HHS Public Access

Author manuscript

Epidemiology. Author manuscript; available in PMC 2019 January 01.

Published in final edited form as:

Epidemiology. 2018 January ; 29(1): 151–159. doi:10.1097/EDE.0000000000000747.

Cognitive aging in black and white Americans: Cognition, cognitive decline, and incidence of Alzheimer disease dementia

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Abstract

Background—US-based studies have reported that older blacks perform worse than older whites on cognitive tests and have higher risk of Alzheimer disease dementia (AD). It is unclear whether these findings reflect differences in cognitive decline.

Methods—The Chicago Health and Aging Project followed individuals, 65+ years old (64% black, 36% white), for up to 18 years. Participants underwent triennial cognitive assessments; stratified randomized samples underwent assessments for AD. We compared black and white participants' cognitive performance, cognitive decline rate (N=7735), and AD incidence (N=2144), adjusting for age and sex.

Results—Black participants performed worse than white participants on the cognitive tests; 441 participants developed AD. Black participants' incident AD risk was twice that of whites (RR=1.9; 95% CI, 1.4–2.7), with 58 excess cases/1000 occurring among blacks (95% CI, 28 to 88). Among non-carriers of *APOE ε4*, blacks had 2.3 times the AD risk (95% CI,1.5–3.6), but among carriers, race was not associated with risk (RR=1.1; 95% CI, 0.6–2.0; $P_{interaction}$=0.05). However, cognitive decline was not faster among blacks: the black-white difference in 5-year change in global cognitive score was 0.007 standard unit (95% CI, −0.034 to 0.047). Years of education accounted for a sizable portion of racial disparities in cognitive level and AD risk, in analyses using a counterfactual approach.

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DATA AND STATISTICAL CODE SHARING: The statistical computing code and data used to generate the findings are available upon request. The text directly references the more novel components of the statistical code.

CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare.

Conclusions—The higher risk of AD among blacks may stem from lower level of cognitive test performance persisting throughout the observation period rather than faster rate of late-life cognitive decline. Disparities in educational attainment may contribute to these performance disparities.

Keywords

health status disparities; cognition; cognitive dysfunction; dementia; Alzheimer disease; cognitive aging; epidemiology; longitudinal study; epidemiologic methods; education; Apolipoprotein E4

BACKGROUND

In numerous studies of older adults in the United States, blacks have performed worse, on average, than whites on tests of cognitive function.[1,2] Furthermore, many studies have documented higher prevalence and incidence of dementia, including Alzheimer disease dementia (AD) among blacks than among whites.[3] Dementia is typically the consequence of decline in cognitive function, thus racial differences in cognition and dementia risk would be expected to be mirrored in faster longitudinal cognitive decline among blacks than among whites. Investigations of this question, however, have generated mixed results.[1,2,4–9] Although many of these studies recruited community participants, and several enrolled thousands of participants, most included few black participants, making it challenging to compare in detail the cognitive aging experiences of black and white older adults.

The population-based Chicago Health and Aging Project (CHAP) evaluated more than 10,000 older adults, 60% of whom were black, over a period spanning nearly two decades. We used data from CHAP to estimate racial differences in cognitive level and rate of cognitive decline, and to update previous estimates of racial differences in dementia risk. Compared with data used for these previous estimates, the updated data comprise over three times as many dementia assessments and dementia cases.[10] We also compared black and white participants' cognitive outcomes according to whether they carried an *APOE ε4* allele, a major genetic risk factor for AD. Finally, we quantified the extent to which racial differences in the outcomes were mediated by educational attainment.

METHODS

Study population

We conducted our study in CHAP,[10,11] a longitudinal, population-based cohort of older adults, 60% of whom self-identified as black and 40% as white, living in a geographically defined region on the south side of Chicago, Illinois. The study began in 1993 with a census of individuals aged 65 years or older. Of those identified, 6158 persons (79%) participated in a home interview. Additional people enrolled as they turned age 65 years, for a total of 10,802 participants through 2012. Participants were re-interviewed in 3-year cycles (eFigure 1). Each data collection cycle consisted of in-home interviews of all participants; a stratified Bernoulli sample of participants underwent detailed clinical evaluation for AD. The Rush University Medical Center Institutional Review Board approved the study.

