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# Personality and epigenetic aging: A multi-cohort and multi-clock study

Yannick Stephan<sup>a,\*</sup>, Angelina R. Sutin<sup>b</sup>, Martina Luchetti<sup>b</sup>, Antonio Terracciano <sup>c</sup>

- a Euromov, University of Montpellier, France
- <sup>b</sup> Department of Behavioral Sciences and Social Medicine, College of Medicine, Florida State University, USA
- <sup>c</sup> Department of Geriatrics, College of Medicine, Florida State University, USA

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#### ABSTRACT

Epigenetic clocks are measures of biological aging related to critical health outcomes, including mortality. The present study examined whether personality traits are related to epigenetic aging. Participants (Age range: 17-98 years, N>6000) were from the Health and Retirement Study, the Midlife in the United States study, and the UK Household Longitudinal Study. Measures of personality traits, demographic factors, first-generation (Hannum, Horvath), second-generation (PhenoAge, GrimAge), and third-generation (DunedinPoAM38/DunedinPace) epigenetic clocks were obtained in each sample. The strongest evidence emerged for conscientiousness: The meta-analysis indicated that higher conscientiousness was associated with a slower epigenetic aging as indexed by second- and third-generation clocks. The other traits were not consistently associated with the five clocks. Surprisingly, moderation by age indicated agreeableness was associated with slower epigenetic aging among relatively older but not younger adults. The present study suggests that conscientiousness is associated with slower epigenetic aging, particularly second and third-generation clocks trained on health-related outcomes.

# 1. Introduction

Epigenetic clocks are DNA methylation (DNAm)-based estimates of biological age. Attention has been directed toward epigenetic clocks because of their association with critical age-related outcomes (see Chervova et al., 2024; Oblak et al., 2021 for reviews). For example, accelerated epigenetic aging, which reflects an older biological age (as measured by epigenetic clocks) relative to one's chronological age is related to the incidence of chronic health conditions (Belsky et al., 2022; Chervova et al., 2024; Mutambudzi et al., 2024), faster cognitive and functional decline (Belsky et al., 2022; Chervova et al., 2024; Savin et al., 2024) and mortality (Belsky et al., 2022; Chervova et al., 2024). Given these implications, a fairly extensive literature has focused on the factors associated with individual differences in epigenetic aging, and a range of factors, from biological to environmental, have been found to explain in part why some individuals are biologically older compared to other people of the same chronological age (see Chervova et al., 2024; Oblak et al., 2021 for reviews). Among this set of factors, psychological factors, such as subjective age, depression and loneliness have been related to patterns of accelerated epigenetic aging (Stephan et al., 2021; Freilich et al., 2024; Wang et al., 2024). The present study adds to existing knowledge by examining the association between stable psychological dispositions (personality traits) and epigenetic aging.

Personality traits are defined as characteristic patterns of feelings, thoughts, and behaviors (Roberts and Yoon, 2022). There is abundant evidence that Five Factor Model personality traits (FFM, McCrae and John, 1992) are linked to health outcomes across adulthood (Grogan et al., 2024; Luo et al., 2023; Strickhouser et al., 2017; Willroth et al., 2023; Wright and Jackson, 2023). In particular, higher neuroticism (the propensity to be vulnerable to stress and to experience negative emotions) and lower conscientiousness (the propensity to be responsible and self-disciplined) have been consistently related to worse health across a range of indicators, including higher risk of chronic conditions (Leger et al., 2021; Stephan et al., 2023a), worse functional and cognitive functions (Stephan et al., 2022; Sutin et al., 2023), and higher risk of geriatric syndromes such as frailty (Hajek, König, 2021) and urinary incontinence (Stephan et al., 2024b). These traits have also been associated with a higher risk of dementia (Aschwanden et al., 2021) and mortality (Graham et al., 2017). To a lesser extent, higher extraversion (the propensity to experience positive emotions and to be energetic) has been related to better functional and cognitive functioning (Stephan et al., 2022; Sutin et al., 2023) and lower risk of geriatric syndromes (Hajek, König, 2021; Stephan et al., 2024a, 2024b). There is inconsistent evidence that openness (the propensity to be curious and imaginative)

<sup>\*</sup> Correspondence to: Euromov, University of Montpellier, UFRSTAPS, 700, Avenue du Pic St Loup, Montpellier 34090, France. E-mail address: yannick.stephan@umontpellier.fr (Y. Stephan).

and agreeableness (the propensity to be altruistic and trusting) are connected to health in adulthood (Leger et al., 2021; Stephan et al., 2023a; Graham et al., 2017).

