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Article

Nativity differences in allostatic load by age, sex, and Hispanic background from the Hispanic Community Health Study/Study of Latinos

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ABSTRACT

Allostatic load (AL), an index of biological “wear and tear” on the body from cumulative exposure to stress, has been little studied in US Hispanics/Latinos. We investigated AL accumulation patterns by age, sex, and nativity in the Hispanic Community Health Study/Study of Latinos. We studied 15,830 Hispanic/Latinos of Mexican, Cuban, Dominican, Puerto Rican, Central and South American descent aged 18–74 years, 77% of whom were foreign-born. Consistent with the conceptualization of AL, we developed an index based upon 16 physiological markers that spanned the cardiometabolic, parasympathetic, and inflammatory systems. We computed mean adjusted AL scores using log-linear models across age-groups (18–44, 45–54, 55–74 years), by sex and nativity status. Among foreign-born individuals, differences in AL by duration of residence in the US (< 10, ≥ 10 years) and age at migration (< 24, ≥ 24 years) were also examined. In persons younger than 55 years old, after controlling for socioeconomic and behavioral factors, AL was highest among US-born individuals, intermediate in foreign-born Hispanics/Latinos with longer duration in the US (≥ 10 years), and lowest among those with shorter duration in the US (< 10 years) ($P < 0.0001$ for increasing trend). Similarly, AL increased among the foreign-born with earlier age at immigration. These trends were less pronounced among individuals ≥ 55 years of age. Similar patterns were observed across all Hispanic/Latino heritage groups (P for interaction=0.5). Our findings support both a “healthy immigrant” pattern and a loss of health advantage over time among US Hispanics/Latinos of diverse heritages.

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Introduction

Exposure to stressors over the life course is thought to accelerate biological aging by promoting physiological dysregulation and influencing disease trajectories (Masoro, 1997). Allostatic load (AL) is an index of physiological dysfunction from a failure to adapt to chronic and repeated exposure to stressors (Ben-Shlomo & Kuh, 2002). As a multisystem model of biological risk, AL has been a

useful construct in conceptualizing how chronic adversity imposes “wear and tear” on biological systems, increasing morbidity and mortality over the life course (McEwen & Seeman, 1999), and contributing to health disparities in the US (Geronimus, Hicken, Keene, & Bound, 2006). Studies suggest that AL increases with age (Crimmins, Johnston, Hayward, & Seeman, 2003) and can vary by sex (Goldman et al., 2004; Yang & Kozloski, 2011). While some available evidence links AL with cardiovascular disease (CVD) risk factors in Hispanics/Latinos in the US (Mattei, Demissie, Falcon, Ordovas, & Tucker, 2010), there has been a scarcity of studies examining patterns of AL accumulation by age and sex in this

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vulnerable population. A greater understanding of the accumulation of biological mediators of risk may help to explain the increased burden of disease among US Hispanics/Latinos.

Emerging evidence suggests that place of birth (nativity) has an influence on AL. Data from the National Health and Nutrition Examination Surveys (NHANES 1999–2002) showed that while Hispanics/Latinos tend to have CVD risk factor values at high risk levels than do non-Hispanic whites, US-born Hispanics/Latinos (who were predominantly of Mexican origin) had higher levels of AL than foreign-born Hispanics/Latinos (Crimmins, Kim, Alley, Karlamangla, & Seeman, 2007). Similar results from a cross-sectional study of Mexican adults residing in Texas City, TX, showed differences across groups that persisted after controlling for socioeconomic status, smoking, and physical activity (Peek et al., 2010). These findings may suggest an “unhealthy assimilation” effect where increased stress from discrimination (Paradies, 2006), worsening dietary habits (Akresh, 2007), physical inactivity (Ham, Yore, Kruger, Heath, & Moeti, 2007), and adoption of unhealthy behaviors such smoking and drinking (Eitle, Wahl, & Aranda, 2009; Leung, 2014) confer a physiological toll and a deterioration in health with time spent in the US (Antecol & Bedard, 2006). Because each major Hispanic/Latino group living in the US has a distinct history and culture, it is informative to investigate heterogeneity in the relationship between nativity, duration in the US, age at immigration and AL across Hispanic heritage backgrounds. Moreover, the few studies that have investigated these relationships have had limited age ranges and modest sample sizes, precluding the study of AL across age groups.

The objective of this study is to examine differences in AL by age and sex patterns of AL in a diverse, representative sample of Hispanic/Latino adults in the US, and to investigate the influence of nativity status and Hispanic heritage on these observed patterns.

Methods

Sample and procedures

The Hispanic Community Health Study/Study of Latinos is a community based prospective cohort study of 16,415 Hispanic/Latino persons of diverse Hispanic heritages (Mexican, Puerto Rican, Cuban, Dominican, Central and South American) aged 18–74 recruited from four U.S. field centers (Chicago, IL; Miami, FL, Bronx, NY; San Diego, CA), with baseline measurements conducted during 2008–2011. Detailed information regarding the sampling design and cohort selection is available elsewhere (Lavange et al., 2010). Briefly, a stratified two-stage area probability sampling approach was used to select households in each of the four field centers. For the first stage, census block groups were randomly selected with stratification on the basis of Hispanic/Latino concentrations and proportions of high and low socioeconomic status. For the second stage, households were randomly selected with stratification on the basis of whether the occupant had a Hispanic surname from US Postal Service registries that covered the census block groups selected. At each stage, strata were oversampled to increase likelihood of selecting a Hispanic/Latino household. Additionally, Hispanic/Latino participants aged 45–74 were oversampled to facilitate an analyses of cardiovascular disease outcomes. The Institutional Review Boards at each participating institution approved this study and all subjects gave written informed consent.

Study visits

At the time of enrollment, all participants attended a clinical examination at a local field center. Fasting morning blood draw

and two-hour oral glucose tolerance test was obtained with clinical chemistry panels conducted by a core study laboratory. Standardized questionnaires were administered by bilingual interviewers in English or Spanish according to the participant's preference (Sorlie et al., 2010). Other measurements included seated blood pressure, resting electrocardiogram, pulmonary function testing and anthropometry (Sorlie et al., 2010).

