Household Income, Neighborhood Poverty, and Epigenetic Age: Differences Between Men and Women

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Objective: Epigenetic changes may partially explain the socioeconomic status (SES)-health gradient, with lower SES associated with accelerated biological aging. Men and women differ in several aspects of this SES-health gradient, with women having lower income and having more health conditions compared with men. Some research documents an even stronger SES-health link among women. The present study investigated gender differences in SES-epigenetic age associations.

Methods: Using data from the Midlife in the United States Study (men $n = 353$, women $n = 367$), we conducted weighted linear regressions to test the hypotheses that lower household income and greater neighborhood poverty would be associated with accelerated epigenetic age assessed on three epigenetic clocks (ie, PhenoAge, GrimAge, and DunedinPACE), particularly for women.

Results: Household income did not significantly interact with gender in relation to PhenoAge or GrimAge. Higher household income was associated with decelerated DunedinPACE, but only among men (simple slope estimate $= -0.01$, $p < 0.001$), not women (simple slope estimate $= -0.00$, $p = 0.37$). Neighborhood poverty was associated with significantly accelerated PhenoAge (simple slope estimate $= 13.25$, $p < 0.001$) and GrimAge (simple slope estimate $= 6.07$, $p = 0.002$) among women, but was associated with significantly decelerated PhenoAge (simple slope estimate $= -19.52$, $p < 0.001$) and GrimAge (simple slope estimate $= -4.81$, $p = 0.021$) among men.

Conclusions: Findings suggest nuanced associations between SES and epigenetic age and highlight notable differences between men and women. The gender differences observed in the present findings further reiterate the importance of closing the gender gap in SES.

Key words: epigenetic age, gender differences, neighborhood poverty, household income

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INTRODUCTION

Low socioeconomic status (SES) is a risk factor for poor health.[1] The SES-health association has been observed using both income and educational indicators, although some research suggests that income-based indicators are more strongly associated with health.[2–4] Poor health outcomes have also been observed among individuals living in low SES neighborhoods, such as those with higher poverty rates.[5,6] Area-based poverty is thought to relate to residents' health via a deterioration of the social and physical environment.[5] Regarding this latter point, researchers have long written about the challenges of identifying unique associations between neighborhood poverty and health given that poverty rates are driven, in part, by residents' income.[7] This methodological challenge necessitates more research that incorporates income indicators from individual and neighborhood levels.

More recently, scholars have written of another observation, namely that "neighborhood factors may not affect everyone equally."[8] Women suffer from reduced quality of life, greater functional impairments, and more chronic health conditions than do men.[9–11] These health disparities necessitate the identification of risk factors not shared between men and women. Women often maintain positions of less privilege relative to men, and this differential is matched with disparities in health and income.[12,13] Not only are women more likely than men to have low income and to reside in low-income neighborhoods, but women's lower income may compound with health risks related to their relatively marginalized status.[14,15] A few studies have documented that multiple indicators of low SES are more strongly associated with poor health among women than men, although existing studies include SES indicators such as education, marital status, and employment, leaving a remaining question of whether women are more vulnerable to low income than are men.[16–18] The present study extended this research to epigenetic outcomes and investigated potential gender differences in vulnerability to low income at both household and neighborhood levels (although see Phyzo et al[19]).

Recent discoveries have revealed epigenetic markers of accelerated biological aging.[20,21] Accelerated aging predicts the development of chronic illness and has documented associations with premature mortality.[22–25] Initial attempts to quantify accelerated epigenetic aging resulted in the construction of the "first generation" of epigenetic clocks.[26,27] These initial clocks were developed in models predicting chronological age, allowing for the identification of unique, age-related patterns of DNA methylation (DNAm). More recent iterations, or "second generation" clocks, were trained instead on biological risk

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markers for chronic diseases (ie, PhenoAge, GrimAge.[28,29] Representing a third generation, DunedinPace is constructed by tracking 19 biomarkers of organ functioning within participants at 4-time points over 2 decades, resulting in a measure that captures the pace of biological aging.[30] Investigations using these "clocks" have revealed more rapid epigenetic aging among men relative to women but also among those with lower SES at both individual and neighborhood levels.[19,31–33] The present study hypothesized that, like investigations of SES-health associations, the strength of income-epigenetic age associations would be stronger among women than men. The current analyses are particularly urgent from a public health standpoint, given the historical and current gender gap in SES.[34]

