



Stress and Health

A Longitudinal Analysis of Allostatic Load among a Multi-Ethnic Sample of Midlife Women: Findings from the Study of Women's Health Across the Nation



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ABSTRACT

Objectives: We examined longitudinal patterns and sociodemographic correlates of allostatic load (AL), a measure of cumulative biological risk and aging, in a sample of midlife women consisting of non-Hispanic White, African American, Chinese, and Japanese women.

Methods: Longitudinal cohort data from the Study of Women's Health Across the Nation were used to examine AL patterns in midlife women ages 42–53 (n=1,932). AL measures were created using 10 biomarkers representing cardiovascular, inflammatory, neuroendocrine, and metabolic system functioning. We used longitudinal random effects Poisson regression models to assess change in AL over the 7-year follow-up period and associations between sociodemographic factors and AL.

Results: On average, a woman's AL score increased 2% each year over the course of the study. Baseline measures of African American race, low family income, older age, and ability to read and speak only in English were significantly associated with higher levels of AL over the study period. We did not observe significant differences in rates of change in AL by race/ethnicity or socioeconomic status.

Conclusions: This study demonstrates that AL increases in a cumulative manner as women age. Midlife is an especially important time in women's life course with respect to health maintenance and healthy aging. AL can be an early warning indicator of subsequent disease burden, pointing to subclinical conditions and the need for implementation of medical and public health interventions earlier in the disease process.

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Midlife is a significant period in women's life course marked by changing social roles, increases in prevalence of chronic conditions, and transition through menopause (Hardy & Kuh, 2002; Kaeberlein, Rabinovitch, & Martin, 2015; Kuh, Wadsworth, & Hardy, 1997). Midlife is also when racial and socioeconomic disparities in chronic disease, impairments, and disability widen (House, Lantz, & Herd, 2005; House et al., 1994). By 2020, more than 35% of the U.S. population will be age 50 and over; therefore, it is imperative that medical and public health professionals address the physical, mental, and social well-being of this growing demographic group. A better understanding of the ways in which health differentials emerge during midlife can inform possible interventions and policies to impact healthy aging.

Allostatic load (AL), a measure of cumulative biological risk and aging, assesses the impact of environmental and social stressors on multiple physiological systems in the body, and elucidates possible pathways by which these stressors translate into health outcomes and disparities (Crimmins & Seeman, 2004; McEwen, 1998, 2002, 2004; Seeman, Crimmins, et al., 2004; Seeman, McEwen, Rowe, & Singer, 2001; Seeman, Singer, Rowe, Horwitz, & McEwen, 1997; Singer, Ryff, & Seeman, 2004). As individuals age, AL generally increases as the functioning and adaptability of physiological systems decline (Crimmins,

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Johnston, Hayward, & Seeman, 2003). Furthermore, cumulative exposure to social, psychological, or environmental stressors is posited to increase the risk for chronic degenerative health problems via disruption of physiological regulatory systems involved in the generalized physiological stress response (McEwen, 1998; McEwen & Stellar, 1993). Increases in AL are associated with health deterioration, accelerated aging, and shortened longevity (Geronimus, Hicken, Keene, & Bound, 2006; Karlamangla, Singer, & Seeman, 2006).

AL often reflects subclinical dysregulation, and as such, can potentially be used as an early warning indicator of disease risk. AL is associated with increased risk for mortality, cardiovascular disease, diabetes, higher pain scores, and decreased physical and cognitive function (Beckie, Duffy, & Groer, 2016; Karlamangla, Singer, McEwen, Rowe, & Seeman, 2002; Karlamangla et al., 2006; Mattei, Demissie, Falcon, Ordovas, & Tucker, 2010; Sabbah, Watt, Sheiham, & Tsakos, 2008; Seeman, Crimmins, et al., 2004; Seeman et al., 2001; Seeman et al., 1997; Seplaki, Goldman, Weinstein, & Lin, 2004), and is a better predictor of subsequent cardiovascular disease than the single biomarkers that comprise it (Karlamangla et al., 2005). Thus, conceptualizing AL in the context of primary and secondary prevention strategies can provide opportunities to prevent or slow chronic disease development in high-risk groups, reduce disease burden in the long term, and promote healthy aging.

Prior research on AL has typically combined men and women when identifying empirical cutpoints for AL, despite evidence of gender variation in distributions of individual biomarkers and cumulative biological risk (Goldman et al., 2004). Rather than incorporating gender simply as a control variable, we focus on a sample of women in this study to explicitly characterize gender-specific patterns of AL and to account for biological makeup, social factors, and health trajectories unique to women. Moreover, midlife is a dynamic stage in the life course of women, marked by physiological changes, social transitions, and the menopausal transition (Hardy & Kuh, 2002; Kuh et al., 1997). It is also during midlife when chronic health problems emerge and health disparities at the population level are most pronounced (House et al., 2005). With women spending one-third or more of their lives in postmenopause, understanding and promoting healthy aging in midlife has important implications for health in later years. To this end, AL can be a useful composite indicator of subclinical health risks and aging trajectories.

