Accelerated Biological Age among Respondents in Same Sex and Mixed Sex Relationships in Add Health and HRS Data: A Research Note

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Abstract

The minority stress framework proposes that individuals from marginalized and minoritized identities experience greater exposure to discrimination and stress that results in worse health outcomes. Stress and aging research increasingly reveals associations between measures of biological aging and mortality and morbidity outcomes; however, this scholarship has focused almost exclusively on cisgender and heterosexual populations. Sexual minorities' chronic exposure to unique stressors over the life course leads to poor health, but the effects on biological aging are unknown. We bring these two areas of scholarship together to investigate whether sexual minorities experience accelerated aging relative to their heterosexual peers. In this research note, we test for differences in epigenetic age acceleration between individuals reporting same sex and mixed sex partnerships and sexual minority identification in two nationally representative cohorts of US adults: the National Longitudinal Study of Adolescent to Adult Health (Add Health) and the Health and Retirement Study (HRS). In Add Health, estimates of the effect of currently or recently being in a same sex relationship on clocks measured in years range from 0 (no difference) to +.875 years (Vidal-Bralo, p<0.1). In the older HRS sample, estimates of the effect of ever being in a same sex relationship on clocks measured in years range from 0 (no difference) to $+3.40$ years (Levine, p<.05). There is general agreement in direction of effect and relative magnitude across clocks and sample populations. In analyses measuring age acceleration by sexual minority identification and partnership status, age acceleration is consistently greater among uncoupled sexual minority adults when compared with coupled heterosexual adults. Despite data and sample size limitation, these results help to move the field beyond examinations of self-reported health

and single-system measures of health risk and provide a critical first assessment of accelerated aging in sexual minority populations.

Keywords

Biological age, Epigenetic clocks, Same sex relationship, LGBTQ aging, HRS, Add Health

JEL Codes

I1, I12, I14, I18

Accelerated Biological Age among Respondents in Same Sex and Mixed Sex Relationships in Add Health and HRS Data: A Research Note

Traditional approaches to the study of healthy aging are often constrained by focusing on a single aging-related disease or morbidity. In contrast, advances in the field provided by geroscience now characterize the cross-system process of aging as a common risk factor for the onset and progression of many chronic conditions and morbidities among older adults, focusing on genetic, molecular, and cellular mechanisms (Kennedy et al. 2014). We liken this process of aging to similar patterns of weathering or allostatic load described in the minority stress literature, or a process of wear and tear on the body that results in gradual physiological decline. Indeed, a primary explanation for health disparities across sexual orientation is the accumulation of stress because of stigmatization, discrimination, harassment, daily microaggressions, vigilance, and violence experienced on the basis of sexual or gender minority status (Frost, Lehavot, and Meyer 2015; Hatzenbuehler 2014; Meyer 2003; Tan et al. 2020). Such experiences, both during critical periods and cumulatively over the life course, wear down the body by chronically activating the stress response system, leading to poor health (Lick, Durso, and Johnson 2013; McEwen 2017; McEwen and Stellar 1993). In this study, we bring together the literatures on geroscience, aging, and minority stress to investigate biological aging among midlife and older adults in same sex and mixed sex relationships and address two major limitations in current research.

First, research on biological aging is based almost entirely on cisgender and heterosexual adults despite evidence that older sexual minority populations experience heightened stress related to their minority status, which is linked to disparities in morbidity, mental health, disability, and healthcare access relative to heterosexual and cisgender populations (Carpenter et al. 2021; Fredriksen-Goldsen, Kim, and Barkan 2012; Gonzales and Henning-Smith 2015; Mayer et al. 2008; MetLife 2010). Further progress towards the goal of increasing longevity and healthy lifespan relies on understanding the process of biological aging as a common risk factor for mortality and morbidity across the entire population. We contribute to this literature an examination of biological aging among same sex relationships in two nationally representative studies of US adults.

Second, while the theory of the biological embedding of stress in sexual minority and other minority populations is well-articulated, there are few empirical tests using biological data. Much of the current research on sexual minorities, health, and aging relies on self-reported outcomes and cannot test for evidence of the physiological stress process (Correro and Nielson 2019; Flentje et al. 2020). DNA methylation is both a potential generalized biological pathway through which social stress becomes biologically embedded, and a biomarker that captures the biological residue of social experience (Hertzman and Boyce 2010; McEwen 2017; Zannas et al. 2015; Zannas and Chrousos 2017).