Assessment of cognition, Alzheimer disease dementia, and other variables

Cognitive function—During their home interviews, all CHAP participants underwent a brief cognitive assessment comprising four tests of functions that typically decline in AD. The Symbol Digit Modalities Test[12] measures perceptual speed, a component of executive function; the East Boston Memory Test[13] generates measures of both immediate and delayed episodic memory; and the Mini-Mental State Examination[14] measures global cognitive function. For each of the four tests, we transformed the raw scores to *z* scores, using the baseline raw scores as the source of the standard deviation. Our analyses concerned three cognitive measures, all scaled to standard normal distribution to enhance comparisons across tests. The first, the global cognitive score, was created by first averaging the *z* scores from all four tests (composite *z* score) and then converting the resulting score to standard normal, using the baseline composite z score's mean and standard deviation.[15,16] The second, the episodic memory score, was the average of the *z* scores from the two components of the East Boston Memory Test, which we further transformed to standard normal as done for the global score. The third measure, the executive function score, was the *z* score from the Symbol Digit Modalities Test.

Dementia diagnosis—The clinical evaluations to diagnose dementia were confined to a large stratified random sample at each study cycle.[11] The sampling strategy for these evaluations has previously been described.[10,11,17,18] Briefly, from the surviving cohort determined to be free of AD at the previous cycle, sampling for clinical evaluation of incident AD in cycles 2 to 6 was stratified by age, race, sex, and change in cognitive function from the previous home interview, with participants selected randomly from all strata. Clinical examiners were blinded to the cognitive scores used for stratification. A team of clinicians led by a neurologist (Dr. Bennett or Aggarwal) conducted this evaluation, which included a structured medical history, neurologic examination, and a battery of 21 cognitive tests, 11 of which encompassed five domains of function.[10] Diagnosis of dementia required the study clinician's inference of loss of function in two or more cognitive domains. Diagnosis of AD followed the criteria for probable AD of the National Institute of Neurological and Communicative Disorders and Stroke-Alzheimer's Disease and Related Disorders Association.[19] Also classified as AD cases were persons who met these AD criteria and may have had another condition impairing cognition. Nearly all dementia cases diagnosed in CHAP (93%) met clinical criteria for AD alone or AD mixed with another dementia. (The eAppendix [Supplemental text: Dementia diagnosis] contains additional detail about the diagnostic process.)

Other variables—Participants self-reported their race and years of education. We constructed a composite index of childhood socioeconomic resources, based on paternal and maternal educational attainment, family financial status when the participant was a child, and paternal occupation prestige.[20] A higher score indicates more socioeconomic resources during childhood.

Statistical analyses

Cognitive level and decline—For each of the three cognitive measures from the four-test battery, we used generalized estimating equations (GEE) regression models with identity

links to compare black and white participants' baseline cognitive performance and rate of cognitive decline. These analyses were restricted to the 7,735 participants who had at least two cognitive assessments, for a total of 25,806 observations. The primary models included terms for race (black, white), baseline age (years), sex, time since baseline (years), and cross-products of time with age, sex, and race. The coefficient parameters of interest were those for race (the multivariable-adjusted mean difference between black and white participants' baseline cognitive scores) and for the time×race cross-product (the adjusted mean difference in rates of change in cognitive score). For reporting, we transformed differences in annual rate of cognitive change to differences in change over a 5-year interval.

Alzheimer disease dementia—We computed AD prevalence by race using the sampling weights. To compare the risk of incident AD between blacks and whites, we computed age- and sex-adjusted risk ratios and differences (excess cases per 1000), derived from the regression coefficients and variance-covariance matrix of logistic regression models, weighted for the stratified random sampling design, with variance parameters computed by jackknife repeated replication.[11,18] The incidence analyses included data from the 2,904 observations of 2,144 individuals who were selected for and underwent clinical evaluation. (See eAppendix [Supplemental text: Derivation of dementia risks, risk ratios and risk differences] for more detail.)

APOE genotype—We explored the extent to which the estimated associations above varied by carriership of the apolipoprotein (*APOE) ε4* allele (i.e., any *ε4* allele versus none), using cross-product of *ε4* carriership with race (or, in cognitive decline analyses, the three-way cross-product of *ε4* carriership, race and time). In the absence of notable effect modification by *ε4* carriership, we evaluated this variable as a source of confounding.

