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Research Article

Grandparent caregiving and epigenetic aging among midlife and older adults in the United States

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Abstract

Objectives: Grandparents have increasingly taken more active caregiving roles for grandchildren. Given their vulnerability to aging-associated health declines, it is essential to understand how grandparent caregiving, along with grandparent gender and family relationships, may influence aging processes. This study examined how grandparent caregiving status interacts with gender and family affectual solidarity (FAS) to affect epigenetic aging, an indicator of healthspan and mortality risk.

Methods: Our sample included grandparents participating in the Midlife in the United States (MIDUS) study ($N = 492$; mean age = 61.94; female = 59.96%), 18.29% of whom reported being grandparent caregivers for 6+ months. Epigenetic age was measured using the Horvath, Hannum, PhenoAge, GrimAge, and DunedinPACE epigenetic clocks. We tested for moderation by gender and FAS, the degree of positive (and negative) sentiment between family members.

Results: Linear regression found, controlling for sociodemographic characteristics and BMI, associations between grandparent caregiving and DunedinPACE, indicating that more time spent caring for grandchildren is related to a faster pace of aging. Two-way interactions between grandparent caregiving and gender showed epigenetic age acceleration (higher biological age compared to chronological age) for grandfather caregivers versus non-caregiving grandfathers across multiple clocks. Three-way interactions between grandparent caregiving, gender, and FAS indicated that caregiving grandfathers experience epigenetic age deceleration with higher FAS compared to caregiving grandmothers. Similarly, caregiving grandfathers experience epigenetic age deceleration with higher partner affectual solidarity compared to caregiving grandmothers.

Discussion: These results have implications for targeted interventions to benefit the healthy aging of grandparent caregivers.

Keywords: Intergenerational relationships, Epigenetic age acceleration, Social determinants of health, Family systems, Gender

In the United States, economic and demographic shifts, including rising childcare costs, women's increased labor force participation, non-marital childbearing, single-parent households, opioid-related parental incapacitation, and longer life expectancy, have intensified intergenerational family interactions with social and health implications (Baker et al., 2008; Danielsbacka et al., 2022; Hayslip & Kaminski, 2005; Minkler & Fuller-Thomson, 2000). In 2015, 7.3 million grandparents lived with grandchildren, and 37% (2.7 million) were primary caregivers (Baker et al., 2008; Danielsbacka et al., 2022). Over one in 10 had raised a grandchild for ≥6 months (Danielsbacka et al., 2022; Shorey & Ng, 2022). According to role theory, these "second-time parents" face competing demands and physical and emotional strain (Hayslip & Kaminski, 2005). Thus, understanding grandparent caregiving and its health implications is vital in an aging society. Specifically, this study examines associations between grandparent caregiving and epigenetic aging—using multiple indicators that compare individuals' biological age with their chronological age—and assesses whether these associations vary by grandparent gender and familial relationships.

Grandparent caregiving and family stress models

A growing body of literature highlights grandparent caregiving as an important social determinant of health (Danielsbacka et al., 2022; Kelley et al., 2021; Kim et al., 2017), which can be explained through the family stress model. Originally focused on parental caregiving stress from finances and parenting practices influencing child outcomes (Masarik & Conger, 2017), it has been adapted to examine how grandparent caregiver stress and parenting practices affect both grandchild and grandparent caregiver outcomes. Smith and colleagues outline contextual factors of family and partner relationship functioning and social support as contributors to behavioral

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and mental health symptoms for grandparent caregivers (Smith & Hancock, 2010; Smith et al., 2008, 2018). Given adaptive stress process models linking psychosocial stressors to physiological health, including biological aging (Epel et al., 2018), this paper extends the adaptive grandparent caregiver family stress model to assess associations between grandparent caregiving and epigenetic aging.

It is important to consider grandparent caregiving within a family systems context. Cox and Paley (2003) describe the family system framework as overlapping subsystems that account for family dynamics. Interactions within these subsystems, including supportive intergenerational and marital interactions, may protect against accelerated epigenetic aging and adverse health outcomes, whereas strained relationships may exacerbate adverse outcomes (Shorey & Ng, 2022). Family and partner affectual solidarity measures indicate combined relationship support/strain, helping ascertain the effects of these relationships on grandparent caregiver well-being (Grzywacz & Marks, 1999; Srirangarajan et al., 2020; Uphold-Carrier & Utz, 2012). However, limited empirical research has investigated how familial and partner relationships impact grandparent caregiver health (Matzek & Cooney, 2009). Non-partner familial relationships may be especially important for grandparent caregivers who are not partnered or have limited partner support (Barnett et al., 2010). Additionally, involvement of grandchildren's parents or other family members contributes to multigenerational interactions and relationships, influencing grandparent caregiver health (Barnett et al., 2010). With the increase in grandparent caregiving in recent decades, it is crucial to understand how family relationships impact grandparent caregiver well-being.

Grandparent caregiving and gender

A majority (63%) of grandparent caregivers are women (Livingston, 2013). The differential susceptibility hypothesis suggests that some individuals are more influenced by positive or negative components of their environment (Belsky & Pluess, 2009). In this regard, grandmothers appear more satisfied in the grandparent role than grandfathers (Winefield & Air, 2010). Family, friend, and community social engagement protects against mental health issues for both genders of grandparent caregivers, but especially for grandmother caregivers (Notter, 2022); whereas the grandfather caregivers' mental health is more impacted by living with a spouse (Park, 2009). Gender may thus play an important role in the context of the grandparent caregiving family stress model in impacting caregiver health. Notably, grandmother caregivers tend to report less spousal support than grandfather caregivers (Matzek & Cooney, 2009); and in general, women experience greater adverse health impacts from strained partner relationships than men (Smith et al., 2011). Notwithstanding, studies suggest that women have slower rates of epigenetic aging than men across most epigenetic clocks (epigenetic aging clocks will be described in a later section; Crimmins et al., 2021).

Grandparent caregiving and health

Grandparenting has both beneficial and adverse health implications. Having grandchildren can enhance social engagement, purpose, and life satisfaction, supporting psychological well-being and cognitive health (Danielsbacka et al., 2022; Winefield & Air, 2010). However, evidence suggests an ambivalent pattern: moderate involvement may promote well-being, whereas intensive caregiving often imposes psychological and physical strain (Danielsbacka et al., 2022). Grandparents who provide instrumental (frequent or primary) care often experience psychological distress, depressive symptoms, anxiety, marital strain, and poorer cognitive functioning, comparable to other high-stress caregiving groups (Burn & Szoeke, 2015; Grinstead et al., 2003; Kelley et al., 2021; Minkler & Fuller-Thomson, 2001; Winefield & Air, 2010). The burden is compounded when grandchildren have behavioral or developmental difficulties, with grandmothers reporting particularly unmet mental health needs (Smithgall et al., 2009).