Some evidence links personality traits to biological hallmarks of aging. For example, higher neuroticism has been associated with lower mitochondrial DNA copy number (mtDNAcn) (Oppong et al., 2022), and higher immunosenescence, indexed by the ratio between naïve and memory T cells (Stephan et al., 2023b). In contrast, higher conscientiousness and to a lesser extent higher extraversion have been related to higher mtDNAcn (Oppong et al., 2022), and lower immunosenescence (Stephan et al., 2023b). In addition, lower neuroticism, higher extraversion and higher conscientiousness have been associated with lower inflammation, measured by c-reactive protein and pro-and anti-inflammatory cytokines (Luchetti et al., 2014; Wright et al., 2022). Such associations may also extend to biological aging indexed by epigenetic clocks.

The extensive literature linking personality to age-related diseases and overall health, including mortality, provides support for a potential association with epigenetic aging markers. Indeed, it is likely that the higher vulnerability to age-related diseases and poor health outcomes associated with higher neuroticism and lower conscientiousness may result from accelerated epigenetic aging. However, there is limited evidence for an association between personality and epigenetic aging. To the best of our knowledge, only two studies examined this association and reported inconsistent results. One study conducted among older adults suffering from chronic pain (N = 26) found that lower neuroticism and extraversion and higher conscientiousness were related to a younger epigenetic age measured by the Horvath clock (Cruz-Almeida et al., 2019). No associations were found for openness and agreeableness. Another study based on the Lothian Birth Cohort 1936 (N  $\simeq 800$ individuals) found no relationship between personality and the DNA-PhenoAge clock (Stevenson et al., 2019). These mixed findings could be due in part to the relatively small sample size of these studies, their selective nature, and the use of different epigenetic clocks between studies. Therefore, the extent to which personality may be related to epigenetic aging remains unclear.

Using a multi-cohort and multi-clock approach, the present study examined the association between personality and epigenetic aging. This association was examined in three large samples of middle-aged and older adults to test of the replicability of the association. In addition, the association was examined across several epigenetic clocks, namely first-generation clocks such as Horvath clock (Horvath, 2013) and Hannum clocks (Hannum et al., 2013), second-generation clocks such as the PhenoAge (Levine et al., 2018) and the GrimAge clocks (Lu et al., 2019), and third-generation clocks such as the DunedinPoAm38 (Belsky et al., 2020) and DunedinPace (Belsky et al., 2022). Based on the literature linking personality to age-related outcomes (Aschwanden et al., 2021; Luo et al., 2023; Stephan et al., 2023b), it was predicted that higher neuroticism would be related to accelerated epigenetic aging, whereas higher conscientiousness and higher extraversion would be associated with slower epigenetic aging. Building upon recent research (Freilich et al., 2024; Oblak et al., 2021), these associations were expected to be stronger for second and third-generation clocks because these clocks have been trained on health indicators (Belsky et al., 2020, 2022; Levine et al., 2018; Lu et al., 2019), compared to first-generation clocks which were trained on chronological age (Hannum et al., 2013; Horvath et al., 2013). Finally, exploratory analyses tested whether age or sex moderated the association between personality and epigenetic aging.

# 2. Method

## 2.1. Participants

Participants were from the Health and Retirement Study (HRS), the Midlife in the United States study (MIDUS), and the UK Household

Longitudinal Study (UKHLS). The Institutional Review Board (IRB) at the University of Michigan approved the HRS, the Education and Social/Behavioral Sciences and the Health Sciences IRB at the University of Wisconsin-Madison approved the MIDUS, and the University of Essex Ethics Committee and the National Research Ethics Service approved the UKHLS. Written informed consent was obtained from all participants in the three samples. The present analyses did not require IRB approval because the study examined publicly available de-identified data. Table 1 reports descriptive statistics for the three samples. Only individuals with complete data on personality, demographic factors, and epigenetic clocks in each sample were included in the analyses.

The HRS is a nationally representative longitudinal study of Americans older than 50 years and their spouses. A non-random subsample of participants provided data on DNA methylation (N=4018) as part of the 2016 Venous Blood Study. The sample included all participants from the 2016 Healthy Cognitive Aging Project (HCAP) who provided blood samples, plus younger participants designated for future HCAP assessments, and a subsample of non-HCAP participants. Personality traits and demographic factors were obtained in 2014/2016. The final analyzed sample included 2926 participants aged from 50 to 98 years (58 % female, Mean age =68.72, SD =9.57) who had complete data on personality traits, demographic factors and epigenetic clocks.

The MIDUS is an ongoing national longitudinal study of adults in the United States. DNAm analysis was conducted on 1310 whole blood DNA samples from participants in the MIDUS 2 (M2, 2004–2006, N = 511) and MIDUS Refresher 1 sample (MR1, 2011–2014, N = 799). Data on personality traits and demographic factors were obtained from the respective samples and waves (either M2 or MR1). The final analyzed sample included 1276 participants aged from 25 to 81 years (55 % female, Mean age = 51.22, SD = 12.46) who had complete information on epigenetic clocks, personality traits and demographic factors.

