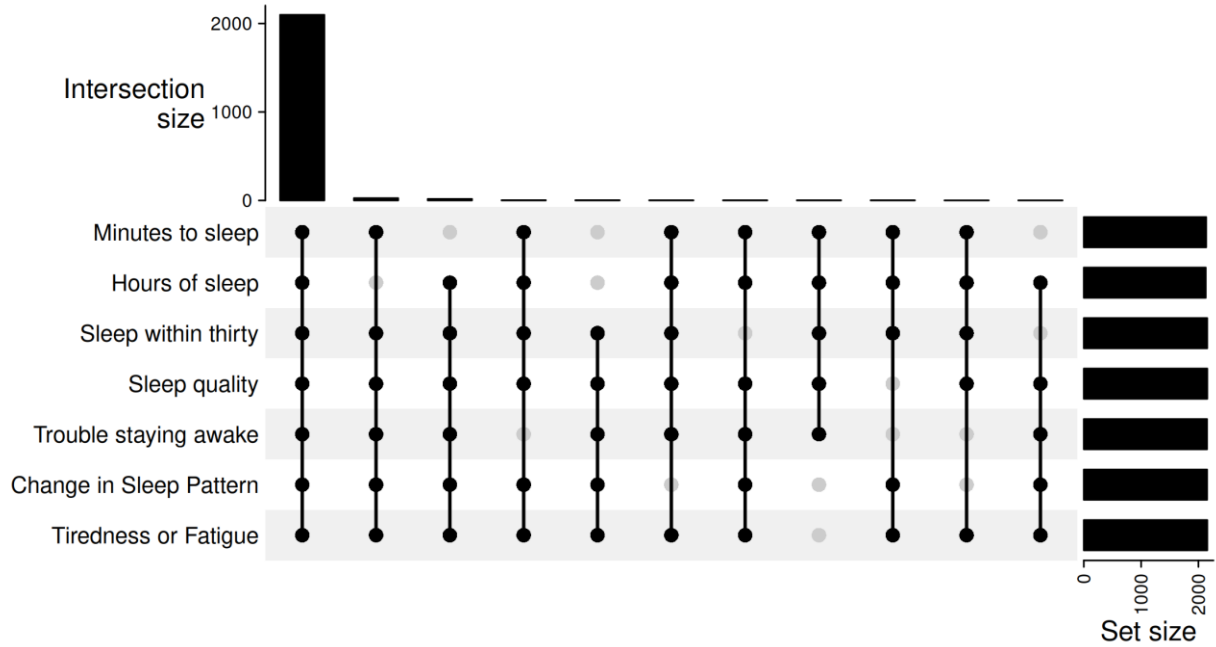


Figure 53: UpSet plot summarizing the joint availability of measures among individuals with one or more visits for the Arousal/Regulatory Systems : Sleep and wakefulness variables across the first 20 visits. The bottom right horizontal barplot shows the number observations for each variable. The filled 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.

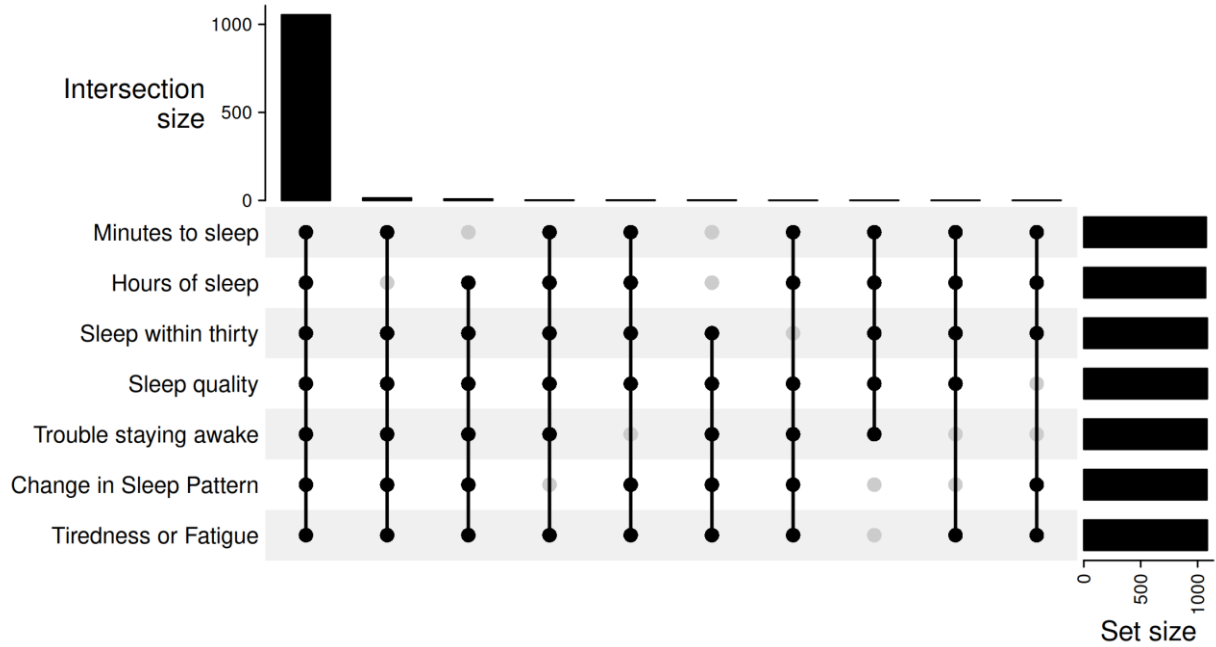


Figure 54: UpSet plot summarizing the joint availability of measures among individuals in the longitudinal cohort for the Arousal/Regulatory Systems : Sleep and wakefulness variables across the first 20 visits. The bottom right horizontal barplot shows the number observations for each variable. The filled 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.

