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Maternal Social Disadvantage and Newborn Telomere Length in Archived Dried Blood Spots from the Michigan Neonatal Biobank

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ABSTRACT

Telomeres are the protective caps at the ends of eukaryotic chromosomes. Short telomere length is associated with morbidity and mortality among adults and may mark the biological impact of social experiences. Using archived dried blood spots from the Michigan Neonatal Biobank, this study examined markers of maternal social disadvantage (educational attainment, receipt of public assistance, marital status, and race/ethnicity) from linked birth certificates as predictors of telomere length at birth in a sample of 192 singleton neonates born to non-Hispanic black, non-Hispanic white, and Latina mothers aged 20–35 years. Consistent with two recent studies in newborns, but counter to the idea that maternal social disadvantage is associated with shorter offspring telomere length, we found that infants born to black mothers had longer telomeres than those born to white mothers (b = 0.12, SE = 0.06, p = .05). However, black/white differences in newborn telomere length varied by receipt of public assistance. Among newborns whose mothers received WIC and/or Medicaid, there were no significant black/white differences in telomere length (b = 0.09, SE = 0.08, p = .25). In contrast, among those whose mothers did not receive public assistance—just 6 out of 69 infants born to black mothers versus 41 out of 69 infants born to white mothers—we found that babies born to black mothers had longer telomere length than babies born to white mothers (b = 0.37, SE = 0.16, p = .03). The interaction between black race/ethnicity and receipt of public assistance did not reach the conventional threshold for statistical significance (b = −0.22, SE = 0.15, p = .13), suggesting that this finding may be due to chance. No other markers of maternal social disadvantage were related to infant telomere length. Although replication of these results in a larger sample with more infants born to black mothers with relatively high socioeconomic status is needed, this study offers preliminary support for the hypothesis that race/ethnic differences in newborn telomere length depend on social context.

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Telomeres cap the ends of chromosomes and promote chromosomal stability. Telomeres shorten both naturally through cell division and due to oxidative damage. Once telomeres become critically shortened, cellular senescence is triggered, and cells lose the ability to divide. Thus, telomere length—which is associated with age-related disease and death among adults—is hypothesized to be a biological marker of aging (see Blackburn, Epel, and Lin 2015 for a review on human telomere biology). Growing evidence also suggests that telomere shortening may be a causal determinant of cardiovascular disease and longevity (Aviv, Kark, and Susser 2015; Codd et al. 2013). Although most epidemiologic studies have focused on predictors of telomere length in adults, a recent study found evidence of tracking and fixed ranking of telomeres throughout adulthood, which suggests that adult telomere length is largely determined by telomere length at birth and telomere attrition during the first 20 years of life (Benetos et al. 2013). Therefore, studies examining risk factors for short telomere length in early life may provide insight into the origins of later life social inequalities in health. Stored blood samples from newborn genetic screening programs have the potential to provide an invaluable source of data for population studies on neonatal telomere length. Using archived dried blood spots from the Michigan Neonatal Biobank, this study examined markers of maternal social disadvantage (educational attainment, receipt of public assistance, marital status, and race/ethnicity) from linked birth certificates as predictors of telomere length at birth.

Telomere Length in Early Life

Previous studies have found substantial inter-individual variation in telomere length at birth, which is hypothesized to be the result of genetic and environmental factors that begin to influence telomere length prenatally (Okuda et al. 2002). Despite evidence of heritability, measured genetic variants explain little of the observed variance in telomere length (Codd et al. 2013; Tellechea et al. 2015), suggesting that environmental factors are responsible for much of the variation across individuals. Previously identified risk factors for shorter telomere length at birth include prenatal cadmium exposure (S. Lin et al. 2013), low maternal folate concentrations (Entringer et al. 2015a), low maternal estriol concentrations (Entringer et al. 2015b), smoking and drug use during pregnancy (Imam et al. 2012), poorly controlled diabetes during pregnancy (Biron-Shental et al. 2015), excess fetal growth (Tellechea et al. 2015), and exposure to maternal psychological stress during pregnancy (Entringer et al. 2013; Marchetto et al. 2016). Evidence regarding associations between newborn telomere length and gestational age (Drury et al. 2015; Friedrich et al. 2001; Menon et al. 2012) and parental age has been mixed (Das, Saini, and Seshadri 2012; Drury et al. 2015; Imam et al. 2012).

