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Cohort Profile Update: High School and Beyond

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Title

Cohort Profile Update: High School and Beyond

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Abstract

Not applicable.

Key features

- High School and Beyond (HS&B:80) has followed a diverse, nationally representative probability sample of 26 830 Americans from high school (in 1980) through midlife (in 2021).
- Survey, administrative, and biomarker data make HS&B:80 valuable for studying the social and biological pathways through which education and early life factors shape later life cognition and health.
- Since the original Cohort Profile, HS&B:80 (1) completed a 2021 data collection round; (b) developed biomarkers reflecting ADRD neuropathology, inflammation, endothelial function, blood-brain barrier disfunction, essential and toxic metals, systemic aging, genetic risk for ADRD, and the oral microbiome; and (c) linked to consumer credit records.
- Of 24 530 surviving panelists, 13 980 participated in the 2021 survey (at age ~60); among survey participants, 4 360 provided blood and 6 260 provided saliva. Among all panelists, 22 340 could be linked to consumer credit records.
- Information about accessing HS&B:80 data is described at www.edshareproject.org.

The original cohort

In 1980, HS&B:80 panelists were selected through a two-stage stratified probability sampling procedure with American public and private high schools as the first stage units and sophomore and senior students as the second stage units.[1] In general, schools were selected with probability proportional to enrollment in a stratified way across regions and urban/rural areas. Within each school, 36 seniors and 36 sophomores were randomly selected (class size permitting). In the end, the achieved sample in 1980 included 1 020 schools and 58 270 students. From that initial sample of 58 270 students in 1980, a random subset of 26 830 students—including 14 830 sophomores and 12 000 seniors—has been re-interviewed on multiple occasions since 1982. All surviving panel members were re-contacted in 1982, 1984, 1986, and 2021; sophomores were also re-contacted in 1992 and 2014; and seniors were also re-contacted in 2015.

HS&B:80 surveys have had remarkably high response rates—ranging from ~90% in the 1980s to ~61% in the 2015 follow-up;[2,3] see Tables 1 and 2 of Grodsky et al.[1] for more details. Carefully constructed cross-sectional and longitudinal sampling weights allow researchers to produce statistical estimates that reflect the population from which students were selected.

The 1980 student questionnaires gathered data on educational experiences; educational and occupational plans and aspirations; health and disability; demographic attributes; family socioeconomic background; students' friendships, and more. They also included standardized multiple-choice assessments of reading, vocabulary, and math. The 1980 survey wave also included a parent survey, a school administrator survey, and a teacher survey. Follow-up surveys of students conducted in the 1980s and in 1992 gathered information about cohort members' educational, employment, and family statuses, activities, and transitions. The 2014 and 2015 surveys—conducted when most sample members were in their early 50s—gathered midlife data on health, work, family, finances, and educational outcomes.

Why has there been a change of focus?

Since the original Cohort Profile[1] was published, fieldwork on the 2021 follow up was completed; the focus of HS&B:80 has changed to include an expanded set of biomarkers; and the project has linked records to consumer credit files.

Data Collection in 2021. The 2021 HS&B:80 follow-up—completed after publication of our original Cohort Profile[1] and conducted when most sample members were approaching age 60—gathered objective data on cognitive functioning and subjective cognitive concerns; health conditions; work; finances; family; COVID 19; and science knowledge. See Table 4 of Grodsky et al.[1] for more details. The follow-up consisted of (1) a 40-minute telephone, web, or (in rare cases) paper survey and (2) an in-person home health visit at which anthropometric measures were gathered and blood and saliva were collected.

Table 1 below describes the contents of the 2021 HS&B:80 surveys and assessments (by mode); the measures constructed from blood and saliva samples; and the number of cases completing surveys, home visits, blood sample donations, and saliva sample donations.

***** TABLE 1 HERE *****

Expanded Biomarkers. Whereas the original Cohort Profile[1] listed only planned blood-based measures of Alzheimer's disease related pathophysiology — including Aβ42/Aβ40, phosphorylated tau 181 (p-tau

181) , neurofilament light (NfL) chain, and glial fibrillary acidic protein (GFAP)—HS&B:80 now includes an extensive set of markers of other factors related to health status and biological aging processes that may both contribute to dementia risk and interact with ADRD pathophysiology.