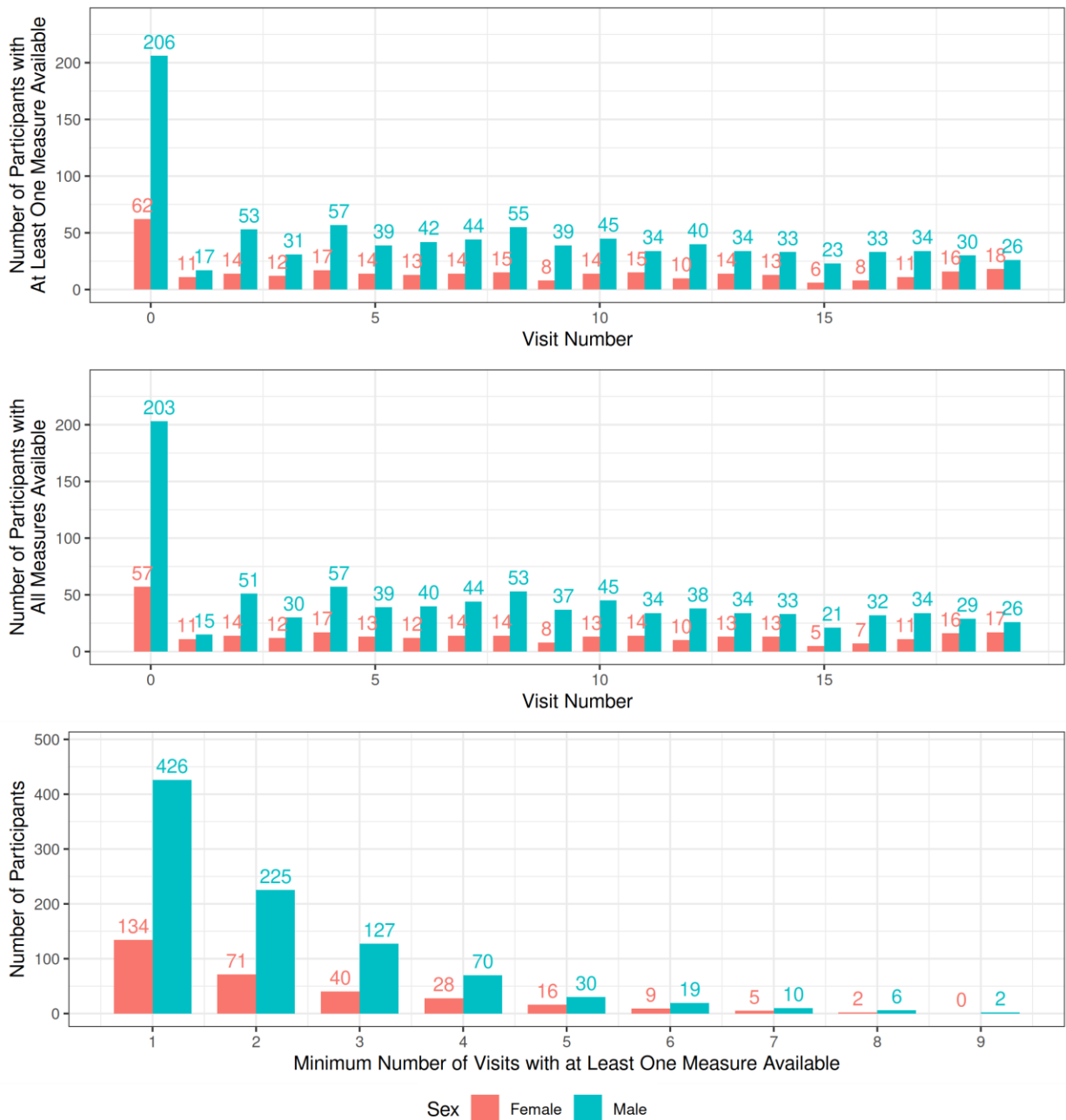


Figure 55: Data availability of participants for Arousal/Regulatory Systems : Sleep and wakefulness variables by sex summarized by the number of participants with at least one measure available at each visit number (top), the number of participants with all measures available at each visit number (middle),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

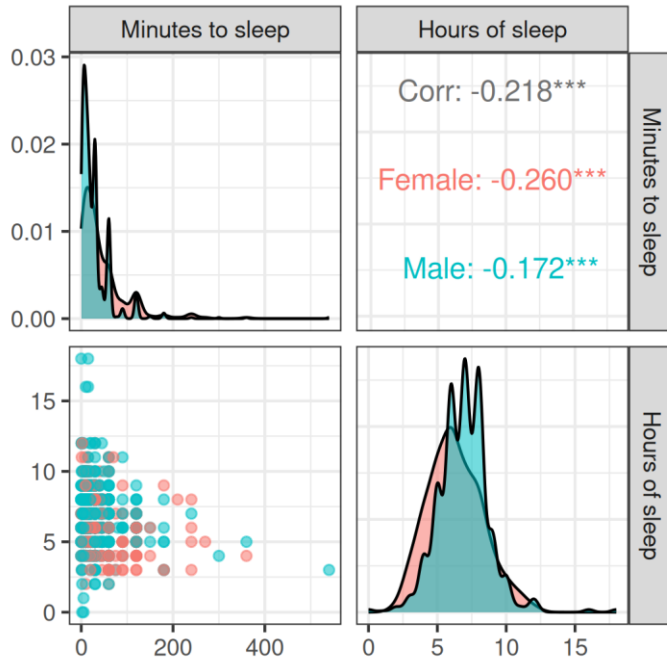
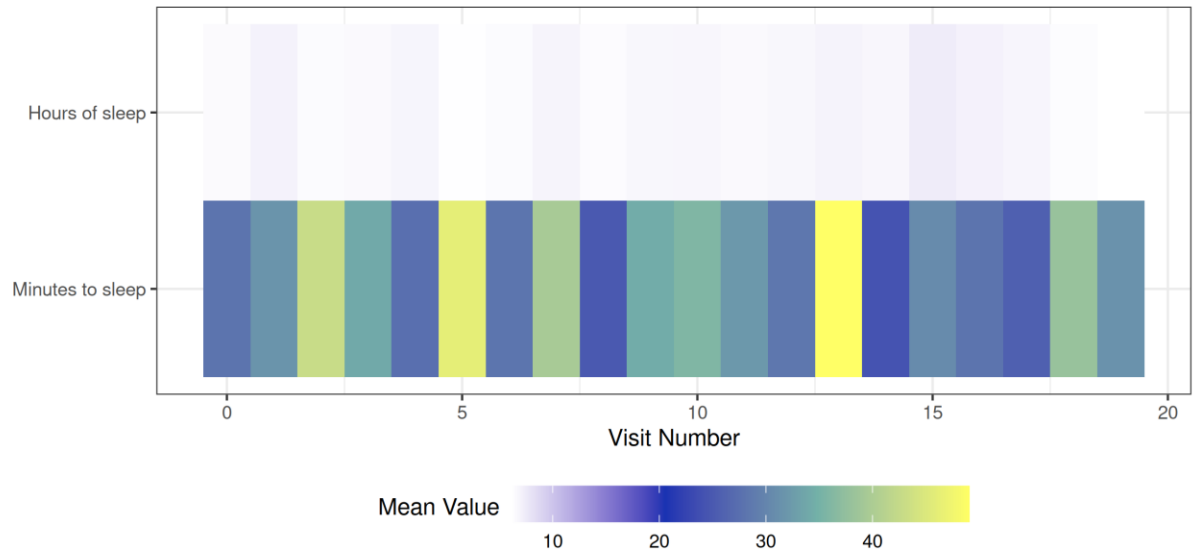


Figure 56: Scatterplot matrix of the Arousal/Regulatory Systems : Sleep and wakefulness variables with points colored by sex. The diagonal shows the estimated density curve for each marginal distribution, and the top right cells show the respective estimated pairwise Pearson correlation values overall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

