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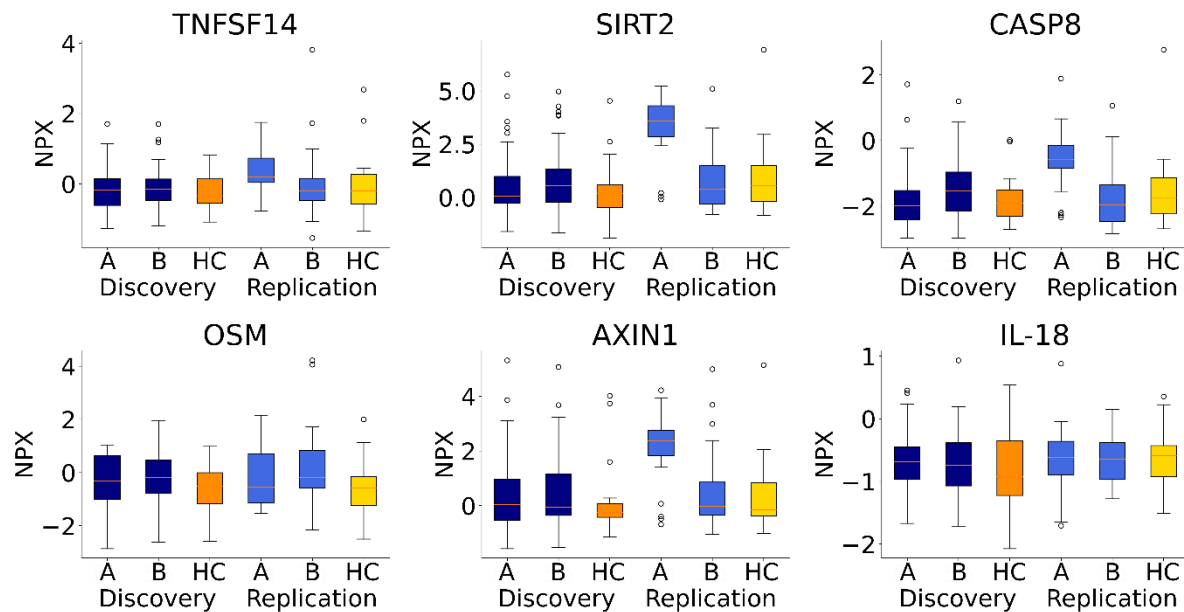


Figure S1 A group (n = 21) of persons with MS (pwMS; Replication cohort group A) had higher expression of several protein markers for delayed sampling handling (TNFSF14, SIRT2, CASP8, AXIN1) in plasma. The figure shows the expression of the six top most affected proteins, also measured on the Olink panel, by sampling handling variability from Table 1 in Huang et al. 2021*. The pwMS from both the discovery and the replication cohort were divided into two groups (A and B), which in both cohorts represents samples from an old collection (A) and from a new collection (B). The remaining groups of pwMS (discovery cohort group A and B, and replication cohort group B) and the healthy controls (HC) did not show any clear effect of sampling or handling variability.

* Huang J, Khademi M, Lindhe Ö, Jönsson G, Piehl F, Olsson T, Kockum I. Assessing the Preanalytical Variability of Plasma and Cerebrospinal Fluid Processing and Its Effects on Inflammation-Related Protein Biomarkers. *Mol Cell Proteomics*. 2021;20:100157. doi:10.1016/j.mcpro.2021.100157.