Although few studies have directly examined markers of parental social disadvantage as predictors of newborn telomere length, mothers with lower levels of disadvantage tend to have greater access to material and psychosocial resources, such as higher income, better medical care, and more stable and supportive social relationships, that promote their own health and the health of their offspring (Gavin, Nurius, and Logan-Greene 2012). Thus, it is reasonable to expect that infants born to more socially advantaged mothers would have longer telomere length at birth than infants born to socially disadvantaged mothers. Consistent with this hypothesis, one recent study reported that babies born to Latina mothers with at least a high school diploma had significantly longer telomere length at

birth than babies born to Latina mothers who did not complete high school (Wojcicki et al. 2016). The results of this study were consistent with previous research that found a positive association between parental education and child telomere length (Mitchell et al. 2014; Needham et al. 2012). Although no prior studies have reported an association between parental marital status and newborn telomere length, previous research suggests that married mothers typically have higher socioeconomic status (SES) than unmarried mothers and that infants born to married mothers tend to have better health-related outcomes than those born to unmarried mothers (Shah, Zao, Ali, and Knowledge Synthesis Group of Determinants of Preterm/LBW Births 2011).

Despite the fact that racial and ethnic minorities in the U.S. tend to be more socially disadvantaged than whites, two previous studies reported longer telomere length in black infants than white infants (Drury et al. 2015; Rewak et al. 2014). These findings are consistent with research on adults, which indicates that blacks have longer telomeres than whites (Needham et al. 2013), but are counterintuitive given that blacks carry a higher burden of social disadvantage and psychosocial stress and that these factors have been linked to shorter telomere length (Epel et al. 2004; Needham et al. 2013). Some have argued that race/ethnic differences in telomere length may be due to genetic differences (Hansen et al. 2016), while others have argued that longer newborn telomere length may mark the fetal programming of accelerated aging in black infants (Drury et al. 2015). In this way, longer newborn telomere length could be indicative of a plasticity response designed to protect against accelerated telomere shortening in response to greater anticipated levels of lifetime stress exposure (see Rewak et al. 2014). However, given marked differences in the social environments of U.S. blacks, whites, and Latinos, others have argued that it is necessary to examine race/ethnic differences in health outcomes, including telomere length, within similar settings, such as those defined by geographic place and/or social strata (Geronimus et al. 2015). Thus, in addition to examining race/ethnic differences in newborn telomere length in the full sample, we also considered whether associations between race/ethnicity and telomere length varied across levels of socioeconomic disadvantage.

Hypotheses

We hypothesized that babies born to mothers with lower SES, as indicated by low educational attainment and/or receipt of public assistance, would have shorter telomere length than babies born to more socioeconomically advantaged mothers and, similarly, that infants born to unmarried mothers would have shorter telomere length than those born to married mothers. Furthermore, we hypothesized that infants born to black mothers would have longer telomere length than those born to white or Latina mothers, but that race/ethnic differences in newborn telomere length would vary by SES.

Methods

Sample and Procedures

Since 1984, the Michigan Neonatal Biobank has stored dried blood spot samples collected from Michigan newborns as part of the state's newborn screening program. Although

samples are de-identified, they can be linked to other statewide databases, including birth and death records, by the Michigan Department of Community Health (MDCH). Detailed information regarding standardized blood specimen collection and handling procedures can be found at https://www.michigan.gov/documents/mdch/MI_NBS_Guide_368636_7.pdf. Since 2009, cards containing dried blood spots have been stored at −20C◦. Cards from 1996 to 2008 have been stored in temperature- and humidity-controlled spaces. The study sample included 213 singleton neonates born to non-Hispanic black, non-Hispanic white, and Latina mothers aged 20–35 years in the state of Michigan between January 1, 2008 and July 31, 2012. Using a simple random sample method in SAS software, an epidemiologist from the MDCH selected an equal number of infants from each of the three race/ethnic groups examined. Out of 213 blood spots selected for this study, 175 were from infants born between August 1, 2011 and July 31, 2012 (stored at −20◦C). In order to determine whether storage conditions and/or year of birth (a proxy for length of time in storage) were associated with newborn telomere length, 19 samples were also selected from infants born between January 1, 2009 and December 31, 2009 (stored at −20◦C), and 19 samples were selected from infants born between January 1, 2008 and December 31, 2008 (stored in temperature- and humidity-controlled spaces). We excluded 17 infants with degraded DNA, one extreme outlier (more than four standard deviations above the mean) on the measure of telomere length, and 3 infants with missing data on study covariates (final n = 192). Human subjects approval for this study was granted by the MDCH and the University of Michigan.