Arousal/Regulatory Systems : Sleep and wakefulness - Mean Value



Arousal/Regulatory Systems : Sleep and wakefulness - Change from Baseline

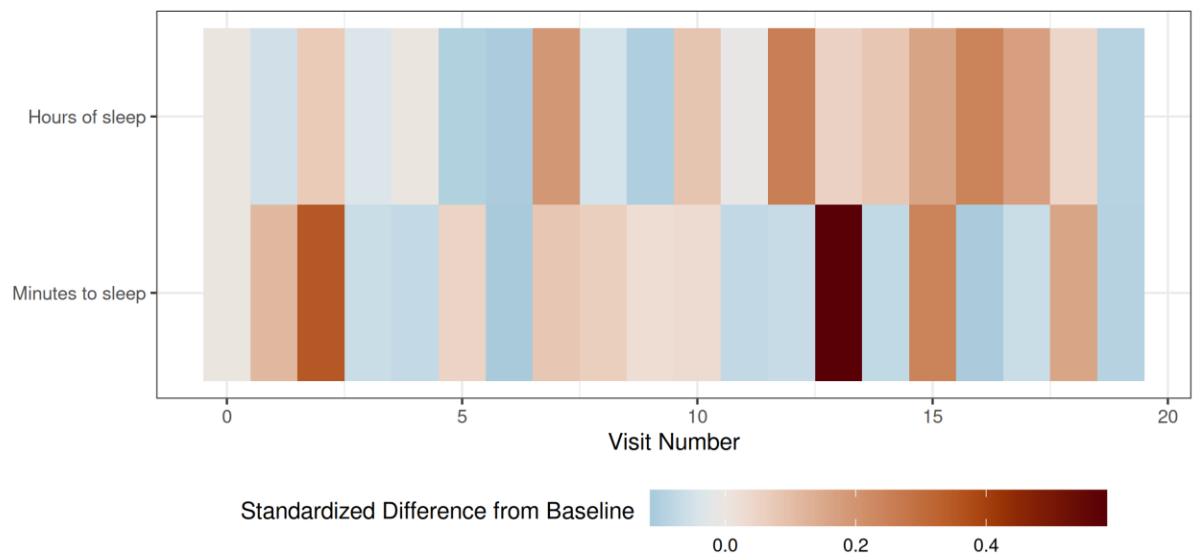


Figure 57: Heatmap of the mean value (top) and standardized mean difference in assessment measurement from baseline (bottom) by visit number for each numeric variable in the Arousal/Regulatory Systems : Sleep and wakefulness construct. Standardized mean difference is the mean difference divided by the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

Sensorimotor Systems: Motor actions

All participants

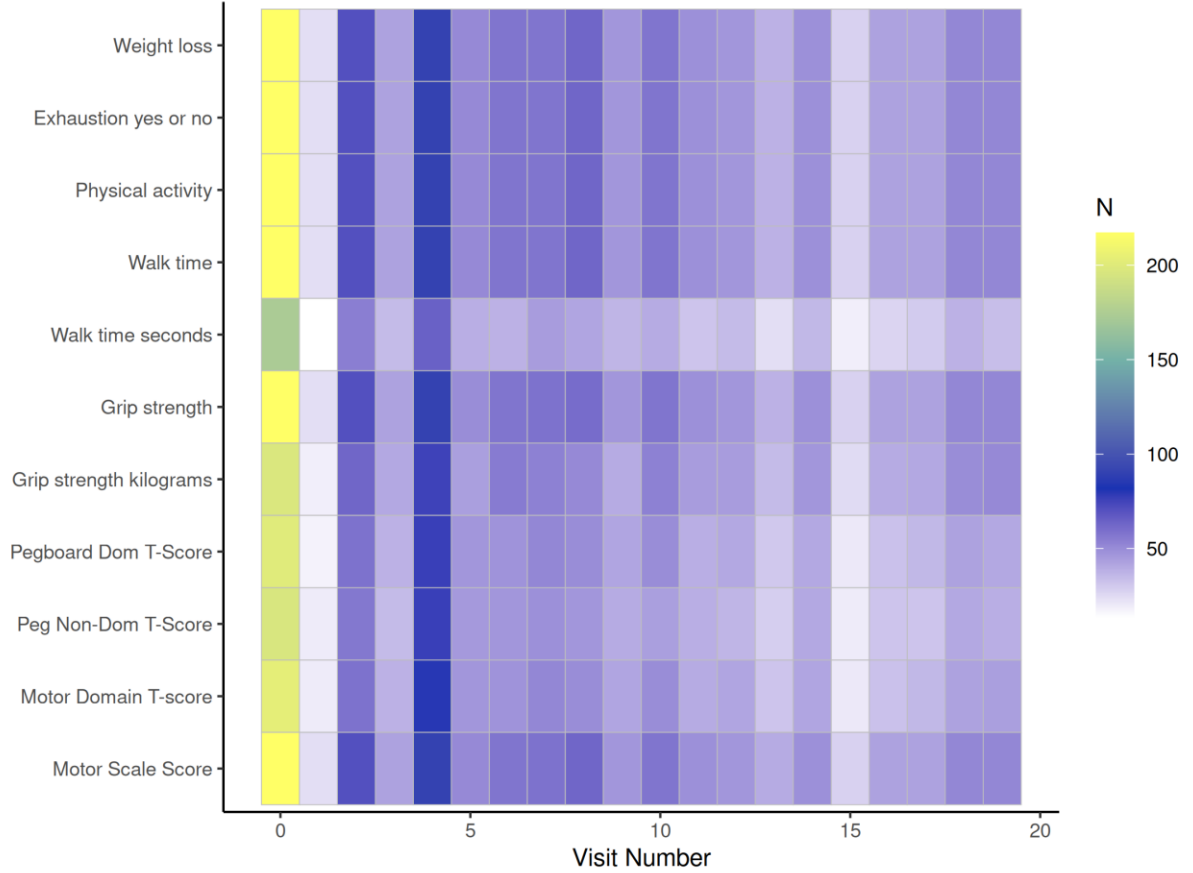


Figure 58: Heatmap showing the number of participants with each Sensorimotor Systems: Motor actions variable measured by visit number for the first 10 years after enrollment in NNTC.

Sensorimotor Systems: Motor actions

Longitudinal cohort

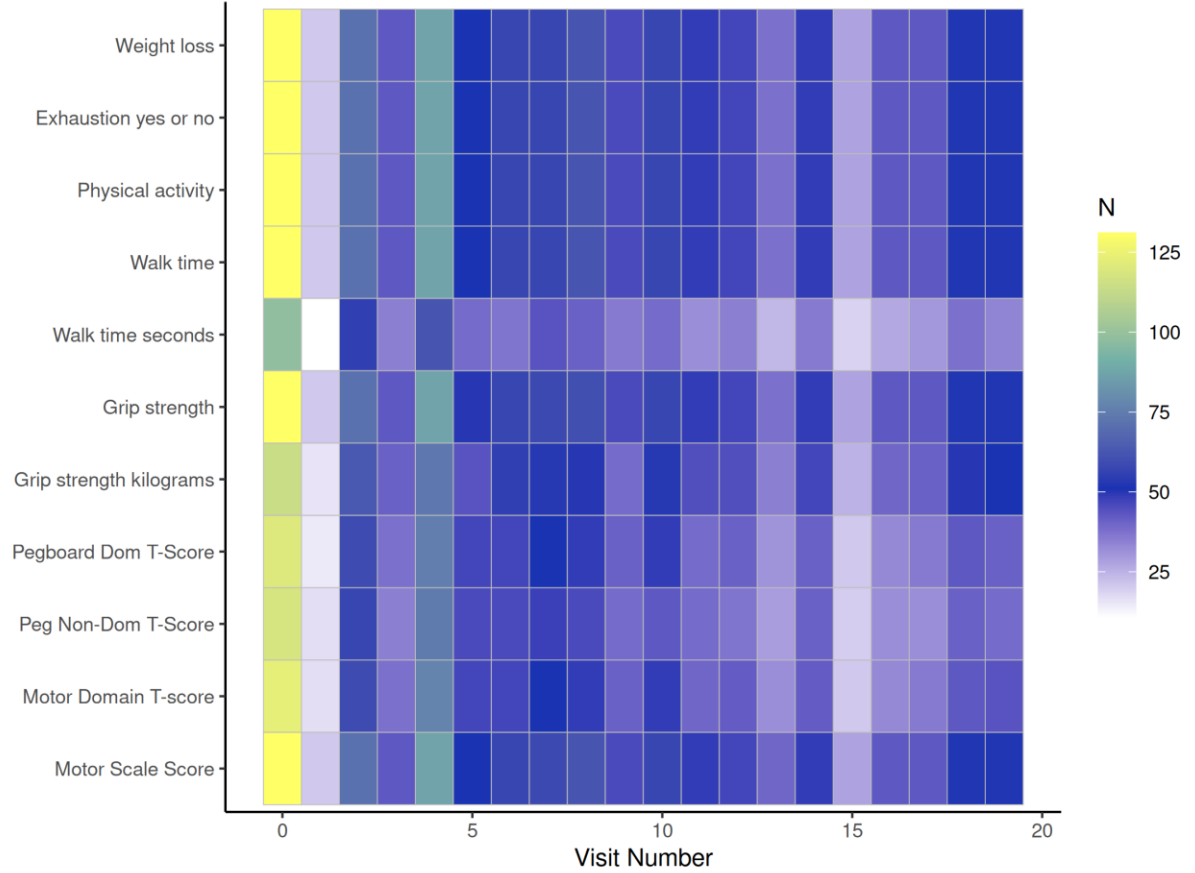


Figure 59: Heatmap showing the number of participants in the longitudinal cohort with each Sensorimotor Systems: Motor actions variable measured, by visit number, for the first 10 years.

