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From culture to chromosomes: A mother-child dyadic study of acculturation, telomere lengths and body fat

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ABSTRACT

Studies suggest that telomere lengths, a biomarker of aging, could also capture the physiological weathering attributable to poor health behaviors and adverse experiences, particularly those experienced in early life. For these reasons, we propose that telomere lengths may be a pivotal biomarker for measuring the heightened susceptibility to illness resulting from the cumulative exposure to acculturation to the US culture. This binational study used an Actor–Partner Interdependence Model to test if maternal acculturation to the US moderates the cross-sectional associations of telomere lengths with percentage of body fat (PBF) among Mexican women, among their children, and the intergenerational associations of mother and children telomere lengths with each other's PBF. Low income Mexican child–mother dyads (n = 108 dyads) were recruited to participate in this cross-sectional study in Mexico and the US. The pooled dataset included measurements of maternal acculturation to the US, mother and children's salivary telomere lengths, PBF measured through bioelectrical impedance, and demographic characteristics. Results showed that the influences of maternal acculturation in the associations of telomere lengths with PBF were different for mothers and their children: Among mothers with higher maternal acculturation to the US, longer salivary telomere lengths were associated with lower PBF. In contrast, among mothers with lower maternal acculturation to the US, salivary telomere lengths were not associated with PBF. There were no significant associations between children's salivary telomere lengths and PBF, and the null associations did not vary across different levels of maternal acculturation to the US. Future longitudinal studies are needed to determine whether acculturation to the US (experienced through immigration or remotely) influences the association of telomere length attrition with obesity risks among immigrant and non-immigrant Mexican children and adults.

1. Introduction

Telomeres are segments of deoxyribonucleic acid (DNA) at the end of the chromosomes that naturally shorten with cell replication over the lifespan [1]. Correspondingly, shorter telomeres are associated with older age, loss of years of healthy life, and higher prevalence of diseases like type 2 diabetes mellitus and cardiovascular disease [2–4]. In addition to aging, there is sufficient evidence suggesting telomere shortening

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is attributable to adverse environmental exposures [1,5–7]. Exposure to poverty, social disadvantage, and chronic physiological stress are associated with shorter telomere lengths [6,8]. Together, these associations suggest that telomere lenghts could serve as a useful 'psychobiomarker' able to quantify the physiological, particularly cardiometabolic damage attributable to adverse environmental exposures [7]).

1.1. Telomere lenghts and obesity

Shorter telomeres and telomere shortening are associated with obesity. Previous studies suggests these associations may be attributable to the increased inflammation and the high levels of reactive oxygen species produced by obesity [9]. It is well-documented that high levels of reactive oxygen species result in single strand breaks in DNA [10]. Compared to genomic DNA, telomeric DNA is more sensitive to damage because in addition to being less capable of DNA repair, it contains G-rich fragments that are highly sensitive to reactive oxygen species [10]. However, while the biological pathways through which obesity could relate with telomere lengths are feasible, this association remains unclear. This is mainly because it is not always consistent. Findings from a recent meta-analysis that included 87 studies suggested the association is age-dependent and varies across different racial/ethnic groups [11]. Age-differences in the association of obesity with telomere lengths may be associated with a stronger effect of early life exposures. Several studies suggest heritability and early life environments are key determinants of telomere lengths [12]. The first 5 years of life, in particular, encompasses a sensitive period of steep telomere loss that sets the course for future telomere trajectories [13].

The racial/ethnic differences in the association of obesity with telomere lengths may be explained by the very low number of Hispanic/Latino adults included in the analyses (less than 3%) [11]. The underrepresentation of Hispanic/Latinos in research studies continues to be a problem that hinders our understanding of telomere trajectories among Hispanic/Latinos, and racial/ethnic differences throughout the lifespan.

The few studies that have examined the association of telomere lengths with obesity among Hispanics/Latinos yielded unexpected findings that merit further investigation. For example, a previous study conducted with the Mano-a-Mano cohort, a large sample of first and second generation Mexican-Americans in the US, showed that shorter telomere lengths were associated with normal weight [14]. In contrast, longer telomere lenghts were most often found among participants with overweight and obesity [14]. Researchers hypothesized that acculturation may explain these differences, but when tested, found no association between parental acculturation and telomere lenghts of children born to Mano-a-Mano participants. Notably, most children in these offspring analyses were born to US-born Mexicans. To our knowledge, no other study has examined the association of telomere lengths with obesity and acculturation in samples of children born to less acculturated Mexican mothers. It is also unknown if the association of obesity with telomere lengths will differ if examined among Mexicans living in Mexico who are exposed to acculturation to the US only through remote cultural vehicles.

1.2. Acculturation and remote acculturation

Acculturation—the gradual multidimensional and behavioral process that takes place when individuals from different cultures have social exchanges—can impact weight gain and telomere lengths of immigrant children and adults through a variety of mechanisms [15,16]. For example, higher acculturation to the US culture is associated with higher levels of sedentary behaviors and changes in dietary behaviors that include lower fruit and vegetable intake, and higher soda and fast-food consumption [16]. Correspondingly, researchers have found that intake of sugar-sweetened soda beverages is associated with shorter telomeres [17].

Exposure to acculturation to the US may not be limited to individuals who migrated to the US. According to Ferguson et al., current intercultural contacts outside the context of migration have opened possibilities to new forms of acculturation known as remote acculturation [18]. In one of the landmark studies of remote acculturation, researchers found that Jamaican adolescents who have never visited the US had a strong Americanized orientation [18]. Their findings on remote acculturation aligned with findings from previous studies that examined acculturation to the US among Jamaican immigrant samples in the US [19].