Socioeconomic differences in AL have been widely reported such that individuals who have lower socioeconomic status (SES) have higher AL relative to their more affluent counterparts (Gustafsson, Janlert, Theorell, Westerlund, & Hammarström, 2011; Karlamangla et al., 2005; Kuzbansky, Kawachi, & Sparrow, 1999; Seeman, Crimmins, et al., 2004; Seeman et al., 2008). Moreover, there is a SES gradient of AL, such that, at incrementally lower levels of SES, AL proportionately increases (Seeman et al., 2008). SES is seen as a fundamental cause of health differentials, whereby individuals of lower SES have fewer flexible resources, such as financial resources, power, social networks, and access to services, that can be leveraged to promote health and reduce disease (Link & Phelan, 1995; Phelan, Link, & Tehranifar, 2010).

Racial differences persist when SES is taken into account (Adler & Rehkopf, 2008; Kawachi, Daniels, & Robinson, 2005; Lillie-Blanton & LaVeist, 1996; Williams & Collins, 1995). African Americans have higher AL compared with Whites; chronic exposure to social and economic adversity and racial and ethnic

discrimination is thought to accelerate the aging process, or weathering, among African Americans and other people of color (Geronimus, 1992, 2001; Geronimus et al., 2006).

Although several studies have identified and characterized African American and White differences, few studies have investigated AL among Asians and Asian Americans (Seeman, Glei, et al., 2004; Upchurch, Stein, et al., 2015). In this study, our sample includes women who identified as Chinese and Japanese. As the fastest growing racial group in the United States, Asian Americans comprise a heterogeneous population, characterized by diverse cultures and representation at both extremes of socioeconomic and health measures (Barnes, Adams, & Powell-Griner, 2008; Hoeffel, Rastogi, Kim, & Shahi, 2012). The common practice of aggregating Asian subgroups in health research masks distinct disease patterns and health inequities among Asians (Ro & Yee, 2010). Nationally representative data have shown that Chinese and Japanese adults are significantly less likely to report fair or poor health, be obese, or have multiple chronic conditions in comparison to other U.S. adults (Barnes et al., 2008; Bloom & Black, 2016). There are also differences in health behaviors, with Chinese women in California reporting less alcohol binge drinking and smoking than their White counterparts (Maxwell, Crespi, Alano, Sudan, & Bastani, 2012). As a predisease indicator, AL can provide insight into underlying cumulative biological risk patterns that may lead to better or worse health outcomes among certain Asian subgroups. This study helps to fill a gap in the literature on AL among Asians, and specifically among Asian subgroups of Chinese and Japanese women in the United States.

A central tenet of AL and physiological dysregulation is that these changes are cumulative as individuals age, reflecting both antecedent and current biopsychosocial challenges (Beckie et al., 2016; Crimmins et al., 2003; Crimmins & Seeman, 2004). However, a significant limitation of much of the prior research is the use of cross-sectional data or only a few longitudinal time points to characterize AL. We use longitudinal biomarker data from the Study of Women's Health Across the Nation (SWAN), measured annually at more time points than available in other datasets, to examine AL patterns among midlife women as they transition through menopause. Leveraging biomarker data collected annually over 7 years, we are able to examine within-woman changes in AL over time and quantify estimated change per year, as well as investigate AL differences between women in different sociodemographic groups. This is one of a few studies to examine the magnitude of change in AL over an extended period of time, a novel contribution to understanding how multisystemic physiological dysregulation accrues.

The objectives of this study are to examine how AL changes over time among midlife women and investigate sociode-mographic correlates of AL, with a specific focus on racial and SES differentials. We hypothesize that within-woman values of AL will increase over time, reflecting health declines and physiological aging over the study period for each woman. We also hypothesize that lower SES, as measured by education and household income, will be associated with higher AL in a stepwise gradient pattern. We expect African American women to exhibit higher AL and Japanese and Chinese women similar or lower AL, relative to their White counterparts.