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.

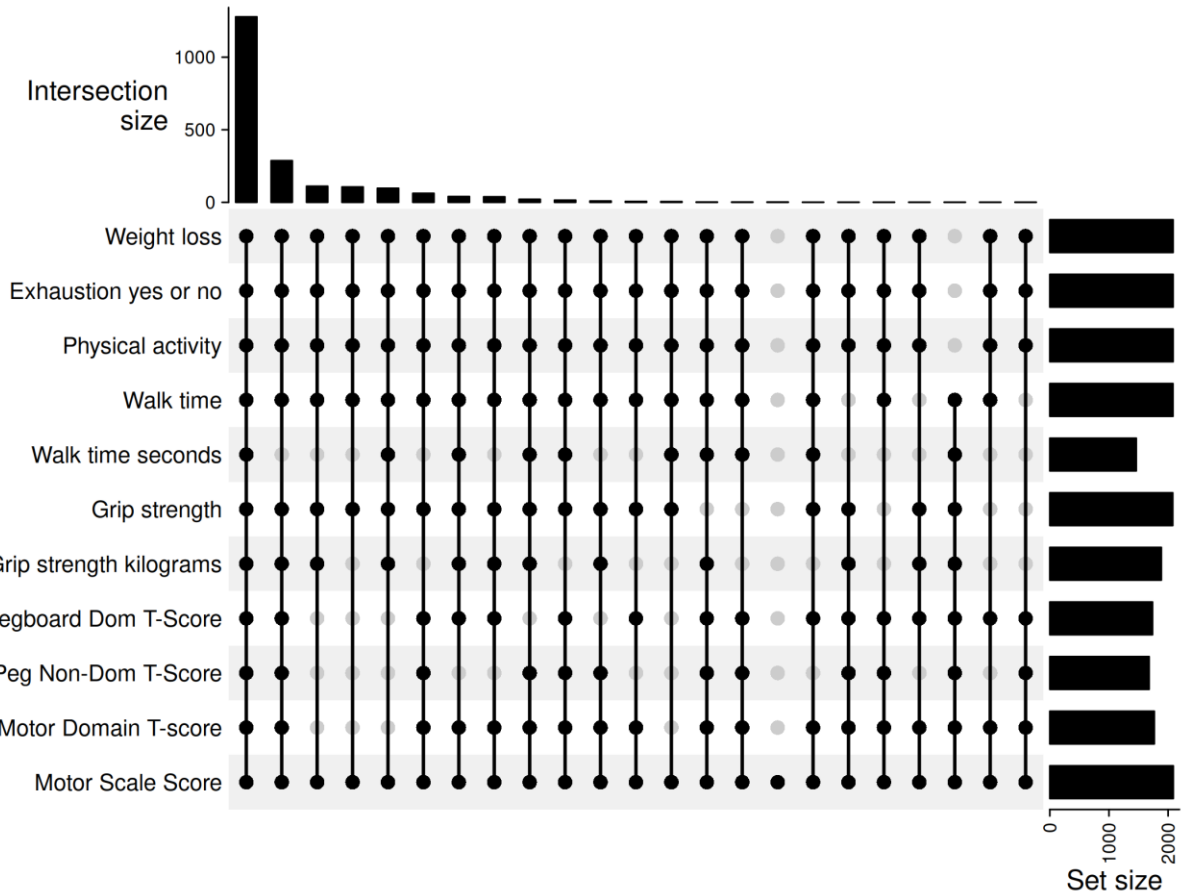


Figure 60: UpSet plot summarizing the joint availability of measures among individuals with one or more visits for the Sensorimotor Systems: Motor actions variables across the first 20 visits. The bottom right horizontal barplot shows the number observations for each variable. The filled circles in the 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.

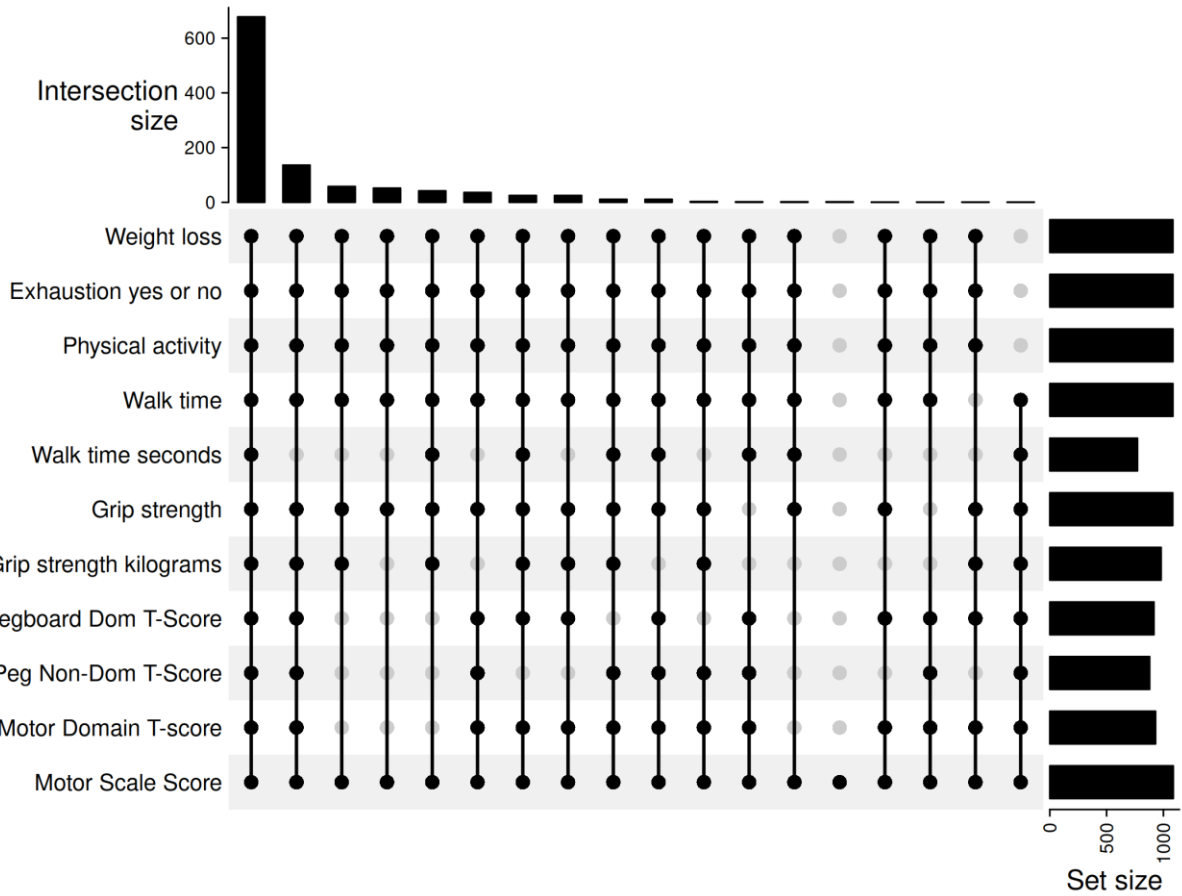


Figure 61: UpSet plot summarizing the joint availability of measures among individuals in the longitudinal cohort for the Sensorimotor Systems: Motor actions variables across the first 20 visits. The bottom right horizontal barplot shows the number observations for each variable. The filled circles in 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.

