# Main & Supplemental Analyses for Probing connections between social connectedness, mortality risk, and brain age: A preregistered study.

Study GitHub: /r/SocConnectionBrainAgeGap-15CF/

## REDACTED

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## Methods

#### Social Connectedness: Positive Relations with Others

This self-report measure was comprised of responses to the following 7 items: 1) "Most people see me as loving and affectionate." (R) 2) "Maintaining close relationships has been difficult and frustrating for me." 3) "I often feel lonely because I have few close friends with whom to share my concerns." 4) "I enjoy personal and mutual conversations with family members and friends." (R) 5) "People would describe me as a giving person, willing to share my time with others." (R) 6) "I have not experienced many warm and trusting relationships with others."

7) "I know that I can trust my friends, and they know they can trust me." (R)

To each item, participants responded: 1= Strongly agree; 2=Somewhat agree; 3=A little Agree; 4=Neither agree or disagree; 5=A little disagree; 6=Somewhat disagree; 7=Strongly disagree.

Further details on MIDUS construct documentation can be found here:

 $for\ Core\ MIDUS\ (M1/M2):\ https://midus.wisc.edu/Projects/M2P1/M2P1\_Survey/Documentation/M2\_P1\_DocumentationOfPsychosocialConstructsAndCompositeVariables\_20201103.pdf$ 

for Refresher MIDUS (MR): https://www.icpsr.umich.edu/web/NACDA/studies/36532/variables

# **Descriptives**

# Power Analyses

```
pwr.r.test(n = NULL, r = .29, sig.level = 0.05, power = .80,
        alternative = c("two.sided"))
##
        approximate correlation power calculation (arctangh transformation)
##
##
##
                 n = 90.19199
##
                 r = 0.29
         sig.level = 0.05
##
##
             power = 0.8
##
       alternative = two.sided
```

## Imputation

The full MIDUS sample and the "mice" package was used to impute the following missing variables: Positive Relations with Others, Instrumental Activities of Daily Living, Basic Activities of Daily Living, Total Chronic Conditions, and Race.

#### **Correlation Table**

	Age	Sex	Latine/x	Race	Income	Sample	Childhood	Childhood	BMI	Panic	Depression	Anxiety	Social	Chronic	ADLs
	Age	SCA	Latine/A	Racc	meome	Sample	Finances	Welfare	DIVII	Dx	Dx	Dx	Connect.	Conditions	ADLS
Age															
Sex	0.02														
Latine/x	0.05	0.04													
Race	0.08	-0.03	-0.18*												
Income	-0.14	-0.22**	-0.10	0.25***											
Sample	-0.41***	-0.14	-0.01	-0.01	$0.19^{**}$										
Childhood Finances	$0.16^{*}$	-0.01	0.01	0.08	-0.05	-0.28***									
Childhood Welfare	0.12	-0.03	-0.09	0.31***	$0.18^{*}$	-0.05	-0.36***								
BMI	0.07	0.11	-0.02	-0.19**	-0.04	0.01	-0.01	-0.13							
Panic Dx	0.08	0.12	0.19**	0.00	0.10	-0.05	0.05	0.02	0.00						
Depression Dx	-0.14	0.04	-0.05	0.00	-0.06	-0.04	0.03	-0.10	$0.15^{*}$	0.04					
Anxiety Dx	0.10	0.07	0.23**	-0.01	-0.07	-0.06	-0.04	0.07	-0.01	0.29***	0.08				
Social Connectedness	0.12	0.21**	-0.08	0.06	-0.02	-0.04	-0.09	0.05	0.01	-0.11	-0.09	-0.14			
Chronic Conditions	0.46***	$0.15^{*}$	$0.18^{*}$	-0.01	-0.21**	-0.22**	0.14	-0.16 <sup>*</sup>	0.27***	0.07	0.12	$0.18^{*}$	0.03		
ADLs	0.22**	0.03	0.18*	-0.33***	-0.25***	-0.12	0.08	-0.25***	0.37***	0.04	0.23**	0.13	-0.17*	0.44***	

Note: Computed correlation used pearson-method with pairwise-deletion. Body Mass Index = BMI, Dx = Diagnosis, ADLs = Activities of Daily Living. <math>p < 0.05 = \*, p < 0.01 = \*\*\*, p < 0.001 = \*\*\*, p < 0.001 = \*\*\*, p < 0.001 = \*\*\*

# Demographics Table

Table 2. Descriptive Statistics for Key Variables by Recruitment Sample

Characteristic	Core <sup>1</sup>	Refresher <sup>1</sup>	Overall <sup>I</sup>
Age (years)	57 (10)	47 (12)	51 (12)
Sex			
Female	50 (68%)	68 (54%)	118 (59%)
Male	24 (32%)	59 (46%)	83 (41%)
Latine/x			
Not Spanish/Hispanic	67 (100%)	125 (100%)	192 (100%)
Race	88 85		100
White	45 (64%)	81 (64%)	126 (64%)
Black and/or African American	20 (29%)	38 (30%)	58 (29%)
Native American or Alaska Native			
Aleutian Islander/Eskimo	3 (4.3%)	2 (1.6%)	5 (2.5%)
Asian	1 (1.4%)	1 (0.8%)	2 (1.0%)
Native Hawaiian or Pacific Islander	0 (0%)	0 (0%)	0 (0%)
Other	1 (1.4%)	5 (3.9%)	6 (3.0%)
Education			
No school/some grade school	0 (0%)	0 (0%)	0 (0%)
Eighth grade/ junior high school	1 (1.4%)	0 (0%)	1 (0.5%)
Some high school	5 (7.1%)	8 (6.3%)	13 (6.6%)
GED	2 (2.9%)	2 (1.6%)	4 (2.0%)
Graduated from high school	21 (30%)	19 (15%)	40 (20%)
1-2 yrs. college, no degree yet	11 (16%)	20 (16%)	31 (16%)
3+ yrs. college, no degree yet	4 (5.7%)	5 (3.9%)	9 (4.6%)
Grad 2-yr/voc. school/Associates degree	7 (10%)	17 (13%)	24 (12%)
Grad 4-5 year college/bachelors degree	9 (13%)	31 (24%)	40 (20%)
Some graduate school	1 (1.4%)	3 (2.4%)	4 (2.0%)
Masters degree	9 (13%)	15 (12%)	24 (12%)
Professional degree (e.g.,Ph.D, JD)	0 (0%)	7 (5.5%)	7 (3.6%)
Income			
Less than \$10,000	4 (6.0%)	11 (8.9%)	15 (7.9%)
\$10,000 to \$19,999	5 (7.5%)	5 (4.0%)	10 (5.2%)
\$20,000 to \$29,999	11 (16%)	5 (4.0%)	16 (8.4%)
\$30,000 to \$39,999	5 (7.5%)	10 (8.1%)	15 (7.9%)
\$40,000 to \$49,999	7 (10%)	6 (4.8%)	13 (6.8%)
\$50,000 to \$59,999	9 (13%)	10 (8.1%)	19 (9.9%)
\$60,000 to \$69,999	5 (7.5%)	13 (10%)	18 (9.4%)
\$70,000 to \$79,999	4 (6.0%)	9 (7.3%)	13 (6.8%)
\$80,000 to \$89,999	4 (6.0%)	10 (8.1%)	14 (7.3%)
\$90,000 to \$99,999	2 (3.0%)	6 (4.8%)	8 (4.2%)
\$100,000 to \$149,999	8 (12%)	28 (23%)	36 (19%)
\$150,000 or more	3 (4.5%)	11 (8.9%)	14 (7.3%)
Total	N = 74	N = 127	N = 201