Epigenetic Age, Gender, and Income

Individuals with accelerated epigenetic age are at greater risk for early mortality, poor cognitive and mental fitness, cardiovascular disease, and cancer.[35–38] The severity of these health consequences necessitates the identification of risk factors that hasten epigenetic changes. For over a decade, the field of environmental epigenetics has investigated the potential for genome x environment interactions that modify gene expression, at least partially through DNAm.[39,40] Furthermore, a growing literature illustrates that social determinants of health, including smoking and SES, are associated with accelerated epigenetic age.[33,41–43]

A recent review describes numerous studies documenting the low individual SES-accelerated epigenetic age link.[43] These studies have observed that both lower income and education relate to accelerated epigenetic aging.[32,44] Further investigations suggest that low SES in childhood and adulthood are associated with accelerated epigenetic aging.[45] An additional review has documented associations between neighborhood SES and accelerated epigenetic age.[33] These studies suggest that, in neighborhoods with lower average income or education, or those with greater unemployment or poverty, epigenetic age is accelerated.[46,47]

Critically, women are more likely than men to experience poor economic circumstances. Women represent 56% of people living in poverty, and in 2018, 12.9% of women lived in poverty compared with 10.6% of men in the United States.[14] Both income and wealth gaps exist between men and women in this country regardless of education.[34,48] Not only are women more likely to have annual incomes below the federal poverty threshold, but they are more likely to live in some of the most poverty-stricken areas of the United States than are men.[15,34]

The Present Study

Data from the Midlife in the United States Study (MIDUS), a national US survey of men and women in midlife and older adulthood, were used in this study. The PhenoAge, GrimAge, and DunedinPACE epigenetic clocks[28–30] were selected given their documented associations with social determinants of health such as household income and neighborhood poverty.[44] This study tests the hypotheses that low household income and greater neighborhood poverty would relate to accelerated epigenetic aging more strongly among women than men (Fig. 1). To our knowledge, no other studies have investigated gender differences in these associations. This paucity of research represents a critical need as women are disproportionately exposed to low income at both individual and neighborhood levels. Moreover, this investigation represents a direct response to calls for more interdisciplinary investigation of health disparities that may stem from gendered life experiences.[40,49]

METHODS

Participants and Procedure

Data from MIDUS II (2004) and the Refresher sample (2011), the latter of which was meant to replenish the original MIDUS cohort, were used in the present study.[50] The MIDUS survey, initiated in 1994, investigated the health and well-being of a US sample of men and women in midlife and older adulthood. Recruitment was conducted via random-digit dialing, with siblings, twins, and city-oversamples also recruited, and all data collection was funded by the John D. and Catherine T. MacArthur Foundations (MIDUS I) and the National Institute on Aging (MIDUS II and III). Participants were eligible if they were 25 to 74 years of age, English-speaking, non-institutionalized, and residing in the co-terminus United States. The core survey, conducted by telephone interview and self-administered questionnaire, asks participants about their sociodemographic, behavioral, psychosocial, and physical health. Although data collection procedures were similar for the Refresher sample, recruitment strategies differed slightly. The multi-frame dynamic sampling plan used to recruit Refresher participants involved landline random-digit dial, cell phone only, and age-targeted list procedures to recruit younger (25 to 54 y) participants, and age-stratified landline random-digit dial and cell phone only lists to recruit older participants (55 to 74 y). More details of the Refresher recruitment can be found elsewhere.[51] No siblings or twins were recruited to the Refresher sample, and to minimize potential sibling-related dependency in the data, siblings and twins from the original MIDUS sample were not included in the current study.

At the second wave, several sub-studies were added to data collection procedures, including the Biomarker Study.[52] Participation in the Biomarker Study involves an overnight stay in 1 of 3 General Clinical Research Centers located across the United States. Participants provide blood samples from which DNA is extracted. In 2022, the MIDUS Genomic Study aimed to quantify and describe DNAm from the Biomarker Study-based blood samples. These DNAm data were used to construct a series of epigenetic clocks, described in the sections that follow ($n = 1310$). Data are available through the Inter-University Consortium of Political and Social Research (https://www.icpsr.umich.edu/web/ICPSR/series/203).

