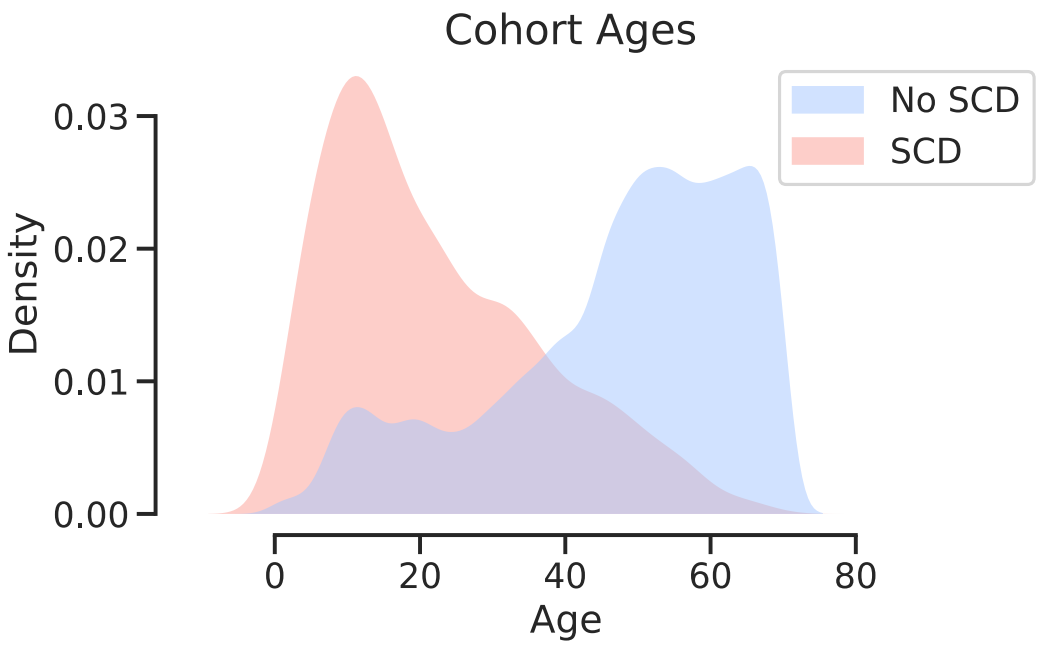
Supplemental Figure 1



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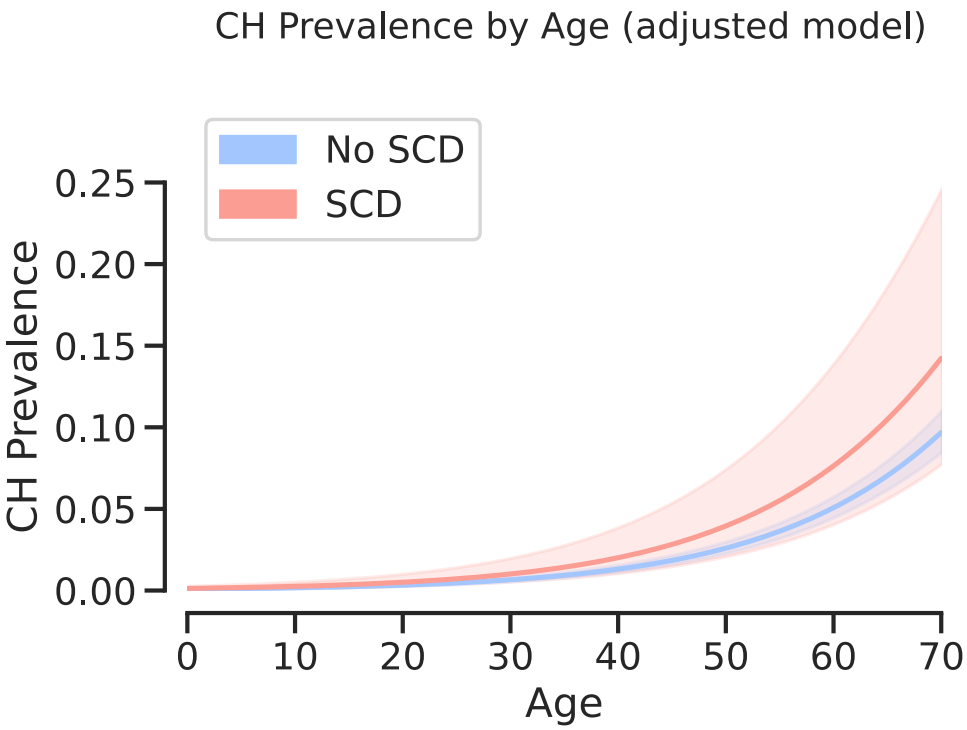