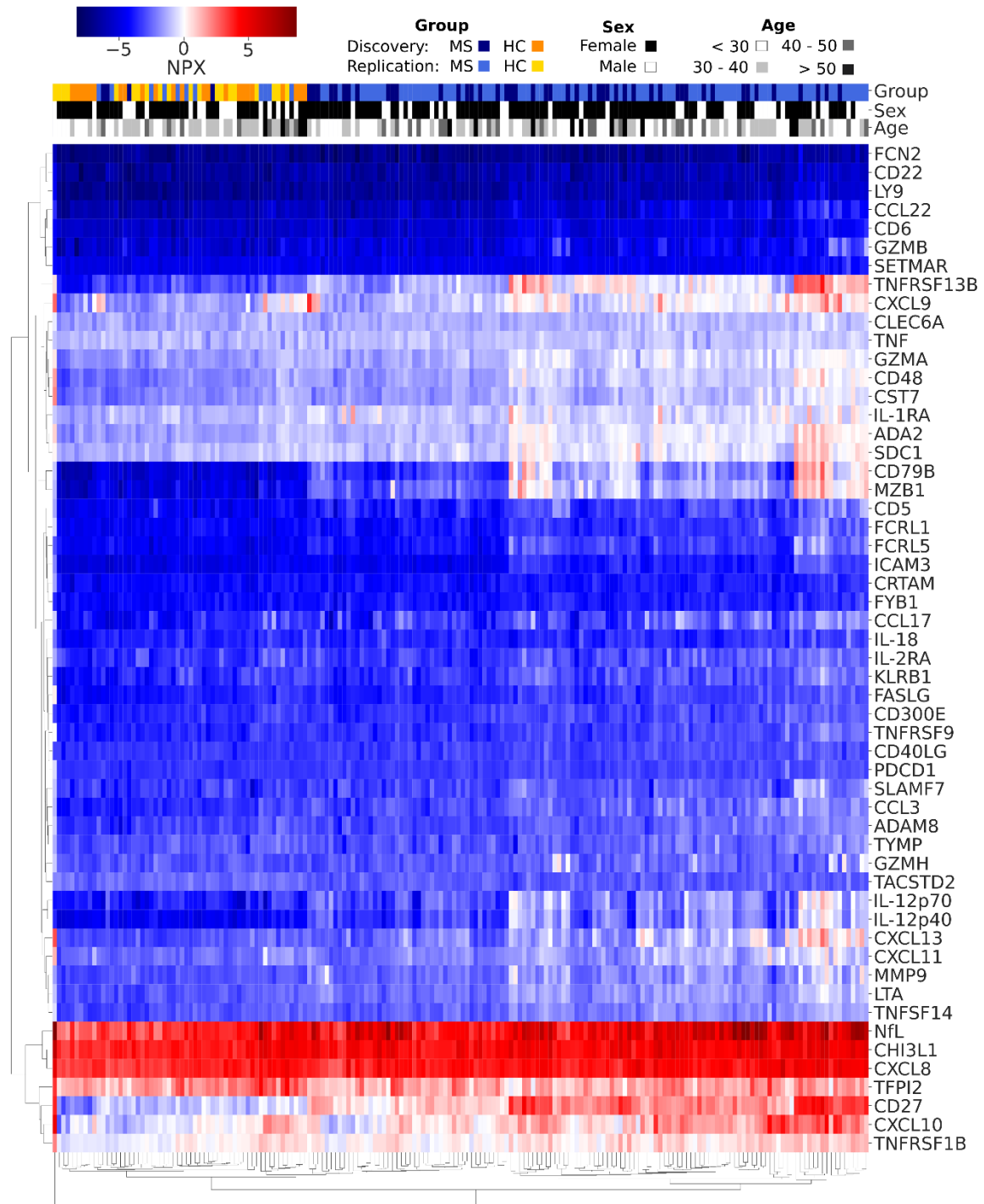


Figure S2 A clustered heatmap showing the protein expression (NPX) of the differentially expressed proteins (FDR < 0.05) either in the discovery cohort or the replication cohort in the CSF. Each column shows the expression of one sample. At the top of the heatmap it is shown which groups a sample is part of (person with MS or healthy control (HC) and discovery cohort or replication cohort), sex (female or male), and age at baseline (16 - 64 years) of each person.