Adding these new biomarkers greatly enhances the project's capacity to shed light on the social and biological pathways through which early life factors (especially education) shape cognitive functioning and ADRD risk in later adulthood. With this change in focus, the data can be used to model the impact of early life factors on vascular, inflammatory, microbiome, and other processes; how those processes in turn shape cognitive functioning; and how those processes interact with ADRD processes to shape risk of mild cognitive impairment (MCI) and, ultimately, dementia.

This change in focus radically expands HS&B:80's utility for research on the biological pathways through which early life factors shape any number of later life health and cognitive outcomes.

Consumer Credit Records. HS&B:80 records also have been or soon will be linked to a variety of administrative and commercial data sources, including secondary and post-secondary school enrollments and transcripts; mortality records; real estate transaction records; voter registration and turnout data; state tumor registries; and pharmacy records. These administrative data are available for analyses, although the way they can be accessed varies across sources. See Table 5 of Grodsky et al.[1] for more details.

Whereas the original Cohort Profile[1] listed the administrative records to which HS&B:80 records have been linked, below we provide results from analyses of HS&B:80 data linked to information obtained from consumer credit records provided by Experian. These records – available in frequent intervals across nearly two decades for about 91% of the cohort – dramatically expand HS&B:80's utility for research on relationships between financial resources and constraints and later life health and cognition.

What will be the new areas of research?

The HS&B:80/21 blood biomarkers that we described in our original Cohort Profile[1] assess the processes related to the amyloid (A), tau (T), and neurodegenerative (N) cascade that define the main pathological features of ADRD; these are critical for the field's understanding of the pathophysiology of cognitive aging and dementia. However, there is growing evidence that *other factors* not necessarily specific to the brain and *biological aging processes* may both contribute to dementia risk and interact with ADRD pathophysiology.

Pathological Factors. We selected biomarkers that may be relevant to cognitive function throughout the lifespan and are of increasing focus to the field, especially in samples outside of clinical settings. In doing so, we integrated established and novel biomarkers reflecting vascular and inflammatory injury to allow researchers to probe their independent impact on cognitive outcomes and the degree to which they interact with A/T/N biomarkers.

Biological Aging. People of the same chronological age experience very different rates of bodily "weathering," known as biological aging. Aging-related dysregulation of metabolic, vascular, and immune function contributes to ADRD risk.[4–6] However, ADRD is not an inevitable consequence of aging, and risk varies across people who are the same chronological age. Better understanding of the molecular mechanisms through which aging affects risk of ADRD could provide insights into disease risk and the identification of potential modifiable preventative targets. Research has linked differences in the pace of biological aging with differences in brain structure, cognitive functioning, and dementia. Accelerated biological aging is associated with risk of ADRD;[8,9] importantly, the strength of those associations may vary across racial/ethnic and socioeconomic groups.[10]

Who is in the cohort?

The original and full HS&B:80 cohort included 26 820 high school sophomores and seniors selected from American public and private high schools; see Grodsky et al.[1] for more details. The first column of Table 2 describes the demographic, spatial, socioeconomic, and educational attributes of sample members in 1980.

The subsequent columns of Table 2 provide parallel information about sample members who responded in 2021; who provided a blood sample in 2021; who provided a saliva sample in 2021; and for whom consumer credit records could be obtained. Women; non-Hispanic whites; and people with better educational outcomes were more likely to participate in the several components of the 2021 follow up. Although 91% of the cohort could be linked to consumer credit records, those who could be linked are also somewhat more likely to be female; White; and with better educational outcomes.

***** TABLE 2 HERE *****

What has been measured?

In addition to ADRD markers, HS&B:80 now includes an extensive set of peripheral biological aging markers that may both contribute to dementia risk and interact with ADRD pathophysiology; it also includes extensive measures derived from consumer credit records. These biomarkers and measures are listed below, and most are included in Tables 3 and 4.

***** TABLE 3 HERE *****

***** TABLE 4 HERE *****

ADRD Neuropathology. Our measures of neurodegeneration along the A/T/N cascade include Aβ42/ Aβ40 (A), phosphorylated tau at threonine 181 (T), neurofilament light chain (N), and glial fibrillary acidic protein.

