Research Paper

Racial and Socioeconomic Variation in Genetic Markers of Telomere Length: A Cross-Sectional Study of U.S. Older Adults

Rita Hamad a,b, Shripad Tuljapurkar b, David H. Rehkopf a

a Stanford University, Department of Medicine, 1070 Arastradero Road, Palo Alto, CA 94304, USA
b Stanford University, Biology Department, Herrin Labs 454, Stanford, CA 94305, USA

1. Introduction

Telomeres are DNA-protein structures that include a repeated nucleotide sequence at the ends of eukaryotic chromosomes, acting to prevent the degradation of functional DNA sequences during cellular replication (Olovnikov, 1973). Shortening of telomeres in human cells in vitro has been shown to lead to cellular dysfunction, senescence, and cell death (Allsopp and Harley, 1995; Blackburn, 2000). Telomere length (TL) has therefore been hypothesized to be a marker of human aging and chronic disease (Zhu et al., 2011a; Hamad et al., 2016). Observational studies in human populations have built on this molecular basis and have shown that chronic and acute stressors, including adverse socioeconomic conditions, are associated with shorter TL, suggesting that TL acts as a marker of biological aging, even if it is not a causal relationship.

The observational literature contains many investigations of racial differences in human TL, with findings that seem to contradict the association between shorter TL and stress. The majority of studies have found that U.S. blacks have longer telomeres than whites, despite on average lower socioeconomic position (SEP) and presumably higher levels of stressors (Adler et al., 2013; Diaz et al., 2010; Hunt et al., 2008; Needham et al., 2013). Research has shown that this is likely the case beginning at birth: several studies have found longer telomeres among black newborns and adolescents, ostensibly before life stressors can accumulate (Rewak et al., 2014; Zhu et al., 2011b), although a single study found similar TL among black and white newborns (Okuda et al., 2002). A smaller number of studies suggest that blacks have shorter TL compared to whites (Diez roux et al., 2009; Geronimus et al., 2010), while others demonstrate more rapid shortening of telomeres among blacks over the life course (Hunt et al., 2008; Rewak et al., 2014).

While it is assumed that most demographic differences in TL are due to environmental factors, this prior evidence is difficult to reconcile with current knowledge of the determinants of TL. A growing body of research has begun to elucidate genetic markers – i.e., single nucleotide polymorphisms (SNPs) – associated with TL, many of which fall in genes known to act on telomere biology (Codd et al., 2013; Levy et al., 2014).
Yet the majority of these studies have been conducted among white or Asian populations, with few examining racial differences in the prevalence of these markers that might explain TL differences across the life course. One prior abstract examined racial differences in TL-associated genetic markers, finding that SNPs strongly associated with TL in whites were only weakly associated when replications were conducted in other racial groups (Kvale et al., 2012). Another included African American participants in a replication sample, but did not conduct comparative analyses as we do here (Levy et al., 2010). In fact, the lack of attention to cataloguing SNPs in populations of African ancestry has been identified as a major gap in the literature: only 4% of genome-wide association studies have been conducted among individuals of non-European descent (Bustamante et al., 2011), although prior research documents racial differences in a variety of genetic markers across the genome (Jorgenson et al., 2005).

This study is one of the first assessments of differences in the demographic distribution of TL-related SNPs identified in genome-wide association studies (GWAS), examining whether genetic makeup explains the variation in TL among various subgroups. We link genetic and survey data from the Health and Retirement Study, a nationally representative diverse U.S. sample, to test the hypothesis that there are differences in the prevalence of TL-associated SNPs in different racial and SEP subgroups.

2. Methods

2.1. Data Set

We used data from the U.S. Health and Retirement Study (HRS), a longitudinal panel study that has collected data biennially since 1992 among a representative sample of over 26,000 men and women over 50 years of age, with an over-sampling of older individuals. The survey also included data on respondents’ spouses, which includes individuals under 50 years of age. Details on the HRS, including survey design, have been previously described (Juster and Suzman, 1999). We restricted our analyses to individuals for whom we have data on genotype or TL (N = 11,934).