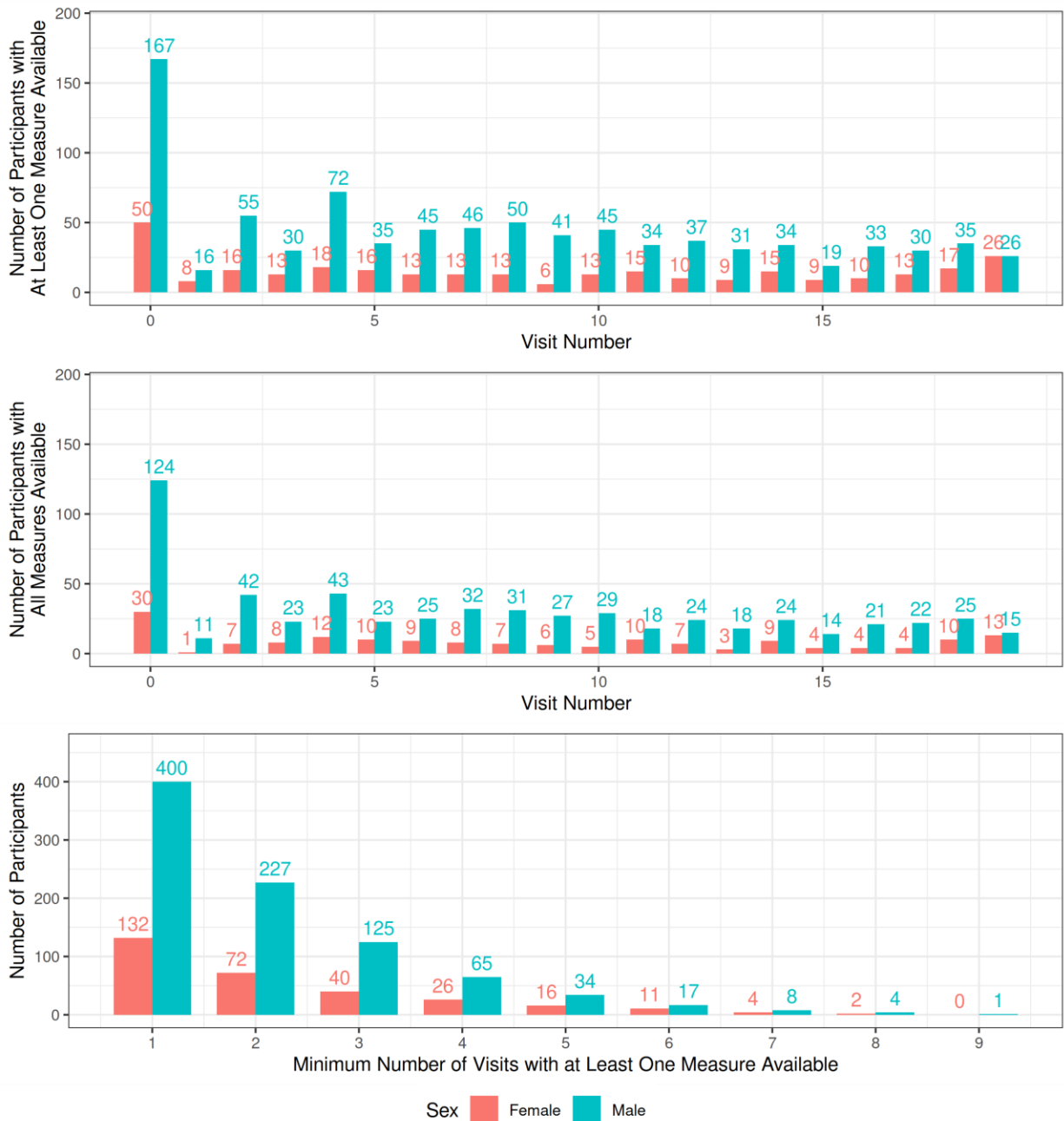
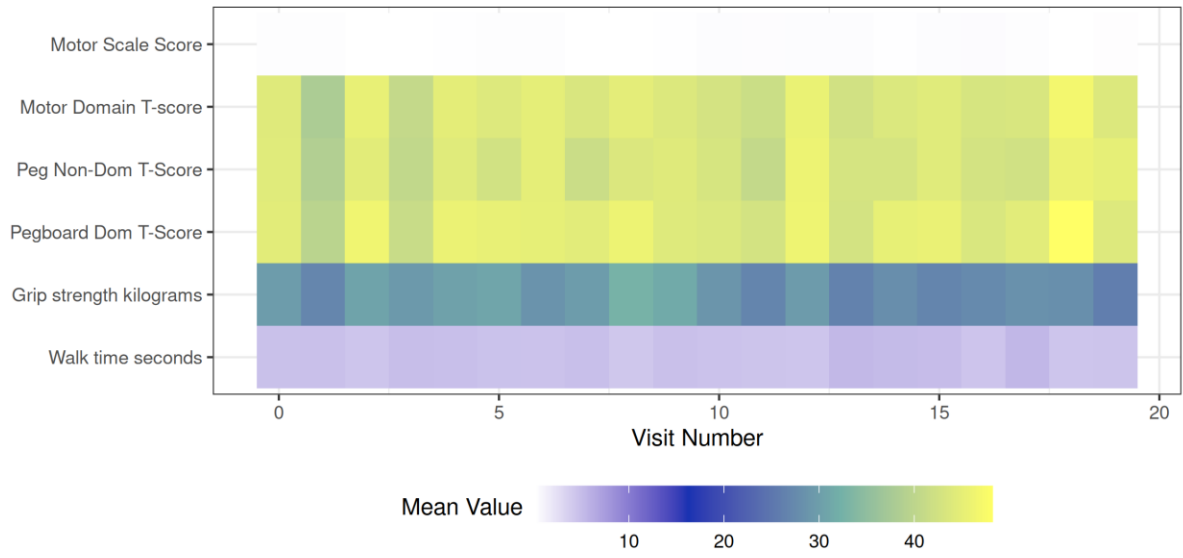


Figure 62: Data availability of participants for Sensorimotor Systems: Motor actions variables by sex summarized by the number of participants with at least one measure available at each visit number (top), the number of participants with all measures available at each visit number (middle), and the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