Pathological Factors. We added new assays that reflect cognition-relevant biological processes. Among these, as shown in Table 3, are: (1) inflammatory markers potentially related to vascular disease and ADRD, estimated through cytokine levels, transforming growth factor-β [TGF-B], soluble urokinase plasminogen activator receptor [suPAR], and the soluble receptor for advanced glycation end-products [sRAGE]; (4) markers of endothelial function, including vascular endothelial growth factor [VEGF-D], placental growth factor [PlGF], and basic fibroblast growth factor [BfGF]; (5) markers of blood-brain barrier dysfunction, including D Dimer; and (1) hemoglobin A1c, an index of prediabetes and untreated diabetes. Other assays completed but not described in Table 3 include C-reactive protein; fibrinogen; blood levels of various metals; and 16s sequencing of the oral microbiome.

Biological Aging. We also added measures of biological changes at the cellular level (e.g., DNA methylation) that occur with aging and that are modifiable causes of many chronic diseases, including ADRD. The biological aging clocks we will construct include – but are not limited to – (1) the GrimAge clock; (2) the DunedinPACE pace of aging measure; (3) the Hannum clock; (4) the Horvath clock; (5) PhenoAge; (6) TAME-BA; and (7) a panel of inflammatory markers allowing quantification of aging-related inflammation, known as “inflammaging.”

Consumer Credit. Consumer credit records from Experian – available for about 91% of HS&B:80 sample members who survived to 2021 – provides snapshots of sample members financial circumstances, including credit scores; estimated income; indicators of bankruptcy proceedings within the preceding 24 months; indicators of medical collections activities; total debt; credit card debt; mortgage debt; and student debts (excluding loans in deferment). Although consumer credit records from 2004 through 2023 were linked to the sample, the results described below are based only on December 2023 records.

What has it found? Key findings and publications

Table 3 describes the distributions of selected HS&B:80 biomarkers from 2021, separately by race/ethnicity and education (Table 3); by secondary school quality (Table 4); and by midlife cognitive functioning (Table 4).

In general, Tables 3 and 4 show that non-Hispanic whites; people with more completed schooling; people who went to higher quality secondary schools (in the metric of "academic press"[11]); and people with higher levels of cognitive functioning as ascertained in 2021 may have more advantageous levels of these biomarkers. This is true for markers of ADRD neuropathology, inflammation, endothelial function, blood-brain barrier disfunction, and diabetes. However, the strength of these associations varies quite a bit across markers.

Table 5 describes the distributions of selected HS&B:80 consumer credit variables as of December 2023, separately by race/ethnicity and education. Credit scores and estimated incomes are higher among Whites and people with more completed schooling; within levels of completed schooling, Whites tend to have better credit scores and higher income. For example, although mean credit scores rise with additional completed schooling for all racial/ethnic groups, Black sample members with college degrees have lower mean credit scores than White sample members who never attended college. Likewise, sample members' chances of experiencing medical collection activity was lowest among Whites and among people with more completed schooling.

As shown in the lower half of Table 5, different forms of debt are associated with race/ethnicity and educational attainment in different ways. In most cases, White people and those with more schooling have more debt – reflecting greater access to credit and higher rates of home ownership. For example, average levels of mortgage debt are substantially higher among people with more completed schooling.

***** TABLE 5 HERE *****

What are the main strengths and weaknesses?

The design and content of HS&B:80 make it invaluable for studying the social and biological pathways through which education and early life factors are embodied biologically to shape later-life cognition and health. The newly added biomarker data make HS&B:80 a key resource for understanding how a broad set of physiological and other processes mediate the effects of education on cognitive and health outcomes in a community-based, diverse, and representative national sample.

Beyond being among just a few prospective U.S. cohort studies that have followed a large, diverse, representative sample of people from adolescence through later adulthood—and beyond the strengths noted in the original Cohort Profile—HS&B:80 has other strengths: (1) The set of blood biomarkers described above are not featured in any other nationally-representative U.S. cohort followed prospectively across the life course; (2) the volume of blood collected in 2021 means that most of it is frozen awaiting future assays (including those not yet developed); and (3) HS&B:80 is among the first large U.S. cohort studies to be linked to many years' worth of consumer credit records.

One weakness of HS&B:80 stems from its being a large, diverse, national, community-based cohort: Panelists were observed at home in 2021—either by telephone or the internet—which constrained the physical and cognitive assessments that could be performed. Another weakness is that we lack "gold standard" ADRD biomarkers that might be collected from cerebrospinal fluid, molecular PET scanning, or brain autopsies; this is probably an insurmountable weakness given the size of this community-based cohort. Still another weakness—to be rectified in the future—is that blood biomarkers were collected at the same time as cognitive and health outcomes were measured; planned future follow-ups of the HS&B:80 cohort will permit understanding how *changes* in biomarkers relate to *changes* in cognitive functioning and health. Finally, the original Cohort Profile explained some minor weaknesses of HS&B:80's initial sampling frame and population coverage.