Despite the geographic and economic proximity between Mexico and the US, studies of remote acculturation among Mexicans in Mexico are lacking. We identified only one study that examined the association of remote acculturation with smoking risks among Mexican youth in central Mexico [20]. Findings from this study showed that greater acculturation to the US culture associated with higher risk of smoking among Mexican youth living in central Mexico [20]. To our knowledge, the influence of remote acculturation to the US has not been examined with other health outcomes or any biomarkers among Mexican samples.

1.3. Telomere lengths and acculturation

Several studies have shown that cumulative exposure to acculturation to the US culture associates with higher physiological weathering [21–23]. In turn, studies have suggested that telomere lengths capture the physiological weathering attributable to poor health behaviors and adverse experiences, particularly those experienced in early life [1,5–7,12]. Together, these studies lay the foundation to suggest that telomere lengths may capture the physiological weathering associated with acculturation to the US culture. However, the few studies that examined the association of acculturation with telomere lengths among Mexican immigrant adults have found conflicting findings. For example, a previous study found that less acculturated, lower-income Mexican immigrants had longer telomere lengths than their more acculturated non-poor Mexican counterparts [8]. Undoubtedly, the influence of acculturation on telomere lengths of Mexican immigrants' merit further investigation. Further, given the heritability of telomere lengths and their heightened sensitivity in early life [12], it is important to examine the influence of acculturation on telomere lengths not only among adult samples, but also test the potential intergenerational influence on the telomere lengths of their offspring who share their US acculturation exposure either through immigration or through remote channels. This intergenerational influence is an important area for research in a population largely understudied.

1.3. The present study

The current cross-sectional study aims to investigate, in an exploratory manner, whether acculturation to the US exerts and influence in the association of telomere lengths with percentage of body fat (PBF), a more precise indicator of obesity. In order to investigate exposure to acculturation to US that occurred through immigration and remotely, this study used a binational design to included Mexican mother-child dyads living in the US and Mexican mother-child dyads living in Mexico. Specifically, this study addresses four exploratory research questions: 1) Does the association of telomere lengths with PBF among Mexican mothers living in Mexico and the US varies with higher acculturation to the US? 2) Does the association of telomere lengths with PBF among Mexican children living in Mexico and the US varies if their mother's have higher acculturation to the US? 3) Does the intergenerational association between mothers' telomere lengths with their children's PBF differs if mother's have higher acculturation to the US? and 4) Is the intergenerational association between children's telomere lengths with mother's PBF moderated by mother's higher acculturation to the US? We hypothesized the association of telomere lengths with PBF among mothers and children's will be moderated by mother's acculturation to the US. Further, given the heritability of telomere lengths, shared environment between mother and children, and the well-established

association between mother's and children's weight, we hypothesized there will be an intergenerational association between mother's telomere lengths and children's PBF that will be moderated by mother's acculturation to the US and an intergenerational association of children's telomere lengths with mother's PBF also moderated by mother's acculturation to the US. Lastly, we hypothesize the moderation tests will show stronger associations amongst the dyads that include mother's with higher acculturation to the US.

2. Methods

A binational cross-sectional sample of Mexican-born mothers and their 4 to 6-year-old children living in Mexico (n = 78) and the US (n = 30) were recruited to participate in the Family-based International Evaluation of Salivary Telomere-lengths and Acculturation (FIESTA!) Study. Mother-child dyads were eligible to participate if the mothers were born in Mexico, had a 4 to 6-year-old child, and spoke Spanish or English. Data from mother-child dyads were pooled and all analyses were conducted using the pooled dataset (n = 108). The sample size was calculated based on recommendations from simulation models that suggest that when the number of dyads is 50 or larger, type 1 error rates of fixed coefficients are closed to 5% across all conditions [24].

In Mexico and the US, recruitment of child–mother dyads and collection of survey data and anthropometric measurements (height, PBF, and saliva samples) took place during one in-person examination. In Mexico, child–mother dyads were recruited using flyers distributed to all parents on the first day of school, and data was collected at their child's government-funded Kindergarten in a low-income semi-urban neighborhood. Data collection in Mexico was conducted from September 2016 to November 2016.

In the US, recruitment materials were posted in local community centers, public parks, laundromats, and at local churches across several semi-urban cities in Illinois. Participants in the US were also recruited using snowball sampling strategies and referrals from community leaders. In the US, data were collected at participants' homes, and in a private office at one of the local churches. Data collection in the US was conducted from April 2016 to March 2017.

Prior to data collection and anthropometric assessments, all mothers (in Mexico and the US) provided informed consent and parental consent on behalf of their child. All children provided assent. All procedures of the FIESTA! Study were approved by the Institutional Review Board of the University of Illinois in Urbana-Champaign, by the Kindergarten's Principal in Mexico, and by the Secretary of Education of the Government of the State of San Luis Potosi, Mexico (Secretaría de Educación de Gobierno del Estado, SEGE). We compensated children in Mexico and the US with an educational toy purchased from Melissa and Doug®. Mothers were compensated with a $20 gift card in the US and $100 pesos ($6 USD) in Mexico, the amount of the compensation in each country was determined based on the estimated local costs of the items needed to prepare a meal for a family of four.

2.1. Measures

Independent variables: Mother and child salivary telomere lengths. Salivary telomere lengths were measured from DNA extracted from children and mother salivary samples. Children and mother's saliva samples were collected using Oragene™ DNA Self- Collection Kit (Oragene, DNA Genotek, Ottawa, Canada). Saliva samples were shipped to the University of Illinois at Urbana-Champaign at room temperature for DNA extractions. Genomic DNA was extracted from 500-μL saliva aliquots using prepIT-L2P (DNA Genotek, ON, Canada), following manufacturer instructions for DNA precipitation with ethanol by centrifugation. Samples were evaluated for quality according to standardized operational procedures established in Dr. Teran-Garcia's Laboratory at the University of Illinois at Urbana-Champaign. Concentrations of DNA were normalized at 40ng/uL and stored at −80° prior to shipping all samples to the University of California, San Francisco for telomere length assay. The telomere length measurement assay was adapted from the published original method by Cawthon [25,26]. The T/S ratio for each sample was measured twice, each in triplicate wells. The average of the two measurements was used for analyses. Whenever variability exceeded 7%, the sample was tested a third time and the average of the two closest values were used. In this study, the average coefficient of variation (CV) was 2.3 ± 1.8%. Telomere lengths ranged from 1.13-2.47 T/S among children and from 1.00-2.14 T/S among mothers and were analyzed as a continuous variable. See Supplement 1 for additional details on laboratory procedures.

