Supplementary Material

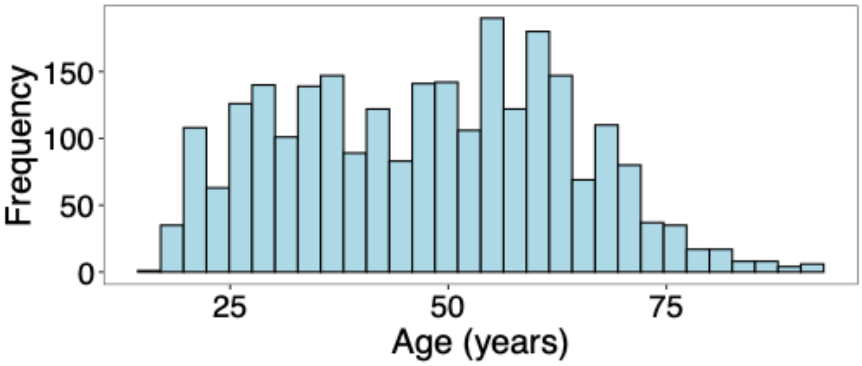

Figure S1. Distribution of age (years) for All of Us participants (n=2,573)

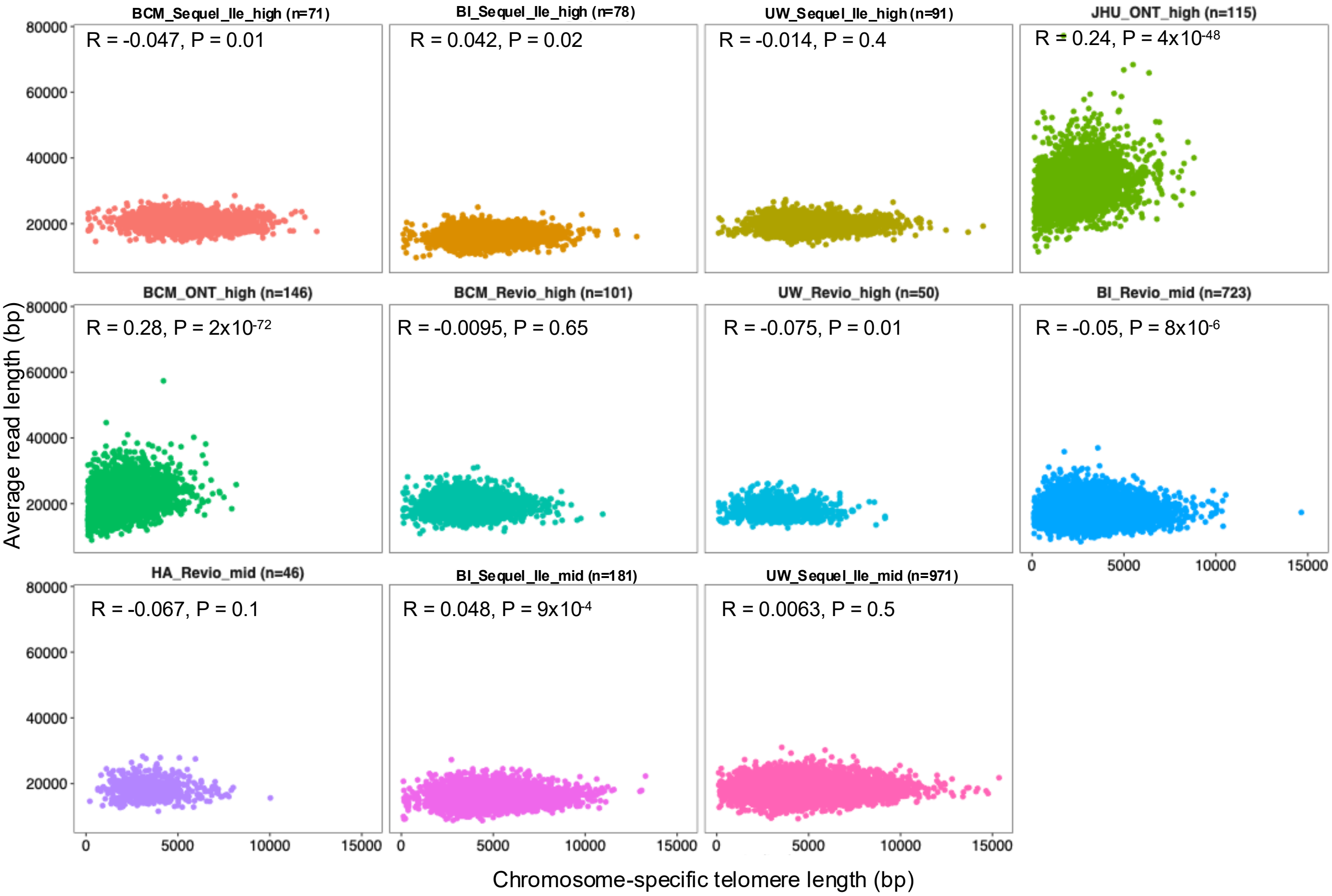

Figure S2. Read length shows moderate correlations with csTLs in ONT samples only. Scatterplot showing the correlation between average read length (length of reads used for estimating csTL) and corresponding csTLs. Pearson correlation and P value displayed.