The UKHLS is a nationally representative panel survey of UK households. Whole blood was obtained from 3654 eligible individuals who consented to both blood sampling and genetic analysis during 2010–2012. Eligibility requirements for genetic analyses meant that the epigenetic samples were restricted to participants of white ethnicity. Personality traits and demographic factors were obtained from the third wave (2011–2013). The analyzed sample included 2211 individuals aged from 17 to 83 years (55 % women, Mean age: 50.46, SD: 15.08) who had complete data on epigenetic clocks, personality and demographic factors.

**Table 1**Descriptive statistics.

	HRS		MIDUS		UKHLS	
Variables	M/%	SD	M/%	SD	M/%	SD
Age (Years)	68.72	9.57	51.22	12.46	50.46	15.08
Sex (% women)	58 %	-	55 %	-	55 %	-
Race (% African	14 %	-	22 %	-	0 %	-
American)						
Ethnicity (% Hispanic)	10 %	-	-	-	-	-
Education	13.26	2.85	7.82	2.52	7.00	6.20
Neuroticism	1.95	0.60	2.09	0.65	3.49	1.41
Extraversion	3.18	0.58	3.12	0.60	4.69	1.30
Openness	2.92	0.56	2.99	0.53	4.61	1.26
Agreeableness	3.51	0.50	3.39	0.52	5.76	0.97
Conscientiousness	3.37	0.48	3.35	0.48	5.60	1.04
Hannum clock	54.97	9.18	42.36	11.44	49.03	11.11
Horvath clock	66.14	9.53	55.37	11.12	56.54	10.87
PhenoAge clock	57.77	10.04	43.54	12.98	43.12	12.38
GrimAge clock	68.21	8.58	56.99	10.92	-	-
Dunedin clock	1.07 <sup>a</sup>	0.09	0.99 <sup>b</sup>	0.14	1.01 <sup>a</sup>	0.07

Note. HRS: N = 2926; MIDUS: N = 1276; UKHLS: N = 2211

<sup>&</sup>lt;sup>a</sup> DunedinPoAM38clock;

<sup>&</sup>lt;sup>b</sup> DunedinPace clock. See Method section for differences in measures.

#### 2.2. Measures

## 2.2.1. Epigenetic clocks

DNA methylation measures were derived from the blood samples. More information on data collection and the derivation of epigenetic variables in the HRS is available in Crimmins et al. (2020), on the MIDUS Colectica Portal (https://midus.colectica.org/), and in Institute for Social and Economic Research (2021) for the UKHLS. Data on DNA methylation profiles were scored using previously published algorithms for two first-generation clocks, the Hannum clock (Hannum et al., 2013) and Horvath clock (Horvath et al., 2013), two second-generation clocks, PhenoAge (Levine et al., 2018) and GrimAge (Lu et al., 2019), and third generation clocks, DunedinPoAm38 (Belsky et al., 2020) and the DunedinPace (Belsky et al., 2022). The UKHLS includes only Hannum, Horvath, Levine, and DunedinPoAM38 clocks.

The Hannum clock was developed to predict chronological age in whole blood samples (Hannum et al., 2013), and the Horvath clock was developed as a predictor of chronological age across multiple tissues and cell types (Horvath et al., 2013). The PhenoAge clock was developed using nine markers of tissue and immune function (albumin, creatinine, serum glucose, C-reactive protein, lymphocyte percent, mean (red) cell volume, red cell distribution width, alkaline phosphatase, and white blood cell count) and age (Levine et al., 2018). GrimAge was developed using seven DNA methylation surrogates of plasma proteins associated with physiological risk and stress factors (adrenomedullin, beta-2 microglobulin, cystatin C, growth differentiation factor 15, leptin, plasminogen activation inhibitor 1, tissue inhibitor metalloproteinase 1) and a DNA methylation-based estimator of smoking pack years (Lu et al., 2019). These four algorithms produce estimates of epigenetic age in years. The DunedinPoAm38 (Belsky et al., 2020) was computed in the HRS and the UKHLS. The DunedinPoAM38 is based on a composite measure of 18 biomarkers that measure the rate of aging in the cardiovascular, metabolic, renal, hepatic, pulmonary, periodontal, and immune systems. The MIDUS used the DunedinPACE (Belsky et al., 2022) which is an updated version of the DunedinPoAM38. The DunedinPACE includes an additional measurement occasion (collected 20 years after inclusion) and only includes the most reliable DNA methylation probes (Belsky et al., 2022). Both DunedinPoAM38 and the DunedinPACE represent individual rate of biological aging (pace of aging) and are expressed in years of epigenetic aging per chronological year. Consistent with existing research (Belsky et al., 2022; Freilich et al., 2024), the Hannum, Horvath, PhenoAge and GrimAge clocks were regressed on chronological age, and residual values indicated accelerated epigenetic aging (positive residuals) or age deceleration (negative residuals). The correlation matrix of the epigenetic markers is in supplementary material (Supplementary Table S1).

