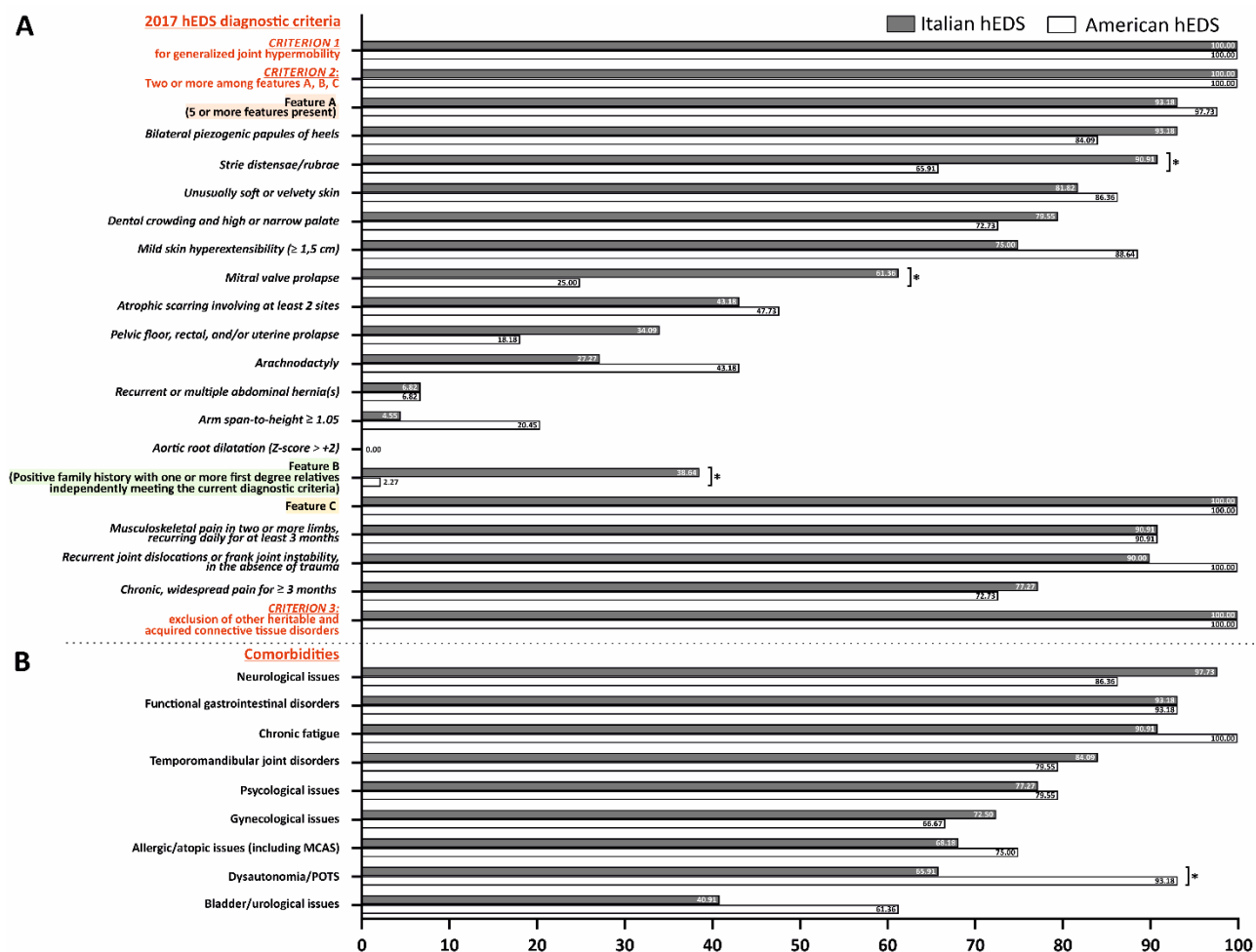
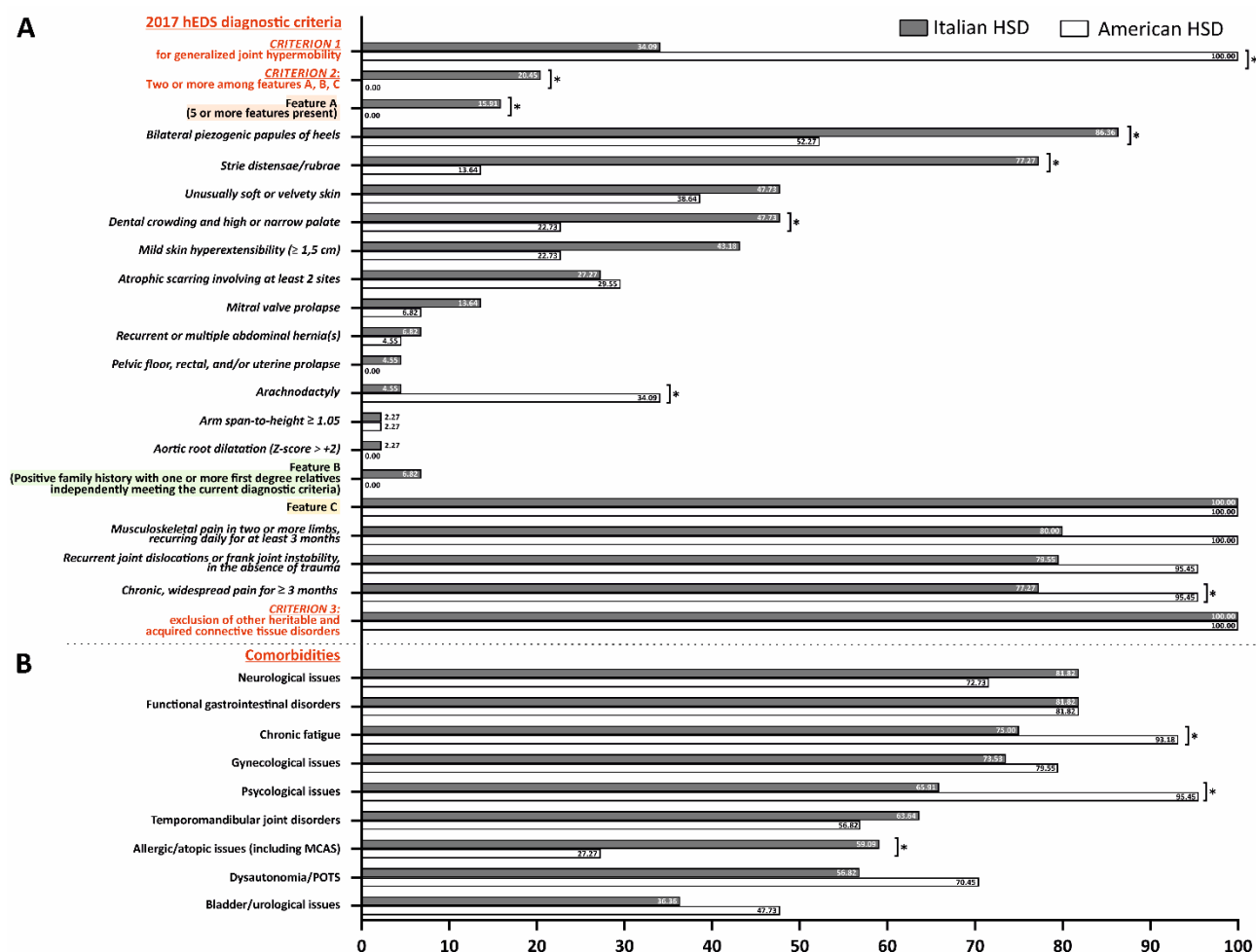
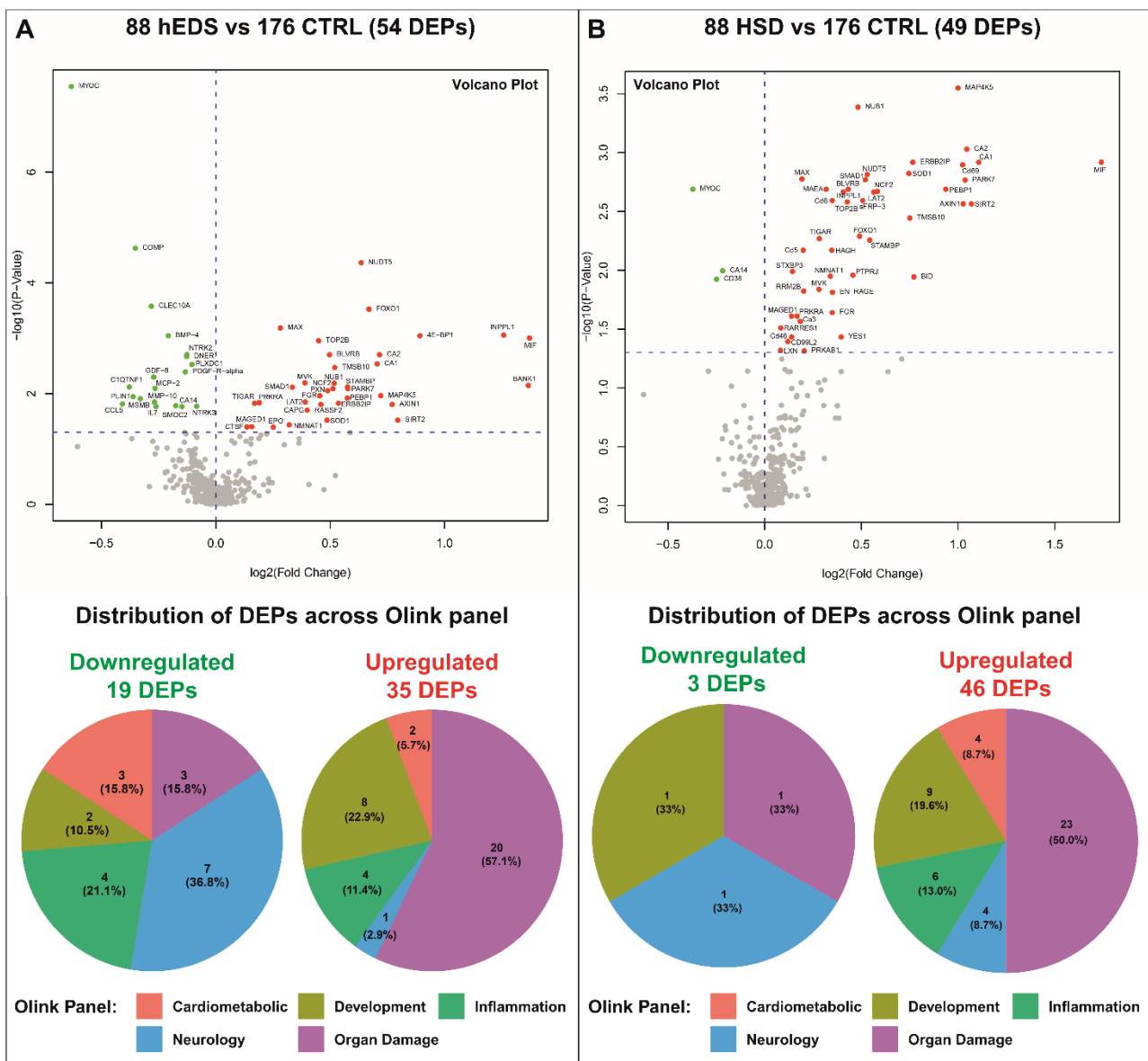




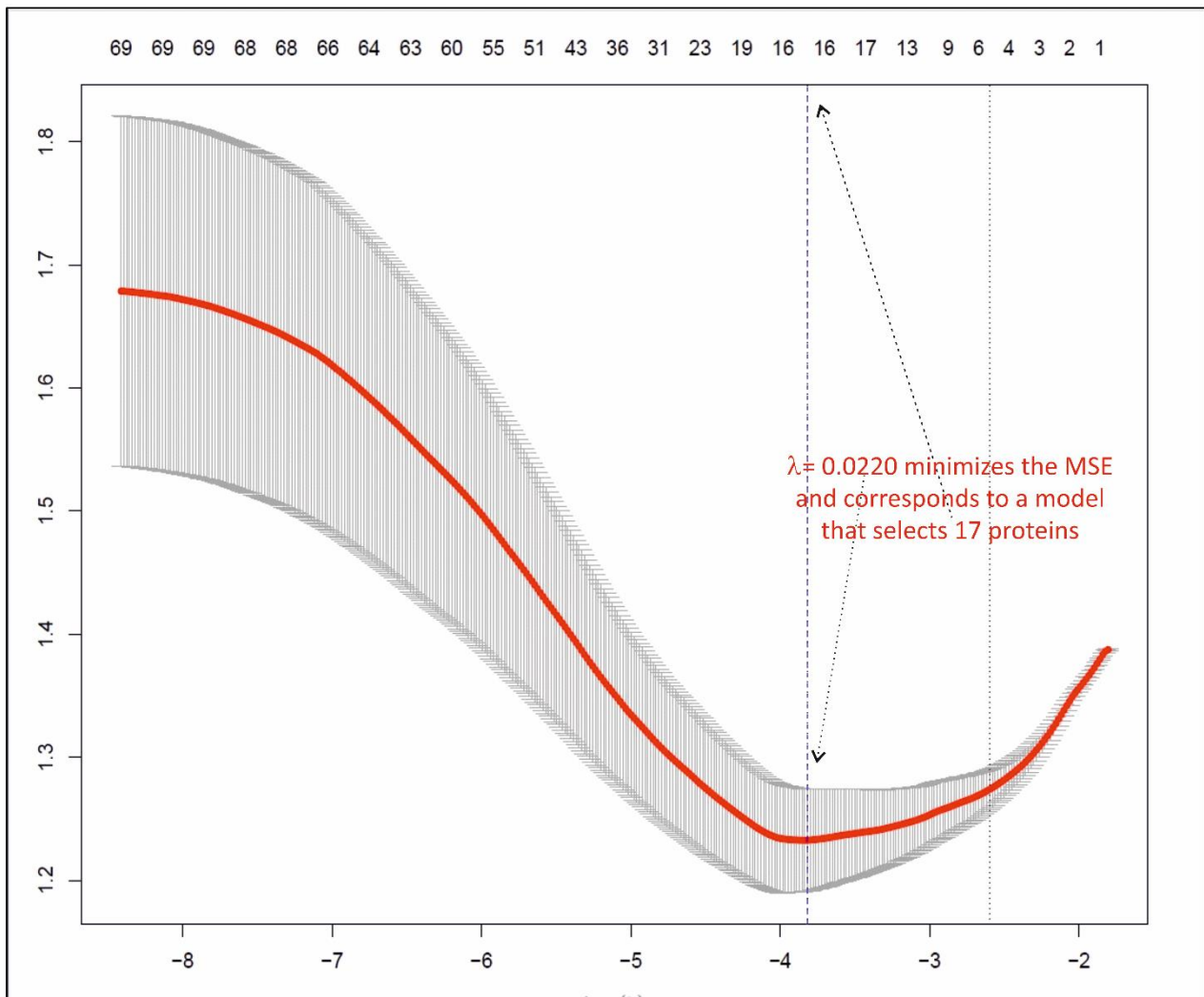
Additional Figure 1: Comparison between Italian and American patients with hEDS. (A) Distribution of the three diagnostic criteria required for an hEDS diagnosis, according to the 2017 EDS classification, in a total cohort of 176 patients: 88 Italian hEDS and 88 American hEDS individuals. (B) Distribution of comorbid conditions in the same cohort. *Indicates statistically significant differences between Italian and American hEDS patients.



Additional Figure 2: Comparison between Italian and American patients with HSD. (A) Distribution of the three diagnostic criteria required for an hEDS diagnosis, according to the 2017 EDS classification, in a total cohort of 176 patients: 88 Italian HSD and 88 American HSD individuals. (B) Distribution of comorbid conditions in the same cohort. *Indicates statistically significant differences between Italian and American HSD patients.



Additional Figure 3: Serum protein dysregulation in patients with hEDS and HSD compared to healthy controls. **(A)** Volcano plot showing 54 DEPs in serum samples from 88 hEDS patients (44 Italian and 44 American) compared to 176 healthy controls. Among these, 35 proteins were upregulated and 19 downregulated. Pie charts display the distribution of upregulated and downregulated DEPs across the five Olink protein panels. **(B)** Volcano plot showing 49 DEPs in serum samples from 88 HSD patients (44 Italian and 44 American) compared to 176 healthy controls, with 46 upregulated and 3 downregulated proteins. Pie charts display the distribution of these DEPs across the same Olink panels.



Additional Figure 4. Cross-validation procedure for identifying the optimal λ parameter used by LASSO for selecting a limited number of proteins