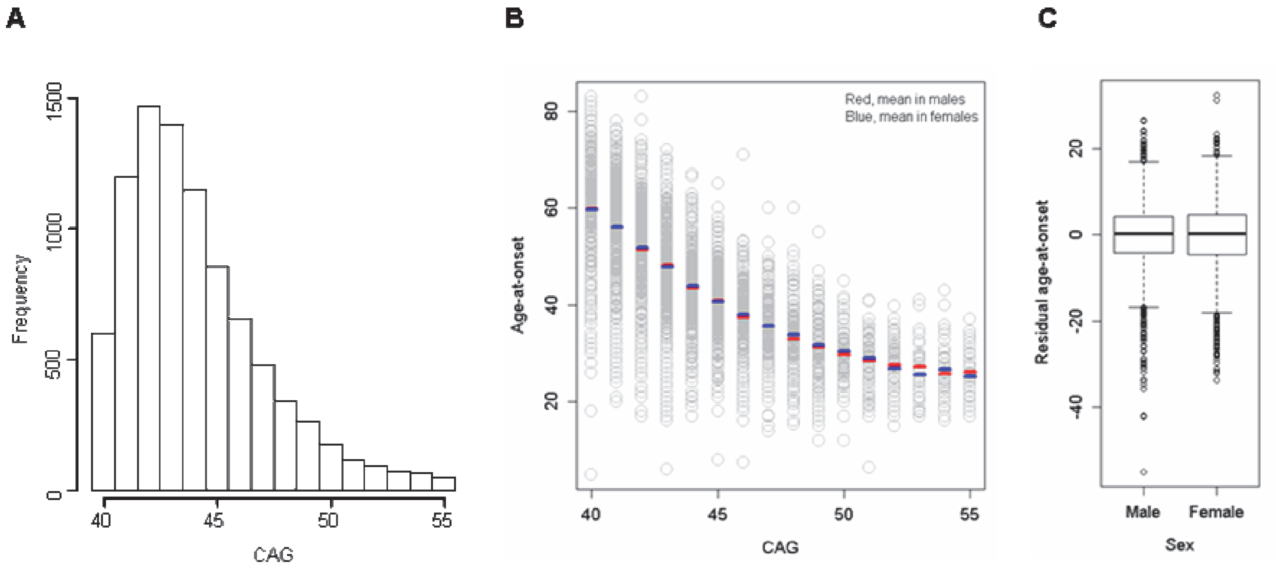
S. Figure 1. CAG, age-at-onset, and residual age-at-onset of study subjects.

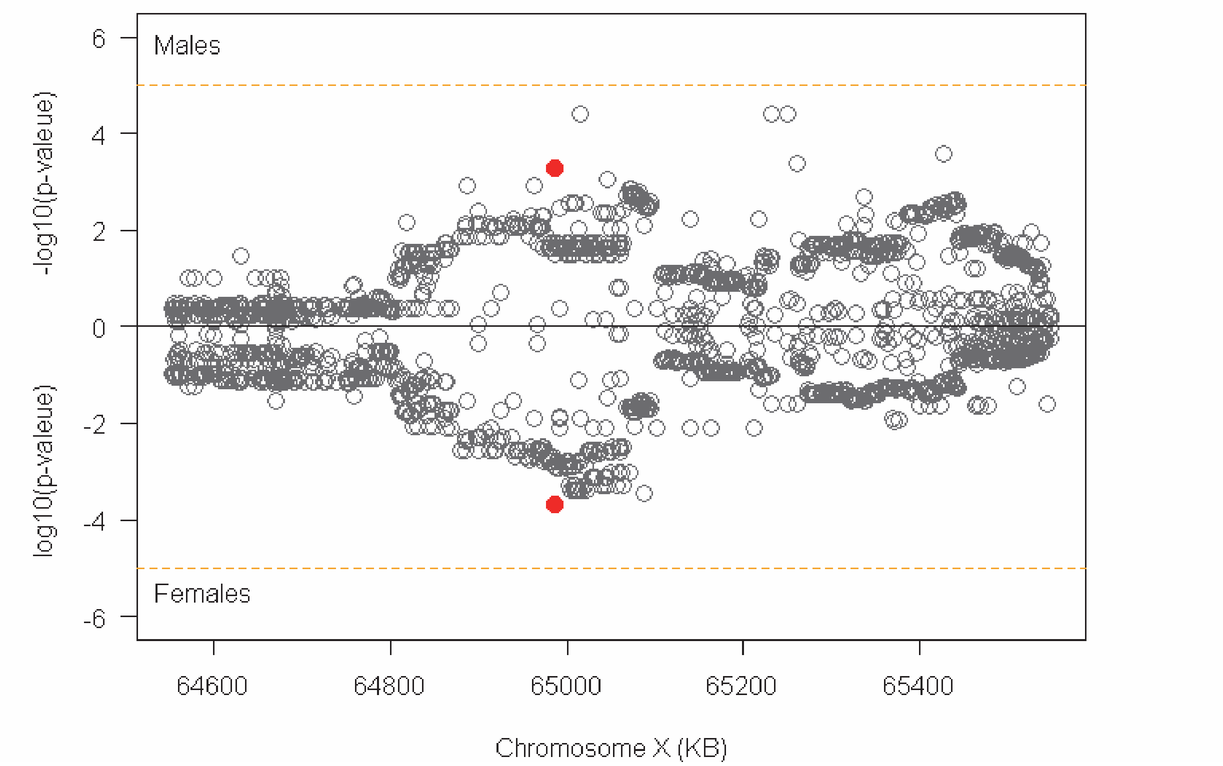


(A) A total of 8,963 HD subjects passed quality control analysis for chromosome X genotype imputation. We analyzed HD subjects carrying CAG repeats between 40 and 55 for XWAS analysis.