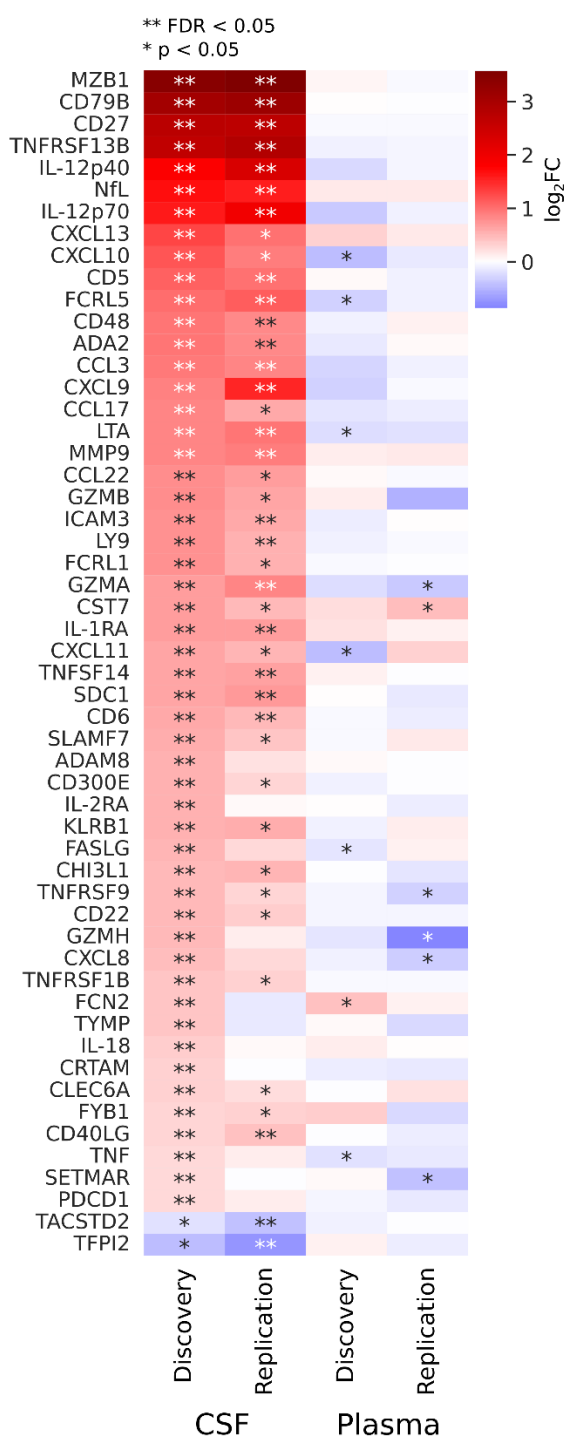


Figure S3 A heatmap showing the $\log_2$ fold-change(FC) values of the differentially expressed proteins (FDR < 0.05) either in the discovery cohort or the replication cohort in the CSF, comparing persons with MS to healthy controls. The $\log_2$ FC values in the CSF are compared to the $\log_2$ FC values in plasma. Differentially expressed proteins: * p < 0.05, ** FDR < 0.05.