Moderator: Maternal acculturation to the US culture. Acculturation was conceptualized as multidimensional concept and measured using a measurement derived from the revised Subscale 1 of the Acculturation Rating Scale for Mexican Americans (ARSMA-II) [27,28]. The original revised ARSMA-II instrument has 30 items that are divided in two subscales: The American or Anglo orientation subscale that includes 13-items and the Mexican orientation subscale that includes 17-items. Both subscales can be used to calculate either bidimensional scores by reporting each subscale separately, or unidimensional scores by subtracting the mean Mexican orientation from the mean American orientation [27,28]. For the purposes of this study, we adopted the bidimensional approach, and focused on the influence introduced by one dimension: the American orientation. This approach is recommended to avoid collapsing two orthogonal dimensions into one dimension which introduces measurement errors and could lead to misinterpretations [28].

In addition, considering the lack of items that examine the influence of acculturation on behavioral preferences, we expanded the instrument by including 2-items from the subscale-2 of the Acculturation Rating Scale for Mexican Americans (ARSMA-II) to each subscale, thus including 4 additional items. The additional items included examined preferences for traditional meals and traditional celebrations, to each culture respectively. Exploratory factor analyses were conducted to examine this adaptation of the revised ARSMA-II scale and the corresponding association between all items with the two factors: maternal acculturation to the US (MA-US), and maternal acculturation to Mexico (MA-MX). Factor analyses were conducted in stages. Models resulted in a 25-item solution with 2-factors with separate loadings of at least 0.30 or higher associated with each cultural orientation (see Supplement 2 for final items and factor loadings). Assessment of the psychometric properties of the derived acculturation subscales indicated overall high internal consistency and reliability in our sample, with a Cronbach's α = 0.91 for the MA-US subscale, and a Cronbach's α = 0.87 for the MA-MX subscale. Data were further assessed for appropriateness for factor analysis by conducting the Kaiser-Meyer-Olkin (KMO) measure of sampling adequacy, which resulted in a value of 0.796 and a significant Bartlett's Test of Sphericity ($P<.0001$). These results confirmed the sample was adequate for factor analysis.

For the purposes of the present analyses, only scores of the derived subscale that assessed MA-US were examined. Measurements of acculturation to the US were collected only from mother due to the complexity of the instrument and the lack of a child-friendly validated tool. Scores were introduced as continuous measurements in all analyses. Responses ranged from 1 to 5. Scores of 1 represented the lowest possible levels of MA-US and 5 represented the highest levels of MA-US.

Outcomes: Mother and child percentage of body fat (PBF). Height was measured to the nearest 0.1 cm, using a portable stadiometer with children and mothers in the standing position (Seca 213, Hamburg, Germany). Body composition measurements of children and mothers were collected during the in-person examination after an overnight fasting following a standardized protocol and using the Inbody230™ (Biospace Ltd., Seoul, Korea) body composition analyzer. This instrument has been validated on both age groups [29,30]. The body composition assessment provides a validated estimate of the PBF. Although body mass index (BMI) is the most commonly used measurement to identify excess

weight, researchers have demonstrated it is not the most accurate indicator of adiposity status and obesity risks [31,32]. BMI measurements often fail to account for the weight of fat-free-mass in adults and do not identify excess body fatness correctly in children [32]. When possible, it is recommended to use more precise measurements of adiposity, like PBF. In adults, bioimpedance analysis (BIA) estimates yield similar results for PBF to those obtained by dual x-ray absorptiometry (DXA), but is a less invasive approach [29]. In a comparison of adiposity assessments that included BMI, CT scans, BIA and DXA, researchers recommended the use of BIA as a more simple and effective way to measure adiposity in young children [30]. Hence, for the purposes of this study, we used the estimate of PBF of children and mothers as the measurement of adiposity proportional to the body size. PBF measurements were treated as continuous variables and assessed as the main study outcome.

Covariates. Mothers self-reported the sex at birth, country of birth, current age in years for themselves and their children, their years of education completed and the number of working light bulbs in the house. Preferred language and country of recruitment were determined from the recruitment forms.

Sex and age for children and age of mothers were included as covariates because previous studies have suggested sex and age differences extend to the association of metabolic health with telomere lengths [33]. We relied on data on the number of working light bulbs in the house to assess socioeconomic status. This measurement has been previously used to characterize differences by socioeconomic status between Mexicans in Mexico and Mexicans in the US given that traditional socioeconomic and income measures may not accurately characterize socioeconomic differences [34]. These data were collected from mothers using a paper questionnaire in their language of preference.

2.2. Analytical approach

Data from both countries were pooled and dyads were analyzed together. Descriptive statistics for the overall sample and by place of residence (Mexico or the US) were tested to confirm dyadic data satisfied the normal univariate distribution criteria and to identify influential observations (DFBETA greater than |0.4|, [35]. Statistical differences between the subsamples from Mexico and the US were determined with Welsh's t-tests for unequal variances. Comparisons across subsamples revealed PBF measurements of mothers recruited in Mexico and the US differed significantly ($p = 0.02$). These differences were addressed by adding a dichotomous variable to control for differences by country.