Census tract data from the 2000 US decennial census and the 2007-2011 American Community Survey (ACS)

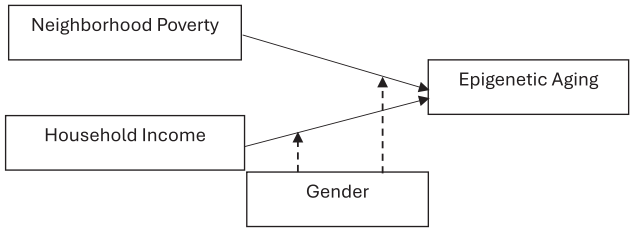

FIGURE 1. Theoretical framework. The 2 solid black lines represent the direct hypothesized associations between neighborhood poverty and household income (left) and epigenetic aging (right). The solid gray line represents the inferred association between household income and neighborhood poverty and is addressed in the current study by including these 2 indices of socioeconomic status in all analytic models simultaneously. The 2 dashed black lines represent the hypothesized moderating effects of gender in both the neighborhood poverty-epigenetic age and household income-epigenetic age associations.

have been linked to 1185 MIDUS II and Refresher respondents with epigenetic clock data, respectively, to evaluate epigenetic age in relation to the poverty rate of the census tracts in which participants lived. Data from all US census tracts were sent to the MIDUS Admin core which, by way of 12-digit Federal Information Processing Information (FIPS) identifiers, linked Census and ACS data to MIDUS respondent data. These data were linked under a restricted data use agreement to the first author. The 720 participants in the analytic sample had complete data on household income (missing 280), neighborhood poverty (missing 53), race/ethnicity (missing 2), body mass index (missing 21), and chronic health conditions (missing 10). All participants signed consent forms before participating in MIDUS projects, and data collection procedures were approved by the University of Wisconsin, Madison Ethical Review Board (IRB protocols 2016-1051 and 2014-0813). All research reported in this paper was guided by the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) standards for reporting observational research. Analysis code is available upon request from the first author.

Measures

Epigenetic Clocks

The primary outcomes in the present study were scores on the PhenoAge and GrimAge clocks which are scaled in years, and DunedinPACE which is scaled to a mean of 1, with values lower than 1 indicating slower pace of aging and values higher than 1 indicating faster pace of aging.[28–30] In 2019, participants in the Biomarker Project provided whole blood samples, which MIDUS staff used to collect DNAm data. In 2022, as part of the MIDUS Genomics Project, these DNAm data were used to construct the epigenetic clocks used in the current analysis.[53]

Household Income

Household income was calculated as the sum of earnings from wages, pensions, and social security payments for the participant and his or her spouse. In the current study, household income was transformed so that model coefficients were interpreted as a change in the outcomes for every $20K increase in household income.

Neighborhood Poverty

Data from the 2000 Census (MIDUS II) and the 2007-2011 ACS (Refresher) were used to calculate census tract poverty rate. Poverty rate was calculated by dividing the number of residents with annual income below the federal poverty threshold by the total population of the census tract whose poverty status was known.

Covariates

Gender was coded as 0 = men and 1 = women. The current analyses used a transformed age variable so that model coefficients could be interpreted as a change in the outcome for every 2-year increase in age. The race/ethnic variable available in MIDUS data sets have codes for multiracial (0), White (1), Black or African American (2), Native American or Aleutian Islander (3), Asian or Pacific Islander (4), and Other (5). Given that both the MIDUS II (94%) and Refresher (81%) samples represented primarily White participants, a race variable was constructed for which 0 = White participants and 1 = non-White participants to adjust for well-known racial/ethnic health disparities. Because the MIDUS II and Refresher samples were pooled in the present analyses, an indicator variable was included where 1 = MIDUS II and 2 = Refresher. Completion of the self-administered questionnaire was required before participants could be recruited to the Biomarker Sub-Study. Given that the time between these sub-studies varied across participants, we also included the number of months between the completion of the self-administered questionnaire and the Biomarker Study as a covariate.

Participants' body mass index was calculated by dividing weight in kilograms by height in meters squared. An additional item, constructed by MIDUS administrators, quantified the total number of chronic health conditions participants had (eg, diabetes, high blood pressure, stroke, asthma). Participants were asked several questions about smoking behaviors including, "Have you ever smoked cigarettes regularly" (yes/no) and "Do you smoke cigarettes regularly now" (yes/no). These questions were used to construct a smoking variable for which 0 = never smoked, 1 = used to smoke, and 2 = currently smokes. The 2 health status covariates (BMI and chronic health conditions) and smoking were included, given known associations between poor health and accelerated epigenetic aging and the inclusion of smoking in the construction of many epigenetic clocks.[28–30]

Statistical Analysis

The purpose of the current analysis was to evaluate epigenetic age in association with household income and neighborhood poverty and gender differences therein. To test the hypotheses that lower household income and higher neighborhood poverty would be more strongly associated with accelerated epigenetic aging among women

relative to men, weighted linear regressions were used. In model 1, epigenetic age was predicted by household income and neighborhood poverty including all covariates simultaneously. Model 2 introduced an interaction term between gender and household income, and model 3 replaced this interaction term with one interacting gender with neighborhood poverty. Models 2 and 3 which included the respective interaction terms included all covariates simultaneously.