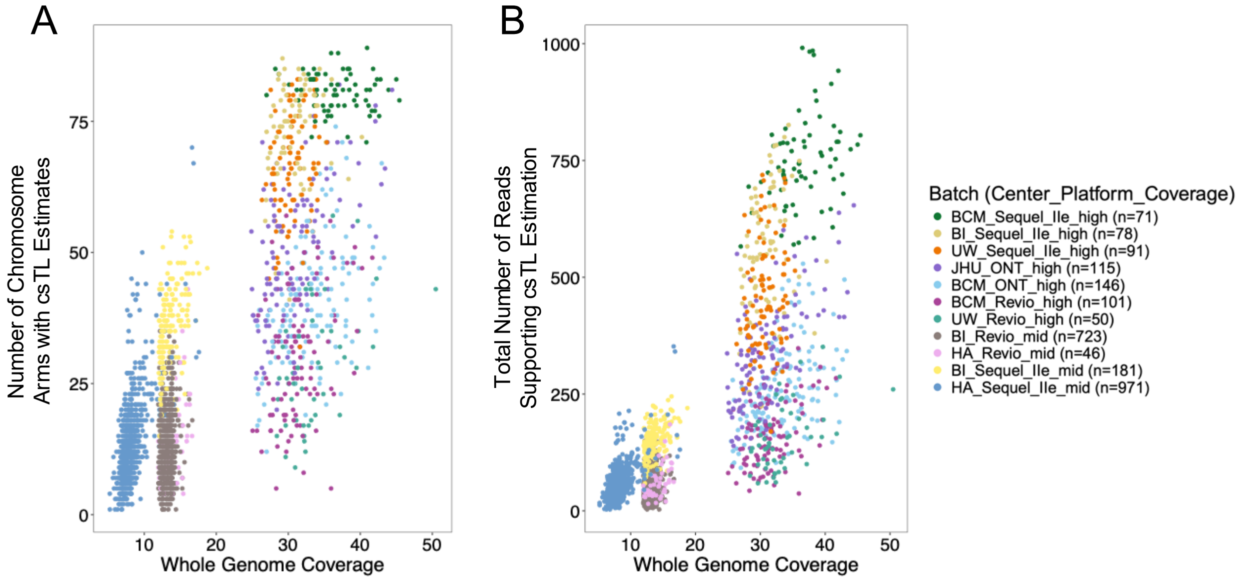

Figure S3. Telogator2 performance shows inter-sample variability independent of whole-genome coverage. Scatterplots showing the relationship between whole-genome coverage and (A) the number of chromosome arms with csTL estimates, (B) total number of reads supporting csTL estimation. Dot colors represent batch.