Telomere Length

The QIAamp DNA Investigator Kit (QIAGEN, cat. #56504) was used to extract DNA from six 1/8-inch punches of the dried blood spots, and the quantitative polymerase chain reaction (PCR) method was used to measure telomere length relative to standard reference DNA (T/S ratio), as described in detail elsewhere (Cawthon 2002; J. Lin et al. 2010). Telomere length is typically measured in whole blood or peripheral blood mononuclear cells, but recent work has shown that the PCR method can be used to measure telomere length in dried blood spots (Zanet et al. 2013). DNA extraction and the telomere length assay were performed in the laboratory of Dr. Elizabeth Blackburn at the University of California, San Francisco. All DNA samples were run on 0.8 percent agarose gels to check DNA integrity. Seventeen degraded DNA samples were excluded from telomere length analysis. Each of the remaining 196 samples was assayed at least twice. T/S ratios that fell into the 7 percent variability range were accepted, and the average of the two was taken as the final value. A third assay was run for samples with greater than 7 percent variability, and the average of the two closest T/S values was used. The inter-assay coefficient of variation was 2.9 percent.

Linked Data from Birth Certificates

Linked birth certificates were used to obtain information on the following characteristics of newborns and their biological parents: maternal education (less than high school, high school or GED, and more than high school), receipt of benefits from the Special Supplemental Nutrition Program for Women, Infants, and Children (WIC) during

pregnancy (yes vs. no), source of payment for the delivery of the child (Medicaid vs. other), maternal marital status (not married vs. married), maternal race/ethnicity (non-Hispanic white, non-Hispanic black, and Latina), infant sex (female vs. male); maternal age (20–24, 25–29, and 30–34), paternal age (less than 25, 25–29, 30–34, and greater than or equal to 35), birth weight (less than 2,500 g vs. greater than or equal to 2,500 g), and gestational age (less than 37 weeks vs. greater than or equal to 37 weeks). Birth certificates were also used to obtain information on the following obstetric complications during pregnancy: prepregnancy or gestational diabetes (yes vs. no); hypertension, preeclampsia, or eclampsia (yes vs. no); premature rupture of the membranes (yes vs. no); and infection (yes vs. no). Data linkage was performed by an MDCH epidemiologist. In order to protect the identity of individuals in this study, no combination of variables in the data set may produce fewer than five records. For this reason, detailed information from the birth certificates (e.g., gestational age in weeks) was collapsed into broad categories (e.g., less than 37 weeks vs. greater than or equal to 37 weeks) by MDCH staff prior to linkage with the telomere length data.

Data Analysis

First, we used *t* tests for variables with two categories and one-way ANOVAs for variables with more than two categories to examine bivariate relationships between telomere length and maternal education, receipt of WIC benefits during pregnancy, source of payment for the delivery, maternal marital status, maternal race/ethnicity, infant sex, maternal age, paternal age, obstetric complications during pregnancy, birth weight, gestational age, and year of birth. Next, we used ordinary least squares (OLS) regression to examine associations of telomere length with markers of maternal social disadvantage, including educational attainment, receipt of public assistance, marital status, and race/ethnicity. Models adjusted for infant sex, maternal age, obstetric complications, birth outcomes, and year of birth. Given the large amount of missing data on paternal age, we did not include this measure in the models. Due to low prevalence, we combined the following obstetric complications of pregnancy into a single dummy variable: prepregnancy or gestational diabetes; hypertension, preeclampsia, or eclampsia; and premature rupture of the membranes. Also due to low prevalence, we combined birth weight less than 2,500 g and gestational age less than 37 weeks into a single dummy variable. Given the high correlation between receipt of WIC benefits during pregnancy and source of payment for delivery ($r = .70$, $p < .0001$), we combined these measures into a single dummy variable. To test the hypothesis that race/ethnic differences in telomere length vary by social class, we examined models with (1) interactions between race/ethnicity and educational attainment and (2) interactions between race/ethnicity and receipt of public assistance. Stratified models were examined for interactions with a p value less than .20. Analyses were conducted in SAS version 9.3 (SAS Institute, Cary, NC, USA).