Discovery cohort: 1 - 24

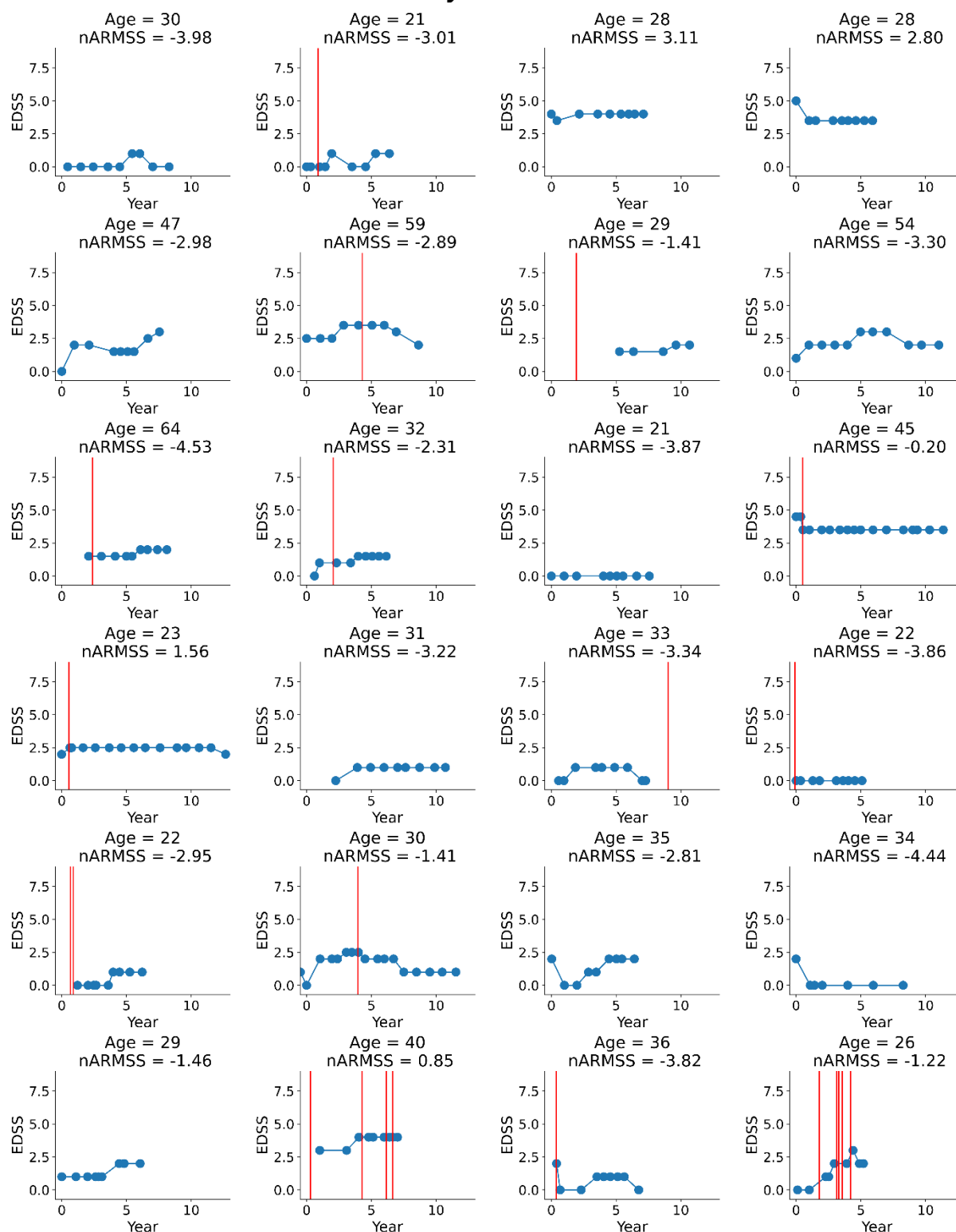


Figure S4 Individual plots for each person with MS showing the person's EDSS scores (blue dots) during the follow-up years after baseline sampling (Discovery cohort: $n = 71$; Replication cohort: $n = 33$). Plots are shown for persons with at least three years follow-up. Documented relapses are shown with a red vertical line. On top of each plot the person's age at baseline sampling and the calculated nARMSS scores are stated.