<sup>&</sup>lt;sup>1</sup> Mean (SD); n (%); N = N

# Results & Analyses

# Research Question 1.

Are there associations between social connectedness and mortality risk?

## C path: Social Connectedness and Chronic Health Conditions (N=8692)

Observations	8692 (3075 missing obs. deleted)
Dependent variable	ChronicConditions
Type	OLS linear regression

F(5,8686)	479.98
$\mathbb{R}^2$	0.22
$Adj. R^2$	0.22

	Est.	S.E.	t val.	p
(Intercept)	-1.96	0.24	-8.09	0.00
PosRelations7	-0.04	0.00	-10.68	0.00
FirstAge	0.11	0.00	48.05	0.00
Sample	0.78	0.06	12.45	0.00
Sex	0.43	0.06	7.11	0.00
Race_Di	-0.02	0.09	-0.18	0.86

## C path: Social Connectedness and ADLs (N = N = 8692)

Observations	8692 (3075 missing obs. deleted)
Dependent variable	$\operatorname{sum} \operatorname{ADL}$
Type	OLS linear regression

F(5,8686)	278.78
$\mathbb{R}^2$	0.14
$Adj. R^2$	0.14

	Est.	S.E.	t val.	p
(Intercept)	2.18	0.12	18.33	0.00
PosRelations7	-0.03	0.00	-18.23	0.00
FirstAge	0.04	0.00	32.48	0.00
Sample	0.04	0.03	1.26	0.21
Sex	0.34	0.03	11.32	0.00
Race_Di	-0.28	0.04	-6.61	0.00

Standard errors: OLS; Continuous predictors are mean-centered and scaled by 1 s.d. The outcome variable remains in its original units.

## C path: Social Connectedness and Chronic Health Conditions (N = 201)

Observations	201
Dependent variable	ChronicConditions
Type	OLS linear regression

F(5,195)	13.92
$\mathbb{R}^2$	0.26
$Adj. R^2$	0.24

	Est.	S.E.	t val.	p
(Intercept)	-1.28	1.33	-0.97	0.34
PosRelations7	-0.03	0.02	-1.21	0.23
ScanAge	0.10	0.01	7.27	0.00
Sample	-0.29	0.33	-0.86	0.39
Sex	0.75	0.32	2.36	0.02
Race_Di	-0.49	0.32	-1.51	0.13

# C path: Social Connectedness and ADLs (N = 201)

Observations	201
Dependent variable	$\operatorname{sum} \operatorname{ADL}$
Type	OLS linear regression

F(5,195)	7.50
$\mathbb{R}^2$	0.16
$Adj. R^2$	0.14

	Est.	S.E.	t val.	p
(Intercept)	3.75	0.78	4.83	0.00
PosRelations7	-0.03	0.01	-2.31	0.02
ScanAge	0.02	0.01	2.67	0.01
Sample	-0.23	0.20	-1.19	0.24
Sex	0.16	0.18	0.86	0.39
Race_Di	-0.97	0.19	-5.11	0.00

Standard errors: OLS; Continuous predictors are mean-centered and scaled by 1 s.d. The outcome variable remains in its original units.

## C path: Social Connectedness and Chronic Health Conditions (N = 197)

Observations	196 (5 missing obs. deleted)
Dependent variable	ChronicConditions
Type	OLS linear regression

F(5,190)	12.98
$\mathbb{R}^2$	0.25
$Adj. R^2$	0.24

	Est.	S.E.	t val.	p
(Intercept)	-1.69	1.30	-1.30	0.20
PosRelations7	-0.02	0.02	-0.94	0.35
ScanAge	0.10	0.01	7.26	0.00
Sample	-0.09	0.33	-0.26	0.79
Sex	0.69	0.31	2.23	0.03
Race_Di	-0.53	0.32	-1.66	0.10

C path: ADLs and Chronic Health Conditions (N=197)

Observations	196 (5 missing obs. deleted)
Dependent variable	$\operatorname{sum} \operatorname{ADL}$
Type	OLS linear regression

F(5,190)	7.97
$\mathbb{R}^2$	0.17
$Adj. R^2$	0.15

	Est.	S.E.	t val.	p
(Intercept)	3.72	0.77	4.84	0.00
PosRelations7	-0.03	0.01	-2.50	0.01
ScanAge	0.02	0.01	2.90	0.00
Sample	-0.17	0.19	-0.85	0.40
Sex	0.13	0.18	0.69	0.49
Race_Di	-1.02	0.19	-5.40	0.00

# Research Question 2.

Are there associations between positive relations with others and the brain-age gap?