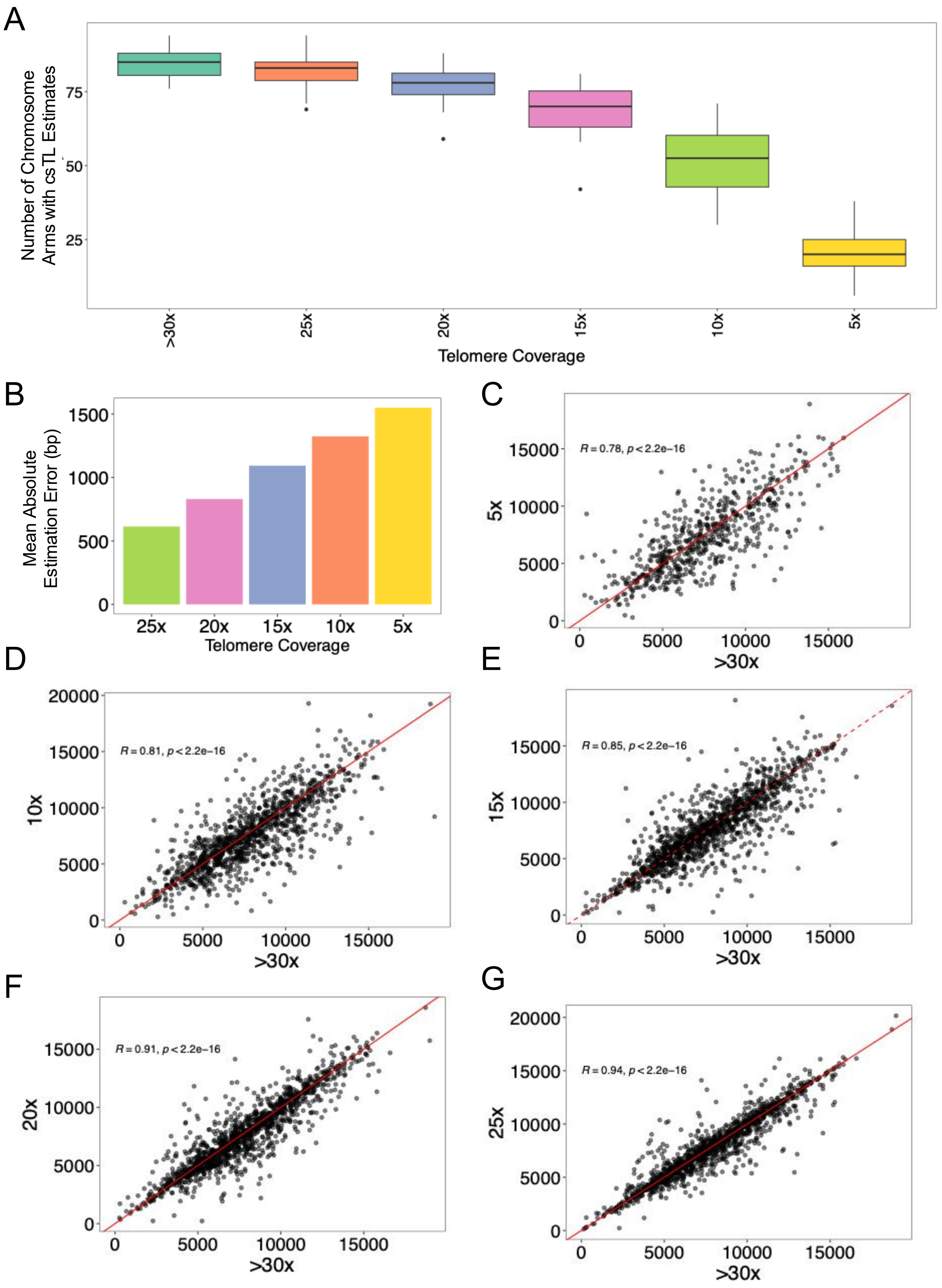

Figure S4. Telogator2 performance across different telomere coverage levels in HPRC samples (n = 36). (A) Box plot showing the number of chromosome arms with csTL estimates across telomere coverage levels. (B) Bar plot showing mean absolute estimation error between high-coverage (>30x) and down-sampled telomeric coverage levels. (C–G) Scatterplots comparing csTLs between >30× coverage and down-sampled telomeric coverage levels of (C) 5×, (D) 10×, (E) 15×, (F) 20× , and (G) 25×.