(B) Age-at-onset (Y-axis) was compared to CAG repeat size (X-axis). For a given CAG repeat size, mean values of age-at-onset for males (red bar) and females (blue bar) are displayed.

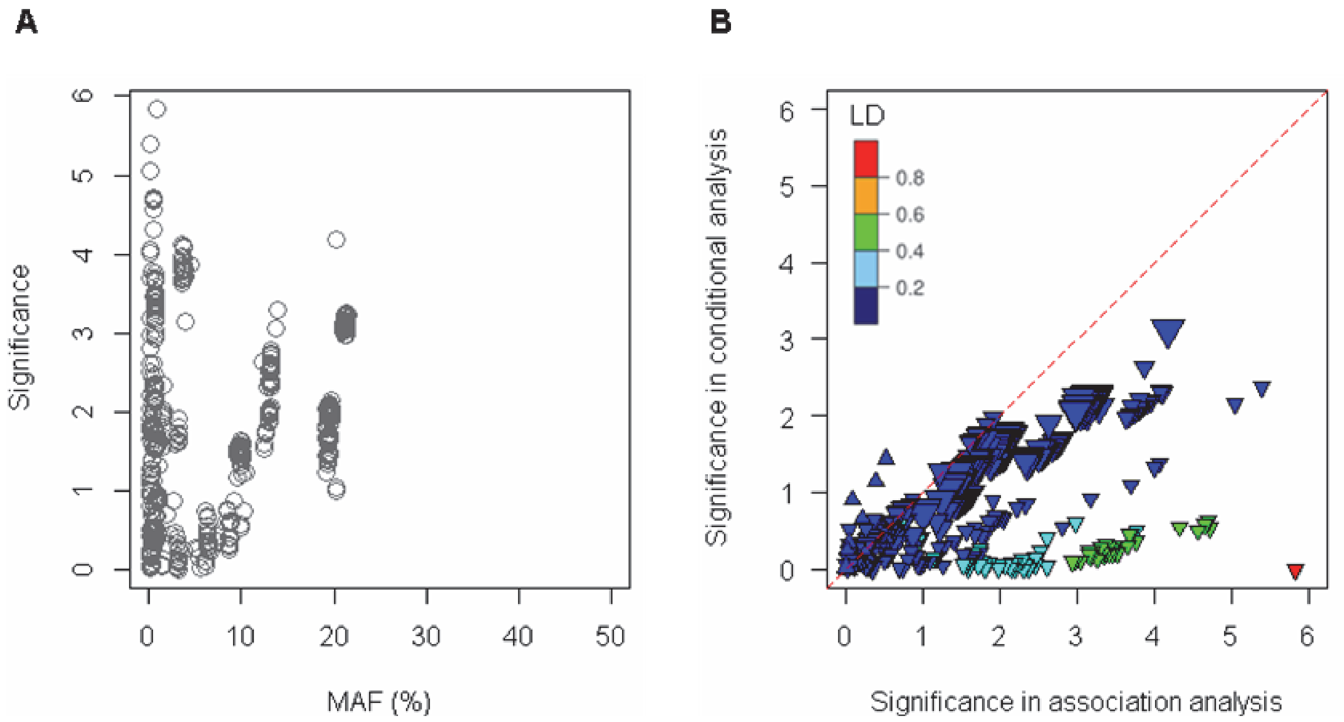
(C) For each study participant, residual age-at-onset was calculated by subtracting expected age-at-onset based on individual CAG repeat from observed age-at-onset. The distributions of residual age-at-onset of male and female HD subjects are plotted and compared by Student t-test (p-value, 0.5415).

S. Figure 2. Male- and female-specific XWAS analysis in the Xq12 region.



Male- (top panel) and female-specific (bottom panel) XWAS analysis results are shown for the Xq12 region. Filled red circles represent rs59098970 that generated the smallest association p-value in the combined XWAS analysis. Orange horizontal lines indicate suggestive significance.

S. Figure 3. Conditional analysis of the Xq12 region.



A) Significance (-log10(p-value)) in our XWAS analysis (Y-axis) was compared to minor allele frequency (X-axis) of SNPs in the Xq12 region.

B) To determine the independence of suggestive association signals, we performed conditional analysis using rs59098970. The Y-axis and X-axis represent significances in conditional and standard XWAS analysis, respectively. Upward and downward triangles represent SNPs whose minor alleles are associated with delayed and hastened age-at-onset, respectively. The sizes of triangles are proportional to MAF.