Results

The mean T/S ratio was 2.24, with a standard deviation of 0.33 and a range of 1.36–3.19. Median T/S ratio was 2.20, with an interquartile range of 0.40.[1] In bivariate analyses, there were no significant differences in T/S ratio by maternal education,

receipt of WIC during pregnancy, source of payment for delivery, maternal marital status, infant sex, maternal age, or paternal age (see Table 1). Infants born to non-Hispanic black mothers had higher T/S ratios than those born to Latina or non-Hispanic white mothers (p = .05). Although only six mothers experienced

Table 1. Differences in mean relative telomere length (T/S ratio) by characteristics of newborns and their biological parents, obstetric complications during pregnancy, birth outcomes, and year of birth.

	n	Mean T/S Ratio (*SD*)	*p* value[a]
Maternal Education			
< High school	42	2.24 (0.31)	.89
High school or GED	57	2.25 (0.30)	
More than high school	96	2.23 (0.35)	
Received WIC			
Yes	117	2.24 (0.31)	.86
No	75	2.23 (0.36)	
Source of Payment			
Medicaid	118	2.26 (0.32)	.29
Other	77	2.21 (0.33)	
Maternal Marital Status			
Not married	106	2.26 (0.33)	.35
Married	89	2.21 (0.32)	
Maternal Race/Ethnicity			
Non-Hispanic white	65	2.19 (0.30)	**.05**
Non-Hispanic black	63	2.32 (0.32)	
Latina	67	2.21 (0.35)	
Sex of Infant			
Female	108	2.23 (0.31)	.78
Male	87	2.25 (0.34)	
Maternal Age			
20–24	88	2.25 (0.33)	.64
25–29	64	2.21 (0.35)	
30–34	43	2.26 (0.29)	
Paternal Age			
< 25	37	2.17 (0.31)	.81
25–29	54	2.22 (0.36)	
30–34	44	2.44 (0.29)	
≥ 35	18	2.21 (0.28)	
Prepregnancy or Gestational Diabetes			
Yes	4	2.18 (0.34)	.73
No	191	2.24 (0.33)	
Hypertension/Preeclampsia/Eclampsia			
Yes	6	1.96 (0.12)	**.001**
No	189	2.25 (0.33)	
Premature Rupture of Membranes			
Yes	2	1.95 (0.26)	.22
No	193	2.24 (0.33)	
Infection			
Yes	32	2.30 (0.31)	.26
No	163	2.23 (0.33)	
Birth Weight			
< 2,500 g	2	2.35 (0.14)	.63
≥ 2,500 g	193	2.24 (0.33)	
Gestational Age			
< 37 weeks	1	2.45 (—)	.52
≥ 37 weeks	194	2.24 (0.33)	
Year of Birth (DBS Storage Conditions)			
Born 2011–2012 (−20◦C)	166	2.18 (0.29)	**<.0001**
Born 2009 (−20◦C)	17	2.41 (0.21)	
Born 2008 (temp/humidity controlled)	12	2.85 (0.21)	

Note. [a]*p* value based on *t* test for variables with two categories and one-way ANOVA for variables with more than two categories. *p* values < .05 are in bold.

hypertension, preeclampsia, or eclampsia during pregnancy, their babies had significantly shorter relative telomere length than infants born to mothers who did not experience these obstetric complications (p = .001). Mean differences in relative telomere length by prepregnancy or gestational diabetes, premature rupture of the membranes, maternal infection during pregnancy, birth weight, and gestational age were not statistically significant, but these findings should be interpreted with caution due to the very low prevalence of obstetric complications during pregnancy, birth weight less than 2,500 g, and gestational age less than 37 weeks in this sample. Out of 175 infants born in 2011–2012 (samples stored at −20◦C), 166 (94.9 percent) had sufficient quality and quantity of DNA for the telomere length assay versus 17 out of 19 infants (89.5 percent) born in 2009 (samples stored at −20◦C) and 12 out of 19 infants (63.2 percent) born in 2008 (samples stored in temperature- and humidity-controlled spaces). Mean T/S ratio was highest among neonates born in 2008, intermediate among those born in 2009, and lowest among those born in 2011–2012 (p < .0001).