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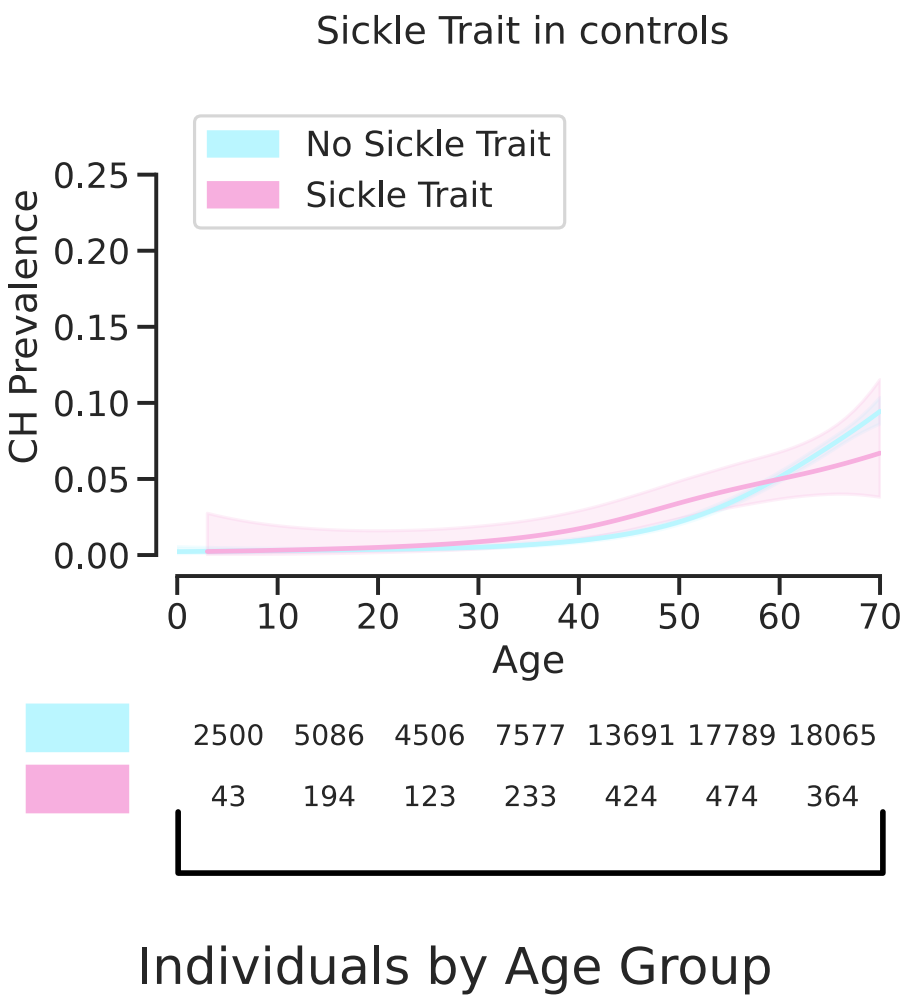