A Path: Social Connectedness and Brain Age Gap (N=201)

Observations	201
Dependent variable	$Kaufmann\_BAG$
Type	OLS linear regression

F(7,193)	40.17
$\mathbb{R}^2$	0.59
$Adj. R^2$	0.58

	Est.	S.E.	t val.	p
(Intercept)	75.66	14.13	5.35	0.00
PosRelations7	0.02	0.08	0.25	0.80
Sample	-2.30	2.15	-1.07	0.29
Race_Di	2.70	1.32	2.05	0.04
Sex	0.50	1.20	0.41	0.68
AGE	-0.85	0.05	-16.21	0.00
CAT12_Grade	-41.40	20.68	-2.00	0.05
ScanLag	0.09	0.16	0.55	0.58

# A Path: Social Connectedness and Brain Age Gap (N=197)

Observations	196 (5 missing obs. deleted)
Dependent variable	Kaufmann_BAG
Type	OLS linear regression

F(7,188)	39.27
$\mathbb{R}^2$	0.59
$Adj. R^2$	0.58

	Est.	S.E.	t val.	р
(Intercept)	74.31	14.53	5.11	0.00
PosRelations7	0.01	0.08	0.18	0.86
Sample	-2.16	2.20	-0.98	0.33
Race_Di	3.14	1.44	2.18	0.03
Sex	0.73	1.23	0.59	0.56
AGE	-0.86	0.05	-15.88	0.00
CAT12_Grade	-40.38	21.13	-1.91	0.06
ScanLag	0.02	0.22	0.08	0.93

# Research Question 3.

Are associations between positive relations with others and all-cause mortality statistically accounted for by the brain-age gap?

B path: Brain Age Gap and Total Chronic Conditions (N=201)

Observations	201
Dependent variable	ChronicConditions
Type	OLS linear regression

F(7,193)	10.14
$\mathbb{R}^2$	0.27
$Adj. R^2$	0.24

	Est.	S.E.	t val.	p
(Intercept)	1.55	3.98	0.39	0.70
Kaufmann_BAG	-0.01	0.02	-0.63	0.53
Sample	0.29	0.57	0.51	0.61
Sex	0.72	0.31	2.30	0.02
AGE	0.09	0.02	4.22	0.00
Race_Di	-0.25	0.35	-0.70	0.49
CAT12_Grade	-5.59	5.53	-1.01	0.31
ScanLag	-0.06	0.04	-1.39	0.17

B path: Brain Age Gap and Total Chronic Conditions (N=197)

Observations	197 (4 missing obs. deleted)
Dependent variable	ChronicConditions
Type	OLS linear regression

F(7,189)	9.37
$\mathbb{R}^2$	0.26
$Adj. R^2$	0.23

	Est.	S.E.	t val.	p
(Intercept)	1.75	3.90	0.45	0.65
Kaufmann_BAG	-0.01	0.02	-0.35	0.73
Sample	0.25	0.56	0.44	0.66
Sex	0.65	0.31	2.13	0.03
Race_Di	-0.52	0.37	-1.41	0.16
AGE	0.09	0.02	4.32	0.00
CAT12_Grade	-5.51	5.40	-1.02	0.31
ScanLag	0.01	0.05	0.24	0.81

B path: Brain Age Gap and ADLs (N=201)

Observations	201
Dependent variable	$\operatorname{sum} \operatorname{ADL}$
Type	OLS linear regression

F(7,193)	6.86
$\mathbb{R}^2$	0.20
$Adj. R^2$	0.17

	Est.	S.E.	t val.	p
(Intercept)	2.06	2.28	0.90	0.37
Kaufmann_BAG	-0.00	0.01	-0.34	0.73
Sample	0.08	0.33	0.24	0.81
Sex	0.09	0.18	0.48	0.63
AGE	0.02	0.01	1.66	0.10
Race_Di	-0.71	0.20	-3.50	0.00
CAT12_Grade	0.10	3.17	0.03	0.97
ScanLag	-0.09	0.02	-3.76	0.00

B path: Brain Age Gap and ADLs (N = 197)

Observations	197 (4 missing obs. deleted)
Dependent variable	$\operatorname{sum} \operatorname{ADL}$
Type	OLS linear regression

F(7,189)	6.85
$\mathbb{R}^2$	0.20
$Adj. R^2$	0.17

	Est.	S.E.	t val.	p
(Intercept)	2.19	2.29	0.96	0.34
Kaufmann_BAG	-0.00	0.01	-0.15	0.88
Sample	0.17	0.33	0.53	0.60
Sex	0.07	0.18	0.39	0.70
AGE	0.02	0.01	1.94	0.05
Race_Di	-0.69	0.22	-3.18	0.00
CAT12_Grade	-0.44	3.17	-0.14	0.89
ScanLag	-0.11	0.03	-3.34	0.00

# Exploratory & Supplemental Analyses

## Mortality

Analyses with mortality records were performed on the entire MIDUS sample using a generalized linear model with a binomial distribution and logit link function to model the effect of variables on a binary outcome (0 = not deceased).

Observations	8692 (3075 missing obs. deleted)
Dependent variable	DeathStatus
Type	Generalized linear model
Family	binomial
Link	logit

$\chi^{2}(5)$	2604.78
Pseudo-R <sup>2</sup> (Cragg-Uhler)	0.42
Pseudo-R <sup>2</sup> (McFadden)	0.31
AIC	5823.41
BIC	5865.83

	Est.	S.E.	z val.	p
(Intercept)	-4.85	0.29	-16.91	0.00
PosRelations7	-0.02	0.00	-5.21	0.00
FirstAge	0.12	0.00	35.49	0.00
Sample	-1.71	0.08	-21.03	0.00
Sex	-0.35	0.07	-5.28	0.00
Race_Di	-0.10	0.10	-0.94	0.35

Standard errors: MLE; Continuous predictors are mean-centered and scaled by 1 s.d. The outcome variable remains in its original units.

