Longer genotypically-estimated leukocyte telomere length is associated with increased adult glioma risk

Supplementary Material

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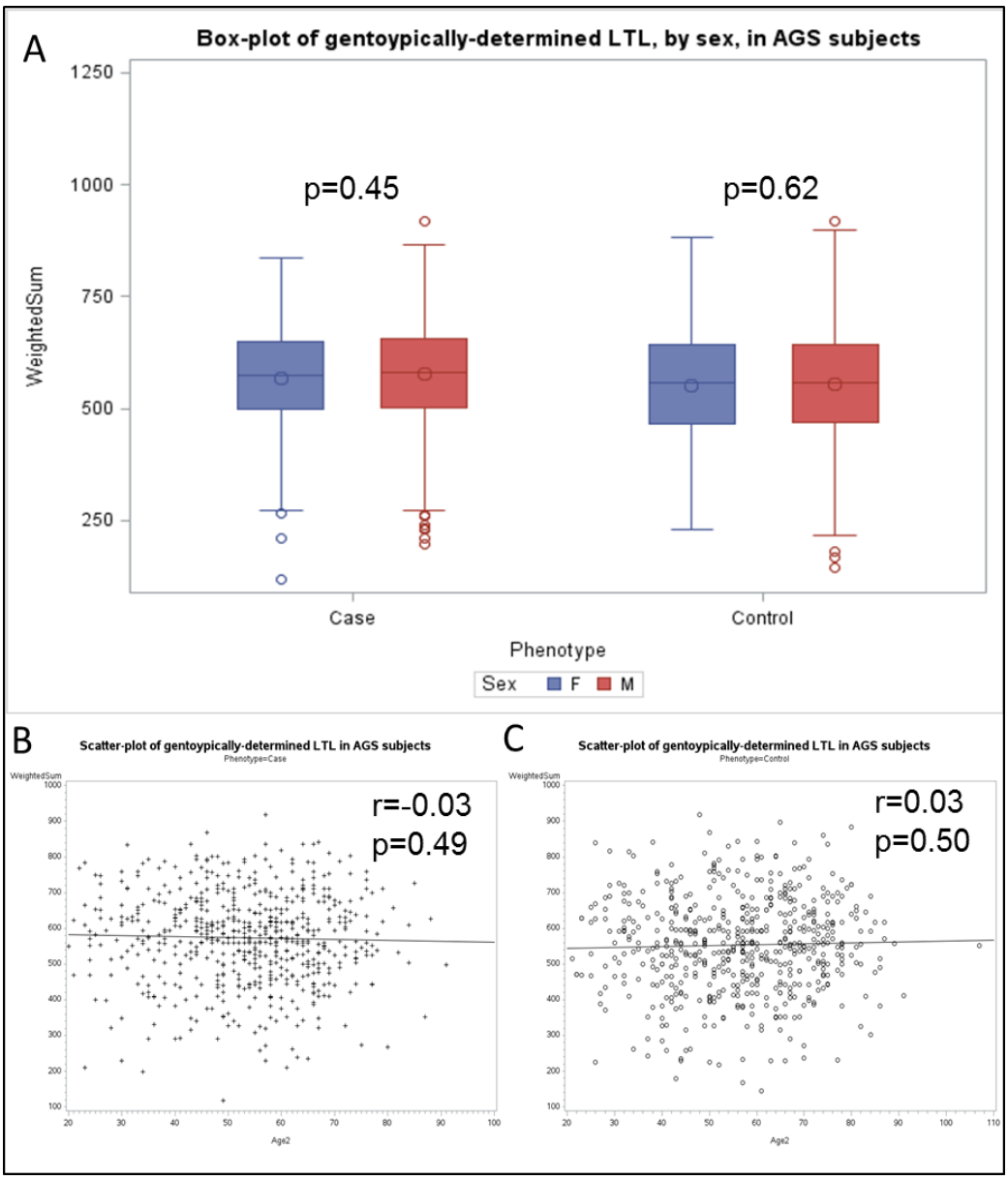
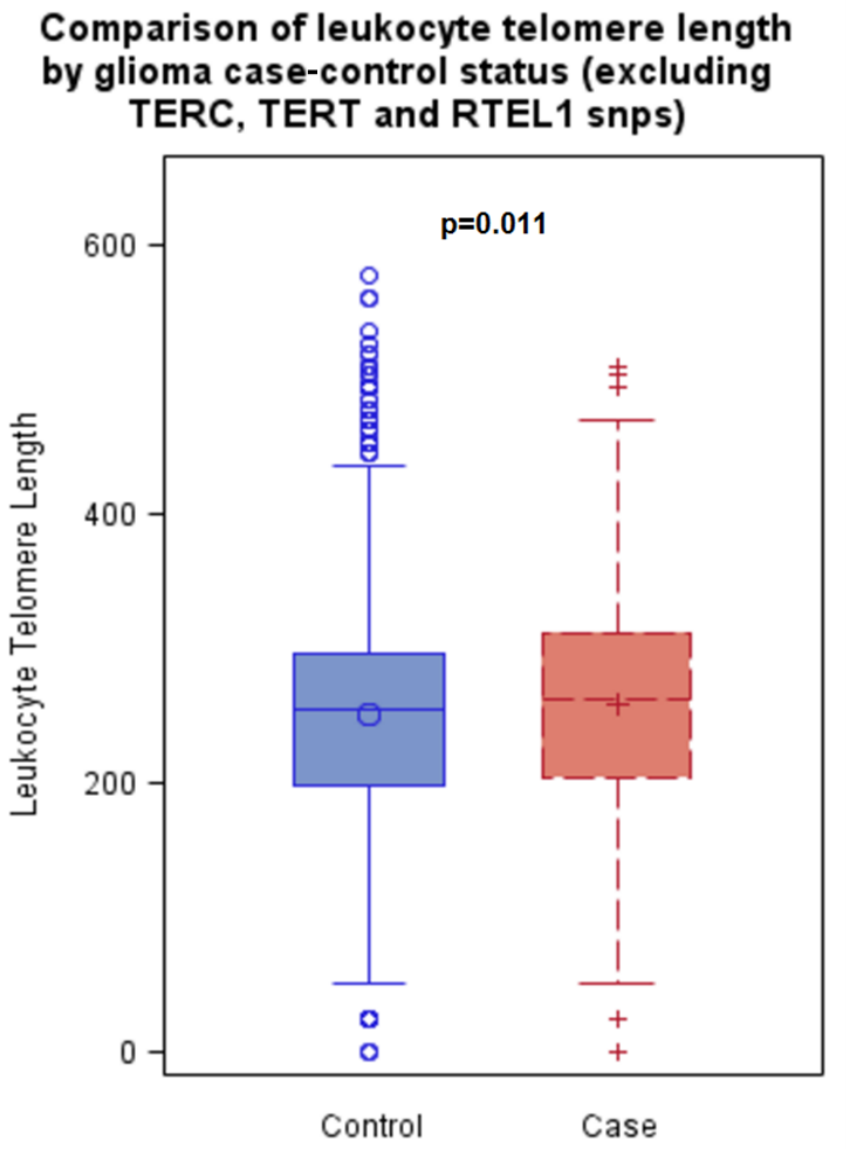
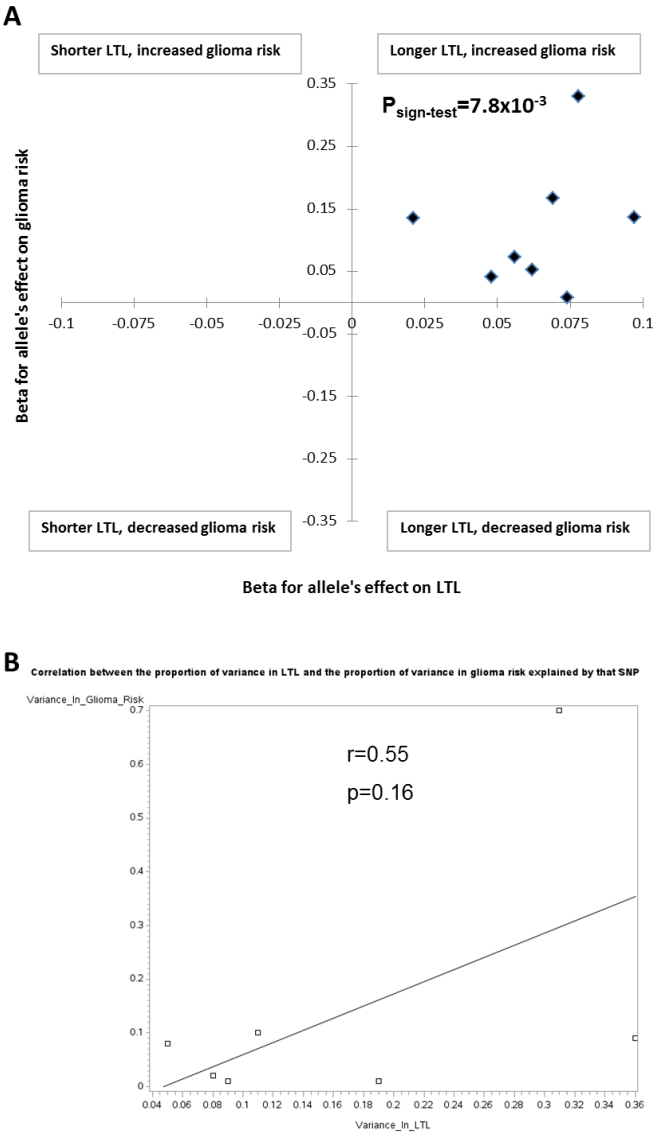