Allostatic load markers

We defined AL based upon values of 16 available biomarkers collected using standardized protocols during the baseline clinical examination. Measures that comprised the AL index were designed to capture (a) cardiometabolic risk: body mass index (BMI), waist-to-hip ratio (WHR), serum triglycerides, and fasting levels of high- and low-density lipoprotein cholesterol (HDL-c and LDL-c); (b) glucose metabolism: fasting plasma glucose (FPG), blood glycosylated hemoglobin (HbA1c), and homeostatic model assessment of insulin resistance (HOMA-IR); (c) cardiopulmonary functioning: systolic blood pressure (SBP), resting pulse pressure, resting heart rate, and lung function (% FEV₁/FVC); (d) parasympathetic functioning using two ultra-short time domain measures of heart rate variability (HRV), including the square root of the mean squared difference of successive NN intervals and the standard deviation of NN intervals; and (e) inflammation: high-sensitivity C-reactive protein (hs-CRP) and total white blood cell count (WBC). These biomarkers span a wide selection of regulatory systems theorized to be involved in adaptive processes related to life stresses and linked to health outcomes later in life (Gruenewald et al., 2012; Juster, McEwen, & Lupien, 2010; Seeman, Epel, Gruenewald, Karlamangla, & McEwen, 2010). We excluded participants who had < 8 h of fasting prior to blood draw ($n=294$, < 2%) and those who had > 2 missing biomarkers of AL ($n=230$, < 2%).

Details of laboratory methods for AL markers in HCHS/SOL are described on the study website (www2.csc.unc.edu/hchs/). Briefly, BMI was computed as weight in kilograms divided by height in meters squared. Plasma glucose was measured using a hexokinase enzymatic method (Roche Diagnostics). HbA1c was measured using a Tosoh G7 Automated HPLC Analyzer (Tosoh Bioscience). Fasting insulin was measured using two commercial immunoassays (ELISA, Mercodia AB, Uppsala, Sweden; and sandwich immunoassay on a Roche Elecsys 2010 Analyzer, Roche Diagnostics, Indianapolis, IN; early measures conducted with the Mercodia assay were calibrated, and values were equivalent to the Roche method (Qi et al., 2015). HOMA-IR was calculated using the following equation: fasting glucose \times fasting insulin/405 (Matthews et al., 1985). The two measures of heart rate variability were assessed through ECG recordings read by the Central ECG Reading Center (EPICARE) using GEMSIT MAC1200 portable electrocardiograph while participants were in a fasting state. Serum hs-CRP was assayed in blood with a RocheModular P Chemistry Analyzer using an immunoturbidimetric method (Roche Diagnostics). Inter-assay coefficient of variation was < 2.5%, and intra-assay coefficient of variation was < 4.7%. White blood counts were measured in EDTA whole blood using a Sysmex XE-2100 instrument, (Sysmex America, Inc., Mundelein, IL). White blood counts were measured in EDTA whole blood using a Sysmex XE-2100 instrument, (Sysmex America, Inc., Mundelein, IL).

Operationalization of allostatic load

We created a count-based summary measure of AL following the approach developed by Seeman and colleagues (Seeman, Singer, Rowe, Horwitz, & McEwen, 1997). Each marker was assigned a score of one if its value reached a high-risk quartile;

lowest quartile for HDL, FEV₁/FVC, and HRV, and highest quartile for all other markers. Participants taking medications designed to lower values of specific markers were considered “high-risk” regardless of biomarker value; specifically, these included: (a) FPG and HbA1c for anti-diabetic medications, (b) SBP for anti-hypertensive medications, (c) heart rate for β -blockers, (d) serum triglycerides for fibrates, and (e) LDL-c for statins, cholesterol absorption inhibitors, niacin, and/or bile acid sequestrants. For each participant, we summed all 16-indicator variables to compute a final AL summary score with a potential range of 0–16.

To examine whether our results were robust to other approaches of operationalizing AL, we developed several additional AL summary measures in sensitivity analyses, including count-based scores that used clinical or sex-specific cut-points, and a measure that summed across standardized z-scores (Box & Cox, 1964; Seplaki, Goldman, Gleib, & Weinstein, 2005). Clinically-defined high-risk cut-points for selected markers were determined upon established criteria (Alberti & Zimmet, 1998; Chobanian et al., 2003; Cleeman et al., 2001; Pauwels et al., 2001; Ridker, 2003).

Nativity, years in the US, and age at immigration

We include information on self-reported nativity status (US-born, foreign-born), with US born defined as birthplace within the 50 states or Washington, DC. Foreign-born individuals were further stratified into categories of duration in the US and age at immigration with cut-points at the median (< 10 , ≥ 10 years and < 24 , ≥ 24 years, respectively). Age at immigration was computed as the number of years of residence in the U.S subtracted from the age at interview. We excluded participants who had missing information on nativity status or Hispanic background ($n=61$, $< 1\%$).

Covariate measures

Covariates assessed included household income, educational attainment, health insurance status, Hispanic background, and field center site. Health behaviors included self-reported smoking status (current, former, never) and current usual alcohol consumption, with at-risk drinkers defined as ≥ 7 drinks/week for women and ≥ 14 drinks/week for men according to the National Institute on Alcohol Abuse and Alcoholism. To ascertain physical activity, we administered a modified World Health Organization Global Physical Activity Questionnaire (Bull, Maslin, & Armstrong, 2009) to obtain estimates of moderate/vigorous levels; physically active was defined as ≥ 150 min/week of moderate-intensity, ≥ 75 min/week of vigorous-intensity, or an equivalent combination of both, as recommended by the 2008 US physical activity guidelines for adults (Pate, 2009). Diet quality was assessed from two 24-h dietary recalls collected during the baseline visit and operationalized using the Alternative Healthy Eating Index 2010 (AHEI-2010). The AHEI-2010 is a summary score of 11 component foods and nutrients; namely, servings/day of: (1) vegetables without potatoes, (2) whole fruits, (3) whole grains, (4) sugar sweetened beverages and fruit juice, (5) nuts and legumes, (6) red/processed meat; total mg/day of: (7) long chain omega-3 fats (docosahexaenoic acid and eicosapentaenoic acid), and (8) sodium; percent (%) energy of: (9) trans-fats and (10) polyunsaturated fatty acids; and number of drinks/day of (11) alcohol. Scores for each individual component were computed using the National Cancer Institute method to estimate usual dietary intakes of foods and nutrients obtained from the dietary recalls (Chiuve et al., 2012). Each component was given a minimal score of 0 and a maximal score of 10, with intermediate values scored proportionally, and has the potential to contribute 0–10 points to the total score (McCullough et al., 2002). All component scores were

summed to obtain a total AHEI-2010 score, which ranges from 0 to 110, with a higher score representing a better quality diet.