DNA methylation age (DNAm age) is a measure of biological age that captures differences in underlying cellular aging relative to chronological age, reflecting accelerated or decelerated aging. The first generation of so-called epigenetic clocks were trained on chronological age, while the second generation were trained to predict mortality or phenotypic age. In brief, each clock algorithm provides a set of weights that are applied to the relevant sites in the sample DNA methylation data and produce a predicted biological age. The clocks were derived in different populations and vary widely in their correlation with chronological age, prediction of morbidity and mortality, and association with social exposures (Marioni et al. 2019; Ryan et al. 2020).

This study uses epigenetic clocks calculated in two nationally representative survey populations, the National Longitudinal Study of Adolescent to Adult Health (Add Health) and the Health and Retirement Survey (HRS), to provide the first estimates of the effects of minority stress on biological aging among sexual minority populations. Although we note limitations to the analyses that follow, the initial evidence suggestive of accelerated aging among sexual minority individuals illuminates several avenues of future research that can contribute to and elaborate on our understanding of the biological embedding of minority stress.

Data and Measures

Samples

Add Health

Add Health is a nationally representative sample of adolescents enrolled in grades 7-12 in 1994 in the United States, with interviews conducted over five waves of data collection (Harris et al. 2019). At the most recent Wave V data collection (2016-2018; average age 37), venous blood was collected in EDTA tubes from a representative subsample of participants during the biomarker home visit. DNA methylation levels were measured using the Infinium Methylation EPIC BeadChip (Illumina). After quality control filtering, DNA methylation data are available for 4,574 participants. For partnered analyses, we limit the Add Health estimation sample to 3,481 Wave V respondents who reported a current coresident spouse/partner or that their most recent relationship was a marriage or coresident partnership, and we expand to 4,469 respondents for analyses including those who do not report being in a current or recent partnership.

HRS

HRS is a population-based, biennial study of aging among older adults (aged 50+) in the United States that began in 1992 with follow-up interviews approximately every two years, and newly eligible cohorts entering every six years. In 2016, the Venous Blood Study (Eileen M. Crimmins et al. 2017) collected blood samples using home visits by a phlebotomist. This collection produced a representative dataset based on DNA methylation data from the Infinium Methylation EPIC BeadChip (Illumina). The Venous Blood Study (VBS) consists of 9,934 respondents. Epigenetic clocks were constructed for a subsample of 4,018 respondents. We limit the HRS estimation sample to 3,300 individuals for who we ever observe in a same-sex or a mixed-sex coresident partnership from 1992 to 2016.

Epigenetic Clocks

Add Health and HRS include thirteen DNA methylation clocks. Each clock was constructed independently by project staff. Descriptive data on each clock as estimated in Add Health and HRS are described elsewhere (Crimmins et al. (2021). Eight of the thirteen clocks are expressed in units of years: Horvath 1 (Horvath 2013), Hannum (Hannum et al. 2013), Levine (Levine et al. 2018), Horvath 2 (Horvath et al. 2018), Lin (Lin and Wagner 2015), Weidner (Weidner et al. 2014), Vidal-Bralo (Vidal-Bralo, Lopez-Golan, and Gonzalez 2016), and GrimAge (Lu et al. 2019). MPOA reflects the pace of aging in 1 year (e.g., in one year, an individual may age slightly slower or slightly faster, data range 0.74 – 1.46 years, Belsky et al. 2020). The four remaining clocks, Yang (Yang et al. 2016), Zhang (Zhang et al. 2017), Bocklandt (Bocklandt et al. 2011), and Garagnani (Garagnani et al. 2012), cannot be interpreted in years. To account for the difference in clock units and scales, we calculated "Accelerated Age" for each clock.

Accelerated Age

Age acceleration is calculated by taking the residual of the clock values regressed on age. For most clocks, the lowest values indicate decelerated aging, and the highest values indicate accelerated aging. An exception is the Bocklandt clock, which is negatively associated with age. Thus, sign on this clock is reversed in interpretation.