Methods

SWAN is a community-based, multisite, prospective study that examines biopsychosocial changes during the menopausal transition among a cohort of midlife women (Sowers et al., 2000). Women were sampled and recruited from seven locations in the United States. Each site enrolled non-Hispanic Whites in addition to a specific racial/ethnic minority group (African Americans in Pittsburgh, Pennsylvania, Boston, Massachusetts, Detroit, Michigan and Chicago, Illinois; Japanese in Los Angeles, California; Chinese in Oakland, California; and Hispanics in Newark, New Jersey) using a community-based sample. From a larger cross-sectional sample, women were considered eligible for the SWAN Longitudinal Cohort if they were: 1) aged 42 to 52 years, 2) had an intact uterus and at least one ovary, 3) were not using exogenous hormone preparations affecting ovarian function in the month before the baseline interview, as well as no hormone use in the 3 months before study screening, 4) had at least one menstrual period in the last 3 months, and 5) selfidentified as non-Hispanic White or the relevant site's designated racial/ethnic group.

Women who were recruited into the longitudinal component completed their baseline assessment during 1996 and 1997 (n=3,302) for an overall participation rate of 51%, and have been followed yearly since then. Overall response rates for participation in the longitudinal cohort varied significantly by SES and smoking status, with women with a high school education or lower and current smokers less likely to participate (Sowers et al., 2000).

Standardized protocols were used during all study visits and were conducted by trained, certified staff. Additional details of recruitment procedures, study design, and study components have been described elsewhere (Sowers et al., 2000). The original SWAN protocol for data collection was approved by each site's institutional review board, and all participants provided written informed consent. The secondary data analysis presented herein was also approved by the Institutional Review Board at the University of California, Los Angeles.

Blood pressure was measured with the respondent seated; two sequential assessments were taken and averaged (SWAN, 2002a). Height and weight were measured without shoes and in light indoor clothing. Waist and hip circumferences were measured with the respondent in nonrestrictive undergarments or over light clothing. Waist circumference was measured at the level of the natural waist, defined as the narrowest part of the torso as seen from the anterior aspect. Hip circumference was measured at the level of maximum extension of the buttocks. Additional information on anthropometric protocols can be found elsewhere (SWAN, 2002a). Blood samples were drawn annually after a 12-hour fast, and laboratory assays are also detailed elsewhere (SWAN, 2002b).

Women recruited at the New Jersey site (n=432), which included all Hispanic women, were not analyzed here because of low retention rate at this site (SWAN, 2013). For all other sites, retention rates were high (82%–92% as of visit 07). The final analytic sample included women who had valid nonmissing baseline data on all 10 biomarkers used to create the AL score, valid AL scores (complete data on all 10 biomarkers) for at least two subsequent visits, and valid (nonmissing; not pregnant or breastfeeding) baseline menopausal transition stage information. From the baseline sample of 3,302 women, we excluded 432 women from the New Jersey site, 923 women with fewer than three valid waves of AL scores (including baseline), and 15 women with invalid data on baseline menopausal status. The final

analytical sample consisted of 1,932 women and 13,391 total observations.

Biomarker Measures and AL Scores

A total of 10 biomarkers was used to represent functioning across cardiovascular, inflammatory, metabolic, and neuroendocrine systems (Chyu & Upchurch, 2011; Crimmins et al., 2003; McEwen & Stellar, 1993; Seeman, Crimmins, et al., 2004; Seeman et al., 2001; Seeman et al., 1997; Seeman, Singer, Ryff, Dienberg Love, & Levy-Storms, 2002). The cardiovascular biomarkers were systolic and diastolic blood pressure, and the inflammatory measure was C-reactive protein. Markers of metabolic functioning were high-density lipoprotein cholesterol, total cholesterol, body mass index, waist-to-hip ratio, fasting serum glucose, and triglycerides. The neuroendocrine marker was dehydroepiandrosterone. Although there is some variation in the biomarkers comprising AL score across studies using different datasets, there is substantial overlap in individual biomarkers used and systems represented.

AL scores were created using high-risk cutoff values based on the distribution of the sample at baseline and a count-based summation method used extensively in previous literature (Chyu & Upchurch, 2011; Crimmins et al., 2003; Crimmins, Kim, Alley, Karlamangla, & Seeman, 2007; Geronimus et al., 2006; Karlamangla et al., 2002; Peek et al., 2010; Seeman, Crimmins, et al., 2004; Singer et al., 2004). Values greater than or equal to the 75th percentile were defined as high risk for all biomarkers, except for high-density lipoprotein cholesterol and dehydroepiandrosterone, for which values lesser than or equal to the 25th percentile were defined as high risk. AL scores were then calculated at baseline and at each follow-up visit by summing the number of biomarkers for which the woman fell into the highest risk quartile. AL scores were not calculated at visit 02 because total cholesterol, high-density lipoprotein cholesterol, triglycerides, glucose, and C-reactive protein were not assessed. Thus, AL score was measured annually at seven time points, with a higher AL score indicating poorer health (range of 0-10 at baseline).