2.2. Measures

The primary outcome variable for this study was a polygenic risk score (PRS) composed of seven SNPs that were previously associated with TL in a genome-wide meta-analysis (Codd et al., 2013). Genetic data collected from respondents during the 2006 and 2008 study waves were used to construct this score (N = 11,143). Subjects provided DNA samples using a mouthwash technique, and genotyping was conducted by the NIH Center for Inherited Disease Research using the Illumina Human Omni-2.5 Quad beadchip, which includes roughly 2.5 million SNPs. Further information on quality control procedures is available from HRS. Of the almost 36,986 individuals interviewed by HRS since 1992, 8151 died before genetic testing became available. These individuals were more likely to be male, white, and less educated. Meanwhile, 17,692 of those who survived did not provide genetic samples because testing was not offered to them or because they refused. These individuals were more likely to be male, non-white, and less educated.

We constructed the PRS for each individual by forming the weighted sum of alleles for these seven SNPs. Weights were assigned using log-odds ratios for each SNP as reported by Codd et al. (Supplemental Table 1), according to the following formula:

$$\text{PRS}_i = \sum_{k=1}^{7} \beta_k \text{allele}_{ki}$$

Here, $\beta_k$ is the log-odds ratio for each of the seven SNPs $k$, and allele$_{ki}$ is the number of alleles present of SNP $k$ for a given individual $i$. We standardized the PRS to have a mean of zero and a standard deviation of one so that associations are more easily interpretable and comparable to other studies; the score itself is only slightly left-skewed. A higher value means that an individual is genetically predisposed to shorter telomeres. Prior research has suggested that analyses using a PRS may be more successful in predicting disease risk than use of individual genetic markers (Dudbridge, 2013). Of note, the meta-analysis by Codd et al. included only individuals of European descent.

The secondary outcome variable was mean TL, which was obtained in 2008 from HRS participants who consented to provide a saliva sample (N = 5808). Samples were analyzed by Telome Health using a standard quantitative polymerase chain reaction (PCR) assay. TL was measured in standard fashion, using the telomere-to-single copy gene (T/S) ratio. This ratio was determined by comparing the telomere sequence copy number (T) with a single-copy gene copy number (S). The equation for conversion of the T/S ratio to TL varies by lab, and for this study was: base pairs = (T/S) x 2400.

Covariates included race, age at genotype testing, gender, educational attainment, and total assets. Racial categories were self-reported and included non-Hispanic white (reference group), black, Hispanic, and other. Educational attainment was constructed as a categorical variable with four levels: less than high school education (reference group), high school or GED completed, some college, and college completed. Total assets were highly right-skewed with some negative values, and therefore a Z-score was created by standardizing with a mean of zero and standard deviation of one.

To account for population stratification, we constructed four principal components to represent genetic structure within the sample (Price et al., 2006). We included these as covariates in some models to control for biased estimates that could result from differences in genetic structure between populations being compared.

For each of the variables used, ~3% of values were missing, so imputation was not conducted.

2.3. Data Analysis

We first examined the racial and socioeconomic predictors of the PRS using linear regressions. Each of these predictors was included in bivariate analyses, and then a full multivariable model was constructed using all covariates. In secondary analyses, we also included the four genetic principal components.

Next, we conducted similar bivariate and multivariable linear regressions to examine racial and socioeconomic correlates of TL in the smaller sample of participants who had provided samples. A secondary analysis additionally controlled for genetic principal components. In all models, robust standard errors were clustered at the household level.

We also conducted several supplemental analyses. For each SNP, we graphically examined whether there were differences in the number of risk alleles by race; our study was not powered to examine these individual differences statistically. Next, we examined the association between self-reported race and principal components for genetic structure. Finally, we assessed the association between individual TL-associated SNPs and TL by race.

2.4. Ethics Approval

Ethics approval for this study was provided by the Stanford University Institutional Review Board (protocol # 25818). Approval for the HRS was provided by the University of Michigan Health Services Institutional Review Board.