Physical health findings mirror these patterns. Grandparent caregivers—many managing chronic conditions (Boersma et al., 2020)—report poorer self-rated health, increased functional impairment, exacerbation of chronic illness, and higher viral illness transmission compared to non-caregivers (Choi, 2020; Danielsbacka et al., 2022; Grinstead et al., 2003; Minkler & Fuller-Thomson, 1999). They may also defer medical care due to stigma or fear of disrupting grandchildren's stability (Taylor et al., 2017). Despite evidence of mental and physical strain, little is known about underlying biological pathways. This study examines epigenetic modifications as a potential mechanism linking caregiving stress to accelerated biological aging.

Epigenetic aging

Stress can alter the epigenomic landscape of cells—a dynamic map of how genes are expressed (activated or suppressed) in response to external factors (Faul et al., 2023). Gene expression can be regulated through DNA methylation (DNAm), a fundamental epigenetic marker, which occurs when a methyl group (a carbon atom bonded to three hydrogen atoms) is added to DNA at specific locations: typically, a cytosine followed by a guanine nucleotide base sequence (CpG site; Faul et al., 2023). DNAm patterns underlie epigenetic "clocks," which estimate biological age from DNAm at CpG sites linked to aging markers (Faul et al., 2023). In other words, DNAm at these CpG sites influences gene activity, including genes linked to aging pathways, and serves as a biomarker to estimate biological age. Each clock utilizes a unique set of CpG sites to estimate biological age or other aging phenotypes, such as the pace of aging relative to chronological age (Faul et al., 2023). Compared to chronological age, epigenetic clocks provide more sensitive measures of how stressors influence biological aging and health (Faul et al., 2023).

Five epigenetic clocks are commonly used (all utilized in this study): two first-generation clocks trained to predict chronological age (Horvath pan-tissue and Hannum clocks; Hannum et al., 2013; Horvath, 2013); two second-generation clocks trained to estimate biological age and predict health span and mortality (PhenoAge and GrimAge; Levine et al., 2018; Lu et al., 2019); and a third-generation clock estimating the pace of aging (DunedinPACE; Belsky et al., 2022). Each clock provides an estimate of biological age, except DunedinPACE, which measures the pace of aging—the rate at which an individual is biologically aging relative to chronological time (Belsky et al., 2022).

By comparing estimated biological age from epigenetic clocks with chronological age, epigenetic age acceleration

(EAA) scores can be calculated. EAA occurs when biological age exceeds chronological age, while epigenetic age deceleration reflects the opposite (Faul et al., 2023). Higher EAA and pace of aging are associated with chronic conditions, increased infection risk, cognitive decline, and general all-cause mortality. Conversely, epigenetic age deceleration and a lower pace of aging are associated with better health and a lower risk of the aforementioned conditions (Faul et al., 2023). For all clocks except DunedinPACE, EAA is calculated as the residual from regressing biological age, estimated by the epigenetic clock, on individual chronological age (Faul et al., 2023).

Caregiving responsibilities may harm grandparents' health partly through epigenetic changes. Given family stress models and established links between psychosocial stressors and biological outcomes, including epigenetic aging, these novel clocks offer insight into how caregiving stress may get "under the skin" to influence aging among those already vulnerable to age-related biological decline (Epel et al., 2018; Smith et al., 2008, 2011, 2018).

The current study

This study, to our knowledge, is the first to examine how grandparent caregiving may be linked to epigenetic aging. We specifically investigated how grandparent caregiving status interacts with gender and family affectual solidarity (FAS) to affect epigenetic aging. Using a sample of midlife and older adults in the United States, we examined the following questions:

1. Do grandparent caregivers have stronger evidence of epigenetic aging compared to non-caregiving grandparents? That is, do grandparent caregivers show higher biological aging (beyond chronological age) compared to non-caregiving grandparents?
2. Does the effect of grandparent caregiving on epigenetic aging differ by gender?
3. Do grandparent caregiving, grandparent gender, and family affectual solidarity interact to predict epigenetic aging?

Method

Participants

Data were obtained from the Midlife in the United States (MIDUS) study, which collects a wide breadth of psychosocial, health, and biomarker data from midlife and older adults in the United States. A subsample of participants in the cross-sectional MIDUS 2 (M2) and MIDUS Refresher (MR) waves provided blood samples that were used to create epigenetic aging scores. Specifically, this study utilizes the M2 Survey (2004–2006), M2 Milwaukee Survey (an African American oversample, 2005–2006), M2 Biomarker (2004–2009), MR Survey (2011–2014), MR Milwaukee Survey (2012–2013), and MR Biomarker (2012–2016) projects. From the M2 Biomarker and MR Biomarker projects, DNAm profiling was conducted in 2019, and in 2022, DNAm data were used to compute epigenetic age estimates. A timeline for data collection can be found at https://midus.wisc.edu/data/timeline.php. Participants who reported being grandparents and had complete data on sociodemographic characteristics, BMI (body mass index, a calculated measure of an individual's body weight in kilograms divided by the square of their height in meters), and FAS were included in the final sample ($N = 492$, mean age = 61.94 years, 30.69% Black, 6.50% non-white, 59.96% female, 58.94% partnered). A consort diagram for the final cross-sectional sample can be found in Figure S1 (see online supplementary material).

Measures

Grandparent caregiving

Definitions of grandparent caregiving vary across studies. Some classify caregivers as grandparents with prior or current primary responsibility for a grandchild for ≥ 6 months (Minkler & Fuller-Thomson, 1999, 2000; Smithgall et al., 2009), or distinguish caregiving intensity by hours or nights of care (Fuller-Thomson & Minkler, 2001). Others rely on custodial or co-residential status (Shorey & Ng, 2022). Consistent with prior work, this study defines caregivers as grandparents who have had primary responsibility for a grandchild for ≥6 months.

In the present study, participants who reported being grandparents were asked to respond yes/no to the question "For various reasons, grandparents sometimes take on a major responsibility for raising a grandchild. Have you ever had major responsibility for [your grandchild/any of your grandchildren] for 6 months or more?" 18.29% of the sample reported having taken on such a responsibility (interchangeably referred to as instrumental grandparent caregiving henceforth).