Figure S4

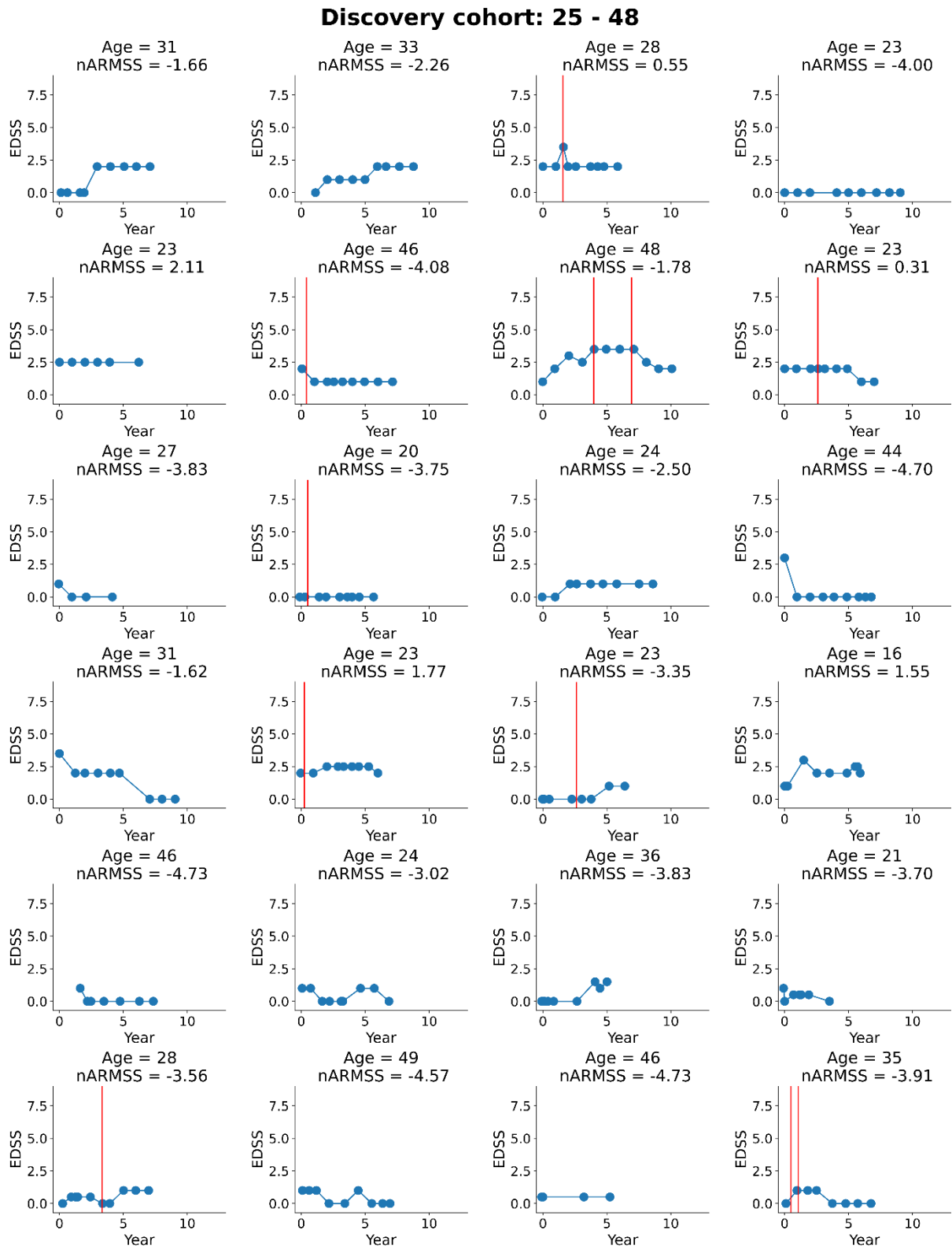


Figure S4

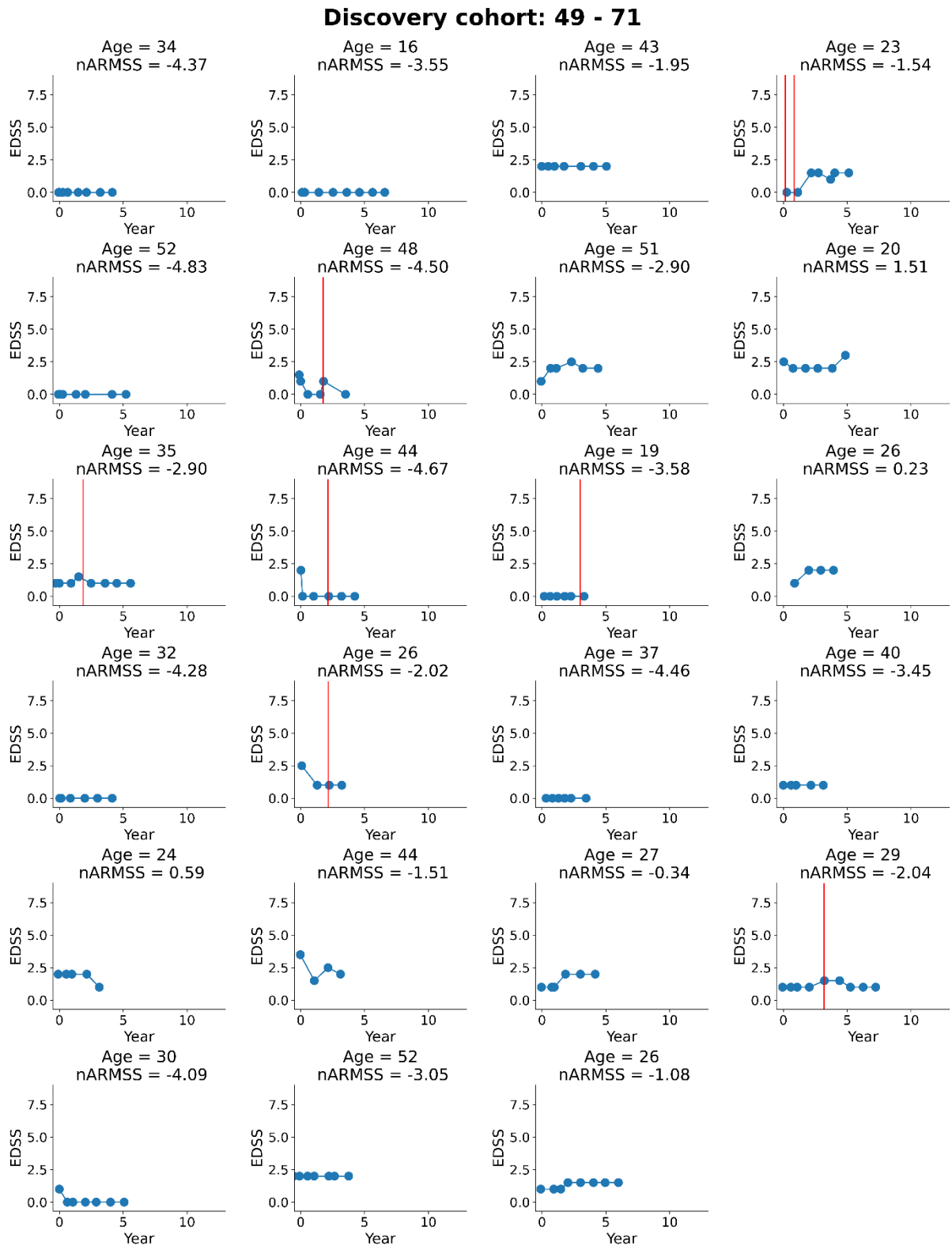