3. Results

3.1. Sample Characteristics

The sample consisted of HRS participants who had provided genetic or telomere data (N = 11,934). Participants were diverse with respect to demographic and socioeconomic characteristics (Table 1).
3.2. Demographic and Socioeconomic Predictors of TL-associated Polygenic Risk Score

We found significant associations of the PRS with both race and SEP in bivariate analyses (Table 2). Black participants were significantly more likely than whites to have a lower PRS (β = −0.92, 95%CI: −0.97, −0.87), where a lower PRS has been associated with longer TL based on a prior genome-wide meta-analysis among individuals of European descent. Compared to whites, those of Hispanic or other race were more likely to have a higher PRS, predicting shorter TL (respectively, β = 0.24, 95%CI: 0.17, 0.31 and β = 0.20, 95%CI: 0.048, 0.35). Those with greater educational attainment were also more likely to have a higher PRS, with coefficients of increasing magnitude for each additional level of education. Similarly, those with higher household assets were more likely to have a higher PRS (β = 0.042, 95%CI: 0.023, 0.061). Each of the four principal components for genetic structure was also strongly associated with the PRS. Gender and age were not significantly associated with PRS. Of note, the variance in PRS explained by each factor was 1% or less, except for race and the genetic principal components, for which the R-squared values were 11% and 12.5% respectively.

In multivariable analyses including race and socioeconomic factors (Table 3A), race/ethnicity remained strongly associated with PRS, with similar magnitude and significance levels as bivariate analyses. Older individuals were more likely to have a lower PRS, predicting longer TL (β = −0.0019, 95%CI: −0.0036, −0.00016), a finding that is consistent with potential mortality selection. Women were more likely to have a higher PRS (β = 0.046, 95%CI: 0.046, 0.076). Education was not significantly associated, while assets were marginally associated with a higher PRS (β = 0.013, 95%CI: −0.0028, 0.028).

When controlling for population stratification (Table 3B), the genetic principal components were strongly associated with PRS. As genetic structure and self-reported race/ethnicity are highly correlated (Supplemental Table 2), race was no longer significantly associated, while assets were marginally associated with a higher PRS (β = 0.0013, 95%CI: 0.0005, 0.0055). Gender, age and several educational attainment were no longer associated with a higher PRS (β = −0.0028, 0.028).

3.3. Demographic and Socioeconomic Predictors of TL

We next examined the association between socioeconomic factors and TL itself using bivariate and multivariable analyses. While some of our results confirmed prior findings of the association between TL and socioeconomic factors, others were inconsistent. In bivariate analyses (Table 4), longer TL was associated with being black and Hispanic (respectively, β = 3.35, 95%CI: 3.46, 7.24 and β = 1.57, 95%CI: 3.35, 281), younger age (β = −8.77, 95%CI: −12.8, −4.75), and lower assets (β = −3.54, 95%CI: −5.34, −1.75), as well as genetic structure. However, shorter TL was associated with college education, relative to less than high school education (β = 8.18, 95%CI: −2.19, −14.6). In multivariable analyses including race and socioeconomic factors (Table 5A), longer TL was associated with black race (β = 0.501, 95%CI: 308, 693) and younger age (β = −7.58, 95%CI: −11.7, −3.46). When controlling for genetic structure (Table 5B), longer TL was associated with genetic principal components, and no longer associated with self-reported race.