C Path: Social Connectedness Predicting Mortality in Full MIDUS (N = 8692)

#### Other Algorithms Deriving the Brain-Age Gap

Various algorithms for predicting brain age have emerged in the past few years. In addition to the algorithm developed by Kaufamann and colleagues (2019), we derived brain age using 4 alternative algorithms. The predicted brain ages from all 5 algorithms can be found on the study GitHub. For further information on all 5 algorithms, please see the following pre-print (Hanson et al., under review; https://www.researchsquare.com/article/rs-3331689/v1)

The additional algorithms considered were developed by:

- Cole and colleagues (2018), referred to as "brainageR"
- Bashyam and colleagues (2020), referred to as "DeepBrainNet"
- Han and colleagues (2021), referred to as "ENIGMA"
- Leonardsen and colleagues (2022), referred to as "pyment"

## a Paths: Social Connectedness Predicting BAG in 4 Alternative Algorithms (N = 201)

Observations	201
Dependent variable	$ANTs\_BAG$
Type	OLS linear regression

F(7,193)	19.14
$\mathbb{R}^2$	0.41
$Adj. R^2$	0.39

	Est.	S.E.	t val.	p
(Intercept)	81.43	19.23	4.23	0.00
PosRelations7	0.10	0.11	0.89	0.38
Sample	-0.31	2.92	-0.11	0.92
Race_Di	4.20	1.80	2.34	0.02
Sex	0.59	1.64	0.36	0.72
AGE	-0.80	0.07	-11.22	0.00
CAT12_Grade	-64.29	28.14	-2.28	0.02
ScanLag	0.19	0.22	0.86	0.39

Observations	200 (1 missing obs. deleted)
Dependent variable	${\rm brainageR\_BAG}$
Type	OLS linear regression

F(7,192)	15.38
$\mathbb{R}^2$	0.36
$Adj. R^2$	0.34

	Est.	S.E.	t val.	p
(Intercept)	94.11	20.42	4.61	0.00
PosRelations7	0.13	0.12	1.09	0.28
Sample	-3.57	3.11	-1.15	0.25
Race_Di	3.56	1.91	1.87	0.06
Sex	1.76	1.75	1.01	0.31
AGE	-0.75	0.08	-9.82	0.00
CAT12_Grade	-77.90	29.87	-2.61	0.01
ScanLag	0.41	0.23	1.75	0.08

Observations	201
Dependent variable	$pyment\_BAG$
Type	OLS linear regression

F(7,193)	19.14
$\mathbb{R}^2$	0.41
$Adj. R^2$	0.39

	Est.	S.E.	t val.	p
(Intercept)	81.43	19.23	4.23	0.00
PosRelations7	0.10	0.11	0.89	0.38
Sample	-0.31	2.92	-0.11	0.92
Race_Di	4.20	1.80	2.34	0.02
Sex	0.59	1.64	0.36	0.72
AGE	-0.80	0.07	-11.22	0.00
CAT12_Grade	-64.29	28.14	-2.28	0.02
ScanLag	0.19	0.22	0.86	0.39

Observations	201
Dependent variable	$ENIGMA\_BAG$
Type	OLS linear regression

F(7,193)	28.91
$\mathbb{R}^2$	0.51
$Adj. R^2$	0.49

	Est.	S.E.	t val.	р
(Intercept)	65.57	16.62	3.95	0.00
PosRelations7	0.05	0.09	0.52	0.61
Sample	-3.58	2.52	-1.42	0.16
Race_Di	1.16	1.55	0.75	0.46
Sex	-1.40	1.41	-0.99	0.32
AGE	-0.85	0.06	-13.73	0.00
CAT12_Grade	-24.81	24.32	-1.02	0.31
ScanLag	0.10	0.19	0.51	0.61

# b Paths: BAG predicting Total Chronic Conditions in 4 Alternative Algorithms (N = 201)

Observations	201
Dependent variable	ChronicConditions
Type	OLS linear regression

F(7,193)	10.06
$\mathbb{R}^2$	0.27
$Adj. R^2$	0.24

	Est.	S.E.	t val.	р
(Intercept)	0.70	3.89	0.18	0.86
$ANTs\_BAG$	-0.00	0.01	-0.06	0.95
Sample	0.32	0.57	0.56	0.58
Race_Di	-0.28	0.35	-0.78	0.44
Sex	0.72	0.31	2.28	0.02
AGE	0.10	0.02	5.62	0.00
CAT12_Grade	-5.15	5.55	-0.93	0.35
ScanLag	-0.06	0.04	-1.41	0.16

Standard errors: OLS; Continuous predictors are mean-centered and scaled by 1 s.d. The outcome variable remains in its original units.

Observations	200 (1 missing obs. deleted)
Dependent variable	ChronicConditions
Type	OLS linear regression

F(7,192)	10.06
$\mathbb{R}^2$	0.27
$Adj. R^2$	0.24

	Est.	S.E.	t val.	p
(Intercept)	1.41	3.93	0.36	0.72
${\bf brainageR\_BAG}$	-0.01	0.01	-0.60	0.55
Sample	0.28	0.57	0.50	0.62
Race_Di	-0.25	0.35	-0.71	0.48
Sex	0.73	0.32	2.30	0.02
AGE	0.09	0.02	5.59	0.00
CAT12_Grade	-5.70	5.58	-1.02	0.31
ScanLag	-0.06	0.04	-1.32	0.19

Observations	201
Dependent variable	ChronicConditions
Type	OLS linear regression

F(7,193)	10.06
$\mathbb{R}^2$	0.27
$Adj. R^2$	0.24

	Est.	S.E.	t val.	р
(Intercept)	0.70	3.89	0.18	0.86
pyment_BAG	-0.00	0.01	-0.06	0.95
Sample	0.32	0.57	0.56	0.58
Race_Di	-0.28	0.35	-0.78	0.44
Sex	0.72	0.31	2.28	0.02
AGE	0.10	0.02	5.62	0.00
CAT12_Grade	-5.15	5.55	-0.93	0.35
ScanLag	-0.06	0.04	-1.41	0.16

Observations	201
Dependent variable	ChronicConditions
Type	OLS linear regression

F(7,193)	10.07
$\mathbb{R}^2$	0.27
$Adj. R^2$	0.24

	Est.	S.E.	t val.	p
(Intercept)	0.35	3.87	0.09	0.93
ENIGMA_BAG	0.00	0.02	0.27	0.79
Sample	0.33	0.57	0.58	0.56
Race_Di	-0.28	0.35	-0.81	0.42
Sex	0.72	0.31	2.29	0.02
AGE	0.10	0.02	5.34	0.00
CAT12_Grade	-4.99	5.49	-0.91	0.36
ScanLag	-0.06	0.04	-1.42	0.16