# 2.2.2. Personality

In the HRS and the MIDUS, the Midlife Development Inventory (MIDI) (Zimprich et al., 2012) was used to assess the five personality traits. Participants were asked to indicate the degree to which 26 adjectives described them on a four-point scale, from 1 (not at all) to 4 (a lot). Example adjectives are nervous (neuroticism), active (extraversion), curious (openness), softhearted (agreeableness), and responsible (conscientiousness). A 15-item version of the Big Five Inventory (BFI, Soto and John, 2017) was used in the UKHLS. Participants rated items that assessed neuroticism (I see myself as someone who gets nervous easily), extraversion (I see myself as someone who is outgoing, sociable), openness (I see myself as someone who values artistic, aesthetic experiences), agreeableness (I see myself as someone who is considerate to almost everyone), and conscientiousness (I see myself as someone who does things efficiently) on a 7-point scale from 1 (does not apply to me at all) to 7 (applies to me perfectly). The mean scores for each trait were taken in the three samples, with higher scores indicative of higher neuroticism, extraversion, openness, agreeableness, and conscientiousness. Cronbach alphas were.71,.73, and.72 for neuroticism,.76,.78 and.66 for extraversion,.79,.75 and.65 for openness,.79,.78 and.53 for agreeableness, and.66,.69 and.56 for conscientiousness respectively in the HRS, the MIDUS, and the UKHLS.

#### 2.2.3. Covariates

Analyses were adjusted for demographic covariates such as age (in years), sex (1 =female, 0 =male), and education in the three samples. Education was reported in years in HRS, and on a scale from 1 (no grade school) to 12 (doctoral level degree) in the MIDUS, and from 0 (none) to 16 (higher degree) in the UKHLS. Race (1 =African/American, 0 =other) was included as a covariate in the HRS and the MIDUS samples and ethnicity (1 =Hispanic, 0 =not Hispanic) and wave of personality assessment (1 =2014, 0 =2016) were also included as covariates in the HRS.

## 2.3. Data analyses

Linear regression was used to test the association between personality and epigenetic aging in the three samples. In each sample, epigenetic aging was regressed on personality traits, controlling for demographic covariates. Separate analyses were conducted for each clock and each trait. Each trait was standardized as z-scores. A random effects meta-analysis was conducted to combine the results from each sample using the JAMOVI 2.6.13 software. The  $\rm I^2$  statistic was used as an indicator of heterogeneity.

Exploratory analyses tested whether age and sex moderated the association between personality and epigenetic aging with an interaction between each trait and either age or sex in each sample. Estimates from these analyses were combined in a random effects meta-analysis conducted with the JAMOVI software. The robustness of the findings was tested with two sensitivity analyses: (1) Analyses were repeated including all five traits simultaneously and (2) Analyses were repeated excluding participants younger than 50 in the MIDUS and the UKHLS. The significance was set at p less than 01 across the analyses and samples.

#### 3. Results

The results of the meta-analysis for the five clocks are in Table 2 and results from the individual studies are in Table 3. The only trait with consistent support across clocks was conscientiousness: Conscientiousness was associated with slower epigenetic aging as indexed by the second- (GrimAge, PhenoAge) and third- (Dunedin) generation clocks (Table 2). There was little heterogeneity in these associations between conscientiousness and clocks as indicated by the I<sup>2</sup> indicator. The difference in DunedinPoAm38 (HRS) between individuals in the top and bottom quartile of the distribution of conscientiousness was d= .11. Effect size for the difference between the top and bottom quartiles of conscientiousness was d= .21 for the GrimAge clock in the HRS. Conscientiousness was unrelated to either of the first-generation clocks (Table 2). In contrast to the hypotheses, across the meta-analyses, there was little evidence of an association between neuroticism and extraversion and the five clocks (Table 2). Agreeableness and openness were unrelated to the five clocks (Table 2).

The meta-analysis indicated a significant interaction between age and agreeableness for the PhenoAge and the Dunedin clocks (Table 4). For each clock, higher agreeableness was related to slower epigenetic aging among older individuals. Results for each sample are in supplementary tables. The meta-analysis also indicated a significant interaction between neuroticism and sex for the PhenoAge clock (Table 5). Higher neuroticism was more strongly related to accelerated epigenetic aging among women compared to men. Results in each sample are in supplementary material (Table S2 and Table S3).