Table 1
Sample characteristics (N = 11,934).

| Variable                              | Value |
|---------------------------------------|-------|
| **Sociodemographic characteristics** |       |
| White                                 | 75.7  |
| Black                                 | 13.4  |
| Hispanic                              | 9.3   |
| Other                                 | 1.6   |
| Age at genetic testing (mean ± SD)    | 68.0 ± 10.6 |
| Female                                | 59.2  |
| Educational attainment (%)            |       |
| Less than high school                 | 19.9  |
| High school                           | 35.7  |
| Some college                          | 22.7  |
| College or more                       | 21.8  |
| Total assets in USD (mean ± SD)       | 500,579 ± 1,199,420 |
| **Genetic characteristics**           |       |
| Polygenic risk score, standardized    |       |
| No. observations                      | 11,143 |
| Mean ± SD                            | 0.002 ± 1.00 |
| Teloemere length in base pairs        |       |
| No. observations                      | 5808  |
| Mean ± SD                            | 3314 ± 1749 |

Table 2
Bivariate (unadjusted) correlations of TL-associated polygenic risk score with race, socioeconomic position, and genetic structure (N = 11,143).

| Variable | β coefficient [95% CI] | R-squared |
|----------|------------------------|-----------|
| Race (ref: white) | Black | −0.92 ** [−0.97, −0.87] | 0.110 |
| Hispanic | 0.24 *** [0.17, 0.31]  |           |
| Other    | 0.20 ** [0.048, 0.35]  |           |
| Age      | −0.0013 [−0.0031, 0.00055] | 0.000 |
| Female   | 0.016 [−0.026, 0.053]  |           |
| Education (ref: less than HS) | High school | 0.061 [0.0072, 0.12] | 0.001 |
|          | Some college | 0.083 *** [0.024, 0.14] |     |
|          | College or more | 0.11 *** [0.048, 0.17] |     |
| Assets z-score | 0.042 ** [0.023, 0.061] | 0.002 |
| Genetic structure | Component 1 | −9.14 *** [−9.64, −8.64] | 0.125 |
|          | Component 2 | −11.7 *** [−13.1, −10.4] |     |
|          | Component 3 | 3.07 [0.0092, 6.14] |     |
|          | Component 4 | 5.66 ** [2.11, 9.21] |     |

TL = telomere length.
** p < 0.01.
* p < 0.05.

Table 3
Multivariable correlations of TL-associated polygenic risk score with race, socioeconomic position, and genetic structure.

| Variable                              | β coefficient [95% CI] | A: Base model |
|---------------------------------------|------------------------|--------------|
| Race (ref: white) | Black | −0.92 ** [−0.97, −0.87] | 0.066 [−0.24, 0.25] |
| Hispanic | 0.23 *** [0.16, 0.30]  | −0.080 [−0.20, 0.040] |
| Other    | 0.19 [0.035, 0.34]  | 0.0042 [−0.21, 0.22] |
| Age      | −0.0010 [−0.0036, −0.00016] | 0.000020 |
| Female   | 0.040 [0.0046, 0.076] | 0.0366 [0.00079, 0.071] |
| Education (ref: less than HS) | High school | −0.017 [−0.068, 0.034] | −0.0087 [−0.059, 0.041] |
|          | Some college | −0.045 [0.067] | 0.017 [−0.039, 0.072] |
|          | College or more | −0.061 [0.035] | 0.0058 [−0.052, 0.064] |
|          | Assets z-score | −0.0028, 0.028 | 0.012 [−0.0027, 0.028] |
| Genetic structure | Component 1 | −9.19 *** [−11.6, −6.82] |     |
|          | Component 2 | −12.9 *** [−15.4, −10.4] |     |
|          | Component 3 | 4.86 [0.058, 9.67] |     |
|          | Component 4 | 4.83 [1.10, 8.55] |     |
| Constant  | 0.21 *** [0.074, 0.35] | 0.089 [−0.048, 0.23] |
| Observations | 11,141 | 11,141 |
| R-squared | 0.111 | 0.126 |

TL = telomere length.
** p < 0.01.
* p < 0.05.
3.4. Secondary Analyses

A secondary analysis is consistent with there being variation in the association between the TL-associated SNPs and TL by race (Table 6), although this study is considerably smaller than a typical GWAS and therefore not powered to detect individual SNP differences. We also found differences in allele frequency by race for several of the SNPs (Supplemental Fig. 1).