# b Paths: BAG predicting ADLs in 4 Alternative Algorithms (N = 201)

Observations	201
Dependent variable	$\operatorname{sum} \operatorname{ADL}$
Type	OLS linear regression

F(7,193)	6.85
$\mathbb{R}^2$	0.20
$Adj. R^2$	0.17

	Est.	S.E.	t val.	р
(Intercept)	1.88	2.23	0.84	0.40
$ANTs\_BAG$	-0.00	0.01	-0.16	0.88
Sample	0.09	0.33	0.27	0.79
Race_Di	-0.71	0.20	-3.52	0.00
Sex	0.09	0.18	0.48	0.64
AGE	0.02	0.01	2.22	0.03
CAT12_Grade	0.18	3.17	0.06	0.96
ScanLag	-0.09	0.02	-3.76	0.00

Standard errors: OLS; Continuous predictors are mean-centered and scaled by 1 s.d. The outcome variable remains in its original units.

Observations	200 (1 missing obs. deleted)
Dependent variable	$\operatorname{sum} \operatorname{ADL}$
Type	OLS linear regression

F(7,192)	6.82
$\mathbb{R}^2$	0.20
$Adj. R^2$	0.17

	Est.	S.E.	t val.	p
(Intercept)	1.76	2.25	0.78	0.44
${\rm brainageR\_BAG}$	0.00	0.01	0.01	0.99
Sample	0.09	0.33	0.29	0.78
Race_Di	-0.72	0.20	-3.55	0.00
Sex	0.09	0.18	0.48	0.63
AGE	0.02	0.01	2.42	0.02
CAT12_Grade	0.25	3.20	0.08	0.94
ScanLag	-0.09	0.02	-3.74	0.00

Observations	201
Dependent variable	$\operatorname{sum} \operatorname{ADL}$
Type	OLS linear regression

F(7,193)	6.85
$\mathbb{R}^2$	0.20
$Adj. R^2$	0.17

	Est.	S.E.	t val.	р
(Intercept)	1.88	2.23	0.84	0.40
pyment_BAG	-0.00	0.01	-0.16	0.88
Sample	0.09	0.33	0.27	0.79
Race_Di	-0.71	0.20	-3.52	0.00
Sex	0.09	0.18	0.48	0.64
AGE	0.02	0.01	2.22	0.03
CAT12_Grade	0.18	3.17	0.06	0.96
ScanLag	-0.09	0.02	-3.76	0.00

Observations	201
Dependent variable	$\operatorname{sum} \operatorname{ADL}$
Type	OLS linear regression

F(7,193)	6.89
$\mathbb{R}^2$	0.20
$Adj. R^2$	0.17

	Est.	S.E.	t val.	p
(Intercept)	1.46	2.21	0.66	0.51
ENIGMA_BAG	0.00	0.01	0.51	0.61
Sample	0.10	0.33	0.32	0.75
Race_Di	-0.72	0.20	-3.62	0.00
Sex	0.09	0.18	0.50	0.62
AGE	0.03	0.01	2.47	0.01
CAT12_Grade	0.37	3.14	0.12	0.91
ScanLag	-0.09	0.02	-3.79	0.00

## Sensitivity Analyses: Covariates Included in Main Models

#### Scan Quality

To assess MRI quality, we generated a quantitative metric ("CAT12 score") using The Computational Anatomy Toolbox 12 (CAT12) toolbox from the Structural Brain Mapping group indicating the quality of each collected MR image (Gaser & Kurth, 2017). This metric considers four summary measures of image quality: noise-to-contrast ratio, coefficient of joint variation, inhomogeneity-to-contrast ratio, and root-mean-squared voxel resolution. The method employed considers four summary measures of image quality: (1) noise to contrast ratio, (2) coefficient of joint variation, (3) inhomogeneity to contrast ratio, and (4) root mean squared voxel resolution. To produce a single aggregate metric that serves as an indicator of overall quality, this toolbox normalizes each measure and combines them using a kappa statistic-based framework, for optimizing a generalized linear model through solving least squares (Dahnke et al., 2015). The score is a value from 0 to 1, with higher values indicating better image quality. Additional information is available at: http://www.neuro.uni-jena.de/cat/index.html#QA.

The following sensitivity analyses modeled all paths (a, b, and c) using only high quality scans. This represents scans with a CAT12 grade of 0.80 or higher.

#### c Path with High Quality Scans (N = 96)

Observations	96
Dependent variable	ChronicConditions
Type	OLS linear regression

F(6,89)	5.43
$\mathbb{R}^2$	0.27
$Adj. R^2$	0.22

	Est.	S.E.	t val.	p
(Intercept)	-2.07	12.75	-0.16	0.87
PosRelations7	-0.03	0.03	-1.07	0.29
Race_Di	-0.54	0.44	-1.22	0.23
Sex	0.25	0.41	0.60	0.55
ScanAge	0.10	0.02	5.58	0.00
ScanLag	0.05	0.23	0.20	0.84
CAT12_Grade	1.75	15.01	0.12	0.91

Observations	96
Dependent variable	$\operatorname{sum} \operatorname{ADL}$
Type	OLS linear regression

F(6,89)	2.92
$\mathbb{R}^2$	0.16
$Adj. R^2$	0.11

	Est.	S.E.	t val.	р
(Intercept)	0.51	7.29	0.07	0.94
PosRelations7	-0.02	0.02	-1.38	0.17
Race_Di	-0.56	0.25	-2.19	0.03
Sex	-0.09	0.24	-0.40	0.69
ScanAge	0.04	0.01	3.68	0.00
ScanLag	-0.20	0.13	-1.52	0.13
CAT12_Grade	2.81	8.58	0.33	0.74