Statistical analyses

To estimate age patterns of AL scores, we computed predicted marginal means from log-linear models (Bieler, Brown, Williams, & Brogan, 2010), with 95% confidence intervals based on Taylor series linearization to account for the complex sampling scheme of HCHS/SOL (Lavange et al., 2010). We grouped individuals into young, middle-aged, and older adults (18–39, 40–54, 55–74 years, respectively); for each age group, we examined whether nativity status was associated with allostatic load (main effect) after adjustment for covariates. Using established methods for multiple imputation (Little & Rubin, 2002) with 20 imputed data sets, key social and behavioral covariates were imputed for 1665 (10.5%) participants who were missing annual household income ($n=1374$), educational attainment ($n=27$), insurance status ($n=216$), and smoking status ($n=74$). Complete case analyses revealed similar results. To further test whether the nativity-allostatic load association differed by sex and Hispanic heritage background, we added (sex*nativity) and (Hispanic heritage background group*nativity) interaction terms in separate models.

All reported values were non-response adjusted, trimmed, and calibrated by age, sex, and Hispanic heritage background to the characteristics of each field center's target population from the 2010 U.S. Census. All analyses account for cluster sampling and the use of stratification in the sample selection, and were performed using SAS 9.3 (Cary, NC) and SUDAAN 11.0 (Research Triangle Park, NC). All tests were two-sided and the level of significance was 5%.

Results

Table 1 depicts the continuous distributions of each physiological marker in the AL index stratified by sex. Mean age was 40 years in men and 42 years in women. On average, men had higher levels of WHR, LDL-c, triglycerides, fasting glucose, SBP, and pulse pressure than women, whereas women had higher mean levels of BMI, HDL-c, resting heart rate, HRV, lung function, CRP and WBC than men (all P values < 0.0001).

Table 2 shows age-adjusted, sex and age-stratified mean AL scores across socio-demographic and behavioral characteristics. We found differences by Hispanic heritage backgrounds ($P < 0.0001$), such that South Americans had the lowest and Puerto Ricans had the highest mean AL scores in both men and women. A notable exception was for Hispanic/Latino men at the oldest age group (55–74 years), where Cubans exhibited the highest levels. When we considered socioeconomic factors, lower income and education levels were associated with higher mean AL scores at all age categories in women (all P values < 0.01 for increasing trend in AL across lower income and education categories). However, no associations between income or education with AL were observed in men. With regard to health behaviors, mean AL scores increased linearly across categories of never, former, and current smoking amongst young (adj means: 2.11, 2.38, 2.64 respectively, $P=0.007$) and middle-aged women (adj means: 3.61, 4.13, 4.28 respectively, $P=0.0007$). We found differences in the relationship of alcohol consumption with AL between men and women. In men aged 18–54, individuals who were classified as low-risk drinkers had the lowest and at-risk drinkers had the highest mean AL scores; whereas amongst women aged 40–74, at-risk drinkers had the lowest but never drinkers had the highest scores. When dietary habits were considered, we found that mean AL scores decreased with better diet quality in both men and women, but only at younger (18–39) and older (55–74) ages. Lastly, AL scores were

Table 1
Distribution of allostatic load markers^a and high risk cut-points in the study population by men and women.

Allostatic load markers by systems	Men (n=6332)		Women (n=9498)		High-risk cut-point ^b	Clinical cut-point
	Weighted means (95% CI)	Weighted medians (IQR)	Weighted means (95% CI)	Weighted medians (IQR)		
Lipid metabolism						
Waist-to-hip circumference ratio	0.94 (0.94, 0.95)	0.94 (0.90, 0.99)	0.89 (0.89, 0.90)	0.90 (0.84, 0.94)	≥ 0.97	≥ 0.85, 0.90 ^c
Body mass index (kg/m ²)	28.9 (28.7, 29.1)	28.3 (25.3, 31.8)	29.8 (29.5, 30.1)	28.8 (25.2, 33.4)	≥ 32.9	≥ 30
High-density lipoprotein cholesterol (mg/dL)	45 (44, 45)	43 (37, 50)	52 (51, 52)	50 (42, 59)	≤ 40	< 40, 50 ^c
Low-density lipoprotein cholesterol (mg/dL) ^d	121 (120, 123)	119 (95, 144)	119 (117, 120)	114 (93, 140)	≥ 145	≥ 160
Serum triglycerides (mg/dL) ^d	147 (143, 151)	117 (79, 176)	119 (117, 121)	101 (70, 146)	≥ 166	≥ 200
Glucose metabolism						
Fasting glucose (mg/dL)	104 (103, 105)	96 (90, 103)	100 (99, 101)	92 (86, 99)	≥ 104	≥ 126
Blood glycosylated hemoglobin (%)	5.7 (5.7, 5.8)	5.4 (5.2, 5.7)	5.7 (5.7, 5.8)	5.4 (5.2, 5.8)	≥ 6	≥ 7
Homeostasis model assessed insulin resistance	3.4 (3.3, 3.5)	2.5 (1.5, 4.1)	3.4 (3.3, 3.5)	2.4 (1.6, 4.0)	≥ 4.2	
Cardiopulmonary						
Systolic blood pressure (mmHg) ^d	123 (123, 124)	121 (113, 130)	117 (116, 117)	112 (103, 125)	≥ 132	≥ 140
Resting pulse pressure (mmHg)	50 (50, 50)	48 (42, 54)	46 (45, 46)	42 (37, 50)	≥ 55	
Resting heart rate (bpm) ^d	64 (64, 65)	63 (57, 70)	67 (66, 67)	66 (60, 72)	≥ 72	≥ 90
Lung function (%FEV ₁ /FVC)	80.3 (80, 80.6)	81.3 (76.5, 84.9)	81.9 (81.7, 82.1)	82.5 (78.6, 86.0)	≤ 77.1	≤ 70
Parasympathetic (heart rate variability)						
R-R interval standard deviation (ms)	32.6 (31.5, 33.7)	25.5 (16.1, 40.8)	33.2 (32.3, 34)	26.8 (17.1, 41.5)	≤ 14.8	
Root mean square successive differences (ms)	38.6 (37.1, 40.1)	29.3 (17.4, 49.3)	41.4 (40.2, 42.6)	32.4 (19.5, 51.6)	≤ 16.5	
Inflammation						
Serum C-reactive protein (pg/ml)	2.9 (2.8, 3.1)	1.6 (0.7, 3.1)	4.6 (4.3, 4.9)	2.5 (1.0, 5.3)	≥ 4.5	≥ 3
Total white blood cell count (per μL)	6.4 (6.3, 6.5)	6.2 (5.2, 7.3)	6.7 (6.6, 6.8)	6.5 (5.4, 7.8)	≥ 7.6	