4. Discussion

This study provides evidence on differences in the genetic determinants of TL by race and SEP. Our sample includes a large nationally representative diverse group of U.S. older adults, allowing for subgroup analyses. The most striking finding is that the longer TL of blacks was markedly attenuated when controlling for four genetic principal components to control for population stratification. These novel findings provide critical insights into prior studies that find that blacks have longer telomeres than whites yet a higher rate of telomere shortening over the life course (Rewak et al., 2014). Our results suggest that black individuals have a higher prevalence of genetic markers associated with longer telomeres, which would reconcile these findings. In other words, blacks appear to be genetically predisposed to longer telomeres, as suggested by studies finding greater TL among black newborns (Rewak et al., 2014; Zhu et al., 2011b). Because of the greater initial length, blacks may continue to have longer TL throughout the lifespan despite higher levels of discrimination and socioeconomic adversity that may lead to more rapid shortening of telomeres among blacks observed in some studies (Chae et al., 2014; Geronimus et al., 2010). Of note, despite the fact that race is widely acknowledged to be a social construct, we found that self-reported race was highly correlated with genetic ancestry for TL-associated genes. The fact that these particular SNPs are associated with race does not change the overarching limitations in the use of race as a primary variable of interest in genetics research (Yu et al., 2016), such as high levels of within-group heterogeneity and subjective classification. Other differences by SEP were significant in bivariate but not multivariate analyses. This suggests that observed relationships in unadjusted regressions are likely confounded by race.

These findings provide evidence of a possible gene-environment correlation (rGE). For example, there may have been greater evolutionary pressure on populations of African ancestry in the past 25,000 years, which may have led to selection favoring genetic predisposition to longer telomeres. This may be similar to the selection of individuals with sickle cell or thalassemia trait that occurred over thousands of years in regions of the world with high prevalence of malaria (Kwiatkowski, 2005), a process that has been hypothesized for other disease processes such as cystic fibrosis (Dean et al., 2002). The role of an infectious etiology in the selection process might be a particularly salient hypothesis, as shorter TL has been associated with increased susceptibility to infection (Cohen et al., 2013). TL in this study, however, was measured in salivary samples rather than leukocytes, and it remains unclear how TL measurements in different tissues are associated with overall health and longevity (Friedrich et al., 2000). Alternatively, it may be that TL-associated SNPs are linked with other genes that experienced selection pressure. Another possible explanation is that there may have been founder effects among populations leaving Africa, such that white and other populations had higher frequencies of genes predisposing to shorter TL. Future studies could examine whether black individuals have similar genetic profiles in other countries in which adverse socioeconomic conditions are not as highly correlated with race.

It is also important to note that the PRS is based on SNPs that were obtained in a genome-wide meta-analysis among individuals of European descent (Codd et al., 2013). It may be the case that the genes that determine TL among blacks and other racial groups differ from those among whites, and future research should focus on conducting genome-wide association studies among more diverse samples. While we examined how each GWAS-associated SNP was associated with TL in difference racial/ethnic groups, we were underpowered to detect whether these differences were statistically significant. Nevertheless, several of the SNPs included in the PRS have been associated with TL and disease in non-white populations, suggesting that their influence may span population subgroups (Shen et al., 2011; Du et al., 2015).

We also find that men are more likely to have a lower PRS predictive of longer TL, but no differences in TL by gender. A recent meta-analysis demonstrated that men in fact typically have shorter TL than women, although this finding depends on the type of measurement method performed (Gardner et al., 2014). In our study, none of the TL-associated SNPs were on sex chromosomes, thus suggesting possible environmental rather than genetic explanations for these gender differences. For

| Variable | \( \beta \) coefficient [95% CI] | R-squared |
|----------|---------------------------------|-----------|
| Race (ref: white) | | |
| Black | 535** [346, 724] | 0.011 |
| Hispanic | 157 [33, 281] | |
| Other | 122 [-184, 428] | |
| Age | -8.77** [-12.8, -4.75] | 0.003 |
| Female | 25.8 [-67.7, 119] | 0.000 |
| Education (ref: less than HS) | | |
| High school | -117 [-267, 31.8] | 0.001 |
| Some college | -570 [-205, 91.2] | |
| College or more | -148 [-283, -13.6] | |
| Assets z-score | -35.4 [-53.4, -17.5] | 0.001 |
| Genetic structure | | |
| Component 1 | 4984 [3306, 6662] | 0.016 |
| Component 2 | -2974 [-5544, -405] | |
| Component 3 | 1374 [-6283, 9030] | |
| Component 4 | -3297 [-8397, 1803] | |

