**Supplementary Tables**

**Table S1. Summary of data corrections used in this study.** Of 13 parameters in the CSS, 6 parameters are purely observational and not amenable to correction of logical inconsistencies. The 7 remaining parameters were corrected for deviations likely resulting from user and/or recording errors. A total of 772 individuals out of 1,819 participants required data correction. An average of ~2 parameters required correction in each of these 772 individuals’ records.

**Table S2. Study Participant Demographics**

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**Figure S1. Rett syndrome severity increases with age and depends on *MECP2* genotype.** A) Baseline clinical severity scores (CSS) plotted with individual age at baseline for 1,451 female RNHS participants with RTT and an identified causal mutation in *MECP2*. Red line: fitted log curve of plotted data points. B) Mean baseline severity scores for common Rett-causing mutations. Error bars represent SEM. C) Heatmap showing pairwise comparisons of baseline CSS by mutation (ANOVA with post-hoc pairwise comparisons using Tukey’s HSD) with color indicating p-value cutoffs as indicated in panel legend.



**Figure S2. Example model predicted clinical severity trajectories for individuals with repeated measures.** Model predicted clinical severity scores (blue line) plotted against observed scores (black points). One individual for each mutation grouping was randomly selected from individuals with greater than thirteen visits in the RNHS to provide a visual assessment of model fit.