Demographic Measures and Menopausal Transition Stage

All independent variables were assessed at baseline and included as time-invariant variables, except for years since interview and menopausal transition stage, which were both time varying. Women's age, measured in years, captured age at the start of the study and allowed for between-women comparisons by baseline age. Years since baseline interview, coded continuously, was included to assess within-woman changes in AL over time.

SES was measured as educational attainment and household income at baseline, and both were coded ordinally. Total household income was categorized based on quintile cutpoints (<\$20,000, \$20,000−34,999, \$35,000−49,999, \$50,000−74,999, and ≥\$75,000). Educational attainment was categorized as less than 12 years, high school graduate/GED, some college/AA degree, college graduate, and more than college degree. Race/ethnicity was based on participants' primary identification with one of the following racial or ethnic groups: non-Hispanic Caucasian or White, Black or African American, Chinese or Chinese American, Japanese or Japanese American, or Hispanic (excluded in this study). Language was coded as English only or bilingual/no English. Data on nativity

status were not collected. Marital status was coded as married/cohabiting, single/never married, and separated/widowed/divorced.

Menopausal transition stage was based on self-reported bleeding patterns, hormone use, and history of hysterectomy or oophorectomy. Using categories developed by the SWAN Coordinating Center, menopausal status was coded as premenopausal (bleeding in the previous 3 months with no change in cycle predictability in the past year); early perimenopausal (bleeding in the previous 3 months with decrease in cycle predictability in the past year); late perimenopausal (3–11 months amenorrhea); postmenopausal (≥12 months of amenorrhea) with no hormone replacement therapy (HT) use; and postmenopausal with HT use.

Following SWAN Coordinating Center protocol, analyses excluded data collected from women at follow-up visits at which they were pregnant, breastfeeding, or reported use of HT before postmenopause. Data from these participants at later follow-up visits were included in analyses when they were no longer pregnant or breast feeding, or had stopped HT with an 18-month wash-out period. Women who had a hysterectomy without bilateral oophorectomy before postmenopause were dropped at the follow-up visit it occurred. Women who had bilateral oophorectomy (with or without hysterectomy) before natural postmenopause were coded as postmenopausal. Menopausal transition stage was time varying in our analysis to account for accompanying physiological changes that occur and could impact AL. Interview site was included to control for differences in recruitment and sampling frames.

There were no missing data on age, race/ethnicity, or site. Single imputation was used for missing values on education, income, and language; estimates were obtained from multivariable regressions using sociodemographic predictors. For marital status, 11 missing cases at baseline were coded to the modal category of married/cohabiting. Results were similar with or without imputation.

Analysis

Median, mean, range, and quartile cutpoint values were computed at baseline for each of the 10 biomarkers that comprise the composite AL score. Univariate distributions of sociodemographic variables and menopausal status were calculated to describe the analytical sample at baseline. Mean AL count scores by sociodemographic variables were also computed, and F-tests were used to assess significance.

Longitudinal random effects Poisson regression was used to model AL as a count score and to identify characteristics associated with women's AL patterns (Cameron & Trivedi, 1998; Long & Freese, 2001). Random intercept models allowed baseline AL values to vary randomly for each woman and accounted for within-woman correlation across follow-up interviews. Moreover, allowing the intercept to vary randomly controlled for a portion of overdispersion (Raudenbush & Bryk, 2002; Singer & Willet, 2003; StataCorp, 2007).

The level 1 component of the model included time-varying variables (years since baseline, menopausal transition stage) and represented effects on within-woman change in AL over time. The parameter estimate for years since baseline interview represents the average rate of change in AL we would expect a woman to experience per year throughout the course of the study. The level 2 component of the model included time-invariant variables of race, age, education, income, language,

marital status, and site measured at baseline. Parameter estimates for these time-invariant variables represented differences in AL levels between women over the study period. Estimated coefficients, count ratios, and CIs for Poisson regression models were computed. Individual-level variance was examined as an indicator of significant variation in baseline AL scores across women. We also tested interaction terms for race and time since baseline, and SES and time since baseline, to examine differences in rates of change in AL. All analyses and estimates were conducted using STATA 12.0 (StataCorp, 2011).

Results

Table 1 presents descriptive statistics, including range, median, quartiles, and high-risk cutpoints, for the 10 individual biomarkers that comprise AL at baseline. The mean AL score at baseline was 2.57, and values ranged from 0 to 10. Figure 1 displays mean AL across all waves.