Exploration of mediation through education—On average, more formal education corresponds to better performance on cognitive tests and lower dementia risk,[21] although education does not appear to be associated with linear trajectory of cognitive decline.[2,22–26] Even if formal education influences cognitive aging, it does not determine race and therefore is not a source of confounding in estimates of race-cognitive aging associations. Rather, in the U.S., racial disparities in educational achievement arise from racially patterned socioeconomic circumstances (e.g., poverty, poor quality schools and limited educational resources), discrimination (limited opportunities, low teacher expectations and biased treatment), and institutional biases (e.g., mechanisms for funding public education, enforcement of compulsory education laws, segregation and tracking).[27] Thus, differences in cognitive performance, trajectory or dementia risk between blacks and whites could be mediated, in part, through racial patterns in educational attainment (eFigure 2). To quantify this mediation, we adopted a counterfactual approach[28] to estimate the effect of race on these outcomes transmitted through years of education (indirect effect) and the effect of race operating through pathways other than years of education (direct effect). For analyses of AD, we modified the approach to incorporate the sampling weights.

To generate valid estimates using this approach, there should be no unmeasured common causes of education ("mediator") and the cognitive outcome.[28] This assumption could be violated if childhood socioeconomic disadvantage (eFigure 2) influences educational

attainment and late-life cognitive outcomes. Thus, we incorporated the composite measure of childhood socioeconomic resources into our mediation analyses as a predictor of both educational attainment and the cognitive outcomes. (See eAppendix [Supplemental text: Mediation by education] for additional assumptions and detail.)

Selection via attrition—To probe the influence of differential post-enrollment attrition on our findings, we computed inverse probability-of-continuation weights[29] and applied them to analyses of race and decline in global cognitive score. (See supplement.)

RESULTS

White participants were, on average, 3 years older than black participants; the groups contained similar percentages of men (Table 1). In unadjusted analyses, black participants' baseline global cognitive scores were substantially lower than whites' scores; rates of change were not substantially different. Of the 2,144 participants selected for clinical evaluation and previously determined to be dementia-free, 474 developed dementia (22%); 441 were identified as having AD, of whom 275 were black.

Cognitive level and cognitive decline

In analyses adjusted for age and sex, the average baseline level of cognitive performance was lower among black participants (Table 2; eFigure 3). The difference in global cognitive score, −0.83 standard units (95% confidence interval [CI], −0.88 to −0.78), was equivalent to the difference in scores between participants who were 12 years apart in age at baseline. Baseline differences in the other two test scores, particularly the executive function score, were also large. With older baseline age, the racial differences in baseline global and episodic memory performance were more pronounced ($P_{interaction} < 0.001$).

By contrast, black participants' cognitive performance did not decline more rapidly (Table 2; eFigure 3), rather, rate of decline in global cognition differed little by race (difference in 5-year change, 0.007 standard units; 95% CI, −0.034 to 0.047). For context, the reference 5-year rate of decline in these analyses (i.e., decline among 75-year-old, white female participants) was 0.361 standard units. On the executive function test, blacks' scores actually declined more *slowly* than whites' scores (difference in 5-year change, 0.138 standard units; 95% CI, 0.110 to 0.166). Although the slower rate of global score decline among black participants was more pronounced among persons with older baseline age ($P_{interaction} < 0.01$), the racial difference in decline was modest in magnitude across the range of baseline age of most participants (e.g., −0.074 among 65-year-olds; 0.015 among 75-year-olds; and 0.087 among 85-year-olds). Likewise, the slower rate of decline in executive function among blacks was less pronounced among younger participants ($P_{interaction} < 0.0001$), with effectively no difference in rates among persons aged 65 at baseline.

Alzheimer's disease and all-cause dementia

Among participants included in the first clinical evaluation cycle, during which only prevalent dementia was assessed, the weighted prevalence of AD among blacks was 19.9% (95% CI, 15.9%–23.9%), more than double the prevalence among whites (8.2%; 95% CI,

5.8%–10.6%). The results on incident AD (Table 3) echoed this pattern: black participants' age- and sex-adjusted risk of AD was twice the risk of AD nearly among whites (RR, 1.93; 95% CI, 1.37–2.73). The burden of AD among black participants was also substantial on an absolute scale: compared with whites, there was an excess of 58 AD incident cases per 1000 persons per assessment cycle among blacks (95% CI, 28 to 88).