Bivariate Pearson correlation tests were used to examine the correlations between mother and child anthropometric measurements. Given the biological and environmental nature of the child–mother relationships, the anthropometric measurements of the 4 to 6-year-old children were presumed to be distinguishable and non-independent from those of their mothers.

Associations of each member of the dyad's (mother and children) salivary telomere lengths with their own PBF and with their dyadic partner's PBF measurements (intergenerational) were tested using two-intercept Actor-Partner Interdependence Model (APIM) [36] as illustrated in Fig. 1. The APIM statistical methodology accounts for the non-independence in the dyad and is a useful approach to simultaneously examine potential intergenerational associations between children and mothers [36,37]. This model implicitly controls for unmeasured and even unknown exposures, common among mothers and children that can influence the predictors (telomere lengths) or the outcomes of interest (PBF) such as genetics, and shared environmental and behavioral factors, and other unmeasured characteristics such as potential prenatal factors. While different analytical models could be used to account for the cluster nature of the mother-child data, the APIM was specifically selected because it is designed to account for a cluster size of two that violates the independent observations assumption which, if ignore can lead to overestimating *p*-values[24,38]. The APIM uses a pooled regression approach and introduces random effects that capture the intraclass correlation which deemed this analytical approach appropriate when the sample size is small [24,38].

In fact, given the small sample size, covariates were determined using the APIM model, and only significant predictors were included in the final models. Variables for socioeconomic status (education and light bulbs) were not included given their non-significant contributions to the model.

Three stepwise APIMs were used to test the associations of telomere lengths with PBF. Model 1 examined the effects of the covariates (sex, age and country). Model 2 examined the main associations of salivary telomere lengths among mother and children with their own PBF, controlling for children's sex, child and mother's ages and country differences. In model 3, we examined the multilevel interaction with MA-US as a level 2 dyadic multiplicative variable. Fig. 1 illustrates the associations

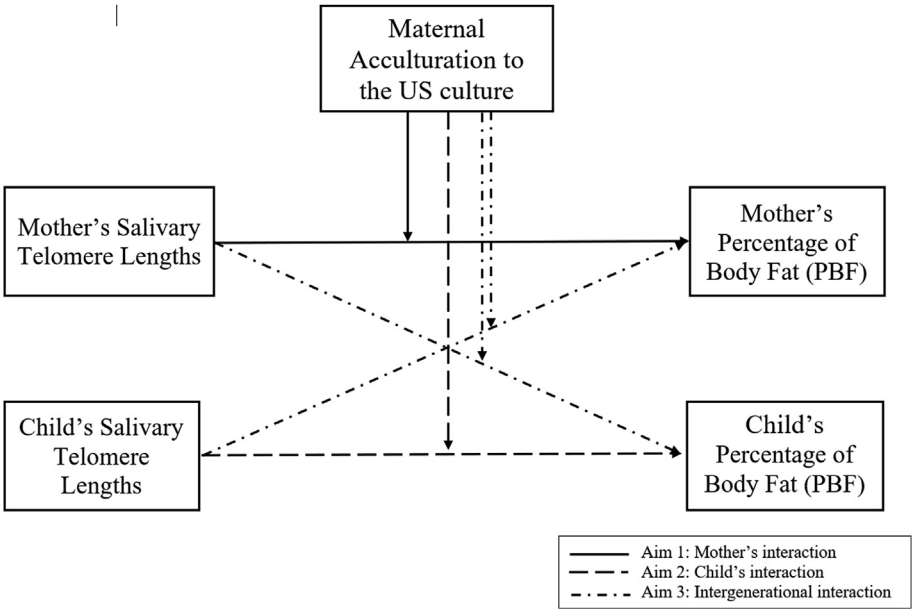

Fig. 1. Actor-partner interdependence model (APIM) with the pathways examined shows the moderation of maternal acculturation to the US in three associations. Aim 1: moderation of maternal acculturation to the US in the association of mother salivary telomere lengths with mother's percentage of body fat (PBF), Aim 2: moderation of maternal acculturation to the US in the association of children's salivary telomere lengths with children's PBF, and Aim 3 moderation of maternal acculturation to the US in the intergenerational associations of mother and child salivary telomere lengths with each other's PBF.

examined with the respective aims associated with each pathway. Results are reported in standardized parameters, with PBF as the only outcome tested. All APIMs were analyzed with hierarchical linear modeling using the APIM two-intercept model method, with restricted maximum likelihood as the estimation method, and PBF as the outcome. Simple slopes were graph to include the association with the mean and one standard deviation. The level of significance for all statistical analyses was set at $\alpha \leq 0.05$. Descriptive statistics were calculated using SPSS version 25 (SPSS, Chicago, IL, USA) and APIM tests were estimated with HLM 7.03 (Scientific Software International, Inc; Skokie, IL, US).

Table 1
Descriptive characteristics of mothers and children by country of residence.