Can I get hold of the data? Where can I find out more?

Survey data and documentation through the 2014-2015 follow ups are available to qualified researchers for research purposes at no cost through NCES's Restricted-use License Program; see https://nces.ed.gov/pubsearch/licenses.asp.

Blood biomarker data will be available through the Global Alzheimer's Association Interactive Network (GAAIN; see http://gaain.org) or a similar venue. A unique and anonymous code will be used to link sample members' blood biomarker data to their survey information at NCES; only NCES will hold the crosswalk between these data files.

See the original Cohort Profile and www.edshareproject.org for more details, and send email inquiries to info@edshareproject.org.

Ethics approval

The protocols for the 2021 wave of HS&B:80 data collection—including the collection of biomarkers—were reviewed and approved by the Institutional Review Boards of the University of Minnesota (approval STUDY00009650) and NORC at the University of Chicago (approval 21-02-148).

Author contributions

All authors were coleaders of the project to design and implement the 2021 wave of HS&B:80 fieldwork and its biomarker components; all are recipients of funding support for that effort. All contributed to drafting and editing this manuscript. Author Warren acts as guarantor for the article.

Supplementary data

Not applicable.

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Note that this manuscript has been subject to disclosure review and has been approved by the U.S. Department of Education's Institute for Education Sciences in line with the terms of the corresponding author's HS&B:80 restricted use data agreement.

Conflict of interest

None declared.

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Table 1. Survey Participation and Content, 2021 Follow-Up, by Mode

	Phone Survey (n=6270)	Web Survey (n=8930)	Paper Survey (n=620)	Home Visit Sample (n=4830)	Blood Sample (n=4360)	Saliva Sample (n=6260)
Education						
Educational attainment	✓	✓	✓			
Post-secondary institution, major field	✓	✓	✓			
Cognitive Functioning & Impairment; Biomarkers for ADRD Risk						
Immediate recall (CERAD[2] word list)	✓					
Semantic fluency (animal naming)	✓					
Phonemic fluency (F task)	✓					
Delayed recall (CERAD[2] word list)	✓					
Working memory (digit span, forward & backward)	✓					
Memory & learning (verbal and visual paired associates)		✓				
Self-reported memory complaints (AD8[2])	✓	✓	✓			
APOE[2] e4 (from saliva or blood)					✓	✓
Markers of neuropathology (Aβ40, Aβ42, tau, NfL, p-tau 181, and GFAp from blood)					✓	
Markers of immunological response; prediabetes and untreated diabetes; inflammatory processes; endothelial function; blood-brain barrier dysfunction; blood lead levels; and systemic aging					✓	
Health						
Self-assessed overall adult health	✓	✓	✓			
Self-assessed overall childhood health	✓	✓	✓			
COVID-19 testing, infection, vaccination	✓	✓	✓		✓	
Pain	✓	✓	✓			
Cervical, colon, and breast cancer screening	✓	✓				
Self reported diagnoses of cancer, diabetes, hypertension, stroke, coronary heart disease, kidney disease, periodontal disease, and mental health condition	✓	✓	✓			
Opioid use	✓	✓	✓			
Height and weight	✓	✓	✓	✓		
Blood pressure, pulse				✓		
Hip, Waist circumference				✓		
Health risk behaviors (smoking, alcohol use)	✓	✓	✓			
Depression	✓	✓	✓			
Loneliness	✓	✓	✓			
Mortality; Cause of death (from National Death Index)						
Labor Market						
Labor force status, number of jobs	✓	✓	✓			
Industry and occupation	✓	✓	✓			
Income	✓	✓	✓			
Other measures						
Marital status	✓	✓	✓			
Science knowledge	✓	✓	✓			
Oral microbiome collection and sequencing				✓		✓

[1] Sample members were asked to complete either the telephone or web survey; those who refused were eventually offered the paper survey. All sample members completing telephone, web, or paper surveys were invited to complete a home health visit for anthropometric measures and blood and saliva collection; those refusing home health visits were mailed a saliva collection kit.