^a Individuals with 1 or 2 missing markers were included in analyses; missing values were imputed at the mean. The distribution of missing markers were as follows: waist-to-hip circumference ratio ($n=39$, 0.2%), body mass index ($n=36$, 0.2%), high-density lipoprotein cholesterol ($n=1$, <0.1%), low-density lipoprotein cholesterol ($n=303$, 2%), fasting glucose ($n=5$, <0.1%), glycosylated hemoglobin ($n=48$, 0.3%), homeostasis model assessed insulin resistance ($n=43$, 0.3%), pulse pressure ($n=8$, <0.1%), resting heart rate ($n=7$, <0.1%), vital capacity ($n=760$, 5%), heart rate variability ($n=684$, 4%), c-reactive protein ($n=4$, <0.1%), and total white blood cell count ($n=962$, 6%).

^b High-risk cut-points derived from the bottom 25th percentile for: high-density lipoprotein cholesterol, lung function, heart rate variability measures; top 75th percentile for all other markers.

^c Sex-specific cut-points for women (first value) and men (second value).

^d Scored as high-risk if on medications that were prescribed to lower these markers, even if the measured marker was below the “high risk” cut point.

lower amongst individuals who met criteria for being physically active as compared to those who did not, irrespective of sex and age.

Nativity differences in allostatic load by age and sex

While scores were higher for the older age groups overall, men exhibited higher mean levels than women at all ages, reaching a peak sex difference in AL scores at 35–44 years (Fig. 1; $P=0.02$ for interaction of age-group*sex). When we plotted age patterns by nativity status, US-born individuals exhibited higher mean scores than their foreign-born counterparts at each age category up to 54 years (Fig. 2a); beyond age 54 years, these differences were no longer apparent. It should be noted, however, that the proportion of foreign-born Hispanic/Latino adults (≥ 55 years) was appreciably higher among older adults than that of their younger counterparts (94% versus 78%, respectively). Similar age patterns of AL

scores by nativity status were observed when the data were further stratified by sex ($P=0.36$ and 0.13 for interaction of sex*nativity in 18–54 year olds and ≥ 55 years, respectively; Fig. 2b,c). However, nativity differences were more pronounced in younger Hispanic/Latino women compared with men.

Stratified results

When foreign-born individuals were further stratified by years living in the US, we observed the lowest mean AL scores in foreign-born persons with <10 years of living in the US (adj. means=3.47, 95% confidence interval [CI]: 3.34–3.61), intermediate AL in those living in the US ≥ 10 years (adj. means=3.78, 95% CI: 3.68–3.88), and the highest AL scores in US-born individuals (adj. means=4.23, 95% CI: 4.03–4.42), after adjustment for age (Fig. 3a; $P < 0.0001$ for trend). These results changed little whether or not adjustment was made for Hispanic background,

Table 2
Age-adjusted means (95% CI) of allostatic load scores across participant characteristics stratified by age and sex.