APOE ε4 carriership

Black participants were more likely than white participants to carry an *APOE ε4* allele (37% vs 26%; Table 1). In analyses restricted to participants with *APOE* data, racial differences in baseline scores or cognitive decline did not vary by *ε4* carriership (all $P_{interaction} > 0.16$). Furthermore, adjustment for *ε4* carriership did not materially change estimated racial differences in baseline performance or cognitive decline (eTable 3).

By contrast, the association between race and AD risk varied markedly by *APOE ε*carriership ($P_{interaction} = 0.05$; Table 4). Among non-carriers, blacks' AD risk was 2.32 times that of whites' (95% CI, 1.50–3.58), but this association was comparably negligible among *ε4* carriers (RR, 1.09; 95% CI, 0.60–1.97).

Mediation by education

On average, black participants had two fewer years of formal education than did whites (Table 1). In age-, sex-, and race-adjusted analyses, more years of education corresponded to higher baseline global cognitive score (0.40 standard unit per each additional 4 years; 95% CI, 0.37 to 0.42) and lower AD risk (RR per each additional 4 years, 0.74; 95% CI, 0.68 to 0.80). We did not further consider cognitive trajectory in these analyses as cognitive decline was not notably faster among blacks in our data.

Educational attainment, as measured by years of education, appeared to mediate a substantial fraction but not the totality of the racial differences in baseline cognitive score and AD risk (Table 5). Under the hypothetical scenario in which education was "controlled" such that each black participant's educational level took on the level it would have been had the participant been white, all covariates being equal, black participants' baseline global cognitive scores were an average of 0.45 standard units lower than whites' scores (95% CI, −0.49 to −0.41), a difference smaller than without controlling years of education (−0.69; Table 5), and translating to about 35% of the total effect of race on cognitive performance mediated through years of education. The racial disparity in cognitive performance was narrower among those with more years of education ($P_{interaction} < 0.001$), echoing previous analyses.[26,30] This interaction manifested itself in the controlled direct effects. In the scenario in which everyone obtained 12 years of education, the black–white difference in global cognitive score dropped to 0.57 standard units (95% CI, −0.62 to −0.53), but in the scenario in which everyone obtained 16 years of education, the difference dropped even further to −0.29 standard units (95% CI, −0.35 to −0.24), eliminating 58% of the total racial disparity in performance. There was no notable interaction between race and education in relation to AD risk. Thus, equally distributing of years of education across race, regardless of the educational level, would eliminate about 37% of the excess relative risk among black

participants. (For more detail, see eAppendix [Supplemental text; Mediation by education and eTable 1a and eTable1b].)

Selection via attrition

Applying inverse probability-of-continuation weights to our analyses did not reveal more rapid decline on the global score among blacks than among whites (see eAppendix [Supplemental text; Assessment of selection via attrition, and eTable 2).

DISCUSSION

In this large, population-based study of older adults, black participants performed worse, on average, on cognitive tests and were more likely to have prevalent AD than white participants at baseline; they also were at higher risk for incident AD. By contrast, the rate of cognitive decline among blacks differed little from or was slightly slower than the rate among whites. Collectively, these results suggest that persistent racial differences in cognitive level—rather than differences in cognitive decline in old age—likely underlie the higher risk of incident AD among blacks.

The large deficits among blacks in average level of cognitive test performance fall in line with the vast body of previous research. Moreover, the elevated risk of incident AD and all-cause dementia among blacks in CHAP is consistent with the age- and education-adjusted AD hazard ratio (HR) of 2.6 (95% CI, 1.6–4.2) from the Washington Heights-Inwood Community Aging Project[31] and the age-, sex-, and *APOE ε4*-adjusted all-cause dementia HR of 1.44 (95% CI, 1.20–1.74) from the Dynamics of Health, Aging, and Body Composition study.[32] By contrast, in the Aging, Demographic, and Memory Study, blacks and whites did not differ substantially in incident AD risk, after adjustment for age, education, sex, and *APOE ε4* (cumulative incidence ratio [CIR]=1.22; 95% CI, 0.58–2.57), and risks of incident all-cause dementia in the two groups were nearly identical (CIR=0.98; 95% CI, 0.50–1.95).[33] An older study from the Duke Established Populations for Epidemiologic Studies of the Elderly reported a small, imprecisely measured difference between blacks and whites in three-year dementia incidence; the analyses were not age-adjusted, however, and included only 77 dementia cases.[34] In the Cardiovascular Health Study, compared with white participants, the age-adjusted incidence rate of AD among blacks was 81% higher, and the corresponding rate of all-cause dementia was 72% higher. However, the study's diagnostic procedures varied by race, and the investigators posited that this could largely explain the racial difference in incidence.[35]