[2] CERAD=Consortium to Establish a Registry for Alzheimer's Disease; AD8=an eight items Alzheimer's Disease screener; APOE=Apolipoprotein E

NOTE: All sample sizes are rounded to the nearest 10 as per restricted-use data licensing requirements.

Table 2. Distributions of Demographic, Spatial, Socioeconomic, and Education Variables across Response Statuses, HS&B:80/21 Data Collection

	Unweighted (i.e., No Adjustment for Selective Attrition or Sample Design)										**Weighted** (to Adjust for Selective Attrition and Sample Design)									
	Full HS&B:80 Sample (n=26 820)		Survey Respondent in 2021 (n=13 980)		Provided Blood Sample in 2021 (n=4360)		Provided Saliva Sample in 2021 (n=6260)		Experian Sample (22 340)		Full HS&B:80 Sample (n=26 820)		Survey Respondent in 2021 (n=13 980)		Provided Blood Sample in 2021 (n=4360)		Provided Saliva Sample in 2021 (n=6260)		Experian Sample (n=22 340)	
	Avg or %	(sd)	Avg or %	(sd)	Avg or %	(sd)	Avg or %	(sd)	Avg or %	(sd)	Avg or %	(sd)	Avg or %	(sd)	Avg or %	(sd)	Avg or %	(sd)	Avg or %	(sd)
Gender																				
Male	48.6%		44.9%		44.7%		45.3%		46.4%		49.4%		47.6%		47.5%		47.5%		47.1%	
Female	51.4%		55.1%		55.3%		54.7%		53.6%		50.6%		52.4%		52.5%		52.5%		52.9%	
Race/Ethnicity																				
White	52.4%		57.3%		60.0%		58.9%		54.4%		72.3%		73.3%		72.7%		72.9%		74.9%	
Black	18.6%		16.9%		14.3%		15.6%		17.4%		11.6%		11.4%		12.2%		11.7%		10.6%	
Latinx	23.0%		20.7%		20.8%		20.3%		22.6%		10.9%		10.8%		10.6%		10.9%		10.2%	
Other	6.1%		5.1%		4.9%		5.2%		5.6%		5.2%		4.5%		4.5%		4.5%		4.2%	
Region in 1980																				
Northwest	21.8%		21.5%		19.9%		20.3%		22.2%		23.3%		22.1%		19.8%		21.1%		23.9%	
Midwest	33.6%		31.7%		30.6%		30.6%		32.9%		30.8%		30.9%		31.2%		30.3%		30.1%	
South	25.1%		27.1%		28.4%		27.6%		25.5%		27.7%		28.3%		30.2%		28.4%		28.2%	
West	19.6%		19.6%		21.1%		21.5%		19.4%		18.1%		18.7%		18.9%		20.2%		17.8%	
Location Type in 1980																				
Urban	26.0%		24.4%		24.0%		24.3%		25.3%		21.6%		21.7%		24.3%		22.7%		20.7%	
Suburban	48.0%		49.4%		50.1%		49.6%		48.9%		49.0%		49.2%		47.8%		48.4%		49.7%	
Rural	26.0%		26.2%		25.9%		26.1%		25.9%		29.4%		29.1%		27.8%		28.9%		29.6%	
Highest Parental Education																				
High School or Less	44.6%		41.1%		36.8%		38.5%		43.5%		41.9%		41.0%		41.0%		40.7%		40.5%	
Some College	29.5%		30.0%		30.3%		30.3%		29.7%		30.8%		31.5%		31.6%		32.1%		31.1%	
BA or More	25.9%		28.8%		32.8%		31.1%		26.8%		27.3%		27.5%		27.5%		27.2%		28.4%	
Educational Attainment																				
High School or Less	18.6%		18.6%		15.5%		16.9%		17.6%		20.4%		24.0%		23.6%		23.5%		19.3%	
Some College	38.3%		38.3%		36.3%		36.9%		38.2%		38.5%		40.6%		40.6%		40.9%		38.5%	
BA or More	43.1%		43.1%		48.2%		46.2%		44.2%		41.1%		35.5%		35.8%		35.6%		42.2%	
GPA in 12th Grade	2.86	(0.72)	2.95	(0.71)	3.01	(0.71)	2.99	(0.71)	2.89	(0.71)	2.85	(0.72)	2.87	(0.72)	2.85	(0.72)	2.87	(0.73)	2.89	(0.71)
Reading Test Score, Gr. 12	0.00	(1.00)	0.19	(0.99)	0.33	(0.98)	0.27	(0.99)	0.05	(0.99)	0.05	(0.99)	0.08	(0.98)	0.07	(0.98)	0.08	(0.97)	0.10	(0.98)
Math Test Score, Gr. 12	0.00	(1.00)	0.19	(0.99)	0.33	(1.01)	0.28	(1.00)	0.07	(0.99)	0.06	(0.98)	0.09	(0.98)	0.07	(1.00)	0.09	(0.99)	0.12	(0.98)
Vocab. Test Score, Gr. 12	0.00	(1.00)	0.18	(0.99)	0.31	(0.98)	0.26	(0.98)	0.05	(0.99)	0.05	(0.98)	0.08	(0.98)	0.07	(0.97)	0.08	(0.97)	0.10	(0.97)