	Men				Women			
	n	18–39 yr (n=2180)	40–54 yr (n=2426)	55–74 yr (n=1726)	n	18–39 yr (n=2726)	40–54 yr (n=3914)	55–74 yr (n=2858)
Overall	6332	2.77 (2.65, 2.88)	4.53 (4.38, 4.68)	6.58 (6.39, 6.77)	9498	2.23 (2.11, 2.35)	3.82 (3.66, 3.97)	5.86 (5.68, 6.03)
National background								
Dominican	489	2.76 (2.33, 3.20)	4.22 (3.72, 4.73)	6.22 (5.75, 6.68)	929	2.19 (1.88, 2.49)	3.39 (3.10, 3.69)	5.77 (5.39, 6.14)
Puerto Rican	1079	3.02 (2.70, 3.35)	5.04 (4.68, 5.40)	6.55 (6.13, 6.98)	1512	2.86 (2.53, 3.18)	4.53 (4.10, 4.95)	6.23 (5.90, 6.56)
Cuban	1069	2.48 (2.20, 2.75)	4.55 (4.26, 4.84)	6.93 (6.57, 7.28)	1213	1.89 (1.66, 2.13)	3.71 (3.47, 3.96)	5.97 (5.65, 6.29)
Mexican	2398	2.86 (2.67, 3.06)	4.36 (4.12, 4.59)	6.49 (6.10, 6.88)	3938	2.27 (2.08, 2.45)	3.76 (3.50, 4.02)	5.58 (5.22, 5.95)
Central American	660	2.51 (2.26, 2.76)	4.60 (3.99, 5.22)	6.41 (5.91, 6.90)	1026	2.11 (1.86, 2.37)	3.72 (3.31, 4.12)	6.14 (5.66, 6.62)
South American	417	2.21 (1.72, 2.69)	3.96 (3.51, 4.40)	5.61 (5.02, 6.20)	619	1.52 (1.17, 1.87)	3.00 (2.67, 3.33)	5.20 (4.61, 5.78)
Other/more than 1	220	2.92 (2.37, 3.47)	4.85 (3.93, 5.78)	6.13 (5.24, 7.02)	261	2.11 (1.67, 2.55)	4.82 (3.20, 6.45)	6.06 (4.82, 7.30)
P group difference ^a		0.0045	0.0056	0.0036		< 0.0001	< 0.0001	0.0316
Annual household income								
< \$10,000	709	2.96 (2.53, 3.40)	4.57 (4.14, 5.01)	6.63 (6.22, 7.03)	1519	2.73 (2.41, 3.05)	4.17 (3.80, 4.55)	5.96 (5.65, 6.27)
\$10,001–\$20,000	1768	2.78 (2.54, 3.03)	4.64 (4.38, 4.90)	6.70 (6.39, 7.01)	2937	2.40 (2.22, 2.58)	3.96 (3.72, 4.21)	6.12 (5.84, 6.39)
\$20,001–\$40,000	2124	2.82 (2.61, 3.02)	4.62 (4.38, 4.86)	6.79 (6.43, 7.15)	2799	2.19 (2.00, 2.38)	3.71 (3.45, 3.98)	5.66 (5.33, 5.98)
\$40,001–\$75,000	964	2.95 (2.66, 3.23)	4.24 (3.95, 4.54)	6.24 (5.78, 6.70)	1000	1.98 (1.70, 2.27)	3.38 (2.93, 3.83)	5.47 (5.03, 5.90)
> \$75,000	358	2.57 (2.11, 3.03)	4.29 (3.62, 4.97)	5.97 (5.07, 6.87)	278	1.56 (1.15, 1.97)	2.91 (2.13, 3.69)	4.15 (2.79, 5.51)
P trend ^a		0.651	0.1666	0.1572		< 0.0001	0.0002	0.0043
Highest educational attainment								
< 9th grade	1351	2.79 (2.48, 3.09)	4.61 (4.26, 4.97)	6.73 (6.40, 7.05)	2368	2.42 (2.10, 2.74)	4.15 (3.85, 4.44)	6.11 (5.78, 6.44)
9th grade–< HS	990	2.79 (2.51, 3.07)	5.00 (4.65, 5.35)	6.79 (6.27, 7.30)	1264	2.59 (2.30, 2.87)	4.23 (3.89, 4.58)	6.11 (5.67, 6.56)
HS or equivalent	1770	2.78 (2.58, 2.99)	4.47 (4.22, 4.73)	6.39 (5.93, 6.85)	2276	2.28 (2.08, 2.48)	4.21 (3.89, 4.53)	5.82 (5.48, 6.15)
> HS	2215	2.73 (2.54, 2.92)	4.39 (4.15, 4.63)	6.49 (6.20, 6.78)	3569	2.00 (1.85, 2.16)	3.30 (3.12, 3.49)	5.53 (5.29, 5.77)
P trend ^a		0.6647	0.0734	0.2069		0.0001	< 0.0001	0.0033
Has health insurance								
No	3258	2.72 (2.58, 2.87)	4.54 (4.35, 4.73)	6.50 (6.17, 6.84)	4479	2.21 (2.07, 2.34)	3.77 (3.59, 3.94)	5.68 (5.41, 5.95)
Yes	2990	2.81 (2.58, 3.05)	4.53 (4.29, 4.77)	6.60 (6.38, 6.83)	4887	2.22 (2.04, 2.39)	3.87 (3.62, 4.12)	5.94 (5.70, 6.19)
P value		0.555	0.9606	0.6213		0.9372	0.4966	0.1732
Smoking status								
Never	3054	2.69 (2.53, 2.85)	4.31 (4.11, 4.52)	6.42 (6.13, 6.72)	6567	2.11 (1.99, 2.23)	3.61 (3.42, 3.80)	5.71 (5.50, 5.92)
Former	1649	2.88 (2.54, 3.22)	4.73 (4.43, 5.03)	6.78 (6.47, 7.09)	1480	2.38 (2.00, 2.75)	4.13 (3.76, 4.51)	6.16 (5.83, 6.50)
Current	1614	2.86 (2.61, 3.10)	4.74 (4.47, 5.01)	6.50 (6.12, 6.88)	1435	2.64 (2.29, 3.00)	4.28 (3.99, 4.56)	6.11 (5.72, 6.50)
P group difference ^a		0.3794	0.1049	0.6247		0.0073	0.0007	0.1651
Alcohol consumption ^b								
Not current drinker	2407	2.82 (2.61, 3.02)	4.70 (4.48, 4.91)	6.54 (6.24, 6.84)	5900	2.29 (2.14, 2.43)	4.05 (3.85, 4.24)	6.06 (5.88, 6.24)
Low-risk drinker	3391	2.63 (2.48, 2.78)	4.30 (4.10, 4.50)	6.70 (6.45, 6.96)	3315	2.16 (1.98, 2.35)	3.40 (3.20, 3.60)	5.33 (4.97, 5.70)
At-risk drinker	527	3.32 (2.81, 3.84)	5.36 (4.84, 5.89)	6.11 (5.57, 6.65)	268	2.18 (1.58, 2.79)	3.84 (3.26, 4.42)	5.48 (4.57, 6.38)
P group difference ^a		0.03	0.0002	0.1437		0.5446	< 0.0001	0.0011
Meets physical activity guidelines ^c								
No	1634	3.21 (2.88, 3.55)	5.06 (4.80, 5.33)	6.88 (6.55, 7.21)	4066	2.37 (2.17, 2.57)	4.10 (3.87, 4.32)	6.12 (5.87, 6.37)
Yes	4650	2.68 (2.55, 2.80)	4.33 (4.17, 4.49)	6.37 (6.15, 6.59)	5406	2.16 (2.02, 2.30)	3.61 (3.43, 3.79)	5.56 (5.34, 5.78)
P value		0.0039	< 0.0001	0.0122		0.0822	0.0004	0.0006
AHEI-2010 scores ^d								
Bottom tertile	3410	3.76 (3.63, 3.88)	2.30 (2.13, 2.46)	4.16 (3.90, 4.41)	1771	4.15 (4.02, 4.28)	2.72 (2.55, 2.90)	4.97 (4.69, 5.26)
Middle tertile	3159	3.41 (3.27, 3.56)	2.11 (1.91, 2.30)	3.81 (3.57, 4.05)	2085	4.06 (3.91, 4.21)	2.87 (2.65, 3.08)	4.32 (4.08, 4.57)
Highest tertile	2849	3.27 (3.10, 3.45)	2.27 (1.97, 2.58)	3.27 (3.02, 3.52)	2402	3.86 (3.71, 4.00)	2.70 (2.46, 2.93)	4.31 (4.06, 4.55)
P trend ^a		< 0.0001	0.4017	< 0.0001		0.0044	0.8919	0.0004

^a P-values for group difference based on Wald F-statistic from age-adjusted models.

^a P-values for test of linear trend with the variable treated as ordinal.

^b At-risk drinking defined as 7+ drinks per week in women and 14+ drinks per week in men.

^c According to self-report using the Global Physical Activity Questionnaire, which recommends at least 150 min/week of moderate-intensity, 75 min/week of vigorous intensity, or an equivalent combination.