## a Path with High Quality Scans (N = 96)

Observations	96
Dependent variable	$Kaufmann\_BAG$
Type	OLS linear regression

F(6,89)	31.67
$\mathbb{R}^2$	0.68
$Adj. R^2$	0.66

	Est.	S.E.	t val.	p
(Intercept)	-17.56	58.24	-0.30	0.76
PosRelations7	0.20	0.14	1.46	0.15
Race_Di	3.46	2.03	1.70	0.09
Sex	0.32	1.89	0.17	0.87
ScanAge	-1.05	0.08	-13.49	0.00
ScanLag	1.05	1.06	0.99	0.32
CAT12_Grade	66.32	68.57	0.97	0.34

# b Path with High Quality Scans (N = 96)

Observations	96
Dependent variable	$\operatorname{sum} \operatorname{ADL}$
Type	OLS linear regression

F(6,89)	2.60
$\mathbb{R}^2$	0.15
$Adj. R^2$	0.09

	Est.	S.E.	t val.	p
(Intercept)	-1.62	7.19	-0.23	0.82
Kaufmann_BAG	0.01	0.01	0.55	0.58
Race_Di	-0.50	0.25	-1.97	0.05
Sex	-0.11	0.24	-0.48	0.63
ScanAge	0.04	0.02	2.46	0.02
ScanLag CAT12_Grade	-0.20 3.93	0.13 8.62	-1.48 0.46	$0.14 \\ 0.65$

Standard errors: OLS; Continuous predictors are mean-centered and scaled by 1 s.d. The outcome variable remains in its original units.

Observations	96
Dependent variable	ChronicConditions
Type	OLS linear regression

F(6,89)	5.27
$\mathbb{R}^2$	0.26
$Adj. R^2$	0.21

	Est.	S.E.	t val.	p
(Intercept)	-4.97	12.51	-0.40	0.69
Kaufmann_BAG	0.01	0.02	0.62	0.53
Race_Di	-0.47	0.44	-1.08	0.28
Sex	0.22	0.42	0.53	0.60
ScanAge	0.11	0.03	3.67	0.00
ScanLag	0.04	0.23	0.19	0.85
CAT12_Grade	3.03	15.00	0.20	0.84

## Age

We ran analyses using the brain-age gap (i.e., a and b path models) excluding chronological age. The inclusion of this variable in models is currently a point of debate in the field.

## a Path Model without Age as a Covariate

Observations	201
Dependent variable	$Kaufmann\_BAG$
Type	OLS linear regression

F(6,194)	1.31
$\mathbb{R}^2$	0.04
$Adj. R^2$	0.01

	Est.	S.E.	t val.	р
(Intercept)	26.71	21.16	1.26	0.21
PosRelations7	-0.20	0.12	-1.63	0.11
Sample	5.68	3.20	1.77	0.08
Race_Di	-0.23	2.00	-0.12	0.91
Sex	1.72	1.84	0.94	0.35
${\rm CAT12\_Grade}$	-40.55	31.70	-1.28	0.20
ScanLag	-0.37	0.24	-1.52	0.13

## $\boldsymbol{b}$ Path Models without Age as a Covariate

Observations	201
Dependent variable	ChronicConditions
Type	OLS linear regression

F(6,194)	8.15
$\mathbb{R}^2$	0.20
$Adj. R^2$	0.18

	Est.	S.E.	t val.	p
(Intercept)	8.66	3.76	2.30	0.02
Kaufmann_BAG	-0.07	0.01	-5.72	0.00
Sample	-0.21	0.58	-0.36	0.72
Race_Di	0.06	0.36	0.15	0.88
Sex	0.73	0.33	2.22	0.03
CAT12_Grade	-8.08	5.73	-1.41	0.16
ScanLag	-0.03	0.04	-0.79	0.43

Standard errors: OLS; Continuous predictors are mean-centered and scaled by 1 s.d. The outcome variable remains in its original units.

Observations	201
Dependent variable	$\operatorname{sum} \operatorname{ADL}$
Type	OLS linear regression

F(6,194)	7.48
$\mathbb{R}^2$	0.19
$Adj. R^2$	0.16

	Est.	S.E.	t val.	p
(Intercept)	3.66	2.08	1.76	0.08
Kaufmann_BAG	-0.02	0.01	-2.48	0.01
Sample	-0.03	0.32	-0.10	0.92
Race_Di	-0.64	0.20	-3.22	0.00
Sex	0.09	0.18	0.48	0.63
CAT12_Grade ScanLag	-0.46 -0.09	3.16 0.02	-0.14 -3.55	0.88

# a Path Model with Older Sample (> 50 years; N = 101).

Observations	101 (5 missing obs. deleted)
Dependent variable	Kaufmann_BAG
Type	OLS linear regression

F(7,93)	9.19
$\mathbb{R}^2$	0.41
$Adj. R^2$	0.36

	Est.	S.E.	t val.	p
(Intercept)	83.43	21.64	3.86	0.00
PosRelations7	0.03	0.12	0.25	0.81
Race_Di	3.78	1.98	1.91	0.06
Sample	-6.18	2.99	-2.06	0.04
AGE	-0.88	0.13	-6.95	0.00
Sex	1.64	1.61	1.02	0.31
CAT12_Grade	-44.41	29.59	-1.50	0.14
ScanLag	-0.12	0.32	-0.36	0.72

# b Path Model with Older Sample (> 50 years; N = 102).

Observations	102 (4 missing obs. deleted)
Dependent variable	ChronicConditions
Type	OLS linear regression

F(7,94) 2.30 R<sup>2</sup> 0.15 Adj. R<sup>2</sup> 0.08

	Est.	S.E.	t val.	p
(Intercept)	-1.35	6.84	-0.20	0.84
Kaufmann_BAG	0.03	0.03	1.12	0.27
Race_Di	-0.98	0.60	-1.61	0.11
AGE	0.14	0.05	3.04	0.00
Sample	0.88	0.91	0.96	0.34
Sex	0.52	0.46	1.12	0.26
CAT12_Grade	-5.66	8.93	-0.63	0.53
ScanLag	-0.06	0.09	-0.65	0.52

Standard errors: OLS; Continuous predictors are mean-centered and scaled by 1 s.d. The outcome variable remains in its original units.