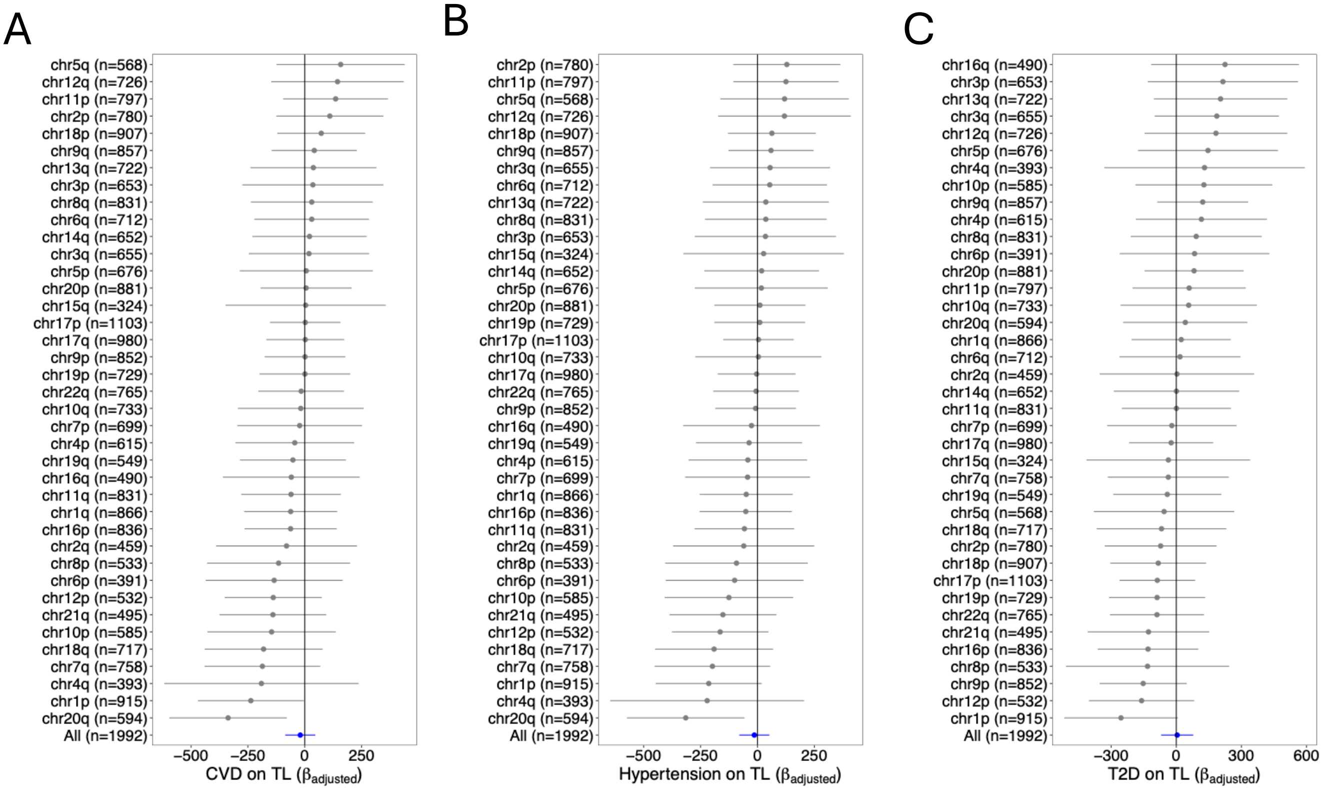

Figure S5. Associations between chronic disease status and csTL at individual chromosome arms and across all arms (in blue). Results are shown for (A) cardiovascular disease (844 cases, 1,148 controls), (B) hypertension (832 cases, 1,160 controls), and (C) type 2 diabetes (452 cases, 1,540 controls).