Same Sex or Mixed Sex Relationship

Add Health: Currently/Recently in Same Sex or Mixed Sex Relationship

We identified respondents who indicated a current marital or coresident partner in the Wave V survey of Add Health, as well as respondents who indicated they were not currently in a relationship but that their most recent relationship was a marriage or with a coresident partner. To generate currently/recently in a same sex relationship or mixed sex relationship, we compared selfreported sex at Wave V for respondents with the reported gender of the current/recent spouse/partner.

Add Health: Sexual Minority Identification

Add Health asks directly about sexual orientation, allowing us to identify single sexual minority adults. Respondents were asked to identify themselves on a spectrum from "100% heterosexual" to "100% homosexual", or asexual. We classify individuals who report anything other than 100% heterosexual or mostly heterosexual at Wave V as a sexual minority, including those who identify as asexual.

HRS: Ever in a Same Sex or Mixed Sex Relationship

We identified 2016 Venous Blood Study respondents with same sex and mixed sex coresident partners and spouses in each HRS wave from 1992 to 2016. To generate a measure of whether the respondent had ever been in a same sex relationship or mixed sex relationship, we compared selfreported sex for each HRS respondent (fixed) with the coresident spouse or partner's gender (timevarying). Two respondents report both a male and a female spouse/partner in their household at different waves; we include both respondents as "ever in a same sex relationship." Respondents who reported no coresident spouse/partner or whose spouse/partner was not living in the same household at the time of interview are not included in the analysis.

Covariates

In adjusted analyses, we control for respondent chronological age, sex (male/female), whether the respondent ever smoked, and cell composition estimates. Sex and smoking status are highly predictive of accelerated age (Crimmins et al. 2021). We control cell composition, including percentages of 6 cell subsets (total CD4 and CD8 cells, CD8 naïve, monocytes, B cells, and natural killer cells), because individual heterogeneity in cell composition may affect DNA methylation patterns (Houseman et al. 2015, 2016; Koestler et al. 2013).

Analytic Approach

We performed OLS regressions of each accelerated age measure on whether the respondent currently/recently reported being in a same sex marital/cohabiting relationship as of Wave V in Add Health or had ever reported being in a same sex marital/cohabiting relationship in any wave prior to 2016 in HRS. In Add Health, we repeated this analysis using direct self-identification of sexual minorities and examine differences in accelerated age measures across four categories: uncoupled heterosexual, uncoupled sexual minority, coupled heterosexual (reference), and coupled sexual minority. Appropriate sampling weights are applied to the data. Tables A1 and A2 present descriptive statistics for each measure of accelerated age by relationship status. For same sex versus mixed sex relationship analysis in both Add Health and HRS, we estimate: 1) an unadjusted model, 2) a model controlling for chronological age and respondent sex, 3) a model controlling for chronological age and whether the respondent ever smoked, and 4) a model controlling for chronological age and sample cell composition. We introduce controls in this manner because of the small sample size of respondents who were ever in a same sex relationship in HRS, and we do not apply additional controls. We address this further in the Limitations section below. For analysis of coupled/uncoupled heterosexual/sexual minority categories in Add Health, we estimate one model for each accelerated aging measure controlling for respondent chronological age, respondent sex, whether the respondent ever smoked, and sample cell composition.

Results

Table 1 presents results of regression analyses in Add Health predicting accelerated age in an unadjusted model (Model 1) and models controlling for chronological age and sex (Model 2), for chronological age and whether the respondent ever smoked (Model 3), and for chronological age and cell composition (Model 4). Results from Add Health show consistent effects within clocks and across models with and without controls. Apart from the Bocklandt clock and GrimAge, the effect of currently/recently being in a same sex relationship on accelerated aging is positive, but non-significant. The Bocklandt clock, which is negatively associated with age, consistently shows a significant negative effect across all models ($p < 0.01$). This is interpreted as evidence of greater acceleration of aging among respondents currently/recently in a same sex relationship compared with adults currently/recently in a mixed sex relationship. Estimates of the effect of currently or recently being in a same sex relationship on clocks measured in years range from 0 (no difference) to $+.875$ years on the Vidal-Bralo clock ($p < 0.1$).