Family affectual solidarity

Participants reported family support and family strain; these scales are revised from Schuster et al. (1990) and have since been used in various publications utilizing MIDUS data (Grzywacz & Marks, 1999; Srirangarajan et al., 2020; Uphold-Carrier & Utz, 2012). For family support, participants responded to the following four items: (a) "Not including your spouse or partner, how much do members of your family really care about you?"; (b) "How much do they understand the way you feel about things?"; (c) "How much can you rely on them for help if you have a serious problem?," and (d) "How much can you open up to them if you need to talk about your worries?." For family strain, participants responded to the following four items: (e) "Not including your spouse or partner, how often do members of your family make too many demands on you?," (f) "How often do they criticize you?"; (g) "How often do they let you down when you are counting on them?," and (h) "How often do they get on your nerves?." Across all items, participants responded on a four-point Likert scale where 1 = Often, 2 = Sometimes, 3 = Rarely, and 4 = Never. The FAS scale is an 8-item scale combining the four-item "family support" and four-item "family strain" subscales, and provides the benefit of assessing the combined effects of support and strain (Grzywacz & Marks, 1999; Srirangarajan et al., 2020; Uphold-Carrier & Utz, 2012). The measure aligns with adaptive grandparent caregiver stress models in assessing both family-based social support and strain or dysfunction as important factors impacting grandparent caregiver stress and health outcomes (Smith & Hancock, 2010; Smith et al., 2008, 2018). The FAS scale is constructed by calculating the mean of the values of the items. Items for the "family support" subscale were recoded so that a high score signifies high levels of FAS. The scale was computed for all cases with valid values for at least one item on the scale. We subtracted 1 from the

FAS scale values to rescale the variable from 0 to 3. The mean for FAS for the sample = 2.19, *SD* = 0.55, range = 0.12–3.00; the alpha for the scale was 0.83.

Partner affectual solidarity

Participants reported spouse/partner support and strain. For spouse/partner support, participants responded to the following six items: (a) "How much does your spouse or partner really care about you?" (b) "How much does he or she understand the way you feel about things?" (c) "How much does he or she appreciate you?" (d) "How much do you rely on him or her for help if you have a serious problem?" (e) "How much can you open up to him or her if you need to talk about your worries?" and (f) "How much can you relax and be yourself around him or her?" For spouse/partner strain, participants responded to the following six items: (g) "How often does your spouse or partner make too many demands on you?" (h) "How often does he or she argue with you?" (i) "How often does he or she make you feel tense?" (j) "How often does he or she criticize you?" (k) "How often does he or she let you down when you are counting on him or her?" and (l) "How often does he or she get on your nerves?" Across all items, participants responded on a four-point Likert scale with 1 = Often, 2 = Sometimes, 3 = Rarely, and 4 = Never. The spouse/partner affectual solidarity scale (PAS) (henceforth referred to as the PAS) is a 12-item scale combining the six "spouse/partner support" items which comprise the "spouse/partner support" subscale and six "spouse/partner strain" items which comprise the "spouse/partner strain" subscale (Grzywacz & Marks, 1999; Srirangarajan et al., 2020). The PAS scale is constructed by calculating the mean of the items. Items for the "spouse/partner support" subscale were recoded so that a high score signifies high levels of PAS. The scale is computed for cases with valid values for at least one item on the scale. We subtracted 1 from the PAS scale values to rescale the variable from 0 to 3. Among participants who reported they were partnered and who had complete data on PAS (comprising 57.72% of the total sample, *N* = 284), the mean of the PAS scale = 2.28, *SD* = 0.54, range = 0.08 to 3.00; the alpha for the scale is 0.92.

Epigenetic age measures

Participants in the present study provided whole blood samples as part of a fasting blood draw on the morning of the second day of the Biomarker visit. These whole blood samples were collected using a BD Vacutainer Tube with EDTA anticoagulant, frozen for storage, and subject to DNA extraction. After extraction, DNA was tested for suitable yield and integrity, and was subjected to genome-wide DNAm profiling using the Illumina Methylation EPIC v1 microarray. The resulting beta values (estimated % methylation at each assayed CpG site) were normalized to control for technical sources of variance (using the noob function in the R minfi package), registered onto the list of CpG sites assayed on the Illumina Methylation 450K microarray, screened using standard quality control metrics for DNAm array data, and scored using previously published algorithms for multiple epigenetic clocks. Details regarding the collection and processing of DNAm data are included in the M2 and MR Biomarker Project Blood, Urine, Saliva documentation, available online at ICPSR or via the MIDUS Colectica Portal (http://midus.colectica.org/).

The current study included Horvath, Hannum, PhenoAge, GrimAge, and DunedinPACE epigenetic clocks. For all clocks, with the exception of DunedinPACE, EAA was calculated as the residual from regressing biological age, estimated by the epigenetic clock, on participant chronological age reported at M2 and MR Biomarker data collection (Faul et al., 2023). Accelerated epigenetic aging was indicated by positive EAA values, while decelerated epigenetic aging was indicated by negative EAA values; except for DunedinPACE, for which values over 1 indicated faster rates of aging, while values less than 1 indicated slower rates of aging. Overall, EAA scores indicated that the sample overall had relatively lower biological age estimates compared to chronological age, although the opposite was found for DunedinPACE. For the regression models, all EAA measures and DunedinPACE were standardized through *z*-scoring.

Sociodemographic and health characteristics

Following Krieger et al. (2023)'s recommendations, chronological age was utilized as a covariate to ensure comparability across clocks and avoid spurious associations from age confounding. Participants self-reported racial background as White, Black/African American, Native American or Alaska Native Aleutian Islander/Eskimo, Asian, Native Hawaiian or Pacific Islander, or other; and were grouped into "White," "Black," and "other" racial groups (these racial groups are often used in MIDUS papers, given the sample demographics; Lawrence et al., 2022). Participants self-reported as male or female, which provided information on the grandparents' genders as a crucial element of the present analyses. Other sociodemographic covariates included partnered status to account for whether grandparents had partners who may impact their caregiving experience (0 = not married/partnered, 1 = married or living with a serious partner); and socioeconomic status indicators including education level (0 = high school or less, 1 = some college or more), and logarithm of household total income from wage, pension, social security, and other sources (minimum possible response = $0, maximum possible response = $300,000) plus 1 to account for responses of $0 (Minkler & Fuller-Thomson, 2000).

Health-related covariates included BMI and smoking status (whether participants smoked at least a few cigarettes every day; never/did not answer, former, or current regular smoker), both established predictors of DNAm and epigenetic clock measures (Faul et al., 2023). Controlling for these reduces confounding and better captures caregiving effects beyond those attributable to health behaviors. Number of chronic conditions ever experienced (ranging from autoimmune, cancer, cardiovascular, diabetes, digestive, lung, neurological, mental health, and substance use-related conditions) was utilized as a covariate in sensitivity analyses (Danielsbacka et al., 2022) to assess whether associations between caregiving and epigenetic aging were independent of health status. Because chronic conditions are often endogenous with epigenetic aging, they were excluded from primary models, but included in sensitivity analyses (Faul et al., 2023).