Table 2 presents the results of the multivariable regression model for the full sample. Maternal education, receipt of public assistance, and maternal marital status were not significant predictors of relative telomere length.[2] Consistent with the bivariate results, neonates born to non-Hispanic black mothers had longer telomere length than infants born to non-Hispanic white mothers (b = 0.12, SE = 0.06, p = .05), but there was no difference in T/S ratio between neonates born to Latina versus those born to non-Hispanic white mothers (b = 0.01, SE = 0.06, p = .87). Babies born to mothers aged 30–34 had higher T/S ratio than those born to mothers aged 20–24 (b = 0.13, SE = 0.06, p = .03), while babies whose mothers experienced hypertension, diabetes, and/or premature rupture of the membranes had significantly lower T/S ratios than those whose mothers did not experience these obstetric complications (b = −0.20, SE = 0.10, p = .04). Compared to neonates born between August 2011 and July 2012, those born

Table 2. OLS regression of relative telomere length (T/S ratio) on characteristics of newborns and their mothers (n = 192).

	Beta	*SE*	*p* value
Mother less than high school (Mother more than high school)	−0.04	0.06	.49
Mother high school or GED (Mother more than high school)	0.00	0.05	.96
WIC and/or Medicaid (No public assistance)	0.05	0.06	.39
Mother not married (Mother married)	0.01	0.05	.79
Mother Non-Hispanic black (Mother non-Hispanic white)	0.12	0.06	**.05**
Mother Latina (Mother non-Hispanic white)	0.01	0.06	.87
Female (Male) infant	−0.01	0.04	.73
Mother age 25–29 (Mother age 20–24)	0.07	0.05	.17
Mother age 30–34 (Mother age 20–24)	0.13	0.06	**.03**
Hypertension, diabetes, and/or premature rupture of the membranes (No obstetric complications)	−0.20	0.10	**.04**
Infection (No infection)	0.01	0.06	.90
Gestational age < 37 weeks and/or birth weight < 2,500 g (Gestational age ≥ 37 weeks and birth weight ≥ 2,500 g)	0.12	0.20	.56
Born 2008 (Born 2011–2012)	0.72	0.08	**<.0001**
Born 2009 (Born 2011–2012)	0.24	0.07	**.001**
Intercept	2.06	0.06	**<.0001**

Note. Reference category is in parentheses. Beta = unstandardized regression coefficient. *SE* = standard error. *p* values < .05 for regression coefficients are in bold. Adjusted R^2 = 0.29. F = 6.86, p = < .001.

in 2008 (b = 0.72, SE = 0.08, p < .0001) and 2009 (b = 0.24, SE = 0.07, p = .001) had significantly higher T/S ratios. Restricting the analysis to infants born in 2009 or later (whose blood spots were stored at −20◦C) produced substantively equivalent results. Infant sex, birth outcomes, and maternal infection were not significant predictors of relative telomere length in the multivariable regression models.

Interactions between race/ethnicity and maternal educational attainment did not reach the predetermined threshold for statistical significance (black × less than high school: b = −0.02, SE = 0.19, p = .92; Latina × less than high school: b = −0.05, SE = 0.18, p = .79; results not shown). However, the interaction between non-Hispanic black race/ethnicity and receipt of public assistance was significant at the p < .20 level (black × receipt of public assistance: b = −0.22, SE = 0.15, p = .13; Latina × receipt of public assistance: b = 0.01, SE = 0.11, p = .90; results not shown). Table 3 presents the results of the multivariable regression model stratified by receipt of public assistance. Among newborns whose mothers received WIC and/or Medicaid, there were no significant black/white differences in telomere length (b = 0.09, SE = 0.08, p = .25). In contrast, among those whose mothers did not receive public assistance, we found that babies born to non-Hispanic black mothers had longer relative telomere length than babies born to non-Hispanic white mothers (b = 0.37, SE = 0.16, p = .03). Results suggest that black/white differences in newborn telomere length are evident only among those who are relatively advantaged socioeconomically. This finding should be interpreted with caution, however, since only 6 out of 69 infants born to black mothers were in families that did not receive public assistance (compared to 41 out of 69 infants born to white mothers and 17 out of 71 infants born to Latina mothers). Predicted values of newborn telomere length for babies born to black, white, and Latina mothers within

Table 3. OLS regression of relative telomere length (T/S ratio) on characteristics of newborns and their mothers, by receipt of public assistance (n = 192).