Table 2 presents results of regression analyses in HRS predicting accelerated age in an unadjusted model (Model 1) and models controlling for chronological age and sex (Model 2), for chronological age and whether the respondent ever smoked (Model 3), and for chronological age and cell composition (Model 4). Estimates of the direction of the effect of ever being in a same sex relationship are consistent across models within 11 of the 13 clocks. Unadjusted estimates of the effect of ever being in a same sex relationship on clocks measured in years range from 0 (no significant difference) to $+3.4$ years on the Levine clock ($p<.05$). Six of the 13 clocks—Levine, Lin, Vidal-Bralo, Zhang, Bocklandt, and GrimAge—consistently indicate significantly faster aging for individuals ever in a same sex relationship compared to those in mixed sex relationships. Controlling for respondent age and sex (Model 2), smoking status (Model 3), and cell composition (Model 4) slightly attenuates observed differences for some clocks (see Figure 2). Of the remaining 7 clocks where no significant differences were detected, 5 have positive coefficients for ever in a same sex relationship. Two clocks, the Hannum and Weidner clocks, change sign after controlling for cell composition.

Next, we examined accelerated aging using direct self-identification of sexual minorities and heterosexuals who are coupled and uncoupled using Add Health (Table 3, Figure 3). In analyses adjusting for all covariates, we find that coupled heterosexual adults and coupled sexual minority adults are aging more similarly compared to either uncoupled group. However, the effects of being an uncoupled sexual minority compared to a coupled heterosexual range from 0 to $+3.566$ (p $<$ 0.05) years on the Levine clock. Here we find statistically significant accelerated age among uncoupled sexual minorities for the Hannum, Levine, Zhang, Bocklandt, GrimAge, and MPOA clocks. Additionally, we find statistically significant accelerated aging among uncoupled sexual minorities compared to uncoupled heterosexuals for the Hannum clock ($p < 0.05$).

Discussion

Using data from two representative surveys with linked measures of biological aging, this paper provides the first evidence suggestive of accelerated aging among sexual minority adults relative to heterosexual adults in the US. Overall, we find that most clocks show either no difference or evidence of faster aging among individuals ever or currently/recently in a same sex relationship compared to individuals ever or currently/recently in a mixed sex relationship. We also show general agreement across analyses in two sample populations with and without a limited set of relevant controls. Analyses using the self-identified sexual minority sample in Add Health suggest that uncoupled adults, especially uncoupled sexual minority adults, experience faster aging relative to coupled heterosexual adults.

Limitations

There are limitations to using the Add Health and HRS samples for these analyses. First, the sample size of respondents ever observed in a same-sex cohabiting partnership or marriage is very small in HRS. Because of this, we have limited the number of covariates in any one model.

Second, we rely on report of a same sex marital or coresidential partner to identify sexual minorities in HRS. Married individuals are selected in many ways, including being healthier than unmarried peers. Marriage may also promote changes in health and stress for sexual minority couples. Because HRS did not collect self-identified sexual orientation until after the 2016 Venous Blood Study, we are unable to identify sexual minorities who are single, never married, or who have nonresident partners in these data. Additionally, we are unable to identify individuals who identify as bisexual when they are in a mixed sex relationship. To address this, we replicate our analyses in Add Heath using both indirect and direct identification of sexual minorities. Findings from Add Health are generally consistent with findings from HRS and are suggestive of likely age acceleration among sexual minorities. Our results also suggest that in younger cohorts like Add Health, focusing on coupled individuals obscures the disparity in accelerated age between sexual minority and heterosexual adults. Although we largely understand the differences in magnitude of age acceleration effects across Add Health and HRS as due to differences in age across the two samples, there may also be period or cohort effects that have changed the trajectories of minority stress accumulation across these two cohorts, which we cannot address.

Third, our analysis is limited to sexual orientation and cannot address disparities by gender identity. In Add Health, respondent gender is collected as a binary measure and, therefore, transgender and gender diverse individuals cannot be identified. HRS also used a binary gender measure prior to 2016.

Conclusions

The minority stress framework suggests generalized biological consequences rather than a single mechanistic pathway (Doyle and Molix 2016; Everett et al. 2014; Hatzenbuehler, McLaughlin, and Slopen 2013), which researchers can explore using DNAm measures. The incorporation of DNA methylation measures of biological stress and aging into existing population surveys and surveys focusing on minority populations provides a path for the field to move beyond selfreported health status measures and test the minority stress framework at the molecular level among sexual minority and other minority populations. Costs of DNA methylation arrays and sample size limitations currently limit the collection and analysis of epigenetic measures of aging, but population-based surveys are increasingly incorporating these measures in subsample studies. The novel incorporation or linkage of DNAm measures to survey data focused on the minority stress experiences of sexual minority and other minority populations will fill key gaps in the literature on the aging experiences of minority populations across age, geography, and across other intersectional identities, thereby contributing to our understanding of the etiology and development of poor health and aging among minority populations and improving our collective ability to reduce health disparities.