Table 1 describes variables in the main analytic sample (*N* = 492). Descriptive variables for the partnered grandparent subsample (*N* = 284) are in Table S1 (see online supplementary material). Table S2 (see online supplementary material)

Table 1. Descriptive statistics for main analytic sample ($N = 492$).

Variable	%	Mean	*SD*	Range
Grandparent variables				
Grandparent caregiver	18.29			
Live with grandchild(ren)	17.07			
Years of care among grandparent caregivers		5.46	5.73	0, 21
0–3	54.44			
4+	45.56			
Sociodemographic variables				
Age		61.94	9.78	36, 86
Race				
White	62.80			
Black	30.69			
Other	6.50			
Gender				
Male	40.04			
Female	59.96			
Partnered status				
Not partnered	41.06			
Partnered	58.94			
Highest educational level				
High school or less	33.94			
Some college or more	66.06			
Total household income		65851.66	55207.89	0, $3x10^5$
Health variables				
Body mass index		30.82	6.89	17.08, 64.06
Smoking				
Never/refused	49.39			
Former	34.96			
Current	15.65			
Chronic conditions		5.00	3.13	0, 23
Affectual solidarity variables				
FAS		2.19	0.55	0.12, 3.00
Epigenetic age variables				
Horvath clock		62.15	8.84	36, 107
Horvath acceleration		−0.006	4.92	−21.14, 38.31
Hannum clock		49.29	9.58	26, 110
Hannum acceleration		−0.005	5.18	−18.70, 53.68
PhenoAge clock		51.58	9.96	24, 85
PhenoAge acceleration		−0.03	6.08	−20.86, 26.08
GrimAge clock		59.34	8.85	33, 104
GrimAge acceleration		−0.006	4.93	−21.20, 38.43
DunedinPACE of aging		1.03	0.14	0.68, 1.45

Note. FAS = family affectual solidarity; PACE = Pace of Aging Calculated from the Epigenome.

provides a correlation table of variables in the main analytic sample ($N = 492$).

Statistical analysis

All analyses used linear regression in R (https://www.R-project.org/). Epigenetic clock outcomes (EAA measures and DunedinPACE) were *z*-scored (mean = 0, *SD* = 1). Predictors were left in original coding. Thus, regression coefficients are unstandardized with respect to predictors but expressed as changes in outcome standard deviation (*SD*) units, representing the expected change in *z*-scored EAA or DunedinPACE for a one-unit change in the predictor. This facilitates comparison of caregiving effects across clocks while maintaining interpretability of predictors. Coefficients can be back-translated into original units by multiplying by the pre-standardization *SD* of the outcome (main sample *SD*s in Table 1; partnered sample in Table S1, see online supplementary material). R^2 (total model variance) and *F* statistics (overall model significance) for each model were reported.

The first analysis examined associations between grandparent caregiving and epigenetic aging ($N = 492$). Direct associations were tested, followed by models including covariates ($\alpha = 0.05$). Two-way interaction models assessed grandparent caregiving × gender effects; three-way models assessed grandparent caregiving × gender × FAS. All were rerun with covariates. Given the limited sample size, the power to detect interactions may be insufficient (Bauer & Curran, 2005). To address this, we applied simple effect and slope analyses to probe all interactions, since significant simple effects can occur even when interaction terms are nonsignificant (Bauer & Curran, 2005).

Table 2. Linear regression models of grandparent caregiving on EAA/pace of aging ($N = 492$).

	Horvath acceleration		Hannum acceleration		PhenoAge acceleration		GrimAge acceleration		DunedinPACE	
Variable	*B* (95% CI)	*p*	*B* (95% CI)	*p*	*B* (95% CI)	*p*	*B* (95% CI)	*p*	*B* (95% CI)	*p*
Model 1										
Grandparent caregiver (Ref = No)										
Yes	0.08 (−0.15, 0.31)	.51	0.05 (−0.18, 0.28)	.65	0.10 (−0.13, 0.33)	.39	0.07 (−0.16, 0.30)	.53	**0.41 (0.18, 0.64)**	**<.001**
R^2	0.001		0.0004		0.001		0.001		0.025	
F	0.429		0.211		0.729		0.398		12.690	
Model 2										
Grandparent caregiver (Ref = No)										
Yes	0.13 (−0.10, 0.37)	.26	0.12 (−0.11, 0.36)	.30	0.10 (−0.13, 0.33)	.39	0.13 (−0.10, 0.37)	.26	**0.22 (0.03, 0.41)**	**.03**
Age	−0.01 (−0.02, 0.005)	.30	−0.01 (−0.02, 0.002)	.11	−0.001 (−0.01, 0.01)	.92	−0.01 (−0.02, 0.005)	.29	*0.01 (−0.001, 0.02)*	*.09*
Race (Ref = White)										
Black	−0.01 (−0.24, 0.22)	.96	**−0.25 (−0.48, −0.02)**	**.03**	−0.05 (−0.28, 0.18)	.67	−0.01 (−0.24, 0.22)	.92	**0.43 (0.24, 0.62)**	**<.001**
Other	0.02 (−0.34, 0.39)	.90	−0.06 (−0.43, 0.31)	.75	0.17 (−0.20, 0.53)	.37	0.02 (−0.34, 0.39)	.90	*0.26 (−0.05, 0.56)*	*.10*
Gender (Ref = Male)										
Female	**−0.45 (−0.64, −0.25)**	**<.001**	**−0.33 (−0.53, −0.14)**	**<.001**	**−0.25 (−0.44, −0.06)**	**.01**	**−0.45 (−0.64, −0.26)**	**<.001**	**−0.20 (−0.36, −0.04)**	**.01**
Partner status (Ref = Unpartnered)										
Partnered	0.02 (−0.19, 0.23)	.86	0.02 (−0.19, 0.23)	.86	0.10 (−0.10, 0.31)	.32	0.02 (−0.19, 0.23)	.85	*−0.17 (−0.34, 0.005)*	*.06*
Education (Ref = High school −)										
College +	**0.20 (0.001, 0.39)**	**.05**	0.14 (−0.06, 0.33)	.17	0.15 (−0.05, 0.34)	.14	**0.20 (0.002, 0.39)**	**.05**	*−0.14 (−0.30, 0.02)*	*.09*
Log household income	*−0.05 (−0.09, 0.001)*	*.06*	−0.01 (−0.06, 0.03)	.56	*−0.04 (−0.09, 0.01)*	*.09*	*−0.05 (−0.09, 0.002)*	*.06*	−0.03 (−0.07, 0.01)	.11
Body mass index	0.002 (−0.01, 0.02)	.74	0.01 *(−0.003, 0.02)*	.12	**0.03 (0.01, 0.04)**	**<.001**	0.002 (−0.01, 0.02)	.73	**0.04 (0.03, 0.05)**	**<.001**
Smoking (Ref = Never)										
Former	0.04 (−0.16, 0.23)	.72	0.12 (−0.08, 0.32)	.23	0.16 (−0.03, 0.36)	.11	0.04 (−0.16, 0.23)	.73	**0.38 (0.22, 0.54)**	**<.001**
Current	0.03 (−0.24, 0.29)	.85	−0.02 (−0.29, 0.24)	.86	0.21 (−0.06, 0.47)	.12	0.03 (−0.24, 0.29)	.85	**1.01 (0.79, 1.23)**	**<.001**
R^2	0.057		0.050		0.064		0.058		0.348	
F	2.631		2.308		2.979		2.667		23.270	

Note. CI = confidence interval; EAA = epigenetic age acceleration; F = F-statistic; HS = high school; PACE = Pace of Aging Calculated from the Epigenome; Ref = reference. Values of $p \leq .05$ are bolded. Values of $p \leq .10$ are italicized.