^d Alternative Healthy Eating Index-2010 (AHEI-2010) is a measure of diet quality is a summary score of 11 component foods and nutrients; servings/day of vegetables without potatoes, whole fruits, whole grains, sugar sweetened beverages and fruit juice, nuts and legumes, red/processed meat; total mg/day of long chain omega-3 fats (docosahexaenoic acid and eicosapentaenoic acid), and sodium; percent (%) energy from trans-fats and polyunsaturated fatty acids; and number of drinks/day of alcohol. Scores for each individual component were computed using the National Cancer Institute method to estimate usual dietary intakes of foods and nutrients obtained from two 24-hr dietary recalls, with each component given a minimal score of 0 and a maximal score of 10, and intermediate values scored proportionally. All the component scores were summed to obtain a total AHEI-2010 score, which ranged from 0 to 110, with higher scores representing better quality diet. The score was categorized into tertiles.

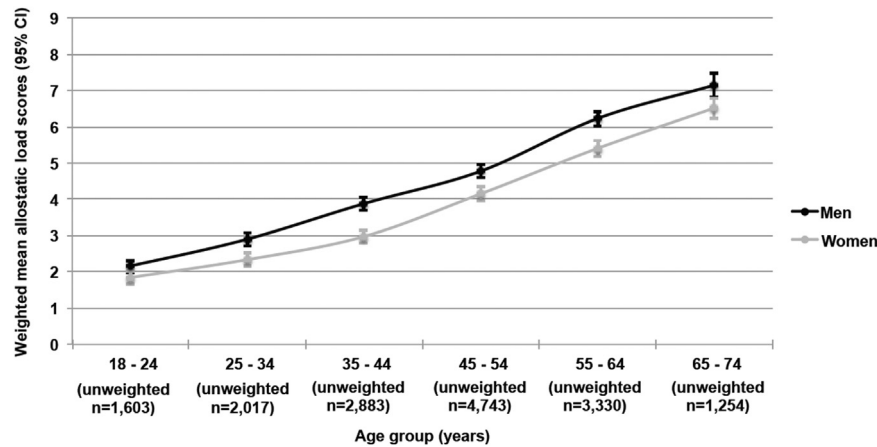


Fig. 1. Age-specific mean allostatic load scores stratified by sex in the overall HCHS/SOL target population (unweighted $n = 15,830$).

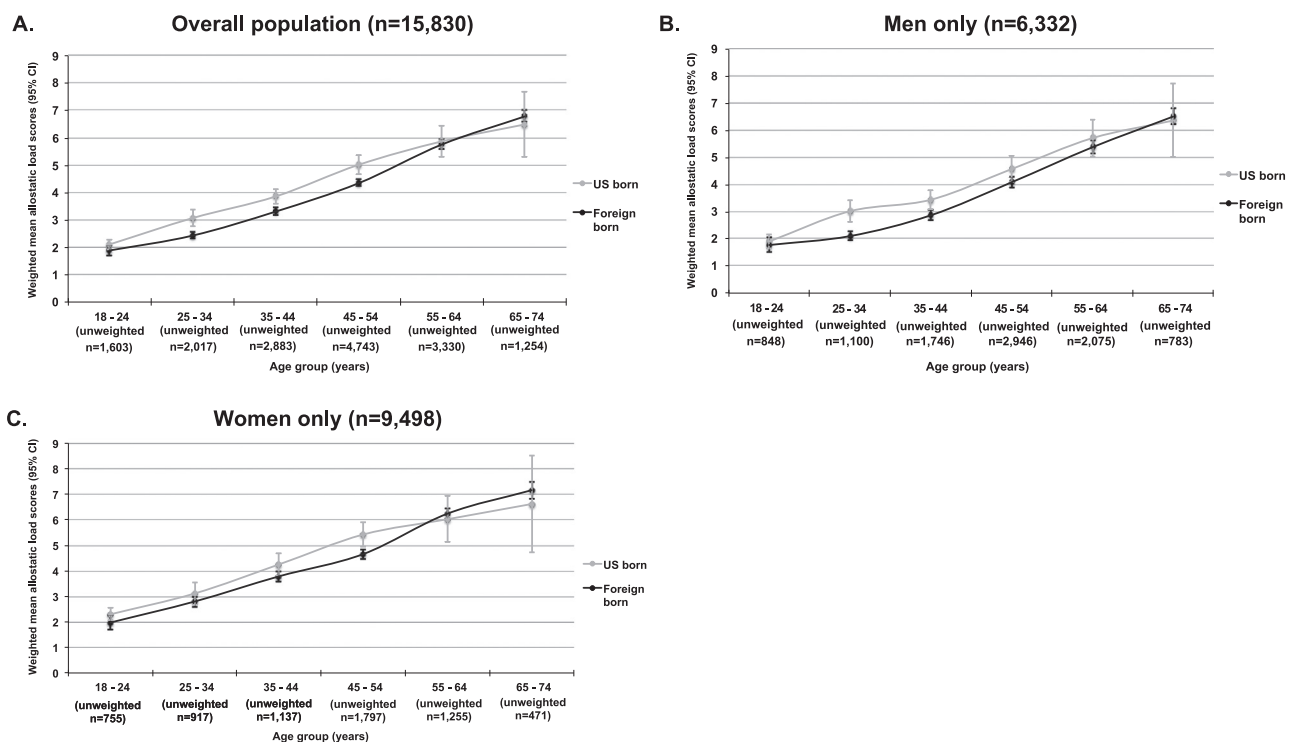


Fig. 2. Age-specific mean allostatic load scores stratified by nativity status in the overall population (panel A; $P = 0.36$ and 0.13 for interaction of sex**nativity* in 18–54 year olds and ≥ 55 years, respectively), in men only (panel B), and in women only (panel C).

field center, socioeconomic position, insurance status, smoking, alcohol consumption, physical activity, and diet quality. Age-stratified models restricted to women showed that this increasing trend in AL scores across categories of nativity/duration was more apparent in persons aged 18–54 years than in those of older age. In men, however, the trend persisted across every age group (P values < 0.01 for trend). Fig. 3b illustrates that similar patterns were observed in analyses in which foreign-born individuals were stratified by age at immigration rather than duration of US residence. Overall, persons who were US born had the highest scores (adj. means = 4.26, 95% CI: 4.06–4.46), those who migrated to the US at younger ages (< 24 years of age) had intermediate mean AL scores (adj. means = 3.75, 95% CI: 3.63–3.87), and persons who migrated at older ages (≥ 24 years of age) had the lowest mean AL scores (adj. means = 3.52, 95% CI: 3.52–3.74, $P < 0.0001$ for trend).