Previous studies of cognitive decline, generally with smaller sample sizes, have found either little racial difference or slower decline among blacks.[1,2,4,5,9] Ours is the third study to observe substantially slower decline among blacks on tests of executive function.[1,9] Of the two previous studies reporting faster cognitive decline among blacks,[6,7] one adjusted for baseline cognitive score, an approach that can severely bias results in the direction of faster decline among blacks when blacks perform markedly worse at baseline.[36]

The racial disparity in dementia risk in CHAP was substantial among persons not carrying an *APOE ε4* allele, but absent among carriers. Equivalently, whereas *ε4* carriership

corresponded to a doubling of risk among white participants, it corresponded to no increase in risk among blacks. This pattern held on the additive (risk difference) scale as well. Similar results emerged from previous analyses of data from CHAP[10] and two other cohorts.[37,38] Nonetheless, the *ε4* allele was associated with increased risk ($P \leq 5 \times 10^{-8}$) in a genome-wide association study of data from 5896 black participants of 15 studies.[39] The limited evidence on cognition and cognitive decline has been mixed as well. In CHAP and two other studies,[7,40] racial differences in cognitive level did not further depend on *ε4* carriership, as opposed to another study in which *ε4* carriership was associated with worse memory performance in white but not black participants.[38] Likewise, in data from CHAP and another cohort,[7] *ε4* carriership had no bearing on racial differences in cognitive decline; in two other cohorts, blacks' decline in semantic memory and working memory scores was slower than whites' cognitive decline among *ε4*-positive persons, whereas no racial differences in cognitive decline were evident among *ε4*-negative persons.[41]

On their surface, the findings on cognitive decline contradict the findings on cognition and dementia risk. Accurately characterizing and effectively intervening on racial disparities in cognitive dysfunction and dementia hinges on understanding these findings. The findings could reflect differences in cognitive reserve caused by racial disparities over the lifespan in, for example, education (both in amount and quality), access to material and social resources, exposure to discrimination, and exposures to neurotoxicants.[27,42] With higher cognitive reserve by older adulthood, on average, white individuals have "farther to fall" cognitively than black individuals before reaching the functional threshold of clinical dementia, so that even if both groups have the same rate of cognitive decline, blacks have poorer cognitive function and disproportionately develop dementia. If this explanation is correct, then intervening on the promoters of cognitive reserve among blacks should enhance cognitive functioning and reduce dementia risk in this group. Another explanation for the discrepancy between the cognitive decline and other results posits that the cognitive and dementia findings—particularly the cross-sectional differences in cognitive performance—reflect measurement bias.[3,43–45] Race-dependent misclassification of dementia status would clearly be problematic and call for unbiased approaches to assessment. Notably, some cognitive tests do not appear to be susceptible to marked, racially differential measurement error.[46,47]

Years of formal education accounted for much but not all of the observed racial disparities in global cognitive score and AD risk. The counterfactual approach we used offers several advantages over the conventional approach of adjusting for putative mediators. However, the education measure—years of education—holds meaning that depends on race, particularly in this generation of participants, representing different drivers, quality, acquired skills,[5] and socioeconomic[48] and health[30] consequences. Thus, our analyses likely failed to fully level the educational playing field, possibly underestimating the extent to which education mediates these associations. For example, in the Washington Heights–Inwood Community Aging Project indicators of educational quality explained racial differences in performance beyond what was explained by years of education.[26] Nonetheless, our findings, together with others, provide support for the claim that early-life education, which social policy can influence at the broad population level, may be one strategy for reducing racial disparities in late-life cognitive health.