The poststratification weight applied to the models was constructed by MIDUS staff to compare the MIDUS II and Refresher sample characteristics (gender, race, age, education) to the 2005 and 2012 Current Population Surveys, respectively. More information about the calculation of poststratification weights can be found elsewhere.[54,55] Identical models were conducted to investigate the PhenoAge, GrimAge, and DunedinPACE clocks separately. All models were conducted in Stata 18. See Table S1, Supplemental Digital Content 1, http://links.lww.com/PSYMED/B84, for weighted linear regressions predicting epigenetic age clocks in a minimally adjusted model. In addition to the above models, zero-order correlations among all analytic variables were examined (Table S2, Supplemental Digital Content 1).

TABLE 1. Weighted Sample Description, Mean (SE)

	Men ($n = 353$)	Women ($n = 367$)
PhenoAge	47.48 (13.97)	46.06 (9.95)
GrimAge	55.56 (11.26)	53.65 (8.17)
DunedinPACE	0.96 (0.11)	1.00 (0.10)
Household Income, $	$118,228 ($61,534)	$77,433 ($53,103)
Neighborhood poverty, %	8.65% (7.32%)	9.27% (6.95%)
Age	54.63 (11.61)	52.11 (8.96)
Race/ethnicity, %		
Non-Hispanic White participants	82%	77%
Non-White participants	18%	23%
Smoking, %		
Never smoked	60%	54%
Quit smoking	25%	38%
Current smoker	15%	8%
Body mass index	27.94 (4.04)	30.32 (6.19)
Number of chronic conditions	2.04 (2.36)	3.51 (2.58)
Months between P1 and P4	31.68 (10.75)	32.62 (12.37)
Cohort, %		
MIDUS II	9	13
Refresher	91	87

P1 = MIDUS self-administered questionnaire. P4 = biomarker project.

RESULTS

Weighted Sample Description

A description of the weighted sample can be found in Table 1. Epigenetic age on the PhenoAge, GrimAge, and DunedinPACE clocks was similar for men and women. Neighborhood poverty rate was also similar between men and women. Men's household income was substantially higher than women's. Of the 720 participants, 51% were women, 83% were White participants (others were non-White participants), and 89% were in the Refresher cohort (others were in the MIDUS II cohort).

Income-Based Predictors of Epigenetic Age

Table 2 reports results of weighted linear regressions predicting epigenetic age by household income, neighborhood poverty, and their interactions with gender. The purpose of model 1 was to examine associations between household income and neighborhood poverty on epigenetic age. Results of model 1 suggested that participants with higher household income had significantly decelerated GrimAge and DunedinPACE, although not PhenoAge. Living in neighborhoods with higher poverty rates was not significantly associated with epigenetic age on any of the clocks.

The purpose of model 2 was to determine whether associations between household income and epigenetic age differed between women and men. The only such significant interaction in model 2 was observed for DunedinPACE where higher household income was significantly associated with decelerated DunedinPACE among men (simple slope estimate = −0.01, SE = 0.00, $p < 0.001$), but not women (simple slope estimate = −0.00, SE = 0.00, $p = 0.37$; Figure S1, Supplemental Digital Content 2, http://links.lww.com/PSYMED/B85). We do note, however, that this interaction was not significant in a minimally adjusted model which included only age as a covariate (Table S1, Supplemental Digital Content 1, http://links.lww.com/PSYMED/B84).