Sensorimotor Systems: Motor actions - Mean Value



Sensorimotor Systems: Motor actions - Change from Baseline

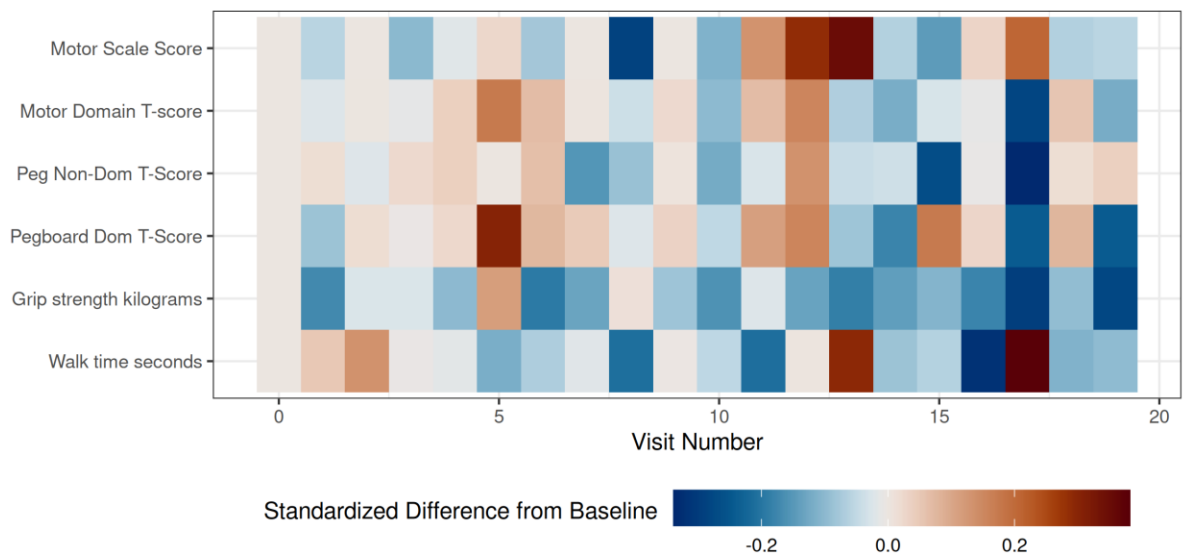


Figure 64: Heatmap of the mean value (top) and standardized mean difference in assessment measurement from baseline (bottom) by visit number for each numeric variable in the Sensorimotor Systems: Motor actions construct. Standardized mean difference is the mean difference divided by the standard deviation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

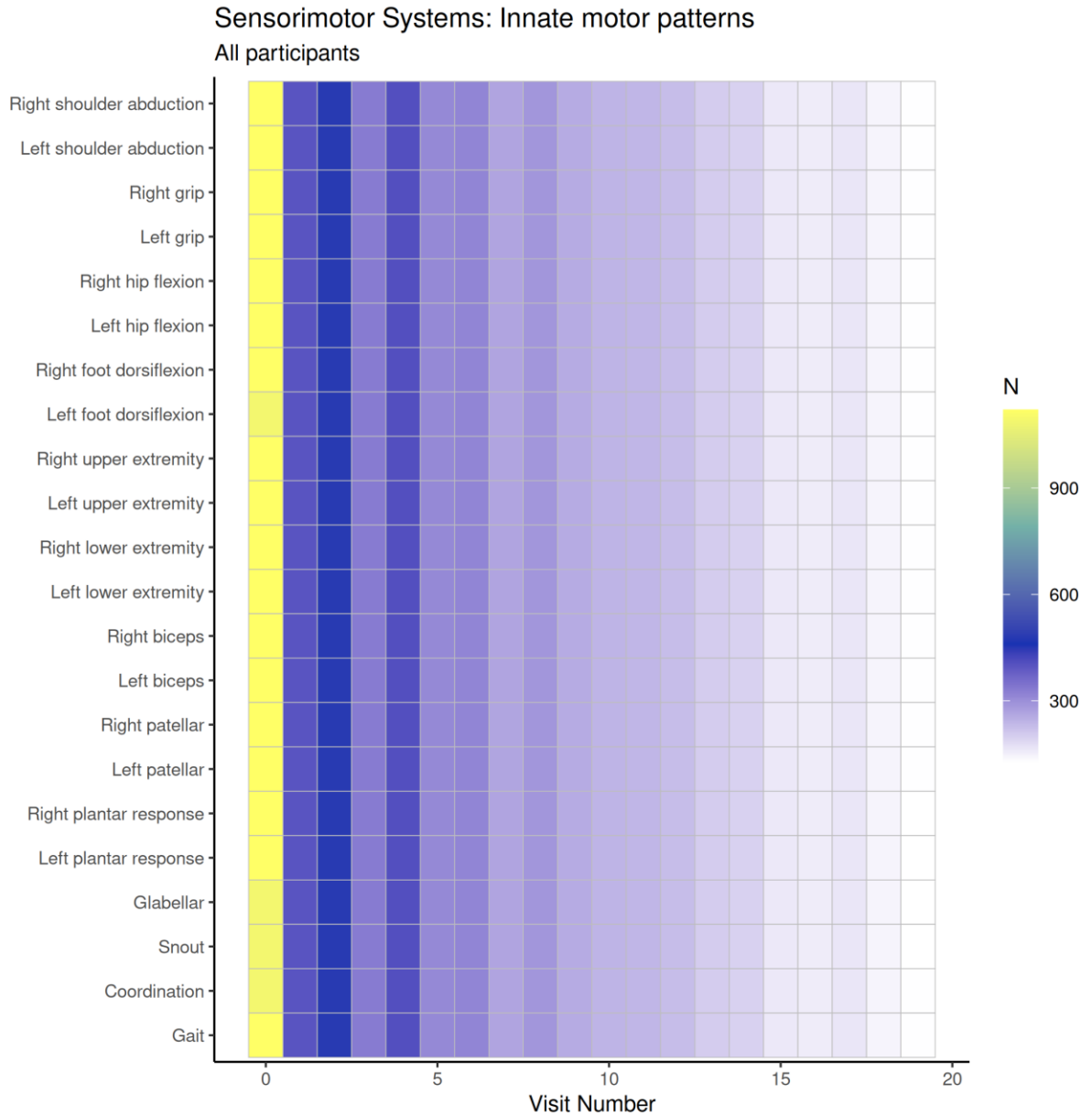


Figure 65: Heatmap showing the number of participants with each Sensorimotor Systems: Innate motor patterns variable measured by visit number for the first 10 years after enrollment in NNTC.

