To calculate the DS-specific GRS, we reweighted each locus in the Sharp GRS using the genotypes of the HTP cohort. New weights were determined using iterative leave-one-out cross validation of logistic regression models. Specifically, for 1,000 iterations at each locus, a random subsample with 1 fewer cases and a selection of controls preserving the original case/control ratio (i.e., 0.1) were input into a logistic regression model with celiac disease status as the binary outcome variable and the SNP dosage as the predictor. The odds ratios for the best performing models, as determined by significance, served as weights in the DS-specific GRS.

The weight of any locus with complete separation cases and controls by genotype was set to 0 to avoid biasing the model.