We observed similar associations of birthplace and length of time in the US with AL when we further stratified the analyses by Hispanic background (Fig. 3c). There was no interaction of nativity/

years in the US with AL by Hispanic background in multivariable analysis ($P = 0.50$ for interaction). While US-born Central and South Americans exhibited similar or lower AL scores than their foreign-born counterparts, their numbers were relatively small ($n = 76$ and 43 , respectively; $< 5\%$ of total sample). Because AL is known to be associated with socioeconomic status, we also tested for interaction by income and education. We found no effect modification by socioeconomic status.

Sensitivity analyses

To assess the robustness of the nativity association, we performed several sensitivity analyses using alternate summary measures of AL that included clinical cut-points, sex-specific cut-points, and standardized z-scores. For each alternate measure of AL, we observed similar nativity differences when we plotted mean levels of each AL measure across age groups (Supplementary Fig. 1). In addition, we adjusted our models for medication use

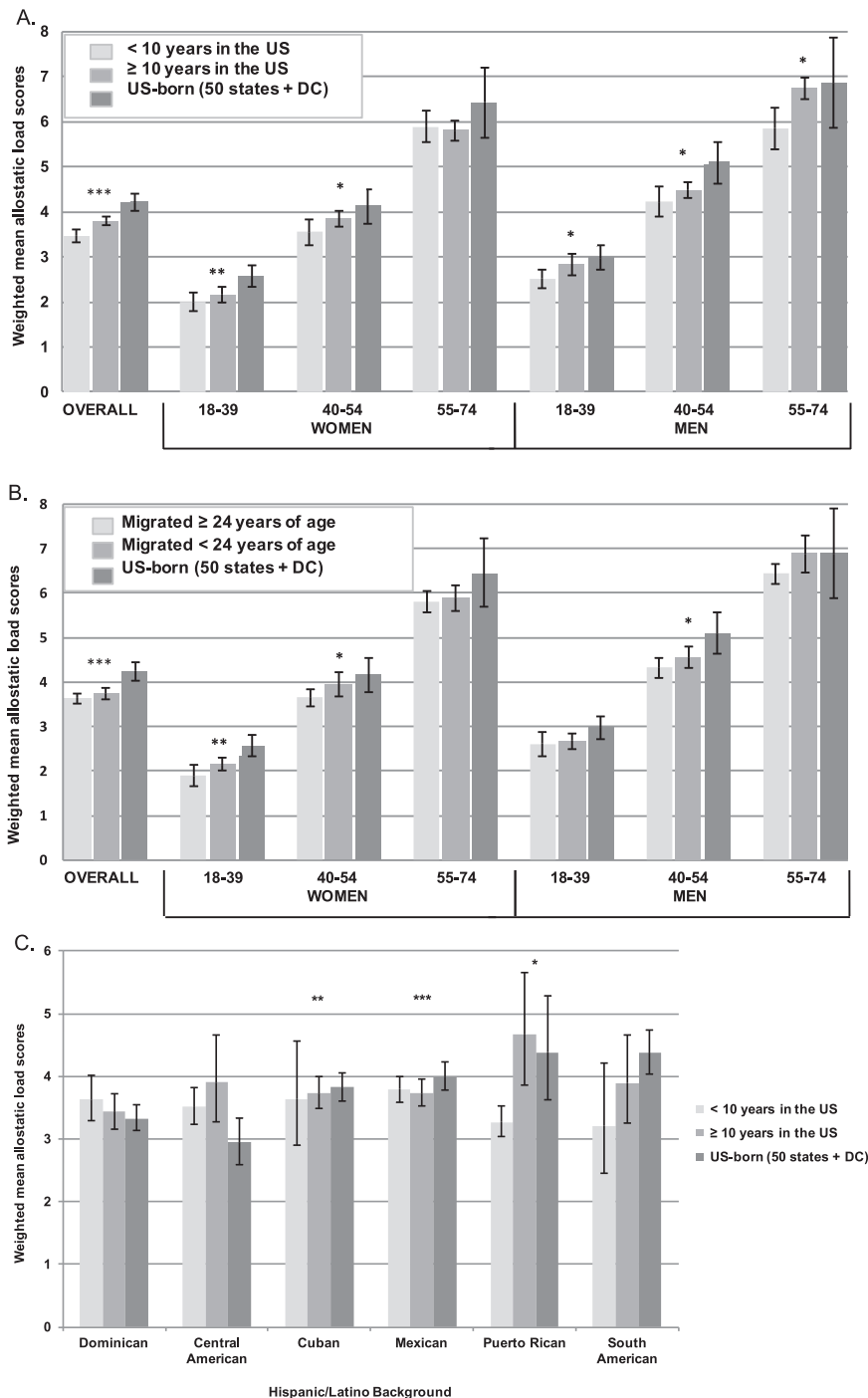


Fig. 3. Adjusted mean allostatic load scores by nativity/duration of US residence (panel A), nativity/age at immigration (panel B), and nativity/duration of US residence further stratified by Hispanic background (panel C), $n = 15,830$. * P for trend < 0.01 , ** P for trend < 0.001 , *** P for trend < 0.0001 , ‡Adjusted for age (continuous), field center (Miami, San Diego, Bronx, Chicago), income ($< \$10,000$, $\$10,001$ – $\$20,000$, $\$20,001$ – $\$40,000$, $\$40,001$ – $\$75,000$, $> \$75,000$), education (< 9 th grade, 9th grade– $< HS$, HS or equivalent, $> HS$), health insurance (yes, no), smoking (current, former, never), alcohol consumption (not current drinker, low risk drinker, at-risk drinker), meets physical activity guidelines (yes, no), and diet quality (tertile scores).

rather than assigning participants into a “high-risk” group and we found that the results were similar.

Discussion

In a sample of individuals drawn from four urban centers with large numbers of Hispanics/Latinos, we found that US-born individuals had higher scores of AL than their foreign-born counterparts, with differences less pronounced at ages 55 or older. The

association persisted in both men and women, across all Hispanic backgrounds, and was independent of selected social factors and health behaviors. The robustness of this finding is further confirmed by the fact that the nativity differences remained unchanged with other measures of AL and was similar across Hispanic backgrounds. Among the foreign-born, we found that greater duration of US residence and younger ages at immigration were related to higher levels of AL. Results from this large population-based study are consistent with those among Mexican Americans (Crimmins et al., 2007; Kaestner, Pearson, Keene, &

Geronimus, 2009; Peek et al., 2010), and extends these findings to US Hispanic/Latinos of other heritage backgrounds.