Figure S4

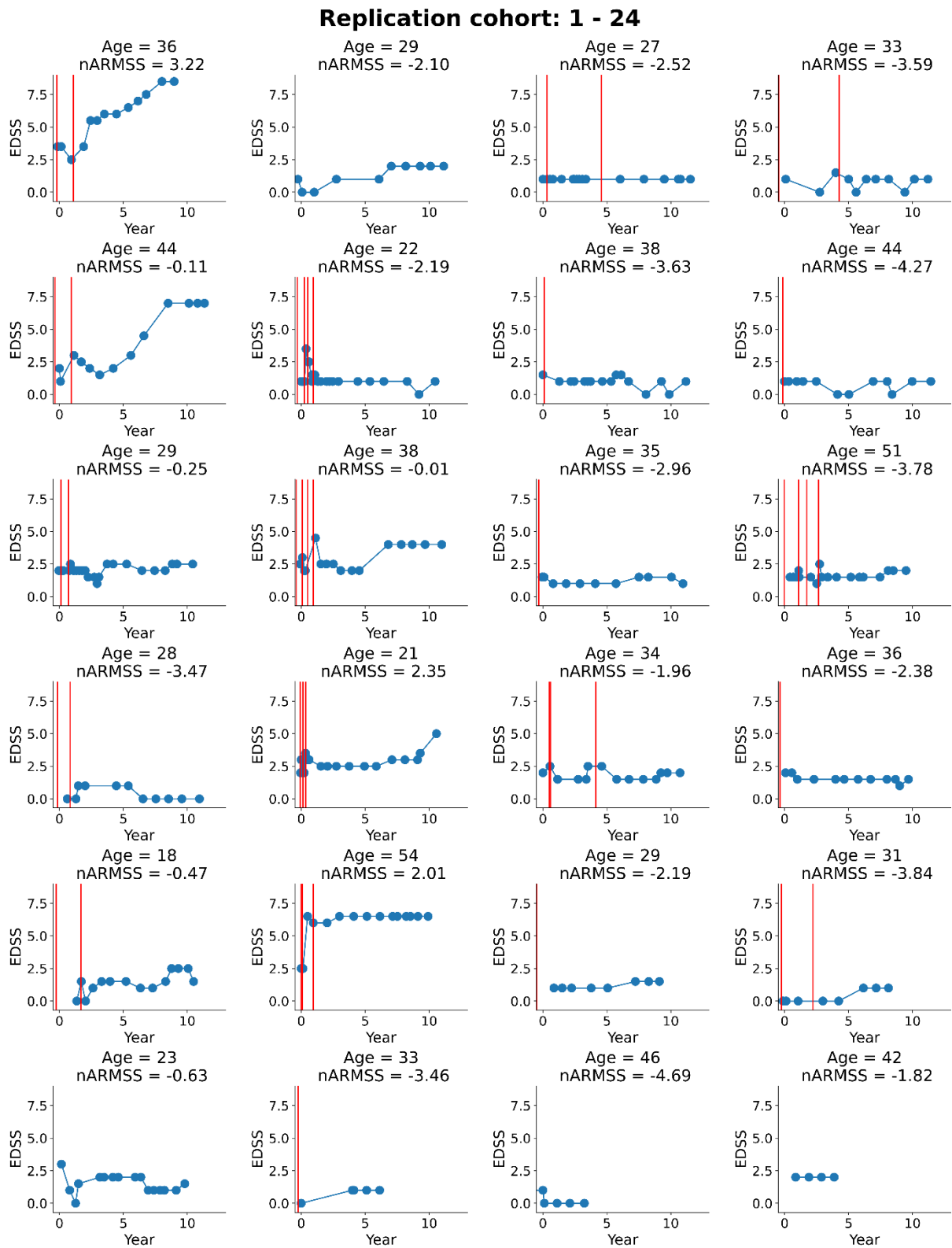
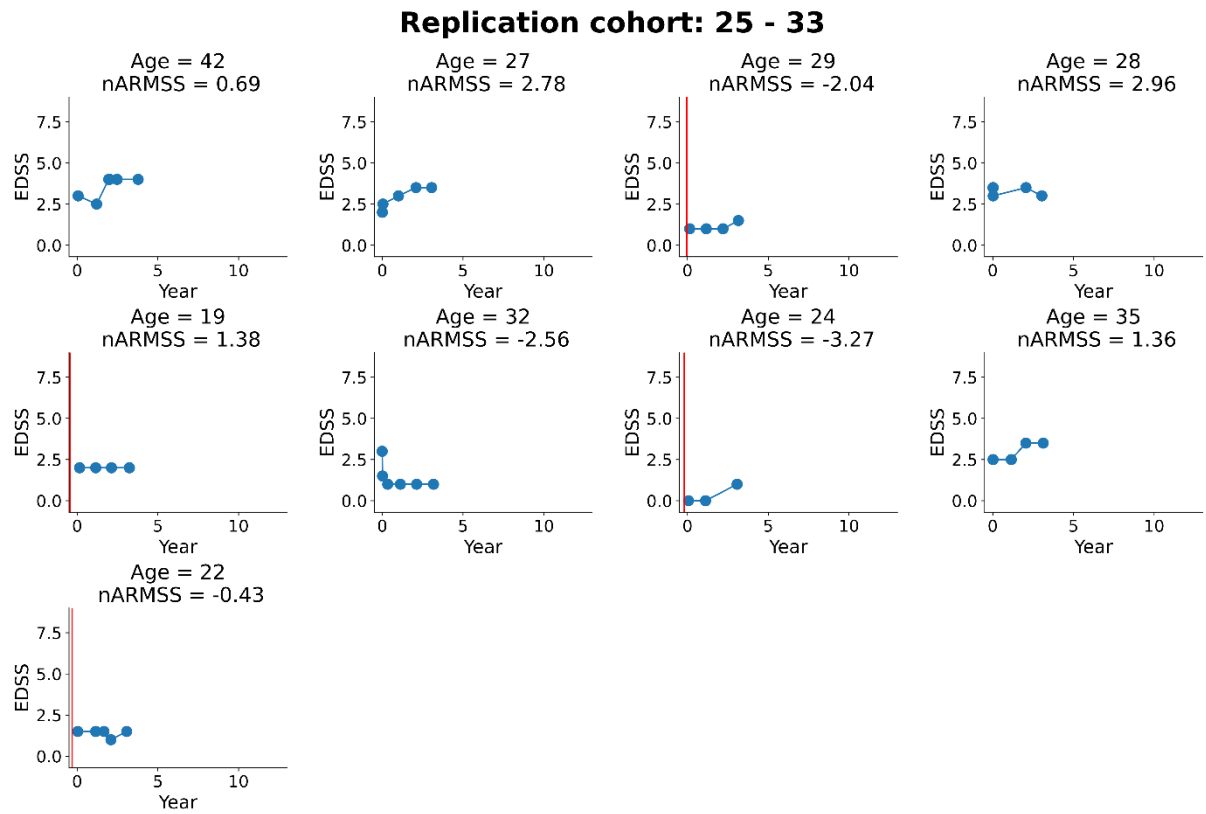