The first column of Table 2 presents the distribution of sociodemographic and other characteristics of the sample at baseline. At baseline, almost one-half of the sample was 42 to 45 years old. Approximately one-half of the women were White and 27% were African American. The study population consisted of 10% Chinese women and 12% Japanese women. Women were generally of high SES, with about 50% having at least a college degree and more than one-half (59%) of women having house-hold incomes of \$50,000 or more. More than two-thirds of women were married or cohabiting, and most women (88%) read and spoke English only. At baseline, slightly more than 55% of women were premenopausal. Women were distributed relatively evenly across the study sites.

The second column of Table 2 displays the mean AL score at baseline by sociodemographic characteristics and menopausal status. All covariates were significant at the bivariate level (p < .001). As expected, the mean AL was higher for women of older ages at baseline. African American women had the highest mean AL at baseline followed by White women; Chinese and Japanese women had the lowest mean AL scores. Generally, lower mean AL scores were associated with higher levels of

Table 1 Biomarker and AL Distribution at Baseline, SWAN (n = 1,932)

	Mean	Median	Range	SD	Quartile Cutoff Value
Cardiovascular					
Systolic blood	115.03	112	80-199	16.19	≥123
pressure (mm Hg)					
Diastolic blood	73.90	73	40-119	10.21	≥80
pressure (mm Hg)					
Metabolic					
Total cholesterol	193.01	190	88-338	33.93	≥213
(mg/dL)					
HDL (mg/dL)	57.28	56	18-138	14.06	≤47
BMI (kg/m ²)	26.90	25.28	14.99-59.13	6.50	≥30.03
WHR	0.79	0.79	0.51 - 1.06	0.07	≥0.84
Glucose (mg/dL)	94.92	91	52-360	23.59	>97
Triglycerides (mg/dL)	107.26	87	31–1185	75.44	≥123
Inflammatory					
CRP (mg/L)	2.09	1.1	0.043-9.9	2.29	≥2.9
Neuroendocrine					
DHEA-S (μg/dL)	135.32	118.65	3.8-621.5	81.64	≤78.45
AL	2.57	2	0-10	2	

Abbreviations: AL, allostatic load; BMI, body mass index; CRP, C-reactive protein; DHEA-S, dehydroepiandrosterone; HDL, high-density lipoprotein cholesterol; SD, standard deviation; SWAN, Study of Women's Health Across the Nation; WHR, waist-to-hip ratio.

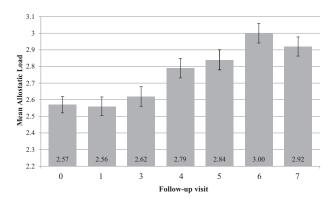


Figure 1. Mean allostatic load by wave, Study of Women's Health Across the Nation (SWAN). Allostatic load score was based on systolic and diastolic blood pressure, C-reactive protein, high-density lipoprotein (HDL) cholesterol, total cholesterol, body mass index, waist-hip ratio, fasting serum glucose, triglycerides, and dehydroepiandrosterone (DHEA-S) values. Values equal or greater than the 75th percentile were defined as high risk for all biomarkers, except for HDL and DHEA-S, which values equal or lesser than the 25th percentile defined as high risk.

education and income, and the differences were more pronounced for income. Married or cohabiting women had the lowest mean AL, whereas single and never married women had the least healthy profiles. Women who only read and spoke English had higher mean AL than women who were bilingual or did not speak or read any English. Early perimenopausal women had slightly higher mean AL than premenopausal women.

Table 3 presents results for the multivariable analysis. On average, a woman's AL score was expected to increase by 2% for each year after baseline, demonstrating significant increases in AL per year over the study period. For each additional year of age at baseline, the AL score was 4% higher. African American women had AL scores 1.21 times higher than White women; Chinese and Japanese women did not differ significantly from White women. Although education was not associated with AL, higher household income at baseline was associated with lower AL. Each income category above \$20,000 was associated with a lower AL score. Women in the highest income category of \$75,000 or more had the greatest health advantage, with AL scores 26% lower than women with household incomes of less than \$20,000. Women who were bilingual or did not speak or read English had AL scores 17% lower compared with women who only spoke and read English. When language read and spoken was not included in analysis, Chinese women had significantly lower AL than White women, but this difference was explained when language was accounted for (results not shown). The individual-level variance term indicated significant variation in baseline AL scores across women. Marital status and menopausal transition stage were not significant. Interaction terms for race and SES by time since baseline were not significant, indicating that there were no differences in rates of AL change by race or SES (results not shown).