NOTE: Weighted analyses for the full sample (n=26 820) use the constructed weight RAWWT. Weighted analyses for 2021 survey, blood, and saliva participants uses the constructed weight CROSS_SECTIONAL_WEIGHT. All sample sizes are rounded to the nearest 10 as per restricted-use data licensing requirements.

Table 3. Distributions of Selected Biomarkers, by Education and Race/Ethnicity, 2021 HS&B:80 Data Collection

	White (n=2620)						**Black (n=630)**						**Latinx (n=910)**					
	High School or Less (n=360)		Some College, No BA (n=840)		Bachelors or More (n=1420)		High School or Less (n=110)		Some College, No BA (n=270)		Bachelors or More (n=250)		High School or Less (n=180)		Some College, No BA (n=410)		Bachelors or More (n=320)	
	Mean	(sd)	Mean	(sd)	Mean	(sd)	Mean	(sd)	Mean	(sd)	Mean	(sd)	Mean	(sd)	Mean	(sd)	Mean	(sd)
ADRD neuropathology																		
AB42/AB40	0.06	(0.01)	0.06	(0.01)	0.06	(0.01)	0.06	(0.02)	0.06	(0.01)	0.06	(0.02)	0.06	(0.01)	0.06	(0.02)	0.06	(0.01)
GFAP	61.15	(33.50)	63.57	(32.31)	69.72	(35.41)	51.60	(29.90)	73.13	(47.38)	77.65	(41.08)	61.53	(32.09)	59.29	(38.80)	65.67	(34.69)
NfL	14.59	(8.92)	13.45	(7.44)	13.27	(7.10)	10.14	(9.20)	11.20	(8.44)	9.57	(6.17)	14.35	(8.24)	13.69	(8.53)	12.03	(5.34)
p-Tau 181	19.16	(8.45)	18.04	(8.48)	17.67	(8.08)	16.72	(8.29)	16.40	(7.57)	16.42	(8.08)	19.29	(8.90)	16.95	(7.86)	17.50	(8.03)
Inflammation																		
IL-6	4.53	(6.51)	4.78	(6.02)	3.72	(4.71)	4.76	(2.64)	6.48	(12.44)	4.81	(4.30)	5.44	(8.09)	4.90	(15.40)	4.68	(4.70)
IL-10	3.27	(1.26)	3.28	(1.79)	3.14	(1.84)	3.47	(1.34)	3.18	(1.33)	3.16	(2.02)	3.44	(1.37)	3.16	(1.46)	2.92	(1.06)
IL-1RA	587	(334)	580	(383)	490	(285)	544	(290)	564	(339)	516	(287)	548	(274)	512	(264)	541	(307)
TNF RII	3163	(955)	3142	(950)	2928	(859)	2756	(825)	2900	(832)	2986	(781)	3287	(1161)	2870	(808)	2934	(830)
TGF-B (x 1000)	58.69	(16.11)	57.93	(13.99)	56.68	(14.34)	72.00	(23.73)	60.77	(16.83)	61.10	(14.03)	59.82	(15.49)	58.66	(14.00)	58.09	(12.97)
suPAR	2572	(687)	2421	(665)	2291	(566)	2271	(589)	2306	(684)	2320	(589)	2653	(567)	2295	(676)	2368	(657)
sRAGE	704	(308)	737	(325)	746	(309)	453	(351)	526	(342)	452	(289)	671	(296)	666	(311)	767	(391)
Endothelial Function																		
VEGF-D	600	(228)	597	(234)	603	(212)	722	(407)	634	(309)	564	(261)	588	(231)	598	(226)	574	(260)
PlGF	29.76	(10.29)	29.25	(12.67)	28.09	(8.05)	26.96	(6.51)	25.01	(6.30)	24.35	(5.50)	27.26	(6.77)	28.14	(6.26)	27.77	(7.19)
bFGF	1.07	(1.10)	0.91	(0.97)	0.91	(1.02)	0.77	(0.81)	0.94	(1.01)	1.00	(1.36)	1.19	(1.20)	0.98	(1.04)	0.81	(0.83)
Blood-Brain Barrier Disfunction																		
D-dimer (x 1000)	583	(753)	663	(940)	678	(948)	571	(793)	773	(1034)	826	(1231)	550	(654)	458	(575)	592	(926)
Diabetes																		
Hemoglobin A1C	5.78	(0.83)	5.67	(0.64)	5.64	(0.68)	6.14	(0.79)	6.02	(0.77)	5.91	(0.65)	5.94	(0.84)	5.91	(0.85)	5.98	(0.97)