Supplementary Figure 1: Genotypically-estimated leukocyte telomere length (LTL) is not associated with subject age or sex. (A) Boxplots comparing genotypically-estimated LTL in females (blue) and males (red), stratified by glioma case-control status, in AGS subjects. (B) Scatter-plot of genotypically-estimated LTL and subject age in AGS glioma patients. (C) Scatter-plot of genotypically-estimated LTL and subject age in AGS glioma controls.



Supplementary Figure 2: Boxplot comparing genotypically-estimated leukocyte telomere length (LTL) in 1130 glioma patients and 6294 controls from the UCSF AGS, TCGA, and WTCCC after excluding contributions from known glioma risk genes (*TERC*, *TERT*, and *RTEL1*) and retaining contributions from *ACYP2*, *NAF1*, *OBFC1*, *CTC1* and *ZNF208*. P-values are adjusted for the first two ancestry-informative principal components and for genotyping platform.



Supplementary Figure 3. Associations between the effects of eight SNPs on leukocyte telomere length (LTL) in the ENGAGE Consortium and glioma risk in the UCSF AGS, TCGA, and WTCCC. (A) For all eight LTL-associated SNPs, the allele associated with longer LTL was associated with increased glioma risk ($P_{sign-test}=7.8x10^{-3}$). (B) The proportion of variance in LTL explained by each SNP was positively but non-significantly correlated with the proportion of variance in glioma risk explained by that SNP (r=0.55, P=0.16). The proportion of variance explained is expressed as a percentage.

Supplementary Table 1. Subject characteristics of glioma patients and controls, the University of California, San Francisco (UCSF) Bay Area Adult Glioma Study (AGS) 1997-2011, Illumina iControls, The Cancer Genome Atlas (TCGA) glioma patients and Wellcome Trust (WTCCC) controls.

Populations	N (cases/controls)	Histopathology	Genotyping array	Ethnicity	% Female (cases/controls)	Median Age (cases/controls)
Discovery						
UCSF Adult Glioma Study	620 / 602	Glioblastoma (85%)[a]	Illumina 370k	Caucasian	36% / 47%	56 / 57
TCGA glioblastoma cases	70 / 0	Glioblastoma	Illumina 550k	Caucasian	43% / -	55 / -
Illumina iControls	0 / 3390	-	Illumina 370k/550k	Caucasian	- / 63%	- / 31
Validation						
TCGA glioblastoma cases	323 / 0	Glioblastoma	Affymetrix 6.0	Caucasian	38% / -	60 / -
TCGA lower-grade glioma	176 / 0	Grade II/III Glioma[b]	Affymetrix 6.0	Caucasian	41% / -	43 / -
Wellcome Trust controls	0 / 2603	-	Affymetrix 6.0	Caucasian	- / 48%	- / -[c]

[a] 15% of the high-grade glioma samples were Grade 3 anaplastic astrocytomas

[b] 35% astrocytoma, 39% oligodendroglioma, 25% mixed oligoastrocytoma

[c] Precise age data were unavailable, but >50% of the included samples were members of the 1958 UK Birth Cohort.