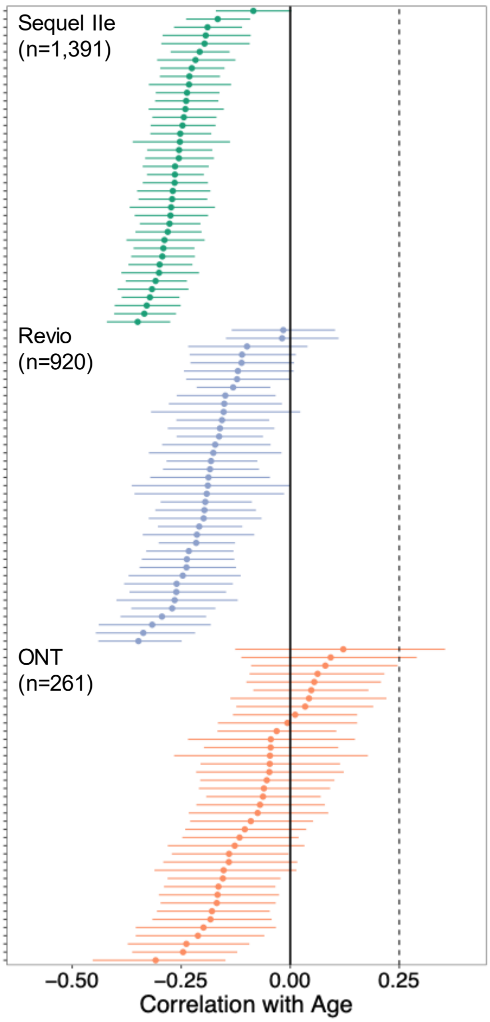

Figure S6. ONT-derived csTLs show weaker associations with Age compared to PacBio-derived csTLs. Forest plot showing Pearson correlations and 95% confidence intervals for the association between age (years) and csTLs for each batch. Batches are aggregated by sequencing platform.