** p < 0.01.
* p < 0.05.
example, this may be a result of men’s higher mortality rates from a number of chronic and acute conditions related to environmental exposures (Cullen et al., 2015), such that men genetically predisposed to longer TL are more likely to be selected into our sample of older adults.

We also find that older individuals are more likely to have genetic profiles predictive of longer TL. These findings are suggestive of the influence of longer TL on mortality, consistent with prior longitudinal studies and population-based studies demonstrating that longer TL is associated with longer survival (Rehkopf et al., 2013; Bakaysa et al., 2007; Ehrlenbach et al., 2009). While studies in humans have not been able to definitively demonstrate the causal effect of TL on longevity, these findings lend further credence to this hypothesis. Because those who provided genetic samples differ from those who died before being tested, future studies should examine samples that include younger individuals. Recent work has suggested that this bias may be substantial, but currently there are not sample weights available to account for this (Domingue et al., 2016).

Our findings with respect to the factors associated with TL itself are largely consistent with the prior literature, showing that blacks and younger individuals are more likely to have longer telomeres (Adler et al., 2013; Diaz et al., 2010; Hunt et al., 2008; Needham et al., 2013), although some of these associations are attenuated when adjusting for other covariates. The association between being Hispanic and longer TL, however, contradicts some of the prior literature that finds telomeres are shorter or not significantly different than those of whites (Diez roux et al., 2009; Gronimius et al., 2015). It also contradicts our finding that Hispanic individuals have higher PRS values predicting shorter TL; this may be suggestive of survivorship bias in this subpopulation or the role of other environmental determinants of TL. For SEP, we find that higher education and greater assets are predictive of shorter telomeres in unadjusted models, contradicting a systematic review that found that higher education is consistently associated with longer TL (Robertson et al., 2013); these findings, however, are no longer statistically significant in adjusted models, suggesting that the associations may be confounded by other sociodemographic factors.

To conclude, this study demonstrates differences in genetic markers for TL by race, gender, and age. The results suggest intergenerational gene–environment correlations in which adverse infectious or social conditions may influence allele frequencies. This study expands our understanding of the role that telomeres play in human aging, as well as the possible effects of socioeconomic factors in driving differences in health and longevity.

### Funding Sources

Dr. Hamad is supported by a KL2 Mentored Career Development Award through the Stanford Clinical and Translational Science Award to Spectrum (KL2-TR001083). Dr. Tuljapurkar is supported in part by a grant from the National Institute of Aging (R24-AG039345). Dr. Rehkopf is supported by a grant from the National Institute of Aging (K01-AG047280).

### Role of Funding Source

The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript. No authors were paid by a pharmaceutical company or other agency to write this article.

### Conflicts of Interests

The authors have no conflicts of interest to disclose.

### Author contributions

RH and DHR conceived of the study. RH conducted the data analysis, and DHR assisted with data analysis. All authors contributed to data interpretation. RH drafted the manuscript. All authors provided critical feedback on the manuscript and approved of the final version.

### Appendix A. Supplementary tables

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.ebiom.2016.08.015.

### References

Adler, N., Pantell, M.S., O’Donovan, A., Blackburn, E., Cawthon, R., Koster, A., Opresko, P., Newman, A., Harris, T.B., Epel, E., 2013. Educational attainment and late life telomere length in the health, aging and body composition study. Brain Behav. Immun. 27, 15–21.