Sensorimotor Systems: Innate motor patterns

Longitudinal cohort

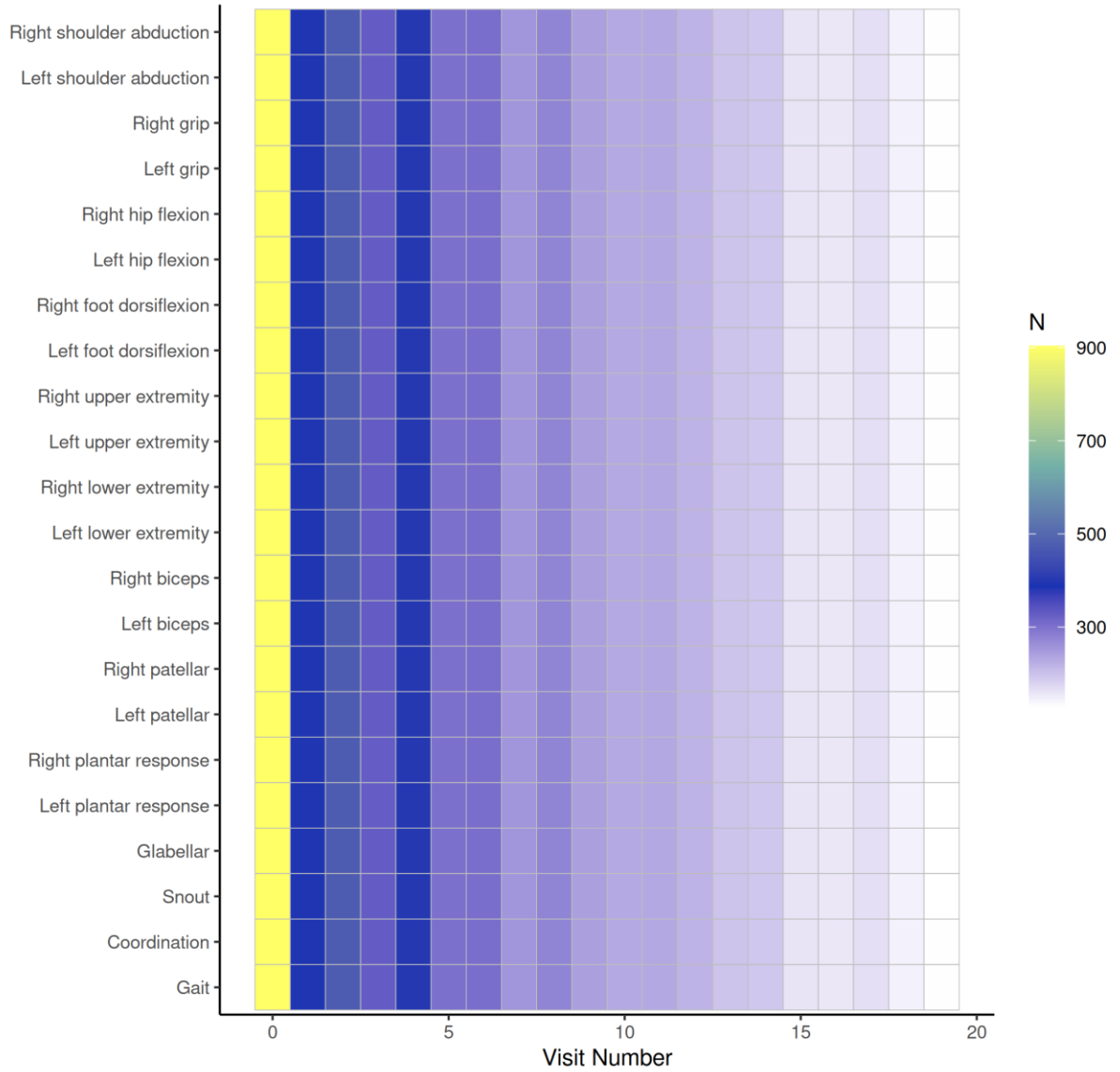


Figure 66: Heatmap showing the number of participants in the longitudinal cohort with each Sensorimotor Systems: Innate motor patterns variable measured, by visit number, for the first 10 years.

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.

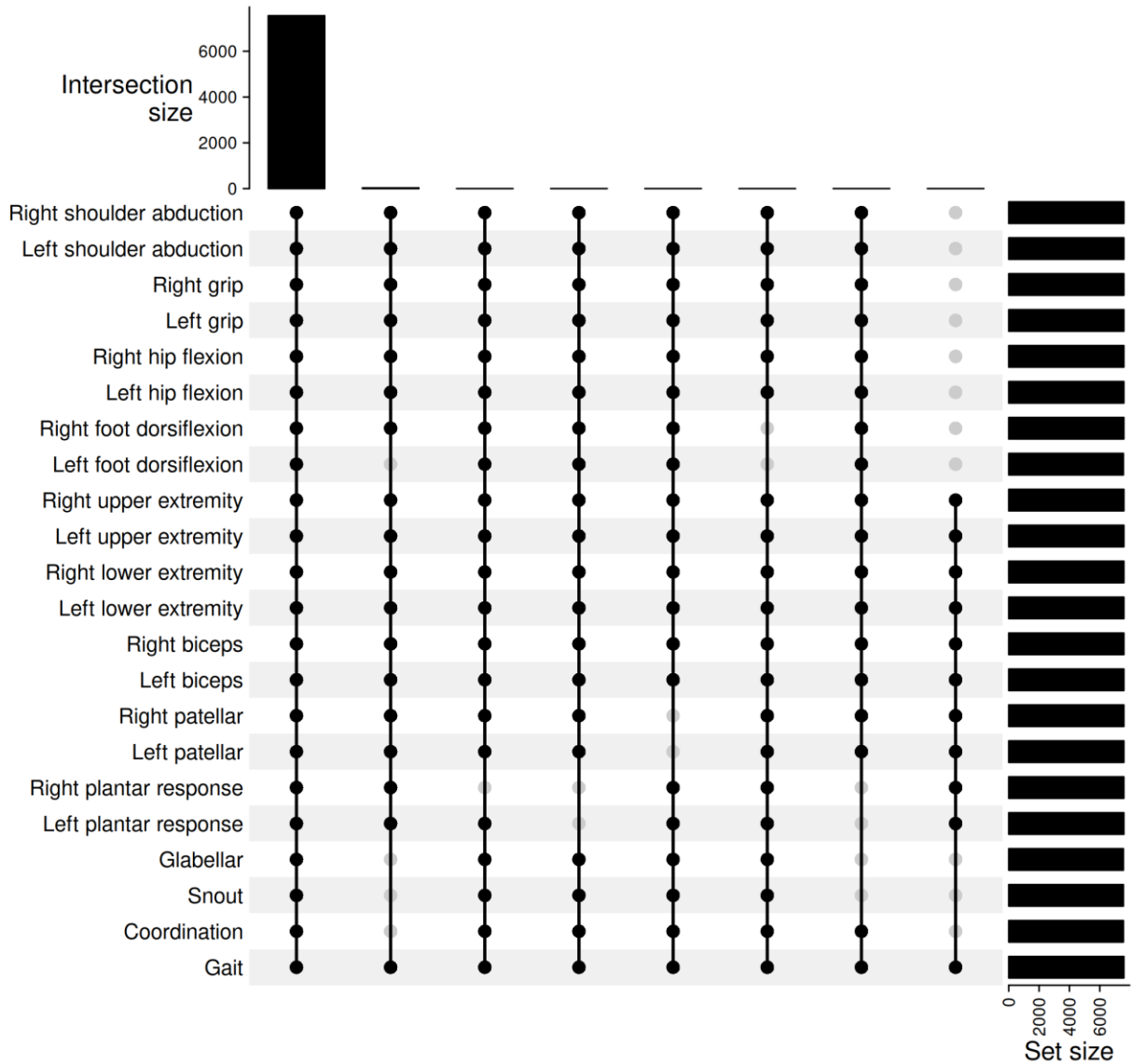


Figure 67: UpSet plot summarizing the joint availability of measures among individuals with one or more visits for the Sensorimotor Systems: Innate motor patterns variables across the first 20 visits. The bottom right horizontal barplot shows the number observations for each variable. The filled circles 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.