NOTE: Analyses weighted by F6WTBLOOD. All values more than four standard deviations from their mean have been censored. All sample sizes are rounded to the nearest 10 as per restricted-use data licensing requirements.

Table 4. Distributions of Selected Biomarkers, by Secondary School Quality and Midlife Cognitive Functioning, 2021 HS&B:80 Data Collection

	Secondary School Quality (Academic Press Measure)						**Midlife Cognitive Functioning** (Global IRT Score)					
	Bottom Third of Distribution (n=1310)		**Middle** Third of Distribution (n=1270)		**Top** Third of Distribution (n=1720)		**Bottom** Third of Distribution (n=930)		**Middle** Third of Distribution (n=1160)		**Top** Third of Distribution (n=320)	
	Mean	(sd)	Mean	(sd)	Mean	(sd)	Mean	(sd)	Mean	(sd)	Mean	(sd)
ADRD neuropathology												
AB42/AB40	0.06	(0.01)	0.06	(0.01)	0.06	(0.01)	0.06	(0.01)	0.06	(0.01)	0.06	(0.01)
GFAP	63.65	(36.09)	67.02	(35.73)	65.63	(34.44)	60.91	(34.98)	64.11	(34.47)	70.97	(35.75)
NfL	13.58	(7.83)	13.15	(7.63)	13.27	(7.93)	14.02	(9.36)	12.67	(6.87)	12.98	(6.70)
p-Tau 181	18.09	(8.61)	18.31	(8.51)	17.57	(7.66)	18.80	(9.46)	17.86	(8.42)	17.02	(6.68)
Inflammation												
IL-6	5.09	(7.89)	4.44	(8.18)	4.18	(4.38)	5.80	(8.21)	4.50	(8.52)	3.63	(3.34)
IL-10	3.24	(1.44)	3.25	(1.81)	3.14	(1.68)	3.49	(1.72)	3.10	(1.43)	3.11	(1.78)
IL-1RA	553	(314)	545	(326)	522	(337)	594	(331)	555	(367)	496	(280)
TNF RII	3031	(914)	3104	(968)	2964	(862)	3244	(1075)	2969	(825)	2931	(878)
TGF-B (x 1000)	60.10	(17.06)	58.05	(14.88)	57.76	(15.02)	59.86	(18.27)	59.01	(14.42)	57.30	(14.70)
suPAR	2436	(676)	2389	(638)	2336	(622)	2563	(747)	2358	(626)	2274	(568)
sRAGE	685	(335)	683	(328)	718	(332)	626	(350)	701	(338)	746	(303)
Endothelial Function												
VEGF-D	625	(271)	582	(219)	607	(241)	613	(282)	615	(254)	600	(223)
PlGF	28.47	(11.62)	28.12	(7.41)	28.43	(8.92)	28.87	(12.91)	28.10	(8.72)	28.34	(8.19)
bFGF	0.97	(1.03)	0.97	(0.98)	0.91	(1.04)	1.01	(1.08)	0.97	(1.00)	0.90	(0.98)
Blood-Brain Barrier Disfunction												
D-dimer (x 1000)	650	(933)	668	(919)	661	(885)	644	(928)	689	(930)	662	(933)
Diabetes												
Hemoglobin A1C	5.82	(0.79)	5.74	(0.74)	5.72	(0.78)	5.93	(0.87)	5.77	(0.75)	5.60	(0.60)

NOTE: Analyses weighted by F6WTBLOOD. All values more than four standard deviations from their mean have been censored. All sample sizes are rounded to the nearest 10 as per restricted-use data licensing requirements.