Supplementary analyses examined three-way caregiving × gender × PAS interactions in partnered grandparents ($N = 284$). All models were rerun with chronic conditions as an additional covariate for sensitivity analyses. These complementary analyses can be found in Supplementary Material.

Results

Associations between grandparent caregiving and epigenetic aging

The first set of linear regression models examined direct associations between grandparent caregiving and epigenetic aging across five epigenetic clocks (Model 1; Table 2), then the models were rerun, controlling for sociodemographic and health covariates (Model 2; Table 2). Results indicated that grandparent caregiving was associated with faster DunedinPACE measurements ($B = 0.22$; 95% CI = 0.03, 0.41; $p = .03$) even when controlling for covariates. Thus, caregiving was associated with a 0.22 *SD* higher DunedinPACE. Given the sample *SD* of 0.14 for DunedinPACE, this corresponds to ~0.03 additional years of biological aging per chronological year among caregivers compared to non-caregivers. Further, although not significant, all clocks showed the same direction of results (positive association) between grandparent caregiving and epigenetic aging. We obtained similar results when running these models with chronic conditions as an additional covariate (Table S3, see online supplementary material).

Two-way interactions between grandparent caregiving and gender on epigenetic aging

Next, we examined two-way interactions between grandparent caregiving and gender and their association with epigenetic aging; first, only examining grandparent caregiving, gender, and grandparent caregiving interacted with gender as predictors (Model 1; Table 3); then, adding covariates (Model 2; Table 3). We further probed two-way interactions in Model 2 with simple effect analyses. Graphs depicting all Model 2 two-way interactions between grandparent caregiving and gender are in Figure S2 (see online supplementary material). Overall, the Model 2 two-way interactions indicated that grandfather caregivers had higher EAA than non-caregiving grandfathers across Horvath, Hannum, and GrimAge clocks ($p \leq .05$). Such an effect was not found for caregiving versus non-caregiving grandmothers ($p > .10$) except for DunedinPACE ($p = .05$); although given that the DunedinPACE interaction term was not significant ($p = .78$), the significant effect may be a result of low statistical power (Bauer & Curran, 2005). Corresponding regression tables for these two-way interactions, controlling for chronic conditions as an additional covariate, are in Table S4 (see online supplementary material).

Three-way interactions between grandparent caregiving, gender, and FAS on epigenetic aging

Next, we examined three-way interactions between grandparent caregiving, gender, and FAS and their association with epigenetic aging. We first examined grandparent caregiving, gender, FAS, and associated two and three-way interactions as predictors (Model 1; Table 4), and then added covariates to assess whether associations still held (Model 2; Table 4). We probed all Model 2 three-way interactions by conducting simple slope analyses. Graphs depicting all Model 2 three-way interactions between grandparent caregiving, gender, and FAS are shown in Figure 1. Overall, the Model 2 three-way interactions indicated that higher levels of FAS were significantly associated with epigenetic age deceleration for grandfather caregivers but not grandmother caregivers across Horvath, Hannum, PhenoAge, and GrimAge clocks. Corresponding regression tables for these three-way interactions, controlling for chronic conditions as an additional covariate, are found in Table S5 (see online supplementary material).

Finally, we conducted supplementary analyses to examine three-way interactions between grandparent caregiving, gender, and PAS in the partnered grandparent subsample ($N = 284$; Table S6, see online supplementary material). Graphs depicting all three-way interactions between grandparent caregiving, gender, and PAS (using Model 2 results from Table S6, see online supplementary material) can be found in Figure S3 (see online supplementary material). Overall, we found a similar pattern to the three-way interactions with family solidarity, such that higher levels of PAS were significantly associated with epigenetic age deceleration for grandfather caregivers but not grandmother caregivers across Horvath, Hannum, PhenoAge, and GrimAge clocks. All slopes for non-caregiving and caregiving grandfathers and grandmothers were found to be insignificant for DunedinPACE ($p > .10$). Corresponding regression tables for these three-way interactions with PAS controlling for chronic conditions as an additional covariate can be found in Table S7 (see online supplementary material).

Discussion

Results suggest grandparent caregiving may contribute to the increased pace of aging (DunedinPACE). Grandfather caregivers generally evidenced EAA compared to non-caregiving grandfathers, whereas overall, no significant differences emerged for grandmothers. Gendered caregiving expectations may heighten stress for grandfathers, while women's generally slower epigenetic aging may buffer effects (Crimmins et al., 2021; Park, 2009). Three-way interactions indicated that grandfather caregivers benefited from higher FAS and PAS, experiencing epigenetic age deceleration, while grandmothers did not. Grandfather caregivers with high partner and family support may receive more assistance in caregiving tasks compared to grandmother caregivers (Park, 2009). This aligns with evidence that men receive more partner support than women in different-gender relationships (Stronge et al., 2019). Additionally, due to socialized gendered caregiving expectations, grandmother caregivers may overestimate levels of external support compared to grandfather caregivers (Park, 2009).

Interventions should leverage healthcare, social, and parenting supports to improve grandparents' mental and physical health (Sumo et al., 2018). Tailoring parenting programs and support groups for grandparents may help them recall strategies, navigate relationships with their grandchild(ren)'s parents, and cope with stress (Kirby & Sanders, 2012). Policy supports, especially for low-income families, are needed to reduce strain. Most services target custodial grandparents, excluding supplementary caregivers (Burn & Szoeke, 2015). Economic relief through tax credits or direct payments could ease financial burdens (Baker et al., 2008), while reducing barriers to respite care would improve health outcomes (Taylor et al., 2017).

Table 3. Two-way interaction linear regression models of grandparent caregiving and gender on EAA/pace of aging (N=492).