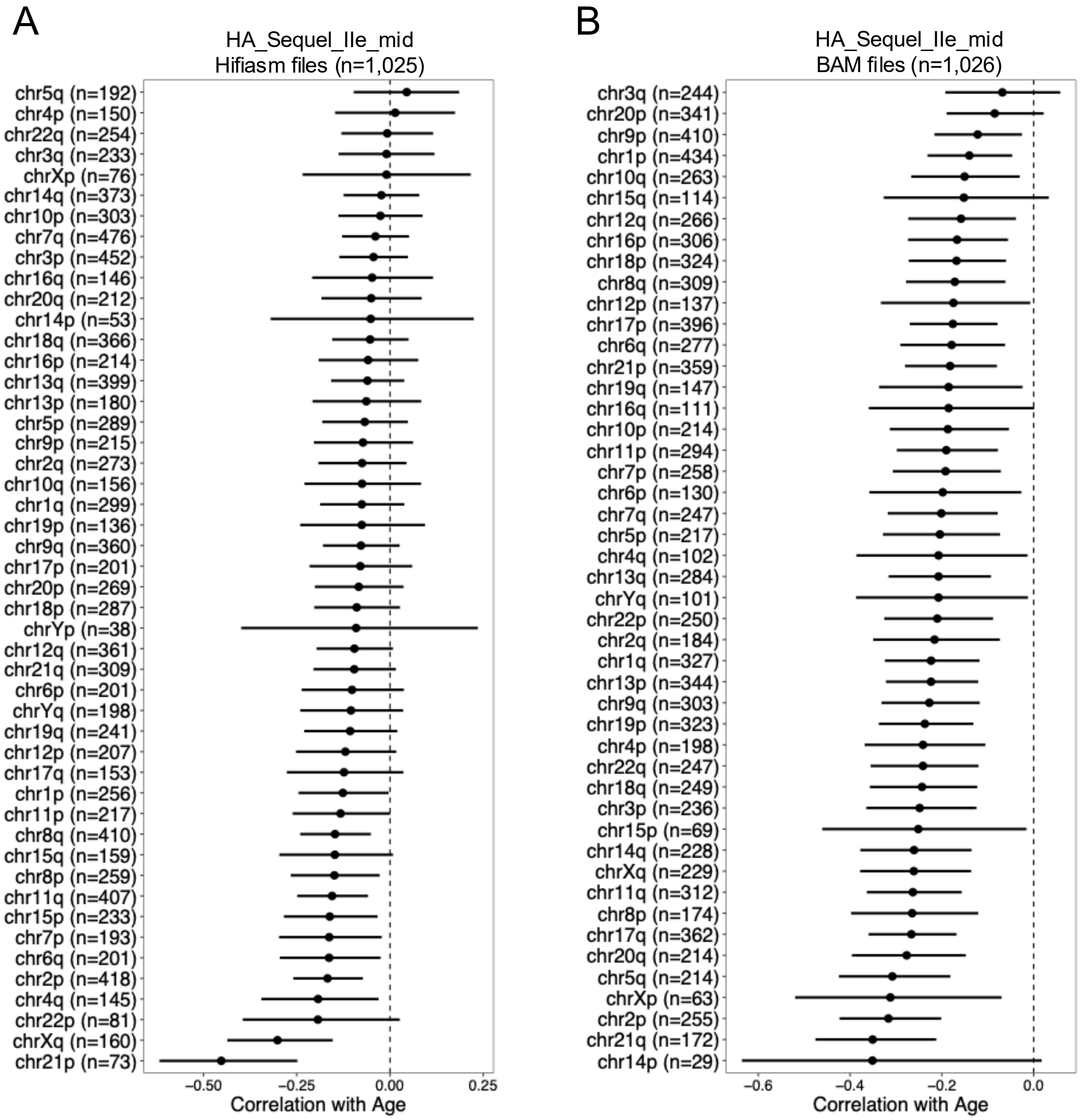

Figure S7. BAM-based csTLs correlate more strongly with Age than hifiasm-based csTLs. Forest plot showing Pearson correlations and 95% confidence intervals for the association between age (years) and csTLs for Hudson Alpha Institute (HA), Sequel IIe, mid-coverage samples, using (A) Hifiasm files as input for (n=1,025) and (B) BAM files as input (n=1,026)

