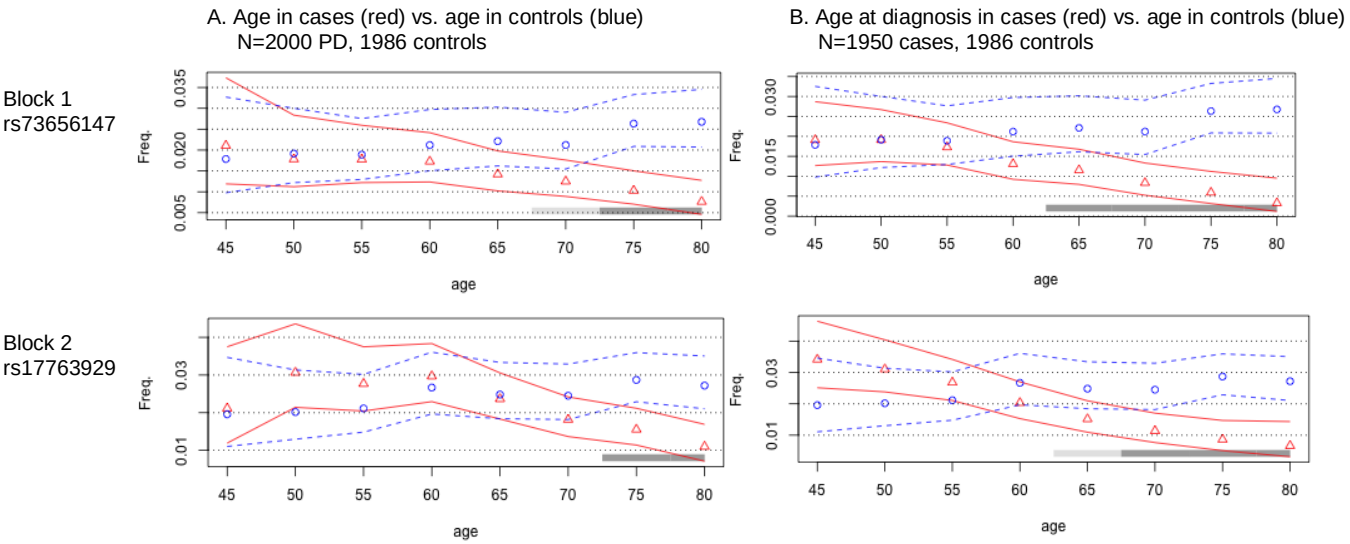
Figure e-3. Moving average allele frequency plots (MAP) of PD-associated variants in *LPPR1*



To visualize the dynamics of allele frequency changes as a function of age and age-at-diagnosis, average minor allele frequencies (MAF) were plotted in a moving window across the age spectrum, using MAP software (freqMAP_v_0.2 in R). NGRC dataset was used. Average MAF (and 95% central posterior interval) was plotted by age in controls (blue circles, N=1986), and age (panel A, N=2000) or age-at-diagnosis (panel B, N=1950) in patients (red triangles). Ages and ages-at-diagnosis ≤45 were collapsed to 45, and ≥80 were collapsed to 80. Significance of difference in MAF between cases and controls is shown by a light gray bar (≥95% posterior probability) or dark gray bar (≥99% posterior probability). The patterns show minor allele frequencies declined by increasing age and age-at-diagnosis in cases, but not in controls, which is consistent with pattern expected for a modifier. Specifically, the MAF for rs73656147 started at ~0.02 at age 45 in both cases and controls and declined steadily as a function of age and age-at-diagnosis in cases, but not in controls, ending at age 80, with MAF~0.009 in cases and MAF~0.028 in controls. The MAF for rs17763929 started at ~0.03 in cases and ~0.02 in controls, decreased by age and age-at-diagnosis in cases but not in controls, ending by age 80 at MAF~0.01 in cases and ~0.03 in controls. Based on statistics (grey bars here, and conditional analysis in **table 2**), the decline in MAF is significant in cases for both SNPs, is driven by age-at-diagnosis, and retains significance when adjusted for age. Conditional analysis (**table 2**) suggests the primary driver of allele frequency decline is the association with age-at-diagnosis, and that the age effect in cases is a by-product of the correlation between age and age-at-diagnosis.