	Horvath acceleration		Hannum acceleration		PhenoAge acceleration		GrimAge acceleration		DunedinPACE	
Variable	*B* (95% CI)	*p*	*B* (95% CI)	*p*	*B* (95% CI)	*p*	*B* (95% CI)	*p*	*B* (95% CI)	*p*
Model 1										
Grandparent caregiver (Ref = No): Yes	**0.45 (0.04, 0.87)**	**.03**	**0.45 (0.04, 0.87)**	**.03**	0.16 (−0.26, 0.58)	.45	**0.45 (0.04, 0.86)**	**.03**	*0.36 (−0.06, 0.77)*	*.09*
Gender (Ref = Male): Female	**−0.35 (−0.54, -0.16)**	**<.001**	**−0.26 (−0.46, −0.06)**	**.01**	**−0.26 (−0.46, −0.07)**	**.01**	**−0.35 (−0.55, −0.16)**	**<.001**	*−0.17 (−0.36, 0.03)*	*.09*
Interactions: Grandparent caregiver × Gender	*−0.45 (−0.94, 0.04)*	*.07*	**−0.50 (−0.99, −0.002)**	**.05**	−0.03 (−0.53, 0.47)	.91	*−0.45 (−0.94, 0.04)*	*.07*	0.11 (−0.39, 0.61)	.67
R^2	0.049		0.035		0.018		0.050		0.031	
F	8.367		5.922		3.048		8.503		5.220	
Model 2										
Grandparent caregiver (Ref = No): Yes	**0.46 (0.05, 0.88)**	**.03**	**0.48 (0.07, 0.90)**	**.02**	0.10 (−0.32, 0.52)	.64	**0.46 (0.05, 0.88)**	**.03**	0.18 (−0.17, 0.53)	.31
Age	−0.01 (−0.02, 0.004)	.28	*−0.01 (−0.02, 0.001)*	*.09*	−0.001 (−0.01, 0.01)	.92	−0.01 (−0.02, 0.004)	.26	*0.01 (−0.001, 0.02)*	*.09*
Race (Ref = White)										
Black	0.00 (−0.23, 0.23)	.99	**−0.25 (−0.48, −0.01)**	**.04**	−0.05 (−0.28, 0.18)	.67	−0.01 (−0.24, 0.22)	.95	**0.43 (0.24, 0.62)**	**<.001**
Other	0.02 (−0.34, 0.39)	.91	−0.06 (−0.43, 0.30)	.74	0.17 (−0.20, 0.53)	.37	0.02 (−0.34, 0.38)	.91	*0.26 (−0.05, 0.56)*	*.10*
Gender (Ref = Male): Female	**−0.38 (−0.58, −0.17)**	**<.001**	**−0.25 (−0.46, −0.05)**	**.02**	**−0.25 (−0.46, −0.04)**	**.02**	**−0.38 (−0.59, −0.17)**	**<.001**	**−0.21 (−0.38, −0.04)**	**.02**
Partner status (Ref = Unpartnered): Partnered	−0.01 (−0.22, 0.20)	.94	−0.01 (−0.22, 0.20)	.93	0.10 (−0.10, 0.31)	.33	−0.01 (−0.21, 0.20)	.96	*−0.16 (−0.34, 0.01)*	*.06*
Education (Ref = High school -): College +	**0.21 (0.01, 0.41)**	**.04**	0.15 (−0.05, 0.35)	.13	0.15 (−0.05, 0.34)	.14	**0.21 (0.02, 0.41)**	**.03**	*−0.14 (−0.31, 0.02)*	*.09*
Log household income	*−0.04 (−0.09, 0.005)*	*.08*	−0.01 (−0.06, 0.04)	.67	*−0.04 (−0.09, 0.01)*	*.09*	*−0.04 (−0.09, 0.005)*	*.08*	−0.03 (−0.07, 0.01)	.11
Body mass index	0.002 (−0.01, 0.02)	.77	0.01 (−0.003, 0.02)	.13	**0.03 (0.01, 0.04)**	**<.001**	0.002 (−0.01, 0.02)	.75	**0.04 (0.03, 0.05)**	**<.001**
Smoking (Ref = Never)										
Former	0.05 (−0.15, 0.25)	.62	0.14 (−0.06, 0.34)	.17	0.16 (−0.04, 0.36)	.11	0.05 (−0.15, 0.25)	.62	**0.38 (0.21, 0.54)**	**<.001**
Current	0.02 (−0.24, 0.29)	.87	−0.03 (−0.29, 0.24)	.83	0.21 (−0.06, 0.47)	.12	0.02 (−0.24, 0.29)	.87	**1.01 (0.79, 1.23)**	**<.001**
Interactions: Grandparent caregiver × Gender	*−0.48 (−0.98, 0.02)*	*.06*	**−0.52 (−1.02, −0.02)**	**.04**	0.0003 (−0.50, 0.50)	1.00	*−0.48 (−0.98, 0.02)*	*.06*	0.06 (−0.36, 0.48)	.78
R^2	0.064		0.058		0.064		0.064		0.348	
F	2.716		2.475		2.725		2.750		21.290	

Note. CI = confidence interval; EAA = epigenetic age acceleration; F = F-statistic; PACE = Pace of Aging Calculated from the Epigenome; Ref = reference. Values of $p \leq .05$ are bolded. Values of $p \leq .10$ are italicized.

Table 4. Three-way interaction linear regression models of grandparent caregiving, gender, and FAS on EAA/pace of aging ($N = 492$).