Characteristics	All (n = 108)	Mexico (n = 78)	US (n = 30)
Mother Characteristics	(%, (n)/*m* ±sd)		
Mother's age (range 19–55)	31.11 ± 7.57	30.48 ± 8.14	32.69 ± 5.72
Under 25	30.6 (33)	39.7 (31)	6.7 (2)
25–30	21.3 (23)	17.9 (14)	30 (9)
31–35	21.3 (23	16.7 (13)	33.3 (10)
35 and older	20.4 (22)	20.5 (16)	20 (6)
Mother's Percentage of Body Fat (PBF)*	39.68 ± 6.16	39.07 ± 6.25	41.34 ± 5.68
Mother's BMI (kg/m^2)	27.90 ± 4.48	27.33 ± 4.34	27.98 ± 4.54
Mother's Weight Status			
Normal	25.9 (28)	33.3 (26)	6.7 (2)
Overweight	25.9 (28)	24.4 (19)	30.0 (9)
Obesity	41.7 (45)	37.2 (29)	53.3 (16)
Mother's salivary telomere lengths (T/S)	1.35 ± 0.21	1.37 ± 0.23	1.30 ± 0.13
Telomere length by age group (T/S)			
Under 25	1.41 ± 0.25	1.41 ± 0.25	1.22 ± 0.02
25–30	1.31 ± 0.16	1.29 ± 0.19	1.35 ± 0.12
30–35	1.32 ± 0.22	1.35 ± 0.22	1.25 ± 0.16
35 and older	1.30 ± 0.19	1.32 ± 0.22	1.24 ± 0.07
Mother's acculturation to US culture (ARSMA-II)**	2.17 ± 1.07	1.69 ± 0.63	3.07 ± 1.15
MA-US range (ARSMA-II)	1.0 to 5.0	1.0 to 4.0	1.55 to 5.0
Years of education	9.56 ± 3.34	9.77 ± 3.42	9.00 ± 3.10
Number of light bulbs in the house*	9.43 ± 5.93	8.43 ± 4.72	12.03 ± 7.76
Child Characteristics			
Children's age**	4.81 ± 0.89	4.58 ± 0.58	5.36 ± 1.23
4 years old	55.6 (60)	64.1 (50)	33.3 (10)
5 years old	30.6 (33)	33.3 (26)	7 (23.3)
6 years old	13.9 (15)	2.6 (2)	13 (43.3)
Children's gender (Male)	49.1 (53)	46.2 (36)	56.7 (17)
Children's Percentage of Body Fat (PBF)	27.10 ± 7.1	27.34 ± 6.8	26.52 ± 7.7
Sex-specific children's BMI-for-age percentile	63.15 ± 30.8	59.87 ± 32.2	71.11 ± 25.8
Children's Weight Status			
Normal (5th to 84.9th percentile)	66.7 (72)	67.9 (53)	63.3 (19)
Overweight (85th to 94.9th percentile)	13.9 (15)	12.8 (10)	16.7 (5)
Obesity (>95th percentile)	19.4 (21)	19.2 (15)	20.0 (6)
Children's salivary telomere lengths (T/S)	1.69 ± 0.28	1.68 ± 0.29	1.69 ± 0.25
Telomere length by age group (T/S)			
4 years old	1.71 ± 0.29	1.71 ± 0.30	1.70 ± 0.23
5 years old	1.68 ± 0.28	1.69 ± 0.29	1.64 ± 0.27
6 years old	1.62 ± 0.28	1.54 ± 0.43	1.66 ± 0.26

*p < 0.05; **p < 0.001.

3. Results

Descriptive statistics for children and mothers are shown in Table 1. All mothers in Mexico and the US selected the Spanish instruments. Analyses revealed that all children born to mothers recruited in Mexico were born in Mexico, and all children born to mothers recruited in the US were born in the US. Given the lack of variability, child nativity and language of preference were not included as potential covariates. Mothers in the US reported they have resided in the country from 5 to 25 years. Mean age of migration was 16.5 years, and only 20% of the mothers in our sample arrived as young children (under the age of 12 years). The combined prevalence of overweight and obesity was 68% among mothers and 33% among children. These prevalence rates closely reflected the current prevalence among Mexican children and adults in Mexico and the US.

Correlations between children and mothers' anthropometric measurements are shown in Table 2. Telomere lengths ($r = 0.36$, $p < 0.01$), and fat-free mass ($r = 0.21$, $p = 0.03$) of children and mothers were significantly correlated. There were no significant correlations between child and mother's PBF ($r = 0.06$, $p = 0.52$). The significant correlations between children and mothers' measurements of telomere lengths and fat-free mass warranted the assumption of non-independence in our distinguishable dyad [36].

Results from associations examined in the APIM are shown in Table 3. Results showed that children and mothers own telomere lengths were not associated with their own PBF (actor effects). In the tests of the intergenerational association, results showed there were no intergenerational associations (partner effects) between children's and mother's telomere lengths with each other's PBF.

3.1. Acculturation to the US (MA-US) as potential moderator in the association of mother's salivary telomere lengths with mothers' PBF

Among mothers, there was a significant cross-level interaction of MA-US with the association of mothers' telomere lengths and their own PBF ($\beta = 25.84$, SE = 8.97, $p = 0.006$). Tests of the simple slopes exploring this interaction revealed the associations of mother's telomere lengths with their own PBF varied for the different levels of MA-US (Fig. 2). Among mothers with lower acculturation to the US (scores of 1/5 and 2/5 in the revised ARSMA-II Sub-scale 1), salivary telomere lengths were not significantly associated with their own PBF ($p = 0.69$ for scores of 1, and $p = 0.17$ for scores of 2). In contrast, among mothers with MA-US scores of 3 or higher, longer telomere lengths were significantly associated with higher PBF ($p = 0.017$).

3.2. Maternal acculturation to the US (MA-US) as potential moderator in the association of children's salivary telomere lengths with children's PBF

In the test of the moderation of MA-US in the child actor path, there was a non-significant trend in the interaction of MA-US with the association between children's telomere lengths and children's PBF ($\beta = 4.63$, SE = 2.51, $p = 0.07$).

3.3. Maternal acculturation to the US (MA-US) as potential moderator in the intergenerational association of mother's telomere lengths with their child's PBF, and of children's telomere lengths with their mother's PBF

The tests of the moderation of MA-US in the intergenerational path evidenced the null-associations of children's and mother's telomere lengths with each other's PBF were not significantly moderated by differences in MA-US. There was, however, evidence of a non-significant trend in the interaction of MA-US with the association between mother's salivary telomere lengths and children's PBF ($\beta = -4.93$, SE = 2.65, $p = 0.067$).

Table 2
Bivariate correlations among children and mother anthropometric measurements.