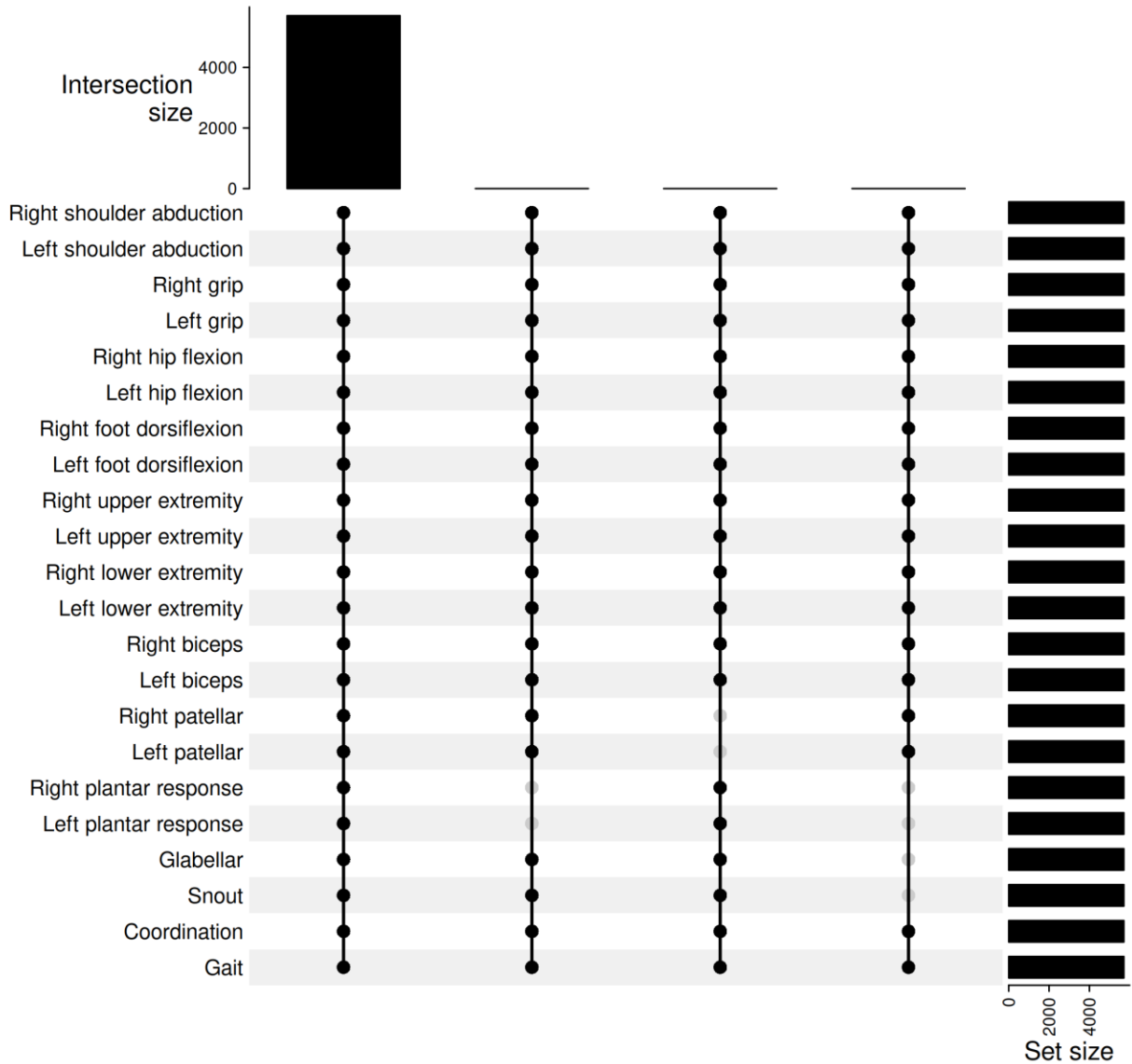


Figure 68: UpSet plot summarizing the joint availability of measures among individuals in the longitudinal cohort for the Sensorimotor Systems: Innate motor patterns variables across the first 20 visits. The bottom right horizontal barplot shows the number observations for each variable. The filled circles 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.

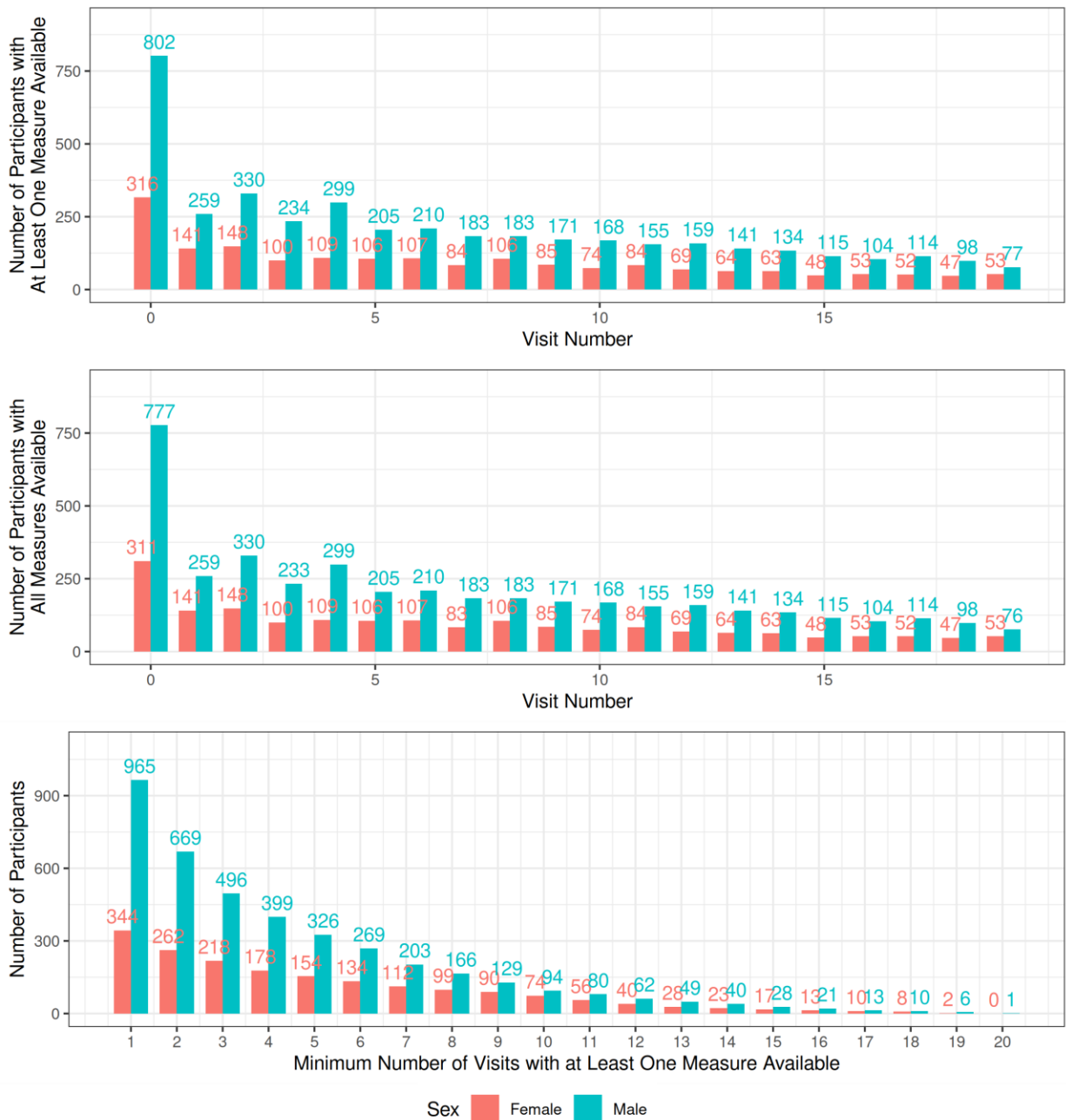


Figure 69: Data availability of participants for Sensorimotor Systems: Innate motor patterns variables by sex summarized by the number of participants with at least one measure available at each visit number (top), the number of participants with all measures available at each visit number (middle), 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 |
|----------------|-----------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
| Glabella | 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 |