The aim of model 3 was to investigate whether neighborhood poverty would have a different association with epigenetic age for women compared with men. The interaction between gender and neighborhood poverty was significant for PhenoAge and GrimAge (Figure S2, panels A-B, Supplemental Digital Content 2, http://links.lww.com/PSYMED/B85). Although the interaction between gender and neighborhood poverty in relation to DunedinPACE was not significant, the pattern was nevertheless similar to those for PhenoAge and GrimAge. Among women, living in neighborhoods with higher poverty rates was significantly associated with accelerated PhenoAge (simple slope estimate = 13.25, SE = 2.86, $p < 0.001$). Among men, however, living in neighborhoods with higher poverty rates was significantly associated with decelerated PhenoAge (simple slope estimate = −19.52, SE = 3.05, $p < 0.001$). Similarly, among women, living in neighborhoods with higher poverty was significantly associated with accelerated GrimAge (simple slope estimate = 6.07, SE = 1.95, $p = 0.002$). Among men, living in neighborhoods with higher poverty was significantly associated with decelerated GrimAge (simple slope estimate = −4.81, SE = 2.07, $p = 0.021$). Finally, the interaction between neighborhood poverty and gender was not significant in relation to DunedinPACE ($p = 0.16$) but revealed the same pattern as those for PhenoAge and GrimAge.

DISCUSSION

Given historic SES gender disparities,[34] the current investigation aimed to determine the degree to which men

TABLE 2. Weighted Linear Regression Predicting 3 Epigenetic Clocks in the Midlife in the United States Survey, Wave 2 and Refresher Cohorts

	PhenoAge		
	Model 1	**Model 2**	**Model 3**
Household Income ($20k increments)	−0.01 (0.05)	−0.02 (0.07)	−0.13* (0.05)
Sex × household income		0.02 (0.11)	
Neighborhood poverty (proportion)	−1.97 (2.23)	−2.01 (2.44)	−19.52*** (3.05)
Sex × neighborhood poverty			32.77*** (3.98)
Womena	1.18*** (0.30)	1.11 (0.60)	−1.99*** (0.48)
Age (2-y increments)	2.04*** (0.03)	2.04*** (0.03)	2.03*** (0.03)
Non-White participantsb	−1.62*** (0.37)	−1.61*** (0.38)	−2.27*** (0.37)
Smokingc			
Quit smoking	−1.49*** (0.34)	−1.51*** (0.37)	−1.17*** (0.33)
Current smoker	−1.43** (0.48)	−1.43** (0.48)	−0.93* (0.47)
Body mass index	−0.03 (0.03)	−0.03 (0.03)	0.01 (0.03)
Number of chronic conditions	0.16** (0.06)	0.16** (0.06)	0.09 (0.06)
Months between P1 and P4	0.04* (0.02)	0.04* (0.02)	0.06*** (0.02)
Refresherd	−1.39** (0.49)	−1.40** (0.50)	−1.22** (0.48)
		GrimAge	
Household income ($20k increments)	−0.13*** (0.04)	−0.12* (0.05)	−0.17*** (0.04)
Sex × household income		−0.03 (0.08)	
Neighborhood poverty (proportion)	1.02 (1.49)	1.09 (1.50)	−4.81* (2.08)
Sex × neighborhood poverty			10.89*** (2.71)
Womena	0.03 (0.20)	0.16 (0.40)	−1.02** (0.33)
Age (2-year increments)	1.69*** (0.02)	1.69*** (0.02)	1.69*** (0.02)
Non-White participantsb	−3.23*** (0.25)	−3.24*** (0.25)	−3.44*** (0.25)
Smokingc			
Quit smoking	−1.38*** (0.23)	−1.35*** (0.25)	−1.27*** (0.23)
Current smoker	−1.42*** (0.32)	−1.43*** (0.32)	−1.25*** (0.32)
Body mass index	−0.01 (0.02)	−0.01 (0.02)	0.01 (0.02)
No. chronic conditions	0.14*** (0.04)	0.14*** (0.09)	0.11** (0.04)
Months between P1 and P4	0.02 (0.01)	0.03 (0.01)	0.03* (0.01)
Refresherd	−0.86** (0.33)	−0.84** (0.33)	−0.80** (0.33)
		DunedinPACE	
Household income ($20k increments)	−0.01*** (0.00)	−0.01*** (0.00)	−0.01*** (0.00)
Sex x household income		0.01*** (0.00)	
Neighborhood poverty (proportion)	−0.01 (0.04)	−0.03 (0.04)	−0.08 (0.05)
Sex × neighborhood poverty			0.09 (0.07)
Womena	−0.00 (0.00)	−0.04*** (0.01)	−0.01 (0.01)
Age (2-year increments)	0.01*** (0.00)	0.01*** (0.00)	0.01*** (0.00)
Non-White participantsb×	0.07*** (0.01)	0.07*** (0.01)	0.07*** (0.01)
Smokingc			
Quit smoking	0.03*** (0.01)	0.02*** (0.01)	0.03*** (0.01)
Current smoker	0.00 (0.01)	0.00 (0.01)	0.00 (0.01)
Body mass index	0.01*** (0.00)	0.01*** (0.00)	0.01*** (0.00)
No. chronic conditions	0.01*** (0.00)	0.01*** (0.00)	0.01*** (0.00)
Months between P1 and P4	0.00** (0.00)	0.00* (0.00)	0.00** (0.00)
Refresherd	0.02* (0.01)	0.01 (0.01)	0.02* (0.01)