Figure S4



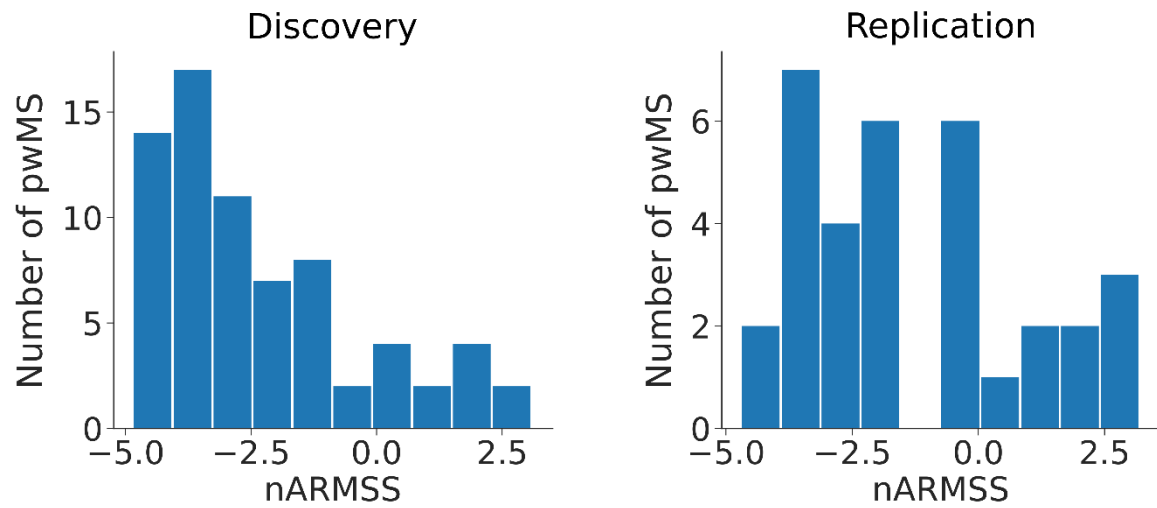


Figure S5 Histograms showing the distribution of nARMSS scores for persons with MS (pwMS) in the discovery cohort (n = 71; left) and the replication cohort (n = 33; right).