Our study included more black participants—often by an order of magnitude—than any previous comparisons of cognitive decline and dementia risk in blacks and whites. CHAP also systematically drew its participants from the population, permitting a potentially more accurate characterization of the cognitive aging experience among community-dwelling black and white older adults. Nonetheless, several limitations and challenges to the interpretation of our results warrant mention.

First, our findings—and those of previous studies—may have been influenced by differential selection. Enrollment is less likely and post-enrollment attrition more likely among individuals with poor cognition.[29] If race is also related to enrollment and attrition, bias in estimated racial differences in cognition, cognitive decline, and dementia risk could result. Findings from inverse probability-of-continuation-weighted analyses indicate that differential post-enrollment attrition, including post-enrollment mortality, does not explain our cognitive decline findings.

However, racial disparities in mortality may shape the initial composition of an older adult cohort, because, among the birth cohorts that generated older adult study populations, blacks were much less likely than whites to survive to the age of 65, a typical minimum age of enrollment (e.g., among those born in 1939–1941, 38% of blacks versus 63% of whites survived to age 65[49]). Specifically, blacks who survived to enrollment age may have been more likely than surviving whites to possess characteristics that both promoted their survival and conferred cognitive benefits.[50] This type of selection is more challenging to address, and if it biases racial comparisons of cognitive outcomes in older age at all, it likely would result in an underestimate of blacks' relative risk of dementia and deficit in cognitive performance. It could also generate the observation of slower cognitive decline among blacks in the true absence of any racial difference, or even in the true existence of faster decline among blacks.[51] All of these biases can be exaggerated in progressively older strata, which are progressively more selected; e.g., as observed in CHAP and in another cohort,[9] the pattern of slower decline in global and executive function among blacks was more pronounced with older age. Without "correcting" this bias, if it exists, our study's estimates describe the experiences of individuals in the population who have survived to an older age; they are essentially a demographic record of a specific time. But the comparisons might not fully capture the total *causal effect*—e.g., the combined effect of social disadvantage and socioeconomic inequality—of being black versus being white on cognitive aging.[52,53] This distinction is important: underestimated racial differences in cognitive aging imply a smaller impact of intervening on the causes of racial disparity in health.[54] Because of this uncertainty, it would be incorrect to conclude, for example, that interventions to slow cognitive decline should be targeted to white individuals.

Selection bias also has been invoked to explain the apparently diminished *APOE ε4* effect on dementia risk among black Americans.[38,55] Alternatively, blacks' dementia risk is largely a function of cognitive level rather than decline, and because the *ε4* allele is more strongly related to cognitive decline than level, it may wield little influence on blacks' dementia risk. Others have proposed that the high prevalence of other unmeasured risk factors among blacks could effectively crowd out *ε4*'s relative contribution to risk, or, equivalently, that the overwhelming dominance of *ε4* as a risk factor diminishes the relative contribution of race

to risk.[38] This purely mathematical construction holds *because* these two factors—the *ε4* allele and being a black American—affect risk, not because of their lack of an effect,[56] a critical point in translating these results to public health and clinical practice.

In conclusion, these findings, from one of the largest studies to date of older black and white Americans, sharpen a pattern of results from other cohorts and suggest that the higher risk of incident AD among blacks observed in this and other studies may reflect persistent differences in cognitive level rather than differences in cognitive decline in older age. Future research is warranted to carefully characterize the causal ties between the manifestations of race and cognitive aging.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

SOURCES OF FUNDING

This investigation was supported by NIH grant AG11101 (PI: Evans).

The authors are grateful to the study participants for their engagement in and dedication to the Chicago Health and Aging Project.

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Table 1

Characteristics of participants, by race, in the analyses of cognitive level, cognitive decline, and incident dementia.