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Figure 1. Effects of currently/recently in same sex relationship on accelerated age measures: Add Health (unweighted). Model 1 is unadjusted. Model 2 controls for chronological age and sex. Model 3 controls for chronological age and ever smoked. Model 4 controls for chronological age and sample cell composition.

Figure 2. Effects of Ever in Same Sex Relationship on Accelerated Age Measures: HRS (weighted). Model 1 is unadjusted. Model 2 controls for chronological age and sex. Model 3 controls for chronological age and ever smoked. Model 4 controls for chronological age and sample cell composition.

Table 1. Effects of currently/recently in same sex relationship versus in a mixed sex relationship on accelerated age measures: Add Health (weighted)

Table 1. (continued)

Table 2. Effects of Ever Being in a Same Sex Relationship vs Ever in a Mixed Sex Relationship on Accelerated Age Measures: HRS (weighted)

Table 2. (continued)

Table 3. Effects of being in a couple versus uncoupled for heterosexuals versus sexual minorities (reference level: coupled heterosexual, $N = 3,341$) on accelerated aging measures: Add Health (weighted). Models include controls for respondent age, respondent sex, and cell composition estimates.

	Hannum Horvath		Levine	Horvath $\overline{2}$	Lin	Weidner	Vidal-Bralo	
	AccelAge	AccelAge	AccelAge	AccelAge	AccelAge	AccelAge	AccelAge	
Coupled sexual minority	-0.033	0.262	0.750	-0.163	0.280	0.916	0.114	
$(N = 157)$	(0.450)	(0.396)	(0.559)	(0.267)	(0.623)	(2.870)	(0.343)	
Uncoupled heterosexual	0.096	-0.069	$0.690**$	-0.003	0.038	2.507	-0.145	
$(N = 903)$	(0.187)	(0.149)	(0.262)	(0.140)	(0.256)	(1.204)	(0.152)	
Uncoupled sexual minority	0.880	$1.623*$	$3.566*$	0.777	1.155	5.802	-0.464	
$(N = 68)$	(0.617)	(0.786)	(1.733)	(0.534)	(1.173)	(4.333)	(0.850)	
Wald X^2								
(Uncoupled: heterosexual v	1.530	$4.603*$	$2.731+$	2.070	0.887	0.556	0.137	
sexual minority)								

	Ever in a Same Sex Relationship		Ever in a Mixed Sex Relationship		Total ^a		
	$\mathbf N$	%	$\mathbf N$	$\%$	$\mathbf N$	$\%$	p-value
Total	89	1.00	3392	1.00	3481	1.00	ns
Age (mean/sd)	38.2	1.92	38.5	1.90	38.4	1.90	ns
Female	47	0.53	2045	0.60	2092	0.60	$\bf ns$
Ever Smoked	47	0.53	1422	0.42	1469	0.42	p < 0.1
Accelerated Age Measures	M	sd	M	sd	M	sd	
Horvath AccelAge	0.36	4.65	-0.01	3.67	0.00	3.70	
Hannum AccelAge	-0.06	4.21	0.00	3.64	0.00	3.65	
Levine AccelAge	0.47	5.72	-0.01	5.31	0.00	5.32	
Horvath 2 AccelAge	0.37	2.74	-0.01	2.75	0.00	2.75	
Lin AccelAge	0.26	5.00	-0.01	4.77	0.00	4.78	
Weidner AccelAge	0.24	23.92	-0.01	23.27	0.00	23.28	
Vidal-Bralo AccelAge	0.50	3.99	-0.01	3.37	0.00	3.39	
Yang AccelAge	0.00	0.01	0.00	0.01	0.00	0.01	
Zhang AccelAge	0.03	0.42	0.00	0.37	0.00	0.37	
Bocklandt AccelAge	-0.01	0.05	0.00	0.05	0.00	0.05	
Garagnani AccelAge	0.00	0.04	0.00	0.04	0.00	0.04	
Grimage AccelAge	0.47	4.39	-0.01	4.05	0.00	4.06	
MPOA AccelAge	$0.01\,$	$0.08\,$	0.00	0.09	0.00	0.09	