The sensitivity analysis indicated that the overall pattern of association was similar when the five traits were included simultaneously in the three samples (supplementary Table S4). In addition, the overall

**Table 2**Meta-analytic findings of the association between personality and epigenetic aging.

	Neuroticism	Extraversion	Openness	Agreeableness	Conscientiousness	
	Random Effect (95 %CI)					
Hannum	0.01	-0.02	-0.04	-0.02	-0.01	
	(-0.012; 0.037)	(-0.068; 0.019)	(-0.070; -0.005)	(-0.043; 0.006)	(-0.036; 0.013)	
p-value	0.299	0.263	0.022	0.138	0.337	
$I^2$	0	65.93	39.46	0	0	
Horvath	0.009	-0.002	-0.02	0.004	-0.01	
	(-0.015; 0.034)	(-0.026; 0.023)	(-0.062; 0.015)	(-0.025; 0.024)	(-0.046; 0.025)	
p-value	0.460	0.895	0.231	0.944	0.571	
$I^2$	0	0	56.48	0	49.9	
PhenoAge	0.02	-0.01	-0.02	-0.02	-0.03	
	(-0.004; 0.045)	(-0.054; 0.029)	(-0.048; 0.001)	(-0.041; 0.008)	(-0.059; -0.010)	
p-value	0.094	0.551	0.064	0.176	0.006	
$I^2$	0.04	63.54	0	0	0	
GrimAge	0.04	-0.02	0.01	-0.01	-0.06	
	(-0.028; 0.110)	(-0.05; 0.015)	(-0.019; 0.041)	(-0.043; 0.017)	(-0.093; -0.018)	
p-value	0.242	0.284	0.477	0.398	0.004	
$I^2$	77.78	13.22	0	0	30.04	
Dunedin	0.04	-0.03	-0.01	-0.006	-0.05	
	(-0.004; 0.085)	(-0.052; -0.003)	(-0.042; 0.020)	(-0.031; 0.018)	(-0.074; -0.018)	
p-value	0.074	0.030	0.474	0.624	0.001	
Î <sup>2</sup>	67.94	0	33.96	0	19.6	

Note. Bold p < .01

 Table 3

 Summary of linear regression analysis predicting epigenetic aging from personality traits in the three samples.

	Hannum		Horvath Pheno.		PhenoAge	ıenoAge		GrimAge		Dunedin	
	β	p	β	p	β	p	β	p	β	p	
HRS											
Neuroticism	0.03	0.132	0.01	0.428	0.02	0.301	0.009	0.590	0.002	0.898	
	(-0.008; 0.06)		(-0.022; 0.052)		(-0.017; 0.056)		(-0.024; 0.043)		(-0.034; 0.039)		
Extraversion	-0.06	< 0.001	-0.01	0.565	-0.05	0.015	-0.03	0.087	-0.04	0.038	
	(-0.096; -0.025)		(-0.047; 0.025)		(-0.081; -0.009)		(-0.063; 0.004)		(-0.073; -0.002)		
Openness	-0.06	< 0.001	0.01	0.438	-0.02	0.248	0.007	0.713	0.006	0.741	
	(-0.10; -0.027)		(-0.022; 0.052)		(-0.060; 0.015)		(-0.028; 0.041)		(-0.030; 0.043)		
Agreeableness	-0.02	0.254	0.02	0.211	-0.01	0.736	-0.01	0.405	-0.01	0.576	
	(-0.058; 0.015)		(-0.013; 0.061)		(-0.043; 0.030)		(-0.049; 0.020)		(-0.047; 0.026)		
Conscientiousness	-0.01	0.570	0.02	0.215	-0.04	0.035	-0.07	< 0.001	-0.06	0.003	
	(-0.047; 0.026)		(-0.013; 0.060)		(-0.076; -0.003)		(-0.10; -0.032)		(-0.092; -0.019)		
MIDUS											
Neuroticism	-0.00	0.993	0.02	0.596	-0.01	0.642	0.08	0.004	0.08	0.002	
	(-0.055; 0.055)		(-0.040; 0.070)		(-0.069; 0.042)		(0.025; 0.127)		(0.028; 0.127)		
Extraversion	-0.02	0.492	-0.02	0.573	0.01	0.616	0.006	0.823	-0.01	0.719	
	(-0.073; 0.035)		(-0.070; 0.039)		(-0.041; 0.069)		(-0.044; 0.056)		(-0.058; 0.040)		
Openness	-0.04	0.174	-0.05	0.060	-0.001	0.964	0.02	0.406	0.001	0.973	
•	(-0.093; 0.017)		(-0.109; 0.002)		(-0.057; 0.054)		(-0.029; 0.072)		(-0.049; 0.050)		
Agreeableness	-0.03	0.289	-0.01	0.603	-0.01	0.676	-0.02	0.355	-0.02	0.439	
o .	(-0.085; 0.025)		(-0.071; 0.041)		(-0.068; 0.044)		(-0.076; 0.027)		(-0.070; 0.030)		
Conscientiousness	-0.02	0.423	-0.03	0.362	-0.01	0.737	-0.03	0.326	-0.06	0.015	
	(-0.077; 0.032)		(-0.081;0.03)		(-0.065; 0.046)		(-0.076; 0.025)		(-0.111; -0.011)		
UKHLS	, , ,		, , ,								
Neuroticism	-0.002	0.933	0.002	0.922	0.04	0.059	-		0.05	0.019	
	(-0.042; 0.039)		(-0.040; 0.045)		(-0.001; 0.084)				(0.008; 0.092)		
Extraversion	0.01(	0.568	0.02	0.456	0.01	0.634	-		-0.02	0.354	
	-0.028;0.051)		(-0.025; 0.057)		(-0.031; 0.052)				(-0.060; 0.021)		
Openness	-0.01	0.636	-0.04	0.069	-0.04	0.082	-		-0.04	0.093	
•	(-0.050;0.030)		(-0.081; 0.003)		(-0.080; 0.004)				(-0.077; 0.006)		
Agreeableness	-0.01	0.589	-0.01	0.658	-0.03	0.227	-		0.007	0.728	
J	(-0.051;0.029)		(-0.051; 0.032)		(-0.068; 0.016)				(-0.034; 0.048)		
Conscientiousness	-0.01	0.632	-0.03	0.150	-0.04	0.047	-		-0.02	0.328	
	(-0.049;0.030)		(-0.072;0.011)		(-0.084;-0.005)	,			(-0.061; 0.020)		