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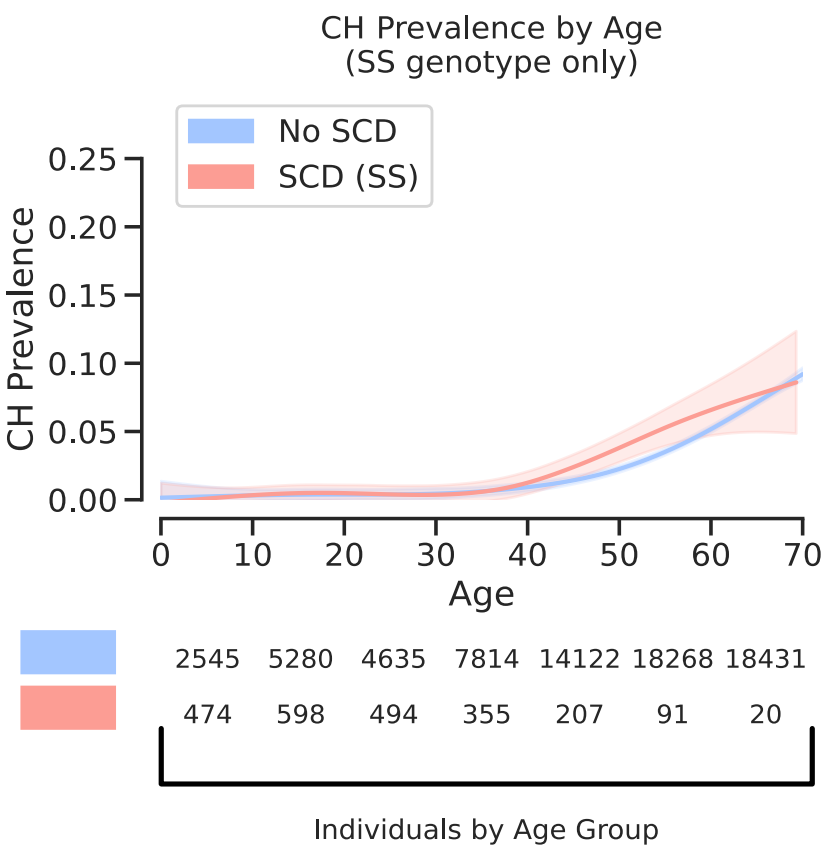

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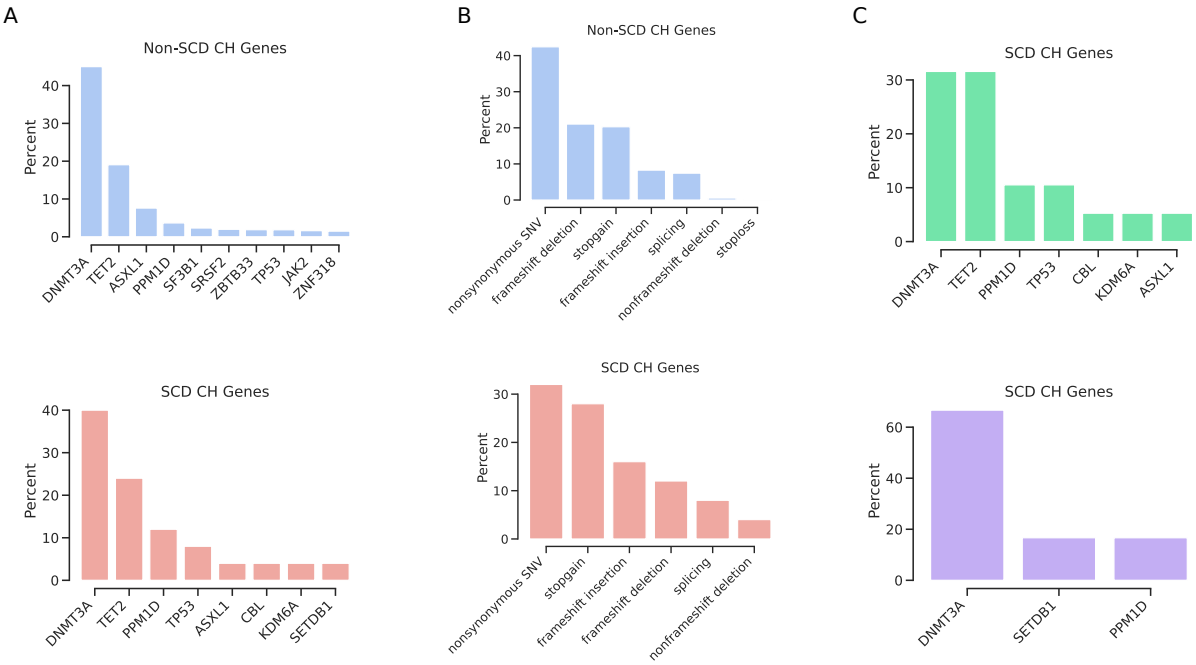