Discussion

This study characterized the longitudinal patterns and sociodemographic correlates of AL, a measure of cumulative biological risk, among a sample of midlife women transitioning from 42 to 53 years of age to 49 to 60 years of age. Older age at baseline, lower household income, African American race, and speaking and reading English only were significant predictors of

Table 2 Demographic and Other Characteristics at Baseline, SWAN (n = 1,932)

Characteristics	Percentage Distribution of Characteristics at Baseline (%)		Mean AL at Baseline
Age at baseline (y)			*
42–45	47.75	911	2.36
46-49	41.72	806	2.63
50-53	11.13	215	3.27
Race			*
White	51.35	922	2.37
African American	26.50	512	3.53
Chinese	10.35	200	1.85
Japanese	11.80	228	1.93
Education at baseline			*
<12 years	2.74	53	3.08
High school graduate	15.27	295	3.12
Some college	31.83	615	2.86
College graduate	23.03	445	2.19
Post-college	27.12	524	2.21
Household income at baseline			*
<\$20,000	7.76	150	3.78
\$20,000-\$34,999	15.27	295	2.95
\$35,000-\$49,999	18.06	349	2.76
\$50,000-\$74,999	26.35	509	2.45
≥\$75,000	32.56	629	2.11
Marital status at baseline			*
Single/never married	13.61	263	3.12
Married/cohabiting	68.74	1,328	2.39
Separated/divorced/	17.65	341	2.86
widowed			
Language read or spoken			*
English only	87.73	1,695	2.68
English + other language	7.40	143	1.83
Non-English only	4.87	94	1.79
Menopausal status			*
Premenopausal	55.64	1,075	2.46
Early perimenopausal	44.36	857	2.72
Site			*
Detroit	16.20	313	3.45
Boston	14.96	289	2.59
Chicago	13.98	270	3.04
Oakland	18.48	357	1.97
Los Angeles	20.13	389	1.86
Pittsburgh	16.25	314	2.86

 ${\it Abbreviations:} \ \, {\it AL, allostatic load; SWAN, Study of Women's Health Across the Nation.}$

Note: *p < .001 based on bivariate F-statistic.

higher AL scores. Longitudinal models also revealed that AL scores increased significantly for women with each additional year. Measuring AL patterns during midlife, a significant stage in a woman's life course, is informative for understanding and promoting healthy aging trajectories.

One of the unique features of this study is the use of longitudinal biomarker data measured consecutively at more time points than available in other datasets to characterize AL patterns over a 7-year period. We use these data to quantify estimated change in AL per year, which uniquely adds to the literature in elucidating temporal patterns of AL and magnitude of change. Results from the longitudinal regression model demonstrated significant increase in AL associated with each year that had passed since a woman's baseline interview. This within-woman increase in AL over time can be attributed in part to biological aging over the course of the study and reduced capacity to adapt to socioenvironmental challenges (Crimmins et al., 2003). An estimated 2% increase in AL score each year after baseline indicated that AL is generally increasing in small, but significant increments throughout midlife. This finding provides support for the cumulative

Table 3 Longitudinal Poisson Regression Model Results with Random Intercept, SWAN (n=1,932)

Variables (Reference Group)	Coefficients	Estimated Count Ratios	p Value	CIs
Years since baseline (continuous)	0.02§	1.02§	<.001	(1.01-1.03)
Age at baseline	0.04§	1.04 [§]	<.001	(1.03-1.06)
(continuous)				
Race (White) African American	0.19§	1.21§	. 001	(1.11. 1.22)
Chinese	-0.19° -0.07	0.93	<.001 .408	(1.11–1.33) (0.78–1.11)
Japanese	-0.07 0.16*	0.93 1.17*	.053	(1.00–1.11)
Education at baseline (less	0.10	1.17	.033	(1.00-1.57)
than high school)				
High school graduate	0.12	1.13	.264	(0.91-1.41)
Some college	0.09	1.09	.423	(0.88–1.35)
College graduate	-0.10	0.91	.375	(0.73–1.13)
Post graduate	-0.11	0.90	.342	(0.72-1.12)
Household income at				` ,
baseline (<\$20,000)				
\$20,000-\$34,999	-0.12^{*}	0.88^{*}	.090	(0.76-1.02)
\$35,000-\$49,999	-0.18^{\dagger}	0.84^{\dagger}	.015	(0.72-0.97)
\$50,000-\$74,999	-0.20^{\ddagger}	0.82^{\ddagger}	.006	(0.72-0.97)
≥\$75,000	−0.30 [§]	0.74 [§]	<.001	(0.63-0.86)
Marital status at baseline				
(married/cohabiting)				
Single/never married	0.08	1.09	.126	(0.98-1.21)
Separated/divorced/ widowed	-0.004	1.00	.938	(0.90–1.10)
Language read or spoken at				
baseline (English only)	0.40 [†]	0.00±	000	(0.70, 0.05)
Bilingual or no English	-0.19^{\ddagger}	0.83 [‡]	.006	(0.72-0.95)
Menopausal status				
(premenopausal) Early perimenopausal	0.01	1.01	.541	(0.07, 1.06)
Late perimenopausal	0.01	1.04	.212	(0.97–1.06) (0.98–1.12)
Postmenopausal, no HT	0.04	1.04	.123	(0.96–1.12)
Postmenopausal, HT	0.07	1.07	.379	(0.98–1.11)
Site (Pittsburgh)	0.03	1.07	.575	(0.50 1.10)
Detroit	0.07	1.07	.260	(0.95-1.20)
Boston	-0.08	0.92	.173	(0.82-1.04)
Chicago	0.13 [†]	1.14^{\dagger}	.030	(1.01–1.29)
Oakland	-0.10	0.90	.178	(0.78-1.05)
Los Angeles	−0.30 [§]	0.74§	<.001	(0.64-0.86)
Constant	-0.82^{\ddagger}	0.44^{\ddagger}	.009	(0.24-0.81)
Individual-level variance	0.44§		<.001	(0.41-0.48)