Note. Bold p < .01

pattern of association between personality and epigenetic aging was similar in the MIDUS and the UKHLS when participants younger than 50 years were excluded in both samples. There was one exception, with the link between neuroticism and GrimAge in the MIDUS was reduced to non significance (supplementary Table S5).

# 4. Discussion

Based on three samples of adults, the present study examined the association between personality traits and epigenetic aging. The meta-analysis indicated that higher conscientiousness had the most consistent association with slower epigenetic aging. In line with expectations,

Table 4

Meta-analytic findings of the association between the interaction between age and personality and epigenetic aging.

	Neuroticism	Extraversion	Openness	Agreeableness	Conscientiousness	
	Random Effect (95 %CI)					
Hannum	-0.01	-0.02	0.009	-0.03	0.01	
	(-0.061; 0.037)	(-0.045; 0.004)	(-0.016; 0.033)	(-0.062; -0.001)	(-0.013; 0.036)	
p-value	0.630	0.100	0.492	0.041	0.354	
$I^2$	73.36	0	0	32.74	0	
Horvath	0.02	0.001	0.02	-0.03	-0.004	
	(0.001;0.050)	(-0.023; 0.026)	(-0.006; 0.043)	(-0.070; 0.015)	(-0.052; 0.044)	
p-value	0.042	0.908	0.149	0.208	0.861	
$\overline{I}^2$	0	0	0	64.52	72.38	
PhenoAge	0.03	-0.005	0.02	-0.05	-0.005	
	(0.003; 0.052)	(-0.029; 0.020)	(-0.006; 0.043)	(-0.070; -0.022)	(-0.029; 0.020)	
p-value	0.025	0.703	0.129	< 0.001	0.717	
$\overline{I}^2$	0	0	0	0	0	
GrimAge	-0.007	-0.02	-0.01	-0.04	-0.004	
	(-0.038; 0.022)	(-0.054; 0.006)	(-0.043; 0.017)	(-0.069; -0.009)	(-0.034; 0.025)	
p-value	0.628	0.121	0.388	0.011	0.774	
$I^2$	0	0	0	0	0	
Dunedin	-0.002	-0.02	-0.002	-0.05	-0.03	
	(-0.027; 0.022)	(-0.041; 0.008)	(-0.029; 0.025)	(-0.094; -0.015)	(-0.058; 0.006)	
p-value	0.850	0.183	0.883	0.007	0.112	
$\tilde{I}^2$	0	0	14.9	59.78	38.73	

Note. Bold p < .01

**Table 5**Meta-analytic findings of the association between the interaction between sex and personality and epigenetic aging.

Neuroticism		Extraversion	Openness	Agreeableness	Conscientiousness	
	Random Effect (95 %CI)					
Hannum	0.02	-0.04	-0.05	-0.01	-0.02	
	(-0.000; 0.049)	(-0.094; 0.018)	(-0.091; -0.008)	(-0.059; 0.037)	(-0.052; 0.020)	
p-value	0.052	0.184	0.020	0.663	0.380	
$I^2$	0	79.69	63.01	72.48	50.01	
Horvath	0.03	-0.03	-0.03	-0.007	0.002	
	(0.008; 0.057)	(-0.052; -0.003)	(-0.051; -0.002)	(-0.032; 0.017)	(-0.048; 0.011)	
p-value	0.010	0.028	0.031	0.571	0.229	
$I^2$	0	0	0	0	0	
PhenoAge	0.06	-0.02	-0.03	-0.02	-0.04	
	(0.038; 0.087)	(-0.044; 0.008)	(-0.068; 0.001)	(-0.048; 0.001)	(-0.068; -0.009)	
p-value	< 0.001	0.165	0.059	0.064	0.011	
$\overline{I}^2$	0	8.84	47.22	0	28.6	
GrimAge	0.02	-0.01	-0.01	-0.004	-0.007	
	(-0.011; 0.049)	(-0.052; 0.033)	(-0.043; 0.017)	(-0.034; 0.026)	(-0.037; 0.023)	
p-value	0.215	0.657	0.398	0.796	0.664	
$I^2$	0	0	0	0	0	
Dunedin	0.01	-0.009	-0.009	0.002	-0.02	
	(-0.012;0.037)	(-0.033; 0.016)	(-0.034; 0.015)	(-0.038; 0.042)	(-0.065; 0.024)	
p-value	0.316	0.493	0.457	0.924	0.368	
$\tilde{I}^2$	0	0	0	59.57	67.97	