		Mother measurements					Child measurements					
		2	3	4	5	6	7	8	9	10	11	12
Mother measurements												
1	Salivary telomere lengths	−0.01	−0.15	−0.15	−0.07	−0.10	0.36**	0.11	−0.15	−0.21*	−0.03	−0.05
2	Percentage of Body Fat (PBF)	–	0.49**	0.03	0.76**	0.71**	−0.02	0.06	0.09	0.07	0.10	0.06
3	Weight (kg)		–	0.83**	0.89**	0.87**	0.05	−0.02	0.18	0.21*	0.11	0.14
4	Fat-free mass (kg)			–	0.50**	0.51**	0.01	0.01	0.17	0.21*	0.10	0.14
5	Body-fat mass (kg)				–	0.95**	0.03	0.03	0.12	0.12	0.10	0.06
6	Body mass index (BMI, kg/m^2)					–	−0.01	−0.03	0.15	0.17	0.09	0.10
Child measurements												
7	Salivary telomere lengths						–	0.07	−0.08	−0.11	−0.02	−0.06
8	Percentage of Body Fat (PBF)							–	0.48**	0.09	0.84**	0.62**
9	Weight (kg)								–	0.90**	0.86**	0.65**
10	Fat-free mass (kg)									–	0.57**	0.49**
11	Body-fat mass (kg)										–	0.69**
12	Body mass index (BMI, kg/m^2)											–

*$p < 0.05$; **$p < 0.01$.

Table 3
Robust coefficients from four two-intercept Actor-Partner Interdependence Models (APIMs) testing the mother–child dyadic association between salivary telomere lengths (sTL), percentage of body fat (PBF), and maternal acculturation to the US (MA-US).

	Model 1: Covariates		Model 2: Tests of main effects		Model 3: Moderation of MA-US		
	β	(SE)	β	(SE)	β	(SE)	*p-value*
Gender	19.72**	1.96					
Age	0.61**	0.07					
Country	7.49**	1.70					
Intercepts							
Child			15.21*	6.13			
Mother			26.54**	6.06			
Actor effects							
Child sTL → Child's PBF			2.46	2.92	−6.36	5.67	0.268
Mother → Mother's PBF			−0.72	4.44	−48.35*	16.83	0.006
Interaction Actor Effects							
MA-US x Child's sTL → Child's PBF					4.63	2.51	0.070
MA-US x Mother's sTL → Mother's PBF					25.84*	8.97	0.006
Partner effects							
Child's sTL → Mother's PBF			3.01	4.91	0.39	6.37	0.951
Mother's sTL → Child's PBF			3.25	3.18	10.62	7.48	0.159
Interaction Partner Effects							
MA-US x Child sTL → Mother's PBF					0.65	5.31	0.904
MA-US x Mother's sTL → Child's PBF					−4.93	2.65	0.067

*$p < .05$; **$p < 0.001$.

4. Discussion

In this study, we showed that MA-US moderates the direct associations of telomere lengths with PBF of the Mexican women in our sample, but does not moderate the direct associations of children's telomere lengths with their own PBF or the intergenerational associations of mother's with their children's and viceversa. Findings evidenced that among women with higher acculturation to the US, longer salivary telomere lengths were associated with higher PBF. In addition our analysis revealed two non-significant trends: the first one in the moderation of MA-US on the association of children's salivary telomere lenghts with their own PBF, and the second one in the moderation of MA-US with the intergenerational association between mothers salivary telomere lenghts and their children's PBF.

Our findings on the association between telomere lengths and PBF among women with higher acculturation to the US merit further investigation. Based on the wide support for the stress-illness model that conceptualizes acculturation as a stressful exposure, we expected more acculturation to the US among immigrant and non-immigrant women would be positively associated with higher adiposity [39,40]. Instead, our results suggest that higher acculturation to the US afforded protective effects to Mexican women. Among Mexican mothers with higher levels of acculturation, higher percentages of body fat were associated with longer telomere lengths. Ours is not the first study to document conflicting associations between telomere lenghts and obesity measurements among Mexican adults. In a previous study with the Mano-a-Mano cohort, a sample of adults of Mexican descent living in the US, researchers found that longer telomere lengths were most often found among participants with overweight and obesity, when compared with normal weight peers [14]. To our knowledge, these are the only two studies that have examined the association of telomere lenghts with adiposity among Mexican samples exposed to different degrees of acculturation to the US.

Several epidemiological studies that assessed the association of adiposity with mortality found that overweight adults were more likely to have lower mortality risks when compared with normal weight counterparts [41]. Studies of this 'obesity paradox' found the associations of BMI with mortality are U or J shaped, particularly when examined among older adult populations [42]. However, these studies relied mostly on BMI measurements as opposed to more precise assesments of body composition [42]. When examining more precise measurements of body composition, findings suggested the different contributions of lean and fat mass may explain the previously paradoxical associations with mortality [42]. Findings from a study conducted with a large cohort of older men (mean age 54 years) showed that fat mass was directly associated with mortaility from cardiovascular disease, cancer, and all other causes, and the protective or paradoxical associations with BMI were mostly attributed to differences in lean mass [42]. While we did not examined lean mass in our study, it can be noted from the simple slopes