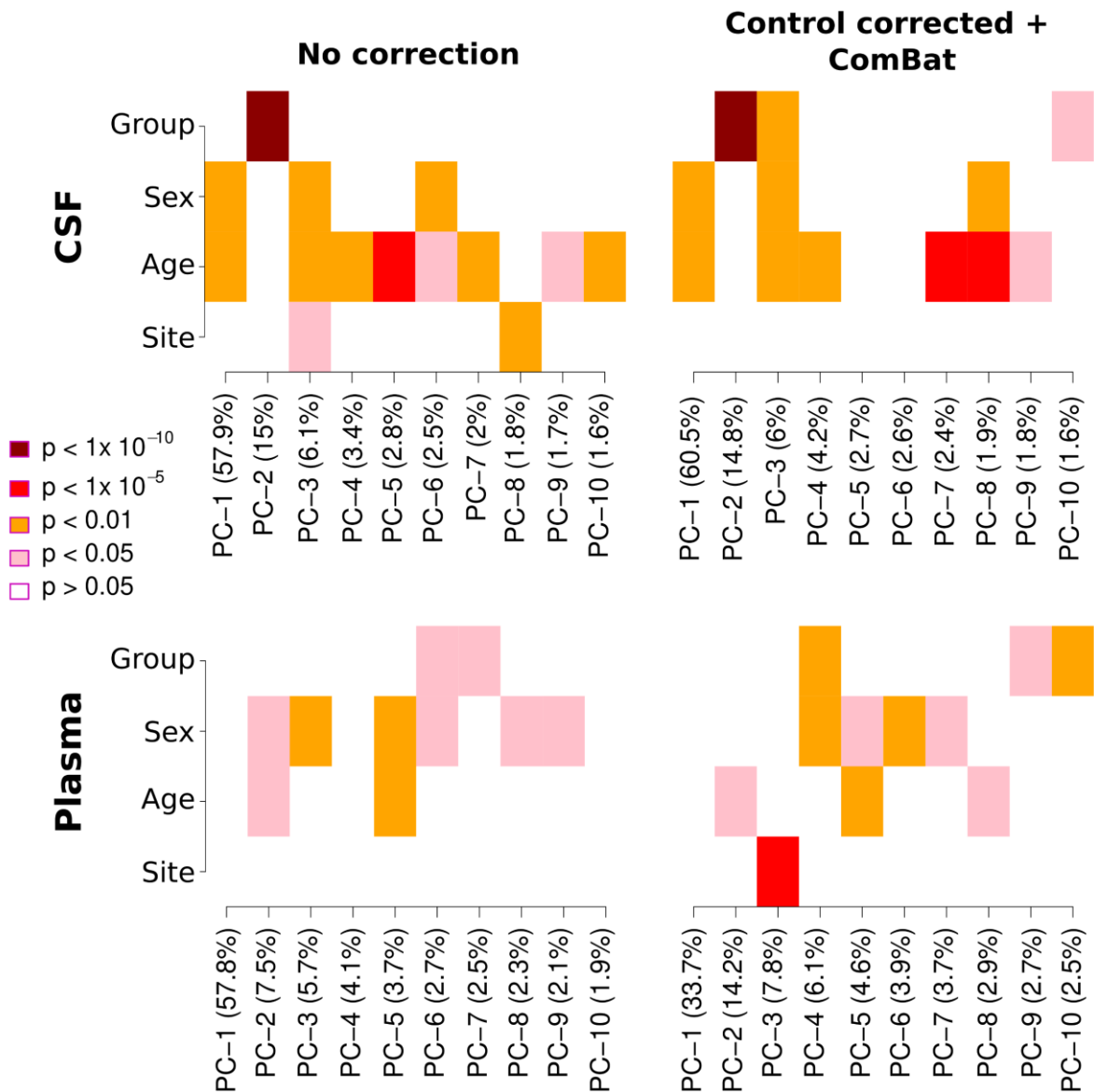


Figure S6 Singular value decomposition analysis of the uncorrected NPX values (left) and the corrected NPX values (right) in both the CSF (top) and plasma (bottom). The NPX values were corrected in two steps: 1) control corrected: NPX values were adjusted so that controls in the discovery cohort and the replication cohort had the same standard deviation and mean, 2) ComBat corrected. The categories investigated were group (person with MS or healthy control), sex (female or male), age at baseline, and site (sampled at Linköping university hospital or Karolinska university hospital). The significance of the correlation of each category with each principal component (PC) is shown in the plot.