[a]Compared with men.
[b]Compared with White participants.
[c]Compared with never smoked.
[d]Compared with MIDUS II cohort.
*$P < 0.05$.
**$P < 0.01$.
***$P < 0.001$.

and women differ in their susceptibility to low income or in the potential benefits gained through high income regarding epigenetic aging. Findings in the current study suggested that the answer to this question depends on the level of SES under investigation (ie, household income vs. neighborhood poverty). First, for both men and women, higher household income was associated with decelerated epigenetic aging on 2 well-established epigenetic clocks (GrimAge and DunedinPACE, although not PhenoAge). This first finding aligns with the larger SES-health literature, where individuals with greater economic resources have better health.[1] Second, at first glance, neighborhood poverty did not appear to be associated with epigenetic aging in these analyses. Following calls for more research

on how gender may differentially shape people's experiences, however,[40,49] we further investigated whether neighborhood poverty would have different associations with the rate of epigenetic aging among men and women.

Our findings consistently suggested that, among women, living in higher poverty neighborhoods was associated with accelerated epigenetic aging (although the interaction in relation to DunedinPACE was not statistically significant and only trended in the same direction as the others). A review of Figure S2, Supplemental Digital Content 2, http://links.lww.com/PSYMED/B85 reveals that women in low-poverty neighborhoods were, on average, 2 to 4 age-adjusted epigenetic years younger than women in the high-poverty areas. This difference is similar to years of life lost in relation to other known risk factors for mortality, such as high cholesterol or hypertension.[56] This pattern is synonymous with the greater neighborhood-health literature in which lower SES neighborhoods are associated with poorer health among their residents.[5] Among men, on the other hand, living in higher poverty areas was significantly associated with decelerated epigenetic aging. This set of results suggested 3 important points. First, neighborhood poverty was explaining unique variation in epigenetic aging beyond that of household income, as these indices of SES were included in models simultaneously. Second, the neighborhood poverty-epigenetic age association was significantly different for women when compared with men, a finding that was hidden in average effects (combining men and women). Third, the gender differences in neighborhood poverty-epigenetic age associations suggested gendered experiences of neighborhood poverty. The evidence in the current report documented a greater detriment for women in higher-poverty neighborhoods. This finding further supports the need to close the socioeconomic gender gap, and identification of the features of higher poverty areas that uniquely associate with accelerated epigenetic aging among women.

Multi-Level Sources of Income and Epigenetic Aging

We hypothesized that low household income would be more strongly associated with accelerated epigenetic aging among women relative to men. This hypothesis was not supported, however. In the current analyses, higher household income was related to decelerated epigenetic aging on 2 of the 3 investigated clocks (GrimAge and DunedinPACE), and this was the case for both women and men. In fact, in the case of DunedinPACE, the association between higher household income and decelerated aging was stronger for men than women. These findings aligned with a large literature documenting the SES-health gradient and were consistent with relatively new research linking higher individual income with younger epigenetic age.[43,57] It is worth noting that this interaction was not statistically significant in the minimally adjusted model for which results are reported in Table S1, Supplemental Digital Content 1, http://links.lww.com/PSYMED/B84. A review of the zero-order correlations among all key analytic variables reported in Table S2, Supplemental Digital Content 1 suggests at least one reason for this null interaction, namely omitted variable bias. Several of our key covariates operated in opposite directions in relation to our epigenetic outcomes and SES-related predictors. For instance, smoking status was positively associated with the epigenetic clocks used in these analyses but was inversely associated with household income. These opposing correlations may have masked the significant interaction observed in the fully adjusted model that included all key covariates.