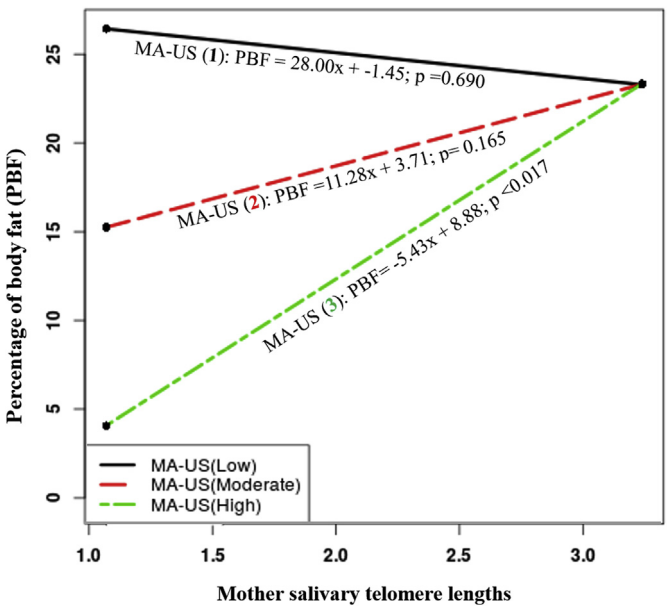

Fig. 2. Intercepts and simple slopes of the association of mother's salivary telomere lengths with their own percentage of body fat (PBF) across three levels of maternal acculturation to the US culture (MA-US).
The association of mother's salivary telomere lengths with their own PBF varies by level of MA-US. When women's acculturation to the US was low (score of 1/5 and 2/5 in the ARSMA-II subscale), salivary telomere lengths were not significantly associated with PBF ($p = 0.690$, and $p = 0.165$, respectively). In contrast, when mothers had high or moderate MA-US (scores of 3/5 and higher) longer salivary telomere lengths were significantly associated with higher PBF ($p < 0.017$).

that the association of higher percentage of body fat with longer telomere lenghts was significant only among women with higher acculturation to the US, who were also leaner than their less acculturated counterparts. Thus, although we examined a younger population, both studies suggest that further examinations using more precise indicators of body composition could reveal differences in the association of fat, and lean masses with overall health, aging and mortality. Future studies should, however, consider including diverse populations and examining these associations across the lifespan, accounting for differences by acculturation as effects may vary by age, race/ethnicity, and acculturation.

In addition, our study found no associations between telomere lenghts with PBF among the children in our sample. This non-significance did not changed across different levels of MA-US. In a previous study of 793 French children ages 2 to 17 with and without obesity, authors found that telomere lengths of children with obesity were 24% shorter than the telomeres of children without obesity [43]. Although our findings did not support this previous study, the authors noted that the association between telomere lengths and excess adiposity varied by age and was stronger among older children [43]. A longitudinal examination of the relationship between telomere lengths and obesity in Latino children found that telomere lengths were not associated with children's adiposity when children were 4 or 5 years old but predicted the development of obesity by age 9 [44]. Findings from these studies suggest that our null findings among children may be explained by the young age of the children in our sample.

Assessments of telomere lengths in children of Mexican descent are particularly scarce. Nonetheless, the limited available evidence is partially consistent with our findings. In a previous study conducted with data from the 'Mano-a-Mano' cohort, researchers found no association between parental acculturation and children telomere lengths [14]. Our study advances this body of literature by showing that in an international sample of young children born to Mexican women, telomere lengths were not associated with PBF, a precise indicator of adiposity, and that these null-association was not modified by MA-US. Further, results revealed that the telomere lengths of young children and their Mexican mothers were not associated with each other's PBF. Prior studies that examined intergenerational mother-child associations found maternal telomere lengths were associated with fetal or newborn telomere lengths [45]. Yet in our study, there was no evidence of any intergenerational contributions. While we cannot discount the role of paternal genetics in the associations between telomere lengths and adiposity accumulation, the lack of an intergenerational association between mother and children suggests that socio-cultural, behavioral, and environmental factors could be largely responsible for children's telomere lengths and attrition after birth. To our knowledge, this study is the first to examine the intergenerational pathway in young children, so we cannot compare this null association with prior evidence. Further research is needed to better understand the intergenerational associations of children's and mother's and potential associations with other family members, like father's and siblings.

An important consideration when assessing our findings in contrast with previous studies is the use of saliva samples to measure telomere lengths as opposed to venous blood. We selected saliva because it was a more cost-effective and minimally invasive approach than blood. These advantages facilitated our access to pediatric populations in Mexico and the US. However, it has been suggested that telomere lengths are not consistent across different biological sample types, and sample differences can potentially translate in differences in effect sizes [46]. In a previous study that compared the association of telomere lengths from blood and saliva with age using samples from the same individual, researchers noted that although telomere length measurements were significantly correlated, the associations with age were stronger on blood samples [46]. These findings suggest the associations previously documented with telomere length measurements from blood may not be consistent if examined with saliva samples.

Longitudinal international studies examining the association of telomere lenghts and telomere attrition with obesity in samples of Mexican immigrant children, adolescents, adults and older adults are needed to adequately characterize the associations between acculturation to the US with telomere lengths and obesity across the lifespan. Previous studies have suggested that findings from attrition studies could be more powerful for detecting environmental influences [47]. It is our hope that findings from this exploratory cross-sectional analyses will justify the need for an in-depth longitudinal examination of the influence of acculturation to the US (from immigration or remote exposures) on telomere lenghts and obestiy, not only among Mexican samples, but also among other Hispanic/Latino populations.

The concept of acculturation and the associations with health are not limited to Mexican populations. Acculturation was originally introduced as a unidimensional process that examined the extent to which immigrants were assimilating to the mainstream European or American (Anglo-Saxon) cultures [48]. The acculturation literature has rapidly evolved from this 'becoming white' approach to a bicultural and even multidimensional approach that aims to better understand the complexity and nuances of increasingly multicultural societies [48]. To date, the study of associations of acculturation to the US with physical and mental health outcomes among Hispanic/Latino immigrants has attracted a large number of scholars. This increasing interest is largely inspired by the "immigrant health paradox", a phenomenon that suggests that despite having lower socioeconomic resources the less acculturated individuals are more likely to have better health outcomes than their more acculturated peers with higher socioeconomic status [49]. However, despite the large number of studies examining the process of acculturation among Hispanics/Latinos, it is not clear whether greater acculturation to the new culture, lower acculturation to the heritage culture, or both processes are hazardous to individual's health [48]. One of the reasons for this is the reliance on the unidimensional measurement of acculturation that results from combining the Mexican and American orientation assessments [48]. As a result, as recognized by Schwartz and

colleges, it is not possible to distinguish which dimension (the Mexican or American) is associated with positive health outcomes [48]. In this study, we sought to address this gap by focusing on the contributions that acculturation to the US introduced to the association of salivary telomere lengths with a precise measurement of adiposity among women and children of Mexican descent.