	WIC and/or Medicaid (n = 131)			No public assistance (n = 61)		
	Beta	*SE*	*p* value	Beta		*p* value
Mother less than high school (Mother more than high school)	−0.08	0.08	.32	−0.10	0.23	.68
Mother high school or GED (Mother more than high school)	−0.04	0.07	.52	0.10	0.11	.36
Mother not married (Mother married)	0.06	0.06	.39	−0.14	0.11	.22
Mother non-Hispanic black (Mother non-Hispanic white)	0.09	0.08	.25	0.37	0.16	**.03**
Mother Latina (Mother non-Hispanic white)	0.01	0.09	.87	−0.02	0.08	.83
Female (Male) infant	−0.02	0.05	.65	−0.02	0.08	.82
Mother age 25–29 (Mother age 20–24)	0.08	0.06	.19	0.01	0.12	.96
Mother age 30–34 (Mother age 20–24)	0.17	0.08	**.04**	0.04	0.12	.74
Hypertension, diabetes, and/or premature rupture of the membranes (No pregnancy complications)	−0.23	0.29	.43	−0.16	0.11	.16
Infection (No infection)	−0.04	0.07	.61	0.09	0.11	.39
Gestational age < 37 weeks and/or birth weight < 2,500 g (Gestational age ≥ 37 weeks and birth weight ≥ 2,500 g)	0.14	0.21	.49	—	—	—
Born 2008 (Born 2011–2012)	0.70	0.12	**<.0001**	0.66	0.13	**<.0001**
Born 2009 (Born 2011–2012)	0.22	0.08	**.007**	0.25	0.22	.26
Intercept	2.12	0.08	**<.0001**	2.11	0.13	**<.0001**
Adjusted R^2	0.19			0.43		
F value (p value)	3.41 (.0002)			4.81 (<.0001)		

Note. Reference category is in parentheses. Beta = unstandardized regression coefficient. *SE* = standard error. p values < .05 for regression coefficients are in bold.

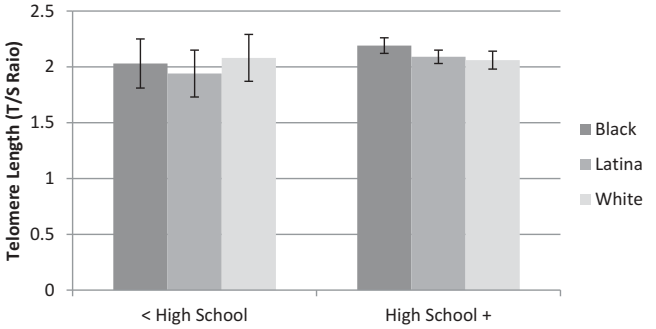

Figure 1. Predicted relative telomere length (T/S ratio) by race/ethnicity and education.

Note. The *p* value for the interaction between black race/ethnicity and educational attainment is .92, and the *p* value for the interaction between Latina race/ethnicity and educational attainment is .79. All covariates were set to zero in the calculation of the predicted values shown in Figure 1. Error bars represent standard error.

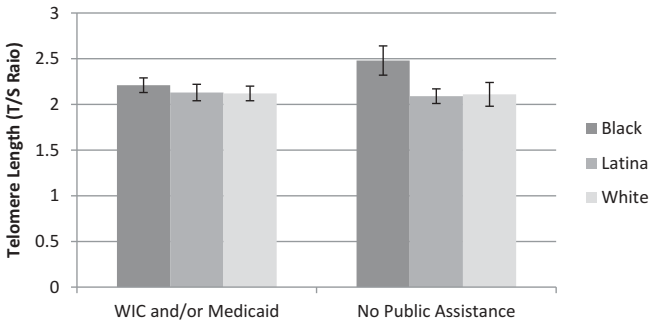

Figure 2. Predicted relative telomere length (T/S ratio) by race/ethnicity and receipt of public assistance.