We further hypothesized that greater neighborhood poverty would be more strongly related to accelerated epigenetic aging among women when compared with men. This hypothesis was driven by research documenting women's relative vulnerability to lower neighborhood SES regarding self-rated health, metabolic functioning, cognitive functioning, chronic health conditions, and mortality.[58–62] Novel to this study, however, was the examination of gender differences in epigenetic aging in the context of neighborhood poverty. We observed partial support for this hypothesis. Specifically, before examining potential interactions between gender and neighborhood poverty, neighborhood poverty was not significantly associated with any of the three epigenetic clocks in the present study. Closer inspection of the interaction with gender, however, revealed divergent patterns with epigenetic age for women and men. As we predicted, living in areas with greater poverty was significantly related to accelerated PhenoAge and GrimAge among women, although there was only a trend suggesting this pattern for DunedinPACE.

We did not expect to find that living in areas with more poverty would significantly relate to decelerated epigenetic aging among men. One possible reason for this finding may be related to downward social comparison. In the present data, neighborhood poverty rates were similar for that of men and women, that is, it was not the case that men were living in areas with more poverty. Yet, men's household income was substantially higher than that of women's. Together, this may mean that there was a larger gap between household income and neighborhood poverty among men relative to women in the current study. Men may have been benefitting from higher individual SES (based on their household income) relative to the SES of their respective neighborhoods (based on their poverty rates).

Another reason for this gender difference may have been related to associations among low neighborhood SES and signs of physical and social disorder.[63] Not only are low SES neighborhoods more likely to exhibit signs of disorder (eg, trash, vandalism), but women are more likely than men to interpret disorder as a safety concern (ie, via a threat to personal safety).[63,64] Women, therefore, may experience low SES neighborhoods differently than do men, and the present analyses support this argument regarding epigenetic aging.

We are not the first to observe an inverse association between higher SES and poor health among men. At least

one other study observed that, among men, greater perceived income adequacy was related to poorer scores on the mini-mental state exam (cognitive functioning) and activities of (instrumental) daily living (physical functioning).[65] Those researchers argued that men's higher pay jobs may lead to greater perceived income adequacy but nevertheless come with cognitive and physical health risks. More research is needed to determine the robustness of this finding.

One final observation worth noting is that our results differed slightly depending on the epigenetic clock under investigation. Regarding household income, there were no significant interactions with gender in relation to PhenoAge or GrimAge. The model investigating DunedinPACE, however, revealed that higher household income was more strongly associated with decelerated aging among men than women. Regarding neighborhood poverty, significant interactions with gender were observed for PhenoAge and GrimAge, but this was only a trend regarding DunedinPACE. Review of the zero-order correlations among these epigenetic clocks indicates that PhenoAge and GrimAge were more strongly correlated with each other than either was with DunedinPACE (Table S2, Supplemental Digital Content 1, http://links.lww.com/PSYMED/B84). These correlations may explain why results diverge somewhat among the three clocks. DunedinPACE is unique in that it uses information about organ functioning at 4 different assessments over 2 decades.[30] This clock quantifies the "pace of aging," and is more strongly associated with morbidity and mortality than other clocks, which may mean it will have different associations with SES. More research is needed that tests these questions in other samples.

Limitations and Future Directions

A few limitations are notable. First, the sample was not sufficiently large to examine interactions between household income and neighborhood poverty in association with epigenetic age. As such, it was not possible to determine whether some of these factors offset risk associated with others, or whether any evidence of buffering differs between men and women. Although MIDUS is a national sample, it nevertheless does not represent the racial/ethnic diversity of the United States. This is a critically important limitation, given clear racial/ethnic disparities in individual SES, neighborhood SES, and health outcomes.[66] Finally, although epigenetic age outcomes can be driven in part by differences in immune cell subsets, MIDUS data sets do not include such information, limiting the ability to determine the degree to which this additional information might have altered our results.

CONCLUSIONS

Although women have a lower risk of mortality from most causes of death compared with men, women nevertheless carry a disproportionate share of chronic illness.[67] Many chronic illnesses have some biological or epigenetic underpinnings.[68] Understanding these epigenetic mechanisms assists with identifying those at greatest risk for poor health and thus preventative measures to slow biological aging.[69] The innovative use of epigenetic markers of accelerated aging in the current analyses suggests that women may be at greater risk for poor health in low SES circumstances than are men. These findings inform the development of targeted interventions, namely those aiming to improve women's economic circumstances that may attenuate existing gender-related health disparities.

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