Table A1. Descriptive Statistics for Respondents Currently/Recently in a Same Sex Relationship, Currently/Recently in a Mixed Sex Relationship, and Total: Add Health (unweighted)

^a Total reflects only Add health Wave V respondents who indicated being in a same sex relationship or a mixed sex relationship with their current or most recent coresident partner/spouse. Analyses

Table A2. Descriptive Statistics for Respondents Ever in a Same Sex Relationship, Ever in a Mixed Sex Relationship, and Total: HRS (unweighted)

of interview for Wave V.

exclude respondents who did not indicate a current or former coresident partner/spouse at the time

^a Total reflects only HRS respondents who were ever observed in a same sex relationship or a mixed sex relationship with a coresident partner/spouse. Analyses exclude respondents who were never married or partnered or who had a nonresident spouse at time of interview.

^b Total N for this item is 3,278, with 24 respondents ever in a same sex relationship due to missingness on ever smoked.

	Heterosexual				Sexual Minority					
	Coupled		Uncoupled		Coupled		Uncoupled			Total ^a
	$\mathbf N$	$\%$	$\mathbf N$	$\%$	${\bf N}$	$\%$	${\bf N}$	$\%$	$\mathbf N$	$\%$
Total	3341	0.75	903	0.2	157	0.035	68	0.015	4469	$\mathbf{1}$
Age (mean/sd)	38.46	1.90	38.42	1.97	38.20	1.83	38.86	1.74	38.45	1.91
Female	2003	0.6	557	0.62	101	0.64	30	0.44	2691	0.6
Ever Smoked	1394	0.42	408	0.45	87	0.55	32	0.47	1921	0.43
Accelerated Age Measures	M	sd	M	sd	$\mathbf M$	sd	M	sd	M	sd
Horvath AccelAge	-0.02	3.67	0.01	3.88	-0.06	4.15	0.88	4.12	0.00	3.74
Hannum AccelAge	0.05	3.60	-0.22	3.71	-0.13	3.82	0.75	4.01	0.00	3.64
Levine AccelAge	-0.10	5.29	0.20	5.67	0.43	5.61	1.40	6.13	0.00	5.40
Horvath 2 AccelAge	0.01	2.76	-0.02	2.92	-0.14	2.74	0.30	3.44	0.00	2.80
Lin AccelAge	0.00	4.78	-0.04	5.06	0.00	4.87	0.32	5.45	0.00	4.85
Weidner AccelAge	-0.33	23.27	1.01	22.40	-0.18	23.39	3.35	22.35	0.00	23.09
Vidal-Bralo AccelAge	0.05	3.38	-0.23	3.38	0.07	3.66	0.21	3.59	0.00	3.39
Yang AccelAge	0.00	0.01	0.00	0.01	0.00	0.01	0.00	0.01	0.00	0.01
Zhang AccelAge	0.00	0.37	0.01	0.41	0.05	0.43	0.06	0.38	0.00	0.38
Bocklandt AccelAge	0.00	0.05	0.00	0.05	0.00	0.05	-0.01	0.04	0.00	0.05
Garagnani AccelAge	0.00	0.04	0.00	0.04	0.00	0.04	0.00	0.05	0.00	0.04
Grimage AccelAge	-0.27	4.04	0.89	4.48	0.44	4.62	0.23	3.92	0.00	4.18
MPOA AccelAge	-0.01	0.09	0.02	0.09	0.02	0.09	0.00	0.09	0.00	0.09

Table A3. Descriptive statistics for respondents in a couple versus uncoupled based on sexual self-identification at Wave V: Add Health (unweighted)

^a Total reflects only Add Health participants who gave sexual self-identification at Wave V exam.

Figure 3 Effects of being in a couple versus uncoupled for heterosexuals versus sexual minorities (reference level: coupled heterosexual) on accelerated aging measures: Add Health (weighted). Models include controls for respondent age, respondent sex, and cell composition estimates. Error bars show 95% confidence intervals.

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