Our data support the healthy immigrant effect, a widely documented and well-established phenomenon in which recent immigrants demonstrate health advantages over demographically similar native-born individuals (Lara, Gamboa, Kahramanian, Morales, & Bautista, 2005). While our data showed that unhealthy behaviors such as cigarette smoking and physical activity were associated with high scores of allostatic load, nativity differences persisted after adjustment for these factors, consistent with prior studies (Crimmins et al., 2007; Kaestner et al., 2009). Proposed alternative explanations for the healthy immigrant effect include selective migration, whereby the healthiest individuals of their respective countries of origin self-select to migrate to a remote and unfamiliar labor market (Bostean, 2013). Given that data on potential emigrants and non-emigrants from participants' countries of origin are not available in the present study, selective migration cannot be ruled out.

Consistent with the notion that newer immigrants' health advantages erode over time, we observed higher AL scores with longer duration in the US and with younger age at immigration. Findings from NHANES (1988–1994) similarly showed a health advantage among Mexican Americans who immigrated at older ages (Kaestner et al., 2009). Moreover, higher AL among those with longer time spent in the US is supported by a large study of Mexican Americans living in Texas that found nativity differences even after adjusting for social factors and health behaviors (Peek et al., 2010). Among immigrants, longer duration of US residence (> 10 years) has been associated with obesity and obesity-related conditions (Goel, McCarthy, Phillips, & Wee, 2004). Exposure to severe challenges and stressors associated with migration and the adoption of a new culture could lead to chronic dysregulation of hypothalamic-pituitary-adrenal axis activity (Mangold, Mintz, Javors, & Marino, 2012; Sapolsky, 2004), with downstream effects on multiple physiological systems.

US-born Hispanics/Latinos consistently had the highest AL scores. Assuming that newer immigrants come with a health advantage and lose that advantage through a process of acculturation to levels comparable of the native born population, it's conceivable that individuals who have already adopted the host culture (US born) would no longer exhibit such health advantage. This is consistent with previous reports using NHANES data (Kaestner et al., 2009; Peek et al., 2010). However, exposure to stressors associated with acculturation might not be the only factor that drives our associations. In addition, the process of acculturation is complex and may be different for each of the Hispanic groups from different countries of origin. Longitudinal studies will be needed to address these questions, which we plan to conduct in future studies using the HCHS/SOL cohort.

The nativity-AL relationship was, however, less pronounced at older ages. This may also reflect an unfavorable influence of increasing acculturation to the US over time among migrants (Antecol & Bedard, 2006), or could also be explained by differences between younger and older individuals in the burden of health conditions and use of medical care. Older individuals are more likely to receive health benefits from the health care system, and the US-born are more likely to take advantage. This may confer a variety of benefits to older US-born Hispanic/Latino persons or among those who have longstanding residence in the US and who therefore have better access to medical and social services. On the other hand, selective survival of older Hispanics with lower AL may offer a competing explanation. Additionally, older individuals with lower levels of AL might have self-selected for inclusion in this study preferentially due to a more favorable health status relative to their similarly aged peers with higher levels of detrimental markers. Another contributory selection factor often cited is the "salmon effect", the selective return of less healthier older

Hispanic/Latino immigrants to their countries of origin (Turra & Elo, 2008). However, our data show differences in AL by nativity/duration in US among Cuban Americans, who would not have easily returned to their country of origin (Abraido-Lanza, Dohrenwend, Ng-Mak, & Turner, 1999). More studies are thus necessary to identify risk and resilience mechanisms that may explain these differences at older ages.

We found that men had higher levels of AL scores than women across every age category, a novel finding among US Hispanics/Latinos of diverse backgrounds. In analyses of specific AL components, metabolic markers were generally higher in men and inflammatory markers were higher in women. Sex differences in components of AL have been previously reported in other cohorts. For instance, results from the Social Environment and Biomarkers of Aging Study in Taiwan, the Wisconsin Longitudinal Survey, and the MacArthur studies of successful aging demonstrated that men had higher cardiovascular/ metabolic markers whereas women had a disadvantage in markers of sympathetic nervous system (SNS) and HPA axis functioning (Goldman et al., 2004). Findings from NHANES (1998–2006) showed a higher overall cumulative burden of inflammation in women than in men, which tended to decline with age (Yang & Kozloski, 2011). Similarly, in the Boston Puerto Rican Study, women exhibited higher levels of inflammatory markers than men (Mattei et al., 2010). It's unclear to what extent sex differences in AL and its components are driven by genetic, hormonal, or contextual influences. There is, however, some empirical evidence from the Texas City Stress and Health Study to show that sex modifies the relationship between duration of residence in a stressful environment and AL (Mair, Cutchin, & Kristen Peek, 2011), suggesting that men and women may manifest stressors differently. Additional work is necessary to further understand the complex inter-relationships between sex, stressors, AL and its components in Hispanics/Latinos.

Our study had several limitations. The cross-sectional design precludes any inferences of a causal effect. Related to this is the possibility that the differences in AL across groups might be influenced, in part, by age and period effects such as shifts in immigration policies. For instance, a rise in late-age immigration due to US admission policies since 1981 (Carr & Tienda, 2013) may create imbalances in the cohort related to family reunification/cohesion and lead to health consequences. Disentangling age, period, and cohort effects on AL and subsequent health outcomes is a target of future study in HCHS/SOL when longitudinal data are made available. Secondly, we did not have neuroendocrine markers available for analyses, which have been previously included in studies of AL. This reduces the ability to compare our findings with some prior studies that included a different set of markers of AL.

In summary, the current study is the first to examine AL patterns in a diverse Hispanic/Latino population in the US. We found nativity differences in age patterns of AL, showed sex-related differences, and conclude that these patterns are consistent across major Hispanic/Latino backgrounds. Future work should focus on identifying risk and resiliency factors that might explain these differences, as well as find additional biological markers such as epigenetic changes that can measure response to stressors. Identification of key determinants of AL patterns among Hispanics/Latinos is an important first step in developing tailored interventions to reduce health disparities. A major strength is the prospective design of HCHS/SOL, which will enable us to monitor the impact of acculturation on AL over time and examine the effects of behavior on these processes.

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Appendix A. Supplementary material

Supplementary data associated with this article can be found in the online version at <http://dx.doi.org/10.1016/j.ssmph.2016.05.003>.

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