Observations	102 (4 missing obs. deleted)
Dependent variable	$\operatorname{sum} \operatorname{ADL}$
Type	OLS linear regression

F(7,94)	2.90
$\mathbb{R}^2$	0.18
$Adj. R^2$	0.12

	Est.	S.E.	t val.	р
(Intercept)	1.42	3.79	0.38	0.71
Kaufmann_BAG	0.02	0.02	1.05	0.30
Race_Di	-1.13	0.33	-3.36	0.00
AGE	0.04	0.03	1.41	0.16
Sample	0.41	0.51	0.81	0.42
Sex	-0.10	0.25	-0.39	0.70
CAT12_Grade	-0.08	4.95	-0.02	0.99
ScanLag	-0.04	0.05	-0.78	0.44

## Sensitivity Analyses: Additional Covariates

As specified in our registered report, we ran regression analyses with the additional independent variables a) income, b) mental health diagnosis, c) childhood social class, and d) BMI predicting both brain age (i.e., a path) and mortality risk (c path) in separate models (i.e., a different model for each additional covariate).

#### Body Mass Index (BMI)

BMI was derived via participant self-report and calculated by dividing respondent's weight (mass) in kilograms by heights in meters squared. Per the MIDUS code book, the height measure (in inches) was multiplied by 0.0254 to get the height in meters, and the weight (in pounds) was multiplied by 0.4536 to get the mass in kilometers.

#### a Path with BMI

Observations	201
Dependent variable	$Kaufmann\_BAG$
Type	OLS linear regression

F(8,192)	34.97
$\mathbb{R}^2$	0.59
$Adj. R^2$	0.58

	Est.	S.E.	t val.	p
(Intercept)	75.27	14.55	5.17	0.00
PosRelations7	0.02	0.08	0.26	0.79
Sample	-2.32	2.16	-1.07	0.28
Race_Di	2.73	1.34	2.03	0.04
Sex	0.48	1.22	0.39	0.70
AGE	-0.86	0.05	-16.07	0.00
$CAT12\_Grade$	-41.27	20.76	-1.99	0.05
ScanLag	0.09	0.16	0.55	0.58
BMI	0.01	0.10	0.12	0.91

Standard errors: OLS; Continuous predictors are mean-centered and scaled by 1 s.d. The outcome variable remains in its original units.

## c Path with BMI

Observations	201
Dependent variable	$\operatorname{sum} \operatorname{ADL}$
Type	OLS linear regression

F(8,192)	10.32
$\mathbb{R}^2$	0.30
$Adj. R^2$	0.27

	Est.	S.E.	t val.	p
(Intercept)	0.44	2.06	0.22	0.83
PosRelations7	-0.03	0.01	-2.48	0.01
Sample	-0.02	0.31	-0.06	0.95
Race_Di	-0.56	0.19	-2.95	0.00
Sex	0.07	0.17	0.38	0.70
AGE	0.02	0.01	3.07	0.00
CAT12_Grade	1.20	2.94	0.41	0.68
ScanLag	-0.09	0.02	-4.05	0.00
BMI	0.06	0.01	4.43	0.00

Observations	201
Dependent variable	ChronicConditions
Type	OLS linear regression

F(8,192)	11.14
$\mathbb{R}^2$	0.32
$Adj. R^2$	0.29

	Est.	S.E.	t val.	p
(Intercept)	-1.70	3.72	-0.46	0.65
PosRelations7	-0.02	0.02	-1.02	0.31
Sample	0.16	0.55	0.29	0.77
Race_Di	-0.06	0.34	-0.18	0.86
Sex	0.64	0.31	2.04	0.04
AGE	0.10	0.01	7.17	0.00
CAT12_Grade	-3.92	5.31	-0.74	0.46
ScanLag	-0.06	0.04	-1.41	0.16
BMI	0.09	0.03	3.50	0.00

#### Childhood Social Class

Participants answered via self-report how they compared to other families in terms of finances growing up. Participants responded a lot better off, somewhat better off, a little better off, same as average family, a little worse off, somewhat worse off, a lot worse off, or I don't know. Participants also responded via self-report whether their family was on Welfare/ADC growing up (0 = no, 1 = Yes). Below, we z-score each of these variables and sum them for a composite measure of childhood social class.

#### a Path with Social Class

Observations	175 (26 missing obs. deleted)
Dependent variable	Kaufmann_BAG
Type	OLS linear regression

F(8,166)	33.36
$\mathbb{R}^2$	0.62
$Adj. R^2$	0.60

	Est.	S.E.	t val.	p
(Intercept)	70.98	17.29	4.10	0.00
PosRelations7	0.08	0.09	0.90	0.37
Sample	-2.38	2.38	-1.00	0.32
Race_Di	1.94	1.51	1.29	0.20
Sex	0.65	1.32	0.50	0.62
AGE	-0.90	0.06	-15.99	0.00
CAT12_Grade	-34.54	24.17	-1.43	0.15
ScanLag	-0.24	0.57	-0.42	0.67
ChildhoodSocClass	1.75	0.60	2.90	0.00

## c Path with Social Class

Observations	175 (26 missing obs. deleted)
Dependent variable	$\operatorname{sum} \operatorname{ADL}$
Type	OLS linear regression

F(8,166)	4.83
$\mathbb{R}^2$	0.19
$Adj. R^2$	0.15

	Est.	S.E.	t val.	р
(Intercept)	4.83	2.30	2.10	0.04
PosRelations7	-0.03	0.01	-2.60	0.01
Sample	0.34	0.32	1.08	0.28
Race_Di	-0.60	0.20	-2.99	0.00
Sex	0.17	0.18	0.99	0.32
AGE	0.03	0.01	4.35	0.00
CAT12_Grade	-3.39	3.21	-1.06	0.29
ScanLag	-0.12	0.08	-1.56	0.12
ChildhoodSocClass	-0.14	0.08	-1.81	0.07

Standard errors: OLS; Continuous predictors are mean-centered and scaled by 1 s.d. The outcome variable remains in its original units.