In addition, in spite of the large number of studies that examined the relationship of acculturation with health, *what* changes with the process of acculturation, or the biological mechanisms through which acculturation-related changes may 'get under the skin' has not been clearly defined [48]. These may be because acculturation is likely not a singular process, and as such, may impact individual's health through a variety of mechanisms [16]. For example, in addition to changes in lifestyle and dietary behaviors, it has been suggested that acculturative stress may be an underlying contributor to behavioral changes and responsible for the resulting excessive weight gain [16,40,48]. To this end, telomere lengths emerge as a very promising biomarker, able to capture the physiological damage attributable to the complex phenomenon of acculturation [47]. In a meta-analysis of the association of telomere lengths with stress and adversity, researchers concluded that a key attribute of telomere lengths is their ability to integrate psychological, social, environmental, and behavioral exposures [47].

Although our aims are exploratory, our findings suggest telomere lengths may be a highly informative biomarker of the physiological changes associated with greater acculturation to the US and perhaps other cultures. Further, the association of greater PBF with greater salivary telomere lengths among women with greater acculturation to the US living in Mexico and the US, even after controlling for country differences, highlights the need to expand the study of acculturation to include the health effects that may be attributed to remote exposures.

4.1. Limitations

Findings should be interpreted with caution in the context of study limitations. Study results could be influenced by the methodological limitations, particularly the small sample size, limited statistical power and uneven subgroup distribution. We tried to address the latter shortcoming by conducting sensitivity analyses accounting for country differences. We also used a statistical model that allowed us to limit the number of covariates and use a pooled regression approach, which is appropriate for small sample sizes [38]. Findings are not generalizable beyond the convenience sample of low-income Mexican women and children recruited. Future studies should consider examining the associations between acculturation to the US, body composition and telomere lengths in a larger binational sample of Mexican adults and their children. Additionally, tests should be replicated with telomere length measurements extracted from venous blood samples to compare findings from saliva samples. A recent study suggested that although telomere length measurements from venous blood and Oragene saliva are correlated, there can be variability in the strength of the associations by sample type [46]. Although saliva samples introduce multiple advantages for being easy to store and minimally invasive, which is convenient for pediatric populations, it is important to recognize the associations of telomere lengths may differ by sample type. Further research to better understand differences across biological sample types [46]. An additional limitation is that our study exclusively focused on the relationship between mothers and children, leaving aside the contribution from fathers, siblings, and other family members. Previous studies have observed that mother's influences on child's weight status are greater than fathers' contribution [50]. In order to understand the mechanisms through which cultural and environmental factors 'get under the skin' and influence obesity and telomere lengths, it is important to examine all potential influences in the family, including children's birth order. Future studies should consider exploring family relationships at the biological and social levels. Birth order, household structure, and other family members may introduce important information about cultural determinants of obesity and loss of telomere lengths within the family context. Lastly, the cross-sectional design of the data and lack of data on acculturative stress precluded us from examining the directionality and potential mechanisms through which acculturation may influence women and children's associations of body fat with telomere lengths. More studies are needed to further examine the directionality of the associations, the mechanisms associated with changes in acculturation to the US and their effect on telomere lengths and PBF.

5. Conclusion

Findings from this study suggest that among women with higher acculturation to the US, salivary telomere lengths are associated with their own PBF, and that maternal acculturation to the US does not influence their children's association of telomere lengths with their adiposity. The lack of an intergenerational effect between mothers' telomere lengths with their child's PBF is an important finding suggesting that after birth, children and their parents have independent telomere trajectories, likely determined in great part by environmental, behavioral, and socio-cultural exposures. In order to adequately characterize the association of acculturation with telomere lenghts and obesity across the lifespan, more assessments of the association of telomere lengths with precise indicators of body composition including adiposity and fat-free mass are needed, particulalry among binational samples that include children and adults and are able to examine the influence of acculturation to the US from immigration, and remote exposures.

Author contributions

Aguayo, Liliana: Conceptualization; Data curation; Formal analysis; Funding acquisition; Investigation; Methodology; Project administration; Resources; and Writing -original draft. Ogolsky, Brian: Conceptualization; Data curation; Investigation; Methodology: Formal analysis; Supervision; and Writing- Reviewing and Editing. Teran-Garcia, Margarita: Conceptualization; Investigation; Methodology; Resources; Funding acquisition; Supervision; Writing- Reviewing and Editing. Pineros-Leano, Maria: Conceptualization; Investigation; Data curation; and Writing-Reviewing and Editing. Wiley, Angela: Conceptualization; Investigation; Methodology; Resources; Funding acquisition; Supervision; Writing-Reviewing and Editing. Lin, Jue: Methodology; Supervision; Writing-Reviewing and Editing. Aguirre-Pereyra, Rosalba: Data curation; Project administration; Writing- Reviewing and Editing; Schwingel, Andiara: Conceptualization; Investigation; Supervision; Project administration; Resources; Writing- Reviewing and Editing.

Submission declaration and verification

The study described in this manuscript has not been published previously (except partly in the form of a dissertation for Liliana Aguayo's qualification of PhD in Community Health). Currently, this manuscript is not under consideration for publication elsewhere, its publication is approved by all authors and tacitly or explicitly by the responsible authorities where the work was carried out, and if accepted, it will not be published elsewhere in the same form, in English or in any other language, including electronically without the written consent of the copyright-holder.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.cpnec.2021.100029.

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