Note. The *p* value for the interaction between black race/ethnicity and receipt of public assistance is .13, and the *p* value for the interaction between Latina race/ethnicity and receipt of public assistance is .90. All covariates were set to zero in the calculation of the predicted values shown in Figure 2. Error bars represent standard error.

socioeconomic strata defined by educational attainment and receipt of public assistance are shown in Figures 1 and 2.

Discussion

A growing body of literature suggests that short telomere length in adulthood is a risk factor for mortality (Rode, Nordestgaard, and Bojesen 2015) and diseases of aging, including coronary heart disease (Haycock et al. 2014) and type 2 diabetes (Willeit et al. 2014), that disproportionately affect individuals from socially disadvantaged backgrounds (Adler and Rehkopf 2008). Given that telomere length in adulthood is thought to be highly dependent on telomere length at birth (Benetos et al. 2013), research on newborn telomere length has the potential to shed light on the origins of later life health disparities. To date, few studies

have examined correlates of newborn telomere length, and, to our knowledge, no prior studies have used archived dried blood spots from a state neonatal biobank.

The primary goal of this study was to examine the hypothesis that infants born to socially disadvantaged mothers have shorter telomere length at birth than those born to more socially advantaged mothers. Contrary to expectations, we found that maternal SES, as indicated by maternal educational attainment and receipt of public assistance, and maternal marital status were not associated with newborn telomere length. Consistent with two recent studies on newborns (Drury et al. 2015; Rewak et al. 2014), but counter to the idea that maternal social disadvantage is associated with shorter offspring telomere length, we found that babies born to non-Hispanic black mothers had significantly longer telomeres than babies born to non-Hispanic white mothers. In models stratified by receipt of public assistance, we found that black/white differences in newborn telomere length were evident only among babies whose mothers were relatively better off (i.e., those who did not receive WIC and/or Medicaid)—just 6 out of 69 infants born to black mothers versus 41 out of 69 infants born to white mothers. These results highlight the fact that blacks and whites tend to live in very different social environments and that race/ethnic differences in health-related outcomes may vary across social contexts (Geronimus et al. 2015). More work is needed to understand why black/white differences in newborn telomere length appear to exist only among those with relatively low levels of socioeconomic disadvantage. Given that high SES blacks report more experiences of racial discrimination than low SES blacks (Cheng, Cohen, and Goodman 2015), longer telomere length among infants born to high SES black mothers may provide evidence for the fetal programming of a compensatory mechanism intended to protect against accelerated telomere shortening in response to greater anticipated levels of lifetime stress exposure. To explore this hypothesis further, future studies should examine more sensitive measures of maternal SES and include more high SES black mothers.

Given that we had greater power to detect interactions between race/ethnicity and educational attainment, the most plausible explanation for our finding of a marginally significant interaction between non-Hispanic black race/ethnicity and receipt of public assistance is that it was due to chance. However, it is well established that traditional measures of SES, such as educational attainment, may not be comparable across race/ethnic groups (Kaufman, Cooper, and McGee 1997; Williams et al. 2010). Previous research suggests that predominantly minority schools have significantly fewer resources than predominantly white schools, which contributes to differential levels of academic achievement (Annie E. Casey Foundation 2006). Moreover, economic returns to education are lower for race/ethnic minorities than for whites (Williams et al. 2010). In this way, the social position of blacks, whites, and Latinos with the same level of educational attainment may differ markedly. Because government assistance programs, such as WIC and Medicaid, are based on financial need, including both income and assets, receipt of these benefits is likely to provide a more comparable indicator of SES across race/ethnic groups. This may explain why we found black/white differences in telomere length according to receipt of public assistance but not according to differences in educational attainment.