Observations	175 (26 missing obs. deleted)
Dependent variable	ChronicConditions
Type	OLS linear regression

F(8,166)	7.98
$\mathbb{R}^2$	0.28
$Adj. R^2$	0.24

	Est.	S.E.	t val.	p
(Intercept)	6.50	4.41	1.47	0.14
PosRelations7	-0.02	0.02	-0.88	0.38
Sample	0.79	0.61	1.30	0.19
Race_Di	-0.22	0.38	-0.57	0.57
Sex	0.74	0.34	2.21	0.03
AGE	0.09	0.01	6.42	0.00
CAT12_Grade	-12.59	6.16	-2.04	0.04
ScanLag	0.17	0.15	1.15	0.25
ChildhoodSocClass	-0.28	0.15	-1.86	0.07

## Income

Participants self-reported their various income sources. We used the variable representing  $household\ total$  income from wage, pension, social security, and other sources.

#### a Path with Income

Observations	195 (6 missing obs. deleted)
Dependent variable	Kaufmann_BAG
Type	OLS linear regression

F(8,186)	36.63
$\mathbb{R}^2$	0.61
$Adj. R^2$	0.60

	Est.	S.E.	t val.	p
(Intercept)	76.64	14.41	5.32	0.00
PosRelations7	0.03	0.08	0.34	0.73
Sample	-1.69	2.15	-0.79	0.43
Race_Di	4.12	1.45	2.83	0.01
Sex	-0.34	1.23	-0.28	0.78
AGE	-0.87	0.05	-16.40	0.00
CAT12_Grade	-39.65	20.71	-1.91	0.06
ScanLag	0.01	0.21	0.05	0.96
Income	-0.00	0.00	-3.09	0.00

Standard errors: OLS; Continuous predictors are mean-centered and scaled by 1 s.d. The outcome variable remains in its original units.

## c Path with Income

Observations	195 (6 missing obs. deleted)
Dependent variable	$\operatorname{sum} \operatorname{ADL}$
Type	OLS linear regression

F(8,186)	7.51
$\mathbb{R}^2$	0.24
$Adj. R^2$	0.21

	Est.	S.E.	t val.	p
(Intercept)	2.91	2.16	1.34	0.18
PosRelations7	-0.03	0.01	-2.42	0.02
Sample	0.20	0.32	0.63	0.53
Race_Di	-0.59	0.22	-2.70	0.01
Sex	0.07	0.18	0.35	0.72
AGE	0.03	0.01	3.40	0.00
CAT12_Grade	0.13	3.11	0.04	0.97
ScanLag	-0.11	0.03	-3.45	0.00
Income	-0.00	0.00	-2.05	0.04

Observations	195 (6 missing obs. deleted)
Dependent variable	ChronicConditions
Type	OLS linear regression

F(8,186)	8.76
$\mathbb{R}^2$	0.27
$Adj. R^2$	0.24

	Est.	S.E.	t val.	р
(Intercept)	2.67	3.74	0.71	0.48
PosRelations7	-0.02	0.02	-0.93	0.35
Sample	0.29	0.56	0.52	0.60
Race_Di	-0.44	0.38	-1.17	0.24
Sex	0.58	0.32	1.81	0.07
AGE	0.09	0.01	6.84	0.00
CAT12_Grade	-5.47	5.38	-1.02	0.31
ScanLag	0.02	0.05	0.35	0.73
Income	-0.00	0.00	-1.74	0.08

#### Mental Health Diagnoses

Participants answered several questions on symptoms for Panic Disorder, Depression, or Anxiety on a commonly-used questionnaire (Wang et al., 2000). Based on their responses, they received a score of 0 if they did not meet criteria for a diagnosis and a score of 1 if they did meet criteria. In this analysis, a Mental health Diagnosis composite variable was derived by summing all three variables.

#### a Path with Mental Health Diagnoses

Observations	197 (4 missing obs. deleted)
Dependent variable	Kaufmann_BAG
Type	OLS linear regression

F(8,188)	35.36
$\mathbb{R}^2$	0.60
$Adj. R^2$	0.58

	Est.	S.E.	t val.	p
(Intercept)	76.50	14.45	5.29	0.00
PosRelations7	-0.02	0.08	-0.20	0.84
Sample	-2.07	2.18	-0.95	0.34
Race_Di	3.37	1.43	2.35	0.02
Sex	1.02	1.23	0.83	0.41
AGE	-0.86	0.05	-16.06	0.00
CAT12_Grade	-41.81	20.93	-2.00	0.05
ScanLag	-0.06	0.21	-0.28	0.78
MentalHealthDx	-2.24	1.23	-1.83	0.07

Standard errors: OLS; Continuous predictors are mean-centered and scaled by 1 s.d. The outcome variable remains in its original units.

#### c Path with Mental Health Diagnoses

Observations	197 (4 missing obs. deleted)
Dependent variable	$\operatorname{sum} \operatorname{ADL}$
Type	OLS linear regression

F(8,188)	8.14
$\mathbb{R}^2$	0.26
$Adj. R^2$	0.23

	Est.	S.E.	t val.	p
(Intercept)	2.19	2.11	1.04	0.30
PosRelations7	-0.02	0.01	-1.93	0.06
Sample	0.12	0.32	0.39	0.70
Race_Di	-0.75	0.21	-3.60	0.00
Sex	0.07	0.18	0.41	0.68
AGE	0.03	0.01	3.72	0.00
CAT12_Grade	0.42	3.05	0.14	0.89
ScanLag	-0.10	0.03	-3.07	0.00
MentalHealthDx	0.48	0.18	2.69	0.01

Observations	197 (4 missing obs. deleted)
Dependent variable	ChronicConditions
Type	OLS linear regression

F(8,188)	9.94	
$\mathbb{R}^2$	0.30	
$Adj. R^2$	0.27	

	Est.	S.E.	t val.	p
(Intercept)	0.51	3.61	0.14	0.89
PosRelations7	-0.00	0.02	-0.17	0.86
Sample	0.18	0.55	0.33	0.74
Race_Di	-0.65	0.36	-1.81	0.07
Sex	0.54	0.31	1.76	0.08
AGE	0.10	0.01	7.35	0.00
$CAT12\_Grade$	-4.11	5.24	-0.79	0.43
ScanLag	0.04	0.05	0.70	0.49
MentalHealthDx	0.97	0.31	3.16	0.00

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