Supplemental Figure 6

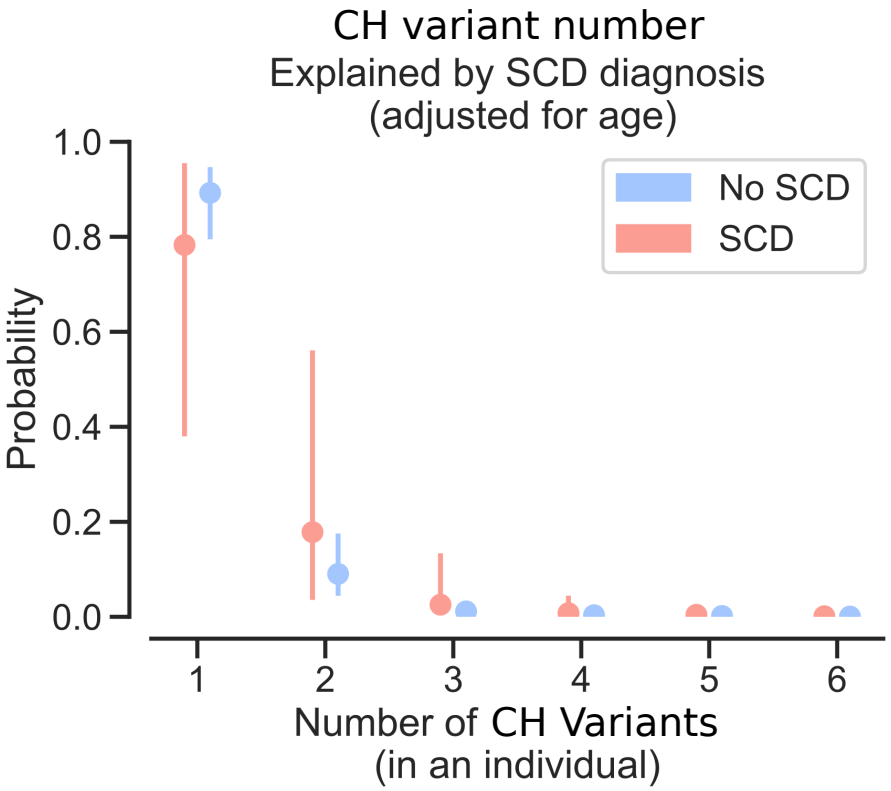

Figure Legends

Supplemental Figure 1. Cohort age distributions. Age distributions of all individuals combined from each of the TOPMed cohorts used in this study, separated by SCD status into those without SCD (blue) and those with SCD (red).

Supplemental Figure 2. A logistic regression model for effect estimates that is adjusted for age, age^2, sex, study, and the first 10 principal components separated by SCD status into those without SCD (blue) and those with SCD (red).

Supplemental Figure 3. CH prevalence when accounting for sickle cell trait. From the group of all control individuals, those individuals who were heterozygous for the sickle cell trait (rs334) SNP are classified as having the sickle cell trait (pink) and those without it are classified as having no sickle cell trait (blue). Even when accounting for the rs334 SNP, there is no significant difference between the two groups.

Supplemental Figure 4. CH prevalence in SS SCD subgroup. Homozygous SS SCD genotypes alone do not show elevated prevalence of CH compared with unaffected individuals (OR=1.34, p=0.22).

Supplemental Figure 5. (**A**) Genes ranked by variant load across all individuals separated by SCD status into unaffected (blue) and affected (red). Percent shown on the y-axis refers to the percent of all observed CH related mutations found within each of the genes shown along the x-axis. (**B**) Type of genetic change ranked by prevalence in all individuals, as a percent of all observed CH related mutations, separated by SCD status into unaffected (blue) and affected (red). (**C**) Genes ranked by variant load across all individuals, as a percent of all observed CH related mutations, with SCD separated by HU treatment status into untreated (green) and treated (purple).

Supplemental Figure 6. CH clone load per individual is unchanged by SCD. Number of variants per individual classified as indicative of CH appear at similar rates in unaffected individuals and individuals with SCD.

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Details provided here for TOPMed are available at https://topmed.nhlbi.nih.gov/topmed-banner-authorship. The TOPMed banner, NHLBI Trans-Omics for Precision Medicine (TOPMed) Consortium, is used to acknowledge individuals who contributed to the overall conduct of TOPMed but do not otherwise meet criteria for by-line authorship for a given manuscript:

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