	Horvath acceleration		Hannum acceleration		PhenoAge acceleration		GrimAge acceleration		DunedinPACE	
Variable	*B* (95% CI)	*p*	*B* (95% CI)	*p*	*B* (95% CI)	*p*	*B* (95% CI)	*p*	*B* (95% CI)	*p*
Model 1										
Grandparent caregiver (Ref = No): Yes	**1.90 (0.18, 3.61)**	**.03**	**3.05 (1.31, 4.78)**	**<.001**	**2.38 (0.63, 4.13)**	**.01**	**1.90 (0.18, 3.61)**	**.03**	**1.76 (0.02, 3.49)**	**.05**
Gender (Ref = Male): Female	−0.05 (−0.87, 0.77)	.90	0.08 (−0.76, 0.91)	.86	0.57 (−0.27, 1.41)	.18	−0.05 (−0.87, 0.77)	.90	*0.82 (−0.01, 1.65)*	*.054*
Family solidarity	−0.15 (−0.43, 0.13)	.30	0.05 (−0.23, 0.33)	.73	0.15 (−0.14, 0.43)	.31	−0.15 (−0.43, 0.13)	.30	0.15 (−0.13, 0.43)	.30
Interactions										
Grandparent caregiver × Gender	**−2.38 (−4.37, −0.38)**	**.02**	**−3.27 (−5.28, −1.26)**	**.001**	**−2.97 (−5.00, −0.94)**	**.004**	**−2.38 (−4.37, −0.39)**	**.02**	−1.49 (−3.51, 0.52)	.15
Grandparent caregiver × Family solidarity	*−0.70 (−1.50, 0.09)*	*.08*	**−1.24 (−2.05, −0.44)**	**.002**	**−1.06 (−1.87, −0.25)**	**.01**	*−0.71 (−1.50, 0.09)*	*.08*	−0.66 (−1.46, 0.14)	.11
Gender × Family solidarity	−0.14 (−0.50, 0.22)	.45	−0.15 (−0.52, 0.21)	.41	**−0.38 (−0.74, −0.01)**	**.05**	−0.14 (−0.50, 0.22)	.44	**−0.45 (−0.81, −0.08)**	**.02**
Grandparent caregiver × Gender × Family solidarity	**0.92 (0.002, 1.84)**	**.05**	**1.33 (0.40, 2.25)**	**.01**	**1.39 (0.45, 2.33)**	**.004**	**0.92 (0.003, 1.84)**	**.05**	0.74 (−0.19, 1.67)	.12
R^2	0.073		0.056		0.039		0.073		0.052	
F	5.439		4.098		2.838		5.484		3.769	
Model 2										
Grandparent caregiver (Ref = No): Yes	**1.82 (0.09, 3.56)**	**.04**	**2.94 (1.20, 4.68)**	**<.001**	**2.23 (0.50, 3.97)**	**.01**	**1.82 (0.09, 3.55)**	**.04**	**1.66 (0.21, 3.12)**	**.03**
Age	−0.002 (−0.01, 0.01)	.71	−0.01 (−0.02, 0.004)	.22	0.001 (−0.01, 0.01)	.87	−0.002 (−0.01, 0.01)	.69	0.01 (−0.002, 0.02)	.13
Race (Ref = White)										
Black	0.01 (−0.22, 0.24)	.94	**−0.23 (−0.46, −0.002)**	**.05**	−0.05 (−0.28, 0.18)	.68	0.004 (−0.23, 0.23)	.98	**0.43 (0.24, 0.62)**	**<.001**
Other	0.04 (−0.33, 0.40)	.84	−0.03 (−0.40, 0.33)	.86	0.18 (−0.18, 0.54)	.33	0.04 (−0.33, 0.40)	.85	*0.26 (−0.04, 0.57)*	*.09*
Gender (Ref = Male): Female	0.03 (−0.81, 0.86)	.95	0.07 (−0.77, 0.91)	.87	0.42 (−0.42, 1.25)	.33	0.03 (−0.81, 0.86)	.95	0.39 (−0.31, 1.09)	.27
Partner status (Ref = Unpartnered): Partnered	0.04 (−0.17, 0.25)	.74	0.02 (−0.19, 0.23)	.88	0.12 (−0.09, 0.33)	.27	0.04 (−0.17, 0.25)	.73	*−0.17 (−0.35, 0.01)*	*.06*
Education (Ref = High school −): College +	*0.19 (−0.01, 0.39)*	*.06*	0.12 (−0.07, 0.32)	.22	0.13 (−0.07, 0.33)	.20	*0.19 (−0.01, 0.39)*	*.06*	*−0.14 (−0.31, 0.02)*	*.09*
Log household income	*−0.05 (−0.09, 0.002)*	*.06*	−0.01 (−0.06, 0.04)	.65	*−0.04 (−0.09, 0.004)*	*.07*	*−0.05 (−0.09, 0.002)*	*.06*	−0.03 (−0.07, 0.01)	.105
Body mass index	0.000 (−0.01, 0.01)	.95	0.01 (−0.004, 0.02)	.18	**0.03 (0.01, 0.04)**	**<.001**	0.001 (−0.01, 0.01)	.93	**0.04 (0.03, 0.05)**	**<.001**
Smoking (Ref = Never)										
Former	0.04 (−0.16, 0.23)	.71	0.14 (−0.06, 0.34)	.16	0.16 (−0.03, 0.36)	.104	0.04 (−0.16, 0.23)	.72	**0.38 (0.21, 0.54)**	**<.001**
Current	−0.03 (−0.29, 0.24)	.84	−0.04 (−0.31, 0.22)	.74	0.19 (−0.07, 0.46)	.16	−0.03 (−0.29, 0.24)	.84	**1.02 (0.79, 1.24)**	**<.001**
Family interactions	−0.13 (−0.42, 0.16)	.38	0.04 (−0.25, 0.33)	.79	0.12 (−0.17, 0.41)	.43	−0.13 (−0.41, 0.16)	.39	*0.24 (−0.002, 0.48)*	*.052*
Grandparent caregiver × Gender	**−2.34 (−4.35, −0.33)**	**.02**	**−3.23 (−5.25, −1.21)**	**.002**	**−2.85 (−4.86, −0.83)**	**.01**	**−2.35 (−4.36, −0.34)**	**.02**	−1.39 (−3.08, 0.29)	.11
Grandparent caregiver × Family solidarity	−0.67 (−1.47, 0.14)	.104	**−1.18 (−1.99, −0.38)**	**.004**	**−1.02 (−1.82, −0.21)**	**.01**	−0.66 (−1.47, 0.14)	.104	**−0.70 (−1.37, −0.02)**	**.04**
Gender × Family solidarity	−0.18 (−0.54, 0.19)	.34	−0.14 (−0.51, 0.23)	.45	−0.30 (−0.66, 0.07)	.11	−0.18 (−0.55, 0.19)	.34	*−0.27 (−0.58, 0.04)*	*.09*
Grandparent caregiver × Gender × Family solidarity	*0.90 (−0.03, 1.83)*	*.06*	**1.30 (0.37, 2.23)**	**.01**	**1.35 (0.42, 2.28)**	**.004**	*0.90 (−0.03, 1.83)*	*.06*	*0.68 (−0.10, 1.46)*	*.09*
R^2	0.085		0.077		0.081		0.086		0.356	
F	2.759		2.468		2.630		2.779		16.430	

Note. CI = confidence interval; EAA = epigenetic age acceleration; F = F-statistic; FAS = family affectual solidarity; PACE = Pace of Aging Computed from the Epigenome; Ref = reference. Values of $p \leq .05$ are bolded. Values of $p \leq .10$ are italicized.