Though not the primary goal of this study, we also considered whether storage conditions and/or year of birth (a proxy for length of time in storage) were associated with newborn telomere length. We found that storage conditions and year of birth were important predictors of DNA quality and telomere length. First, samples from

births in 2008, which were stored in (room) temperature- and humidity-controlled spaces, were more likely to be degraded than samples from births in 2009 and 2011–2012, which were stored at −20◦C. Furthermore, year of birth was strongly positively associated with telomere length. Samples from babies who were born earlier produced longer T/S ratio values than samples from babies who were born more recently. Given that samples from 2011 to 2012 and 2009 were stored under the same conditions (frozen at −20◦C), it is unlikely that observed differences according to year of birth were due solely to differences in storage conditions. More work is needed to understand whether this finding is evidence of a cohort effect or a secular trend in newborn telomere length or whether the PCR assay is sensitive to sample storage time (see Kugler et al. 2011 for more information on the effects of storage time on laborabory assays). Regardless of the reason for our findings, we recommend that researchers adjust for time in storage (proxied by year of birth in this study) and use caution when making inferences about samples that have been stored for different lengths of time.

Limitations, Strengths, and Directions for Future Research

Limitations of this study include small sample size; low prevalence of preterm birth, low birth weight, and obstetric complications; limited measures of the maternal social environment; cross-sectional design; lack of detailed information on time in storage; and lack of data on leukocyte cell subpopulations. The small sample size limited statistical power and resulted in low prevalence of preterm birth, low birth weight, and obstetric complications, which may be important predictors of newborn telomere length. Now that feasibility of the PCR assay has been demonstrated in archived dried blood spots from a newborn genetic screening program, future studies should include larger samples. Future studies should also link data from dried blood spots to more detailed sources of information on exposures, covariates, and outcomes in new or existing cohorts. While birth certificates provide important sociodemographic information about newborns and their biological parents, detailed data on environmental, social, and psychosocial factors are limited. Moreover, longitudinal data are needed to identify correlates of the rate of telomere attrition over time, which may be a better predictor of long-term health outcomes than a single measure of telomere length (Duggan et al. 2014). To better understand effects of storage time on T/S ratio, future studies should obtain information on month and day of birth, in addition to year of birth. Although detailed information on the date of birth can be linked to dried blood spots from the Michigan Neonatal Biobank, a larger sample size is needed in order to gain access to this information. Finally, previous research suggests that, within individuals, telomere length in different cell types varies (J. Lin et al. 2010). Given evidence of black/white differences in leukocyte cell subpopulations (Freedman et al. 1997; Lim et al. 2010), future studies should consider whether racial/ethnic heterogeneity in cell types contributes to racial/ethnic differences in newborn telomere length.

The limitations of this study were balanced by several strengths. Although this was a relatively small study (n = 192), most prior research on newborn telomere length has been conducted in even smaller samples. For example, the two studies that examined race/ethnic differences in newborn telomere length had sample sizes of 71 (Drury et al. 2015) and 143 (Rewak et al. 2014), while the study examining effects of maternal education on

newborn telomere length had a sample size of 54 (Wojcicki et al. 2016). Another strength of this study was the use of a population-based sample, which reduces selection bias and enhances generalizability. Finally, this study demonstrated the feasibility of measurement of telomere length in archived dried blood spots from a newborn genetic screening program. This opens up numerous possibilities for future studies of the environmental antecedents and health-related consequences of newborn telomere length.

Conclusions

Using archived dried blood spots from the Michigan Neonatal Biobank, we found that maternal race/ethnicity was an important determinant of neonatal telomere length, but that black/white differences were evident only among infants born to mothers who did not receive public assistance. Replication studies in larger samples are needed to confirm or refute this finding, which poses a challenge to simplistic biological explanations for race/ethnic differences in telomere length. Given that telomere length during adulthood appears to be largely determined by telomere length at birth and telomere attrition during the first 20 years of life (Benetos et al. 2013), more work is needed to identify early-life determinants of life course telomere dynamics, including the effects of parental —and even grandparental—social disadvantage. Samples obtained from newborn genetic screening programs are currently available to researchers only in Michigan and California but are stored for at least 21 years in 14 states, covering 45% of the newborn population in the U.S. (Therrell et al. 2011). These samples provide an invaluable source of data for population studies on neonatal telomere length.

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Notes

1. T/S ratio values are not directly comparable across labs unless the same reference standard and lab procedures are used. For this reason, the univariate statistics presented here may differ from those presented in other studies of newborn telomere length.
2. Models stratified by race/ethnicity failed to replicate the Wojcicki et al. (2016) finding that maternal educational attainment was associated with newborn telomere length among infants born to Latina mothers.

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