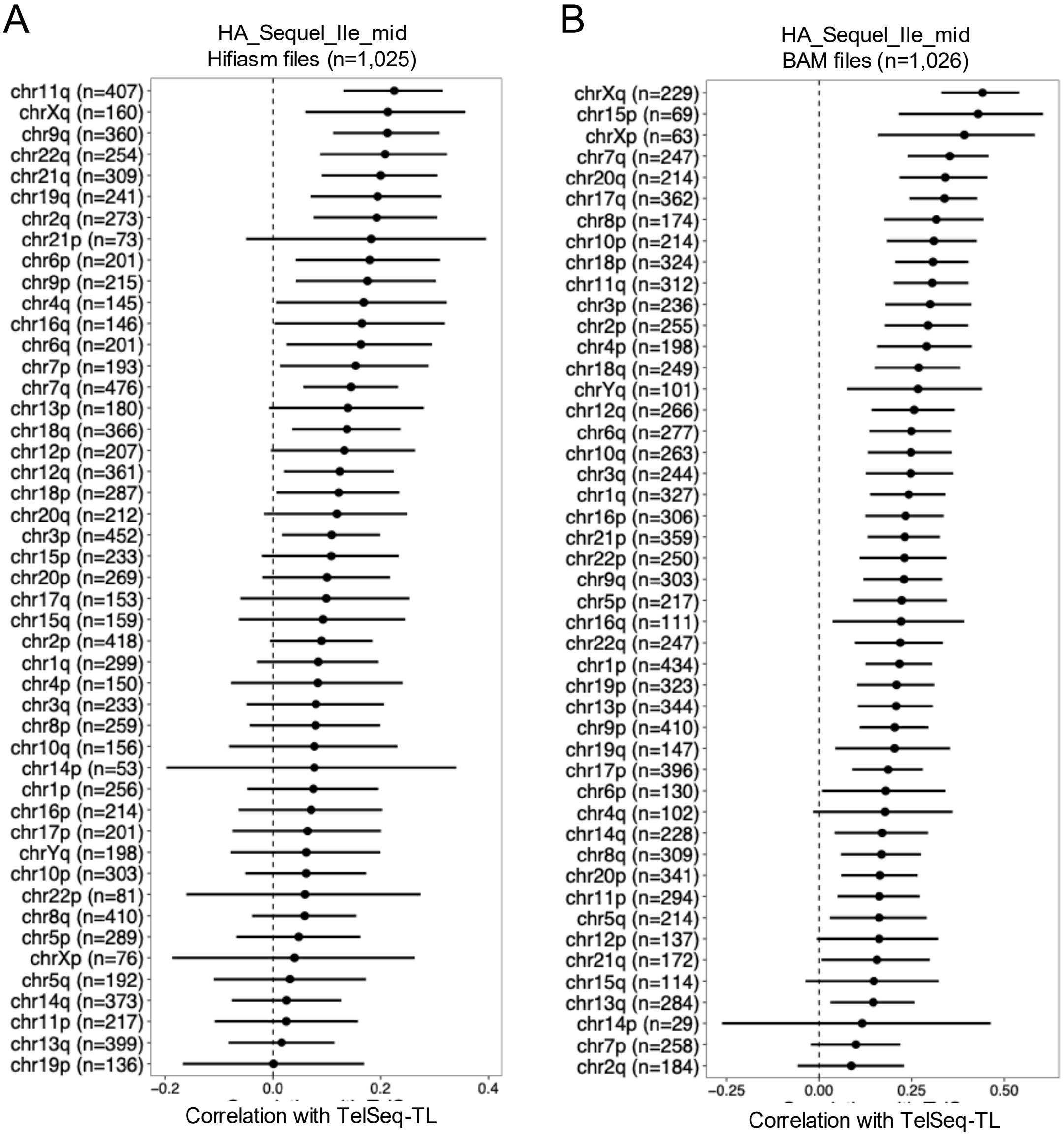

Figure S8. BAM-based csTLs correlate more strongly with TelSeq-TL than hifiasm-based csTLs. Forest plot showing Pearson correlations and 95% confidence intervals for the association between TelSeq-TL and csTL estimates for Hudson Alpha Institute (HA), Sequel IIe, mid-coverage samples, using (A) Hifiasm files as input for (n=1,025) and (B) BAM files as input (n=1,026)

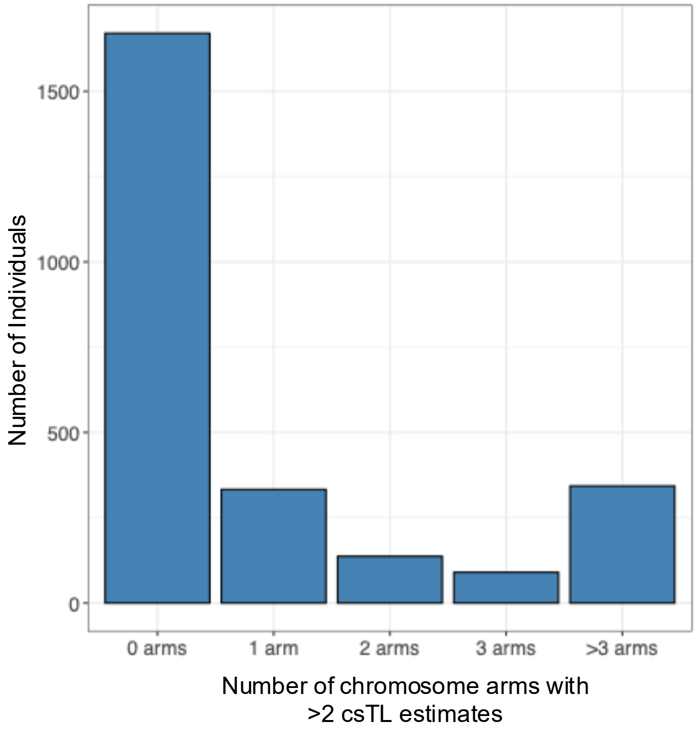

Figure S9. Most individuals have zero chromosome arms with >2 csTL estimates. Bar plot showing the distribution of individuals based on the number of chromosome arms they harbor with more than two csTL estimates.

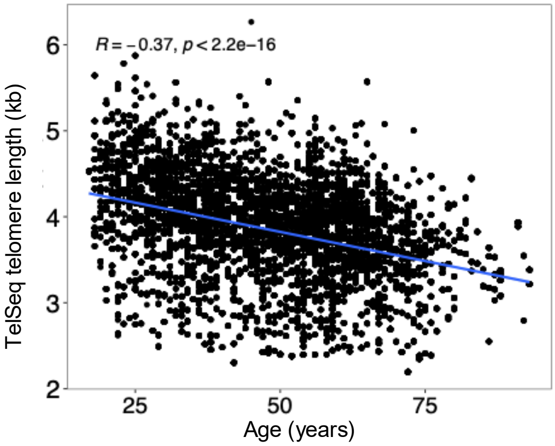

Figure S10. Age is negatively correlated with TelSeq-TL. Scatterplot show the correlation between age (years) and TelSeq-TL. Pearson R and P value displayed.

Table S9. Clinical codes extracted from the All of Us Researcher Workbench for disease identification.

	ICD-10	**ICD-9**
Cardiovascular Disease		
• Hypertension	I10, I11, I12, I13, I15	401, 402, 403, 404, 405
• Ischemic Heart Disease	I20, I21, I22, I25	410, 411, 413, 414
• Heart Failure	I50	428
	Concept ID	
Type 2 Diabetes	201826, 4008576, 4193704, 443732	