Limitations include lack of data on caregiving recency, intensity, custodial context, cultural variation, and partner gender (which could provide insight into the differences in the effects of partner affectual solidarity between same gender and different gender grandparent couples on epigenetic aging), preventing finer-grained analyses. Grandparent caregiving was also

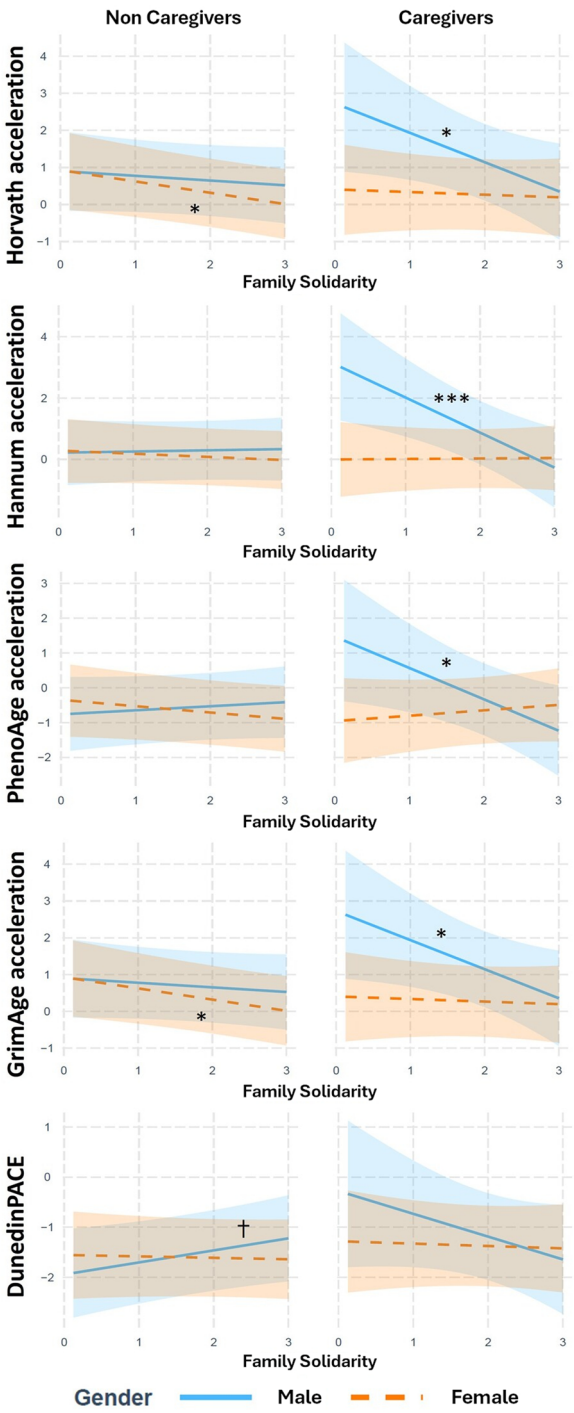

Figure 1. Three-way interaction graphs of grandparent caregiving, gender, and FAS on EAA (N=492). EAA = epigenetic age acceleration; FAS = family affectual solidarity. $^{\dagger}p \leq .10$. $^{*}p \leq .05$. $^{***}p \leq .001$.

assessed in the Survey projects, prior to the collection of epigenetic samples in the Biomarker projects. Additionally, since epigenetic data are only available at M2 and MR, this study was cross-sectional, limiting conclusions around causation and raising the question of whether the associations observed were at least partially due to health selection effects, as we were unable to control for health status at a prior wave (Hoffmann et al., 2019). To further investigate potential health selection effects, Table S8 (see online supplementary material) provides a comparison of sociodemographic and health characteristics of non-caregiving versus caregiving grandparents in the sample. Overall, grandparent caregivers were more likely to be Black, women, unpartnered, lower socioeconomic status, unemployed/homemakers, and in poorer health compared to non-caregiving grandparents. This pattern is consistent with health selection (i.e., the healthy worker effect): healthier grandparents remain employed and are less available for caregiving, leaving relatively less healthy grandparents overrepresented among caregivers (Hoffmann et al., 2019). Additionally, it is notable that minoritized racial groups are overrepresented among the grandparent caregiving sample, as factors related to systemic discrimination (e.g., legacies of redlining, housing discrimination, lower wealth accumulation, incarceration) contribute to health disparities between Black and white populations in the United States (Chen et al., 2015; Epel et al., 2018). Finally, because only a subsample of MIDUS participants provided data for the DNAm project, the sample size of the study was also severely limited, which may affect the power of the analyses (Bauer & Curran, 2005). Generalizability of our results to a wider population of grandparent caregivers should be applied with caution.

Importantly, we found a significant effect between grandparent caregiving only with the DunedinPACE measure (although the direct association between grandparent caregiving and other clocks had a non-significant positive trend). However, the three-way interaction results indicating that grandfather caregivers experienced epigenetic age deceleration when receiving higher family/partner affectual solidarity were significant for most clocks *except* DunedinPACE. The DunedinPACE measure is among the most sensitive indicator of biological aging in most studies, so this was unexpected (Belsky et al., 2022). It is possible that our limited sample size contributed to a lack of a significant three-way interaction for DunedinPACE, but it is also possible that the interaction results found using the other generation clocks are spurious compared to main effects between grandparent caregiving and epigenetic aging (Bauer & Curran, 2005). Future studies are needed to clarify among these differing possibilities.

Despite these limitations, this study extended adaptive stress process models of grandparent caregiving to examine indicators of biological aging. These findings have the potential to provide further insight into the biopsychosocial pathways by which grandparent caregiving stress gets under the skin to impact the aging processes of a group already vulnerable to age-related physiological changes (Epel et al., 2018; Smith & Hancock, 2010; Smith et al., 2008, 2018). Additionally, the three-way interactions examining how family systems impact grandparent caregiver health may provide insight into family and partner interventions aimed at mitigating epigenetic aging, as well as community support groups particularly aimed toward grandmother caregivers to potentially provide additional support outside of the family system (Notter, 2022).

Future research is needed to identify grandparents providing instrumental care to grandchildren, and develop a standardized intensity measure of caregiving to assess how different levels of care may benefit or adversely affect the health of grandparents, exploring whether a "sweet spot" exists for grandparent involvement that benefits grandparent caregiver well-being and grandchild(ren) outcomes. Additionally, future work should assess how custodial and informal caregiving affect

grandparent epigenetic health, and the practice of these types of care in multigenerational households and in the cultural context of immigrant families (Winefield & Air, 2010; Xie & Wang, 2024). Finally, research should also examine non-familial relationships as a moderator between grandparent caregiving and biological health indicators (Notter, 2022).

Supplementary material

Supplementary data are available at *The Journals of Gerontology, Series B: Psychological Sciences and Social Sciences* online.

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Conflict of interest

None declared.

Data availability

The dataset used for this study is available through the MIDUS Colectica Portal (https://midus.colectica.org/), and the analysis code is available upon request from the first author. The MIDUS study was approved by Education and Social/Behavioral Sciences and the Health Sciences IRBs at the University of Wisconsin-Madison. The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study. This study was not preregistered.

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