Note.Bold p<.01

these associations were more apparent for second and third-generation clocks than first-generation clocks. In contrast, there was little evidence for an association with neuroticism, extraversion, openness, or agreeableness in main analysis. Unexpectedly, the association between agreeableness and epigenetic aging was moderated by age, such that higher agreeableness was related to slower epigenetic aging among older individuals, and mostly in second and third generation clocks. Taken as whole, the present multi-cohort, multi-trait, and multi-clock study expands past research on the association between personality and epigenetic aging (Cruz-Almeida et al., 2019; Stevenson et al., 2019).

Conscientiousness was the most consistent personality correlate of epigenetic aging: Conscientiousness was related to slower epigenetic aging across different clocks, including clocks recording the amount of aging experienced across the lifespan and clocks tracking how fast individuals are aging. The link between conscientiousness and epigenetic aging is broadly in line with substantial evidence linking higher

conscientiousness to better age-related health outcomes, including better functional health (Stephan et al., 2022), slower cognitive decline (Sutin et al., 2023), and lower risk of geriatric syndromes (Canada et al., 2020; Gale et al., 2017; Stephan et al., 2024b), musculoskeletal (Stephan et al., 2024a), and neurodegenerative (Aschwanden et al., 2021) diseases. This association extends evidence for conscientiousness and better biological aging as indexed by higher mtDNAcn (Oppong et al., 2022), lower immunosenescence (Stephan et al., 2023b), and lower inflammation (Luchetti et al., 2014; Wright et al., 2022).

Several potential pathways may connect conscientiousness to slower epigenetic aging. A direct pathway suggests that the core characteristics of conscientiousness such as being cautious, dutiful, considerate, organized, and deliberate may manifest into a slower pace of biological aging. Indirect pathways may also operate. Indeed, higher conscientiousness is associated with better overall health (Luo et al., 2023), lower BMI (Sutin and Terracciano, 2016), fewer depressive symptoms

(Hakulinen et al., 2015) and higher involvement in physical activity (Sutin et al., 2016) that have been related to slower epigenetic aging (Chervova et al., 2024; Oblak et al., 2021).

The hypothesis that neuroticism would be associated with faster epigenetic aging was not supported. That is, neuroticism was unrelated to epigenetic aging in the meta-analysis of the five clocks. There was a modest pattern of association between higher neuroticism and a faster pace of biological aging measured by the Dunedin clocks in the MIDUS and the UKHLS. This overall pattern is surprising because neuroticism is associated consistently with worse aging-related outcomes (e.g., risk of frailty; Gale et al., 2017) and other markers of biological aging (e.g., lower DNAm copy number; Oppong et al., 2022), that would suggest faster epigenetic aging. In addition, there was little evidence for an association between extraversion and epigenetic aging. This result contrasts with past research linking extraversion to higher mtDNAcn (Oppong et al., 2022), lower immunosenescence (Stephan et al., 2023b), and better overall health outcomes in old age (Luo et al., 2023; Stephan et al., 2024a, 2024b). More research is needed to determine the reason for these inconsistencies.

The association between agreeableness and epigenetic aging was moderated by age in the meta-analysis and across several clocks. These findings indicate that higher agreeableness was related to a slower epigenetic aging among older adults. Interestingly, these interactions were found mostly for the second and third-generation clocks. This finding contrasts with existing research that found no link between agreeableness and biological markers of aging (Luchetti et al., 2014; Oppong et al., 2022; Stephan et al., 2023b; Wright et al., 2022) or weak associations with overall health across adulthood (Luo et al., 2023). The prosocial orientations associated with higher agreeableness may lead to positive interpersonal relationships and higher social support that may have be associated with positive effects over time, which may explain the associations with slower epigenetic aging. Furthermore, higher agreeableness has been associated with health behaviors such as physical activity (Sutin et al., 2016), treatment adherence (Bucher et al., 2019), and more healthcare use (Atherton et al., 2024), which may be related to slower epigenetic aging over time.