Table 5. Distributions of Consumer Credit and Debt Measures, by Education and Race/Ethnicity, HS&B:80

	White (n=12 080)						Black (n=3830)						Latinx (n=4990)					
	High School or Less (n=1790)		Some College, No BA (n=5280)		Bachelors or More (n=5010)		High School or Less (n=630)		Some College, No BA (n=1990)		Bachelors or More (n=1210)		High School or Less (n=1040)		Some College, No BA (n=2640)		Bachelors or More (n=1310)	
	Mean	(sd)	Mean	(sd)	Mean	(sd)	Mean	(sd)	Mean	(sd)	Mean	(sd)	Mean	(sd)	Mean	(sd)	Mean	(sd)
Credit score	727.7	(92.9)	745.1	(88.8)	782.9	(68.3)	640.8	(95.5)	660.7	(102.7)	701.9	(102.3)	690.9	(99.9)	714.7	(97.6)	757.9	(86.0)
Estimated income (in $1000s)	102.9	(68.4)	121.3	(75.0)	183.1	(111.4)	63.8	(43.4)	77.9	(54.6)	120.0	(88.7)	82.9	(54.8)	101.6	(71.1)	163.1	(108.5)
Any medical collections	4.8%		2.7%		0.9%		9.6%		5.5%		5.9%		5.7%		6.3%		1.4%	
Any debt																		
Total	86.8%		91.4%		96.0%		76.5%		86.8%		93.9%		85.1%		90.3%		95.7%	
Credit card	76.0%		83.5%		92.5%		56.4%		72.2%		85.5%		70.1%		79.6%		91.4%	
Credit card (30-180 days)	10.1%		10.2%		6.5%		16.9%		20.8%		19.9%		14.1%		13.2%		12.9%	
Mortgage	34.3%		42.0%		50.3%		26.9%		31.3%		48.7%		30.3%		40.7%		49.4%	
Student	3.3%		7.1%		9.1%		7.0%		11.9%		26.3%		4.3%		8.5%		13.4%	
Mean debt (among debtors)																		
Total (in $1000s)	82.86	(143.01)	105.67	(150.56)	177.91	(344.96)	69.37	(110.43)	93.10	(144.99)	180.17	(270.97)	73.33	(116.03)	130.57	(374.89)	182.71	(274.56)
Credit card (in $1000s)	7.47	(11.65)	8.76	(12.69)	10.89	(16.50)	7.85	(13.63)	8.35	(11.53)	12.57	(16.25)	7.32	(11.22)	9.27	(13.56)	10.85	(16.50)
Mortgage (in $1000s)	126.23	(130.57)	144.69	(135.14)	221.56	(366.22)	122.44	(124.15)	160.98	(133.57)	192.17	(215.29)	125.06	(123.01)	156.27	(161.11)	228.40	(250.77)
Student (in $1000s)	31.97	(36.34)	28.70	(35.30)	61.43	(80.57)	32.67	(33.81)	33.93	(43.39)	68.62	(72.16)	20.64	(30.43)	31.40	(42.33)	52.28	(53.48)
Mean debt (in full sample)																		
Total (in $1000s)	71.91	(136.14)	96.58	(146.95)	170.74	(339.74)	53.09	(100.97)	80.86	(138.73)	169.23	(266.11)	62.41	(110.18)	117.87	(358.28)	174.81	(271.12)
Credit card (in $1000s)	5.68	(10.65)	7.31	(12.04)	10.07	(16.13)	4.43	(10.95)	6.03	(10.48)	10.75	(15.66)	5.13	(9.97)	7.38	(12.66)	9.92	(16.06)
Mortgage (in $1000s)	43.26	(97.09)	60.76	(113.00)	111.35	(282.25)	32.89	(84.10)	50.31	(105.55)	93.65	(178.34)	37.94	(88.82)	63.65	(128.31)	112.77	(209.94)
Student (in $1000s)	1.06	(8.71)	2.03	(11.91)	5.57	(29.97)	2.30	(12.19)	4.03	(18.54)	18.08	(47.78)	0.89	(7.53)	2.68	(15.14)	6.98	(26.39)

NOTE: Analyses weighted by RAWWT. All sample sizes are rounded to the nearest 10 as per restricted-use data licensing requirements.

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