Allsopp, R.C., Harley, C.B., 1995. Evidence for a critical telomere length in senescent human fibroblasts. Exp. Cell Res. 219, 130–136.

Bakaysa, S.L., Mucci, L.A., Slagboom, P.E., Boomsma, D.J., Mcclearn, G.E., Johansson, B., N.L., P., 2007. Telomere length predicts survival independent of genetic influences. Aging Cell 6, 769–774.

Blackburn, E.H., 2000. Telomeres states and cell fates. Nature 408, 53–56.

Bustamante, C.D., De La Vega, F.M., Burchard, E.G., 2011. Genomics for the world. Nature 475, 163–165.

Chae, D.H., Nuru-Jeter, A.M., Adler, N.E., Brody, G.H., Lin, J., Blackburn, E.H., Epel, E.S., 2014. Discrimination, racial bias, and telomere length in African-American men. J Prev Med–>Am J. Prev. Med. 46, 103–111.

Codd, V., Nelson, C.P., Albrecht, E., Mangino, M., Deelen, J., Buxton, J.L., Hottenga, J.J., Fischer, K., Eko, T., Surakka, I., 2013. Identification of seven loci affecting mean telomere length and their association with disease. Nat. Genet. 45, 422–427.

Cohen, S., Janicki-Deverts, D., Turner, R.B., Casebrazier, M.L., U-Korotky, H.S., Epel, E.S., Doyle, W.J., 2013. Association between telomere length and experimentally induced upper respiratory viral infection in healthy adults. JAMA 309, 699–705.

Cullen, M.R., Baiocchi, M., Eggleson, K., Loftus, P., Fuchs, V., 2015. The Weaker Sex? Vulnerable Men, Resilient Women, and Variations in Sex Differences in Mortality since 1900. National Bureau of Economic Research, Cambridge, Massachusetts.

Dean, M., Carrington, M., O’Brien, S.J., 2002. Balanced polymorphism selected by genetic versus infectious human disease. Annu. Rev. Genomics Hum. Genet. 3, 263–292.

Diaz, V.A., Mainous, A.G., Player, M.S., Everett, C.J., 2010. Telomere length and adiposity in a racially diverse sample. J Obes (Lond)–>Int. J. Obes. 34, 261–265.

Diez roux, A.V., Ranjit, N., Jenny, N.S., Shea, S., Cushman, M., Fitzpatrick, A., Seeman, T., 2009. Race/ethnicity and telomere length in the multi-ethnic study of atherosclerosis. Aging Cell 8, 251–257.

Domingue, B.W., Belsky, D.W., Harrati, A., Conley, D., Weir, D., Boardman, J., 2016. Mortality selection in a genetic sample and implications for association studies. bioRxiv 049635.

### Table 6

| Race          | β coefficient [95% CI] |
|---------------|------------------------|
| PRS           | TERC                   | TERT                   | NAFL                   | OBFC1                   | ZNF208                   | RELI1                   | ACYP2                   |
| Whites (N =   | 3735)                  | 20.2 [−45.6, 86.1]     | −46.2 [−102, 9.5]      | −23.0 [−80.9, 35.0]     | −137 [−279, 4.8]        | 13.2 [−88.4, 62.0]      | 9.46 [−58.9, 31.4]      | −30.0 [−91.5, 31.4]     |
| Blacks (N =   | 691)                   | 143 [−156, 442]       | −359 [−665, −52.9]    | −102 [−288, 84.3]       | 249 [−407, 905]         | 45.7 [−112, 204]        | 140 [−259, 359]         | 212 [−44.6, 469]        |
| Hispanics     | (N = 510)              | −9.51 [−81.1, 62.0]   | 24.0 [−93.0, 141]     | −113 [−155, 64.4]       | 109 [−473, 265]         | 26.0 [−158, 210]        | −40.7 [−183, 102]       | −33.5 [−196, 129]       |

SNP = single nucleotide polymorphism. Individuals of “other” race not included due to small sample size (N = 81). Principal components not included in this analysis.

* p < 0.05.
+ p < 0.1.