The present study adds to existing knowledge on the factors associated with epigenetic aging (Chervova et al., 2024; Oblak et al., 2021). Indeed, existing reviews have identified a range of biological, social, or environmental correlates of epigenetic aging (see Chervova et al., 2024; Oblak et al., 2021). Chervova et al. (2024) also indicated that psychosocial factors were related to epigenetic clocks. However, this category did not include personality traits. Therefore, the present study expands existing literature and reviews by adding psychological factors such as personality traits to the list of factors associated with epigenetic aging.

Of note, conscientiousness was almost exclusively related to second (GrimAge, PhenoAge) and/or third (DunedinPace and edinPoAm38) clocks, which were developed based on multiple physiological systems that are predictive of morbidity and mortality (see Belsky et al., 2022; Oblak et al., 2021). This pattern supports evidence that a range of variables have stronger associations with more recent clocks trained on health than with the first-generation clocks trained only on chronological age (Freilich et al., 2024; Oblak et al., 2021). Furthermore, this study contributes to existing models and research on personality and health across adulthood (Chapman et al., 2014; Friedman and Kern, 2014; Grogan et al., 2024). Indeed, it could inform about potential mechanisms explaining the association between personality and crucial age-related outcomes. For example, lower conscientiousness has been related to an increased risk of dementia (Aschwanden et al., 2021) and mortality (Graham et al., 2017). A faster pace of biological aging, as indicated by higher Dunedin clocks, has been found to predict a higher risk of dementia (Sugden et al., 2022) and mortality (Belsky et al., 2022). A faster pace of biological aging may be one pathway between lower conscientiousness and risk of dementia and mortality.

The present study was based upon existing models which postulate a predictive role of personality on age-related outcomes (Chapman et al.,

2014). An alternative model suggests that epigenetic aging may contribute to personality traits. For example, a faster biological aging may be accompanied by an overall biological dysfunctioning, worsening physical and mental health and a decline in energy, which may manifest into a lower propensity to be self-disciplined, deliberate and organized (lower conscientiousness). In addition, third variables such as genetic factors or childhood trauma and poverty may also explain the association between personality and epigenetic aging.

The present study has several strengths including the examination of the use of three large samples of middle-aged and older adults, using first-, second-, and third-generation clocks, a meta-analysis, and a test of moderators of this association. There are also several limitations to consider. The cross-sectional design limits causal interpretations. Reciprocal relationships are likely to exist between personality and epigenetic aging. In addition to testing reciprocal relations, longitudinal research is needed to test a mediational model in which clinical (e.g., disease burden, obesity) and behavioral (e.g., physical activity, smoking) factors are tested as mechanisms of the association between personality and the epigenetic clocks. Furthermore, the size of the association between personality and epigenetic aging was relatively small. However, epigenetic aging is a multidetermined variable that is influenced by a range of factors (see Chervova et al., 2024). The results of the exploratory analyses may also be inflated by type I error given the number of statistical tests and thus should be interpreted with caution until replicated. The interpretation of the findings needs to take into account the low internal consistency of the BFI-15, which is mainly due to the low number of items (3) used to assess each domain. Importantly, internal consistency is unrelated to stability, heritability, and cross-observer validity of personality scales (McCrae et al., 2011). Still, the poor internal consistency likely attenuates true associations and may increase the risk of spurious findings, particularly in cohorts where traits were measured with very few items. In addition, future research may examine the specific personality facets that are associated with epigenetic aging. Finally, the present study includes samples from the US and UK. Further research is needed to examine whether the pattern of association between personality and epigenetic aging generalizes to other populations.

In conclusion, the present study conducted in three large samples found that personality is associated with epigenetic aging. In particular, higher conscientiousness was related to slower epigenetic aging, with stronger associations with second and third-generation epigenetic clocks trained on health-related outcomes than to first-generation clocks trained on chronological age.

## CRediT authorship contribution statement

Martina Luchetti: Writing – review & editing, Methodology. Antonio Terracciano: Writing – review & editing, Supervision, Formal analysis, Conceptualization. Angelina R. Sutin: Writing – review & editing, Conceptualization. Yannick Stephan: Writing – review & editing, Writing – original draft, Supervision, Project administration, Methodology, Formal analysis, Conceptualization.

# **Ethical approval**

The Health and Retirement Study was approved by the University of Michigan IRB. The Education and Social/Behavioral Sciences and the Health Sciences IRB at the University of Wisconsin-Madison approved the MIDUS Study. The University of Essex Ethics Committee has approved all data collection on the UK Household Longitudinal Study. All participants provided informed consent. This study was based on publicly available de-identified datasets and therefore was exempt from Institutional Review Board review.

#### **Declaration of Competing interest**

None.

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## Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.psyneuen.2025.107582.

#### Data availability

Health and Retirement Study data are publicly available at http://hrsonline.isr.umich.edu/. MIDUS data can be accessed at http://midus.wisc.edu/index.php. UKHLS data are available at: https://www.understandingsociety.ac.uk/documentation/access-data.

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