Abbreviations: HT, hormone therapy; SWAN, Study of Women's Health Across the Nation.

Note: *p < .1; †p < .05; †p < .01; §p < .001.

nature of AL over time by illustrating increasing individual trajectories of AL.

The negative association between household income and AL found in this study confirms the established association between SES and health, and is attributed to factors such as fewer financial and social resources to address life challenges; lesser availability, quality, and use of health care; and increased exposure to environmental hazards and stressors among the socioeconomically disadvantaged (Braveman, Egerter, & Williams, 2011; Phelan et al., 2010; Ross & Wu, 1995; Williams & Collins, 1995). The association between income and AL exhibited the well-documented stepwise gradient pattern, with each higher level of income associated with better health.

Education, in contrast, was not associated with AL. This finding was consistent with another study using SWAN to examine AL, as well as another study of AL among a nationally representative sample of midlife women (Upchurch, Rainisch, & Chyu, 2015; Upchurch, Stein, et al., 2015). Differences in AL patterns by education and income may reflect differential aspects of

SES and corresponding effects on health. AL may be more sensitive to more contemporaneous SES measures, such as income, that represent current availability of resources that affect health (Gustafsson et al., 2011). A study that examined longitudinal patterns of AL among a community-based sample of adults 45 to 85 years of age found that higher educational attainment was associated with lower AL levels and slower increase in AL (Merkin, Karlamangla, Diez-Roux, Shrager, & Seeman, 2014). The differences in the effects of educational attainment could be attributed in part to different sample composition, with SWAN focusing specifically on women in a narrower age range, for whom health status might be less impacted by educational attainment. The operationalization of AL in our study also included a wider range of biomarkers representing multiple biological systems compared with a more restrictive set of cardiovascular and metabolic markers used in the study by Merkin et al. (2014).

Racial differences in AL persisted even after controlling for SES, supporting past research showing that racial/ethnic differences cannot be explained adequately by SES alone. One explanation for worse AL profiles among African American women is that SES indicators used in this study do not fully capture economic status differences beyond income and education, such as inheritance, assets, and intergenerational transfers of wealth (Krieger, Williams, & Moss, 1997; LaVeist, 2005). Systemic racial discrimination over the life course also contributes to higher AL among African American women (Brody et al., 2014; Geronimus et al., 2006; Upchurch, Stein, et al., 2015). Experiencing racial discrimination elicits psychological distress and harmful changes in physiological health, which can be further exacerbated by unhealthy coping behaviors and internalization of negative stereotypes (Bennett, Wolin, Robinson, Fowler, & Edwards, 2005; Borrell, Kiefe, Williams, Diez-Roux, & Gordon-Larsen, 2006; Mays, Cochran, & Barnes, 2007; Pascoe & Smart Richman, 2009; Williams & Mohammed, 2009). Because African American women experience more exposure to adverse socioenvironmental challenges and discrimination over their life course, these experiences may chronically elicit stress responses that ultimately lead to increased cumulative physiological dysregulation and higher disease risk. The AL profiles from this study support previous cross-sectional research demonstrating that African American women are at high risk for development of chronic disease at middle and older ages (Geronimus, 2001; Geronimus et al., 2006). In another study using SWAN that explicitly examined perceived discrimination as a mediator of race and SES differences in AL, the authors found that both African American women and lower SES women reported higher levels of discrimination, which contributed to their higher AL (Upchurch, Stein, et al., 2015). However, discrimination did not completely explain racial and SES differentials. These findings, along with our own, highlight the need to continue to investigate the multiple ways in which both racial and SES disparities in AL

A noteworthy contribution of this paper is an examination of AL in Chinese and Japanese women, Asian subgroups that are not systematically considered in health research. Our findings that Chinese and Japanese women have AL similar to White women confirmed our hypotheses and are consistent with relatively healthy profiles of Chinese and Japanese individuals in the United States. Elucidating cumulative biological risk patterns among Chinese and Japanese women can inform more nuanced characterizations of healthy aging trajectories among racial subgroups.

