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Testing Life Course Models Whereby Juvenile and Adult Adversity Combine to Influence Speed of Biological Aging

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ONLINE SUPPLEMENT ON MEASURES OF AGING

The epigenetic measures of Horvath (2013) and Hannum et al. (2013) are probably the most widely accepted measures of biological aging. They correlate much more strongly with chronological age (r >.90) than any of their competitors and they have been shown to predict all-cause mortality in 13 cohorts (Chen et al. 2016). Further, accelerated aging using these measures has been linked to frailty, some types of cancer, cardiovascular disease, and both Alzheimer's and Parkinson's disease (Jylhava et al. 2017). However, these indices are unrelated to many types of cancer, their relation with cardiovascular disease is weak, and they are not associated with disease risk factors such as smoking, diabetes, hypertension, lipoproteins, insulin, glucose, triglycerides, or C-reactive protein (Horvath et al. 2016). In addition, it is unclear whether the Horvath and Hannum epigenetic clocks are a cause, consequence, or correlate of aging (Jyhava et al. 2017). Finally, it is now a challenge to obtain the methylation data necessary to construct either Horvath's or Hannum's epigenetic measures. Their indices were originally formed using the Illumina 450 Beadchip. Illumina has replaced the 450 beadchip with the new EPIC 850 Beadchip. This new platform has the advantage of providing data on 850,000 methylation sites compared to the previous approach that assayed only 450,000 sites; but, much to the dismay of biomedical researchers, it also omits several of the sites included in both the Horvath and Hannum epigenetic indices.

For much of the new millennium, leucocyte telomere length has been a popular measure of aging. Telomere length correlates roughly .50 with chronological age and several studies have reported that this measure is associated with increased risk of mortality (Jylhava et al. 2017). Meta-analyses also report that telomere length is related to cardiovascular risk (Haycock et al. 2014), and some cancers (Wentzensen et al. 2011). Unfortunately, however, research on

telomeres has often been plagued by inconsistent findings. Even meta-analytic efforts often produce limited conclusions (Gardner et al. 2013; Jylhava et al. 2017). Further, some established findings obtaining with the measure are rather puzzling. Several studies, for example, have failed to find an association between socioeconomic status and telomere length (e.g., Carroll et al. 2013; Steptoe et al. 2011), or between age and telomere length among black Americans (Needham et al. 2013). Further, there is research indicating that telomere length is longer among black Americans than white Americans of the same age (Needham et al. 2013; Rewak et al. 2014), a paradoxical finding given the high rates of adversity, morbidity, and mortality suffered by blacks compared to other ethnic groups living in the United States (Williams 2012). Importantly, DNA extraction methods used to assess telomere length have been shown to have a pronounced influence on telomere length values and this variability likely contributes to spurious or lost associations in epidemiological studies (Raschenberger et al. 2016). Finally, like the epigenetic clocks of Horvath and Hannum, it is not clear whether telomere length is a cause or a consequence of aging (Jylhava et al. 2017). Although the epigenetic clock and telomere studies have furthered our understanding of aging, it is clear that both of these approaches present limitations as measures of biological aging. Indeed, most studies find that the correlation between the epigenetic clocks and telomere length are either very low or non-significant (Jylhava et al. 2017).

References

Blackburn, Elizabeth. 2005. “Telomeres and Telomerase: Their Mechanisms of Action and Effects of Altering Function.” *Federation of European Biochemical Societies* 579(4) 859–62.

Chen, Brian H., Richardo E. Marioni, Elena Colicino….and Steve Horvath. 2016. "DNA Methylation-based Measures of Biological Age: Meta-analysis Predicting Time to Death." *Aging* 8(9): 1844–65.

Hannum, Gregory., Justin Guinney, Ling Zhao,….Kang Zhang. 2013. "Genome-wide Methylation Profiles Reveal Quantitative Views of Human Aging Rates." *Molecular Cell 49*(2): 359–67.

Heycock, Phillip C., Emma E. Heydon, Stephen Kaptoge, Adam S. Butterworth, Alex Thompson, and Peter Willeit. 2014. "Leucocyte Telomere Lengh and Risk of Cardiovascular Disease: Systematic Review and Meta-analysis." *BMJ* 349:g4227 doi:10.1136/bmj.g4227.

Horvath, Steve. 2013. "DNA Methylation Age of Human Tissues and Cell Types." *Genome Biology* 14(R115):1–19.

Jyhava, Juulia, Nancy L. Pedersen, and Sara Hagg. 2017. "Biological Age Predictors." *EBioMedicine* 21: 29–36.

Needham, Belinda L., Nancy Adler, Steven Gregorich, David Rehkopf, Jue Lin, Elizabeht H. Blackburn, and Elissa S. Epel. 2013. "Socioeconomic Status, Health Behavior, and Leukocyte Telomere Length in the National Health and Nutrition Examination Study, 1999–2002." *Social Science & Medicine* 85(May):1–8.

Raschenberger, Julia, Claudia Lamina, Margot Haun, Barbara Kollerits, Stefan Coassin, Eva Boes, Ludmilla Kedenko, Anna Kottgen, and Florian Kronenberg. 2015. "Influence of DNA Extraction Methods on Relative Telomere Length Measurements and its Impact on Epidemiological Studies." *Scientific Reports* 6:25398. doi:10.1038/srep25398.

Rewak, Marissa, Stephen Buka, Jennifer Precott, Immaculata De Vivo, Eric B. Loucks, Ichiro Kawachi, Amy L. Non, and Laura D. Kubrzansky. 2014. “Race-related Health Disparities and Biological Aging: Does Rate of Telomere Shortening Differ across Blacks and Whites?” *Biological Psychology* 99(May) 92–9.

Steptoe, Andrew, Mark Hamer, Lee Butcher, Jue Lin, Lena Brydon, Mika Kivimaki, Michael Marmot, Elizabeth Blackburn, and Jorge D. Erusalimsky. 2011. “Educational Attainment but Not Measures of Current Socioeconomic Circumstances Are Associated with Leukocyte Telomere Length in Healthy Older Men and Women.” *Brain, Behavior, and Immunity* 25(7): 12192–8.

Wentzensen, Ingrid M., Lisa Mirabello, Ruth M. Pfeiffer, and Sharon A. Savage. 2011. “The Association of Telomere Length and Cancer: A Meta-analysis.” *Cancer Epidemiology, Biomarkers, & Prevention* 20(6):1238–50.

Williams, David R. 2012. “Miles to Go Before We Sleep: Racial Inequities in Health.” *Journal of Health and Social Behavior* 53(4):279–5.