Although we found significant differences in levels of AL by race and income, rates of change in AL per year did not differ significantly by race or SES. These findings are consistent with another study using different methodology to examine AL in SWAN, which found that race and income were not directly associated with rate of change in AL, but were indirectly associated through perceived stress (Upchurch, Stein, et al., 2015). Although AL levels reflect differential cumulative exposure to social and environmental stressors, the time period examined in this study may not have been sufficiently long to capture significant differences in rates of change. A study of adults 70 to 79 years old found that increase in AL was associated with higher all-cause mortality (Karlamangla et al., 2006). However, change in AL was based on only two measures of AL over a 2.5-year period, and analyses was based on a relatively small sample of only Black and White individuals.

The healthier AL profiles of women who were bilingual or could not speak English in comparison with women who could only speak English highlight the importance of incorporating measures of nativity status and acculturation in studying socioeconomic and racial/ethnic disparities in health. Some racial and ethnic differences could be explained by nativity status and acculturation, which our findings suggested for Chinese women. Although the variable used in this study (language read and spoken) was a crude proxy for nativity status and acculturation, the significant association with AL supports previous findings that foreign-born and less acculturated individuals tend to be healthier than their U.S.-born counterparts (Crimmins et al., 2007; Franzini, Ribble, & Keddie, 2001; Huh, Prause, & Dooley, 2008; Lara, Gamboa, Kahramanian, Morales, & Hayes Bautista, 2013; Peek et al., 2010; Salazar et al., 2016). Possible explanations for this pattern are migration of healthier individuals from country of origin, protective cultural practices, and health-promoting behaviors among foreign-born individuals and those who have lived in the United States for shorter durations (Crimmins, Soldo, Kim, & Alley, 2005; Franzini et al., 2001; Lara et al., 2013; Palloni & Arias, 2004). Protective factors, such as social support, ethnic enclaves, and strong family ties, could also provide a buffer against acculturative stress and perceived discrimination, particularly among Asian Americans (Lim, Yi, De La Cruz, & Trinh-Shevrin, 2017; Singh, McBride, & Kak, 2015).

There are limitations to this study. First, the biological indicators used to create AL measures in this study were constrained by availability in SWAN. However, previous studies suggest that despite differences in operationalization and composition of AL, substantive findings are robust (Karlamangla et al., 2006; Seeman et al., 2008). Second, our analytical sample is a subset of the original cohort and, thus, subject to selection bias. Analyses indicated that participants of higher education and income were more likely to be in our analytical sample. Despite this selection bias, our findings are consistent with those found in studies on AL using cross-sectional, nationally representative samples of women from the National Health and Nutrition Examination Survey (NHANES) that found older age, African American race, lower income, and being born in the United States were associated with higher AL (Chyu & Upchurch, 2011; Upchurch, Rainisch, et al., 2015). The similar substantive findings between the SWAN and NHANES samples from between-women analyses suggest the validity of our data despite selection bias in our analytical sample. Moreover, the overrepresentation of women of higher SES in our sample suggests that our findings might be underestimates of trends in the original cohort. Third, the data used in this study are based on a community sample of midlife women and findings, thus, cannot be generalized to all midlife women. However, our findings on between-women differences are generally consistent with other studies on AL using nationally representative samples of women, as described. There was limited information on nativity status and acculturation, other than language, in this study. Data limitations also precluded us from examining Hispanic women.

Implications for Practice and/or Policy

Addressing persistent health disparities in the United States remains an important priority for public health research, practice, and policy. We focus on midlife because it is during this life stage that health differentials are most pronounced and decline in health is common. In addition to detecting possible pathways by which socioenvironmental factors impact physiological functioning and lead to chronic disease, AL can help to identify high-risk women and inform early points of prevention and intervention to reduce disease burden and disparities at the population level. Promoting healthy lifestyle behaviors and contexts, such as leisure time physical activity, stress coping strategies, positive social relationships, and emotional support are potential avenues for interventions to reduce AL levels and slow rate of change (Brody et al., 2014; Brooks et al., 2014; Seeman, Glei, et al., 2004; Upchurch, Rainisch, et al., 2015; Upchurch, Stein, et al., 2015). Given aging trends in the U.S. population and associated caregiving and long-term health care needs, public health strategies and interventions aimed at promoting healthy aging are of high priority.

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Clinical Centers

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