	Black participants	White participants	Difference, *ref: white* (95% CI[a])
Analyses of cognitive level and cognitive decline			
	N=4968	*N=2767*	
Mean age, years, at baseline (SD[a])	71 (6)	74 (7)	−3.0 (−3.3, −2.7)
Male (%)	37	38	−1 (−3, 2)
Mean years of formal education (SD)	12 (3)	14 (3)	−2.4 (−2.6, −2.3)
Composite childhood socioeconomic resources score (SD)[b]	−0.1 (0.7)	0.3 (0.7)	−0.44 (−0.47, −0.41)
APOE ε4 allele carrier[c] (%)	37	26	11 (8, 14)
Mean baseline global cognitive score (SD)	−0.2 (1.0)	0.4 (0.9)	−0.59 (−0.63, −0.55)
Mean 5-year change in global cognitive score (SD)	−0.25 (0.63)	−0.26 (0.68)	0.01 (−0.02, 0.04)
Analyses of incident dementia			
	N=1170	*N=974*	
Mean age, years, at baseline (SD)	72 (5)	75 (6)	−3.0 (−3.6, −2.6)
Male (%)	37	39	−2 (−6, 2)
Mean years of formal education (SD)	12 (3)	14 (3)	−2.4 (−2.6, −2.1)
Composite childhood socioeconomic resources score (SD)[b]	−0.1 (1.1)	0.5 (1.1)	−0.5 (−0.6, −0.4)
APOE ε4 allele carrier[c] (%)	35	26	9 (5, 13)
Incident AD[a] case (%)[d]	24	17	6 (3, 10)
Incident dementia case (%)[d]	25	18	7 (3, 10)

[a] CI: confidence interval. SD: standard deviation. AD: Alzheimer disease dementia.

[b] Higher values correspond to more socioeconomic resources and less socioeconomic disadvantage during childhood. Data available for 4587 black and 2748 white participants in the analyses of cognitive level and decline, and for 1107 black and 971 white participants in the analyses of incident dementia.

[c] From a subsample of participants: 2997 black and 1257 white participants (cognitive decline); and 1105 black and 843 white participants (dementia).

[d] Over the entire course of follow-up.

Table 2

Adjusted[a] differences (and 95% confidence intervals [CI]) between black and white participants in baseline cognitive score and rate of change in score.

	COMPOSITE GLOBAL COGNITIVE SCORE	EPISODIC MEMORY SCORE	EXECUTIVE FUNCTION SCORE
	N (obs) = 7735 (25806) **Difference (95% CI)**	**N (obs) = 7696 (25508)** **Difference (95% CI)**	**N (obs) = 7358 (24431)** **Difference (95% CI)**
COGNITIVE PERFORMANCE AT BASELINE			
Difference between black and white participants' scores[b]	−0.83 (−0.88, −0.78)	−0.58 (−0.63, −0.53)	−1.03 (−1.07, −0.99)
Additional difference in scores, per year of age[d]	−0.02 (−0.02, −0.01)	−0.02 (−0.02, −0.01)	−0.01 (−0.01, 0.00)
TRAJECTORY IN COGNITIVE PERFORMANCE			
Difference between black and white participants' 5-year change in scores[b]	0.007 (−0.034, 0.047)	−0.028 (−0.068, 0.013)	0.138 (0.110, 0.166)
Additional difference in 5-year change in scores, per year of age[c]	0.008 (0.002, 0.014)	0.004 (−0.002, 0.009)	0.014 (0.009, 0.018)

[a] Adjusted for age and sex.

[b] The core model contained terms for race, age, sex, time, (race)×(age), (race)×(time), (age)×(time), (sex)×(time), and (race)×(age)×(time). Because of the inclusion of a cross-product of race with age, the differences reported are specific to participants aged 75, the reference value for age.

[c] Based on the (race)×(age) term in context of baseline scores, and on the (race)×(age)×(time) term in the context of trajectory. For example, on average, blacks scored 0.58 standard unit worse than whites in episodic memory. Per year in age above 75, this difference widened by 0.02 unit; equivalently, per age younger than 75, the difference narrowed by 0.02 unit.

Table 3

Adjusted[a] relative risk (and 95% confidence interval [CI]) of incident dementia in black participants compared with white participants.

		Black participants compared with white participants	
	Cases/total observations	Risk ratio (95% CI)[b]	Risk difference, cases per 1000 (95% CI)[b]
Alzheimer's disease dementia	441/2904	2.04 (1.26, 2.82)	52 (24, 80)
All-cause dementia	474/2909	1.99 (1.27, 2.71)	52 (24, 80)

[a] Adjusted for age and sex.

[b] Risk ratios and differences are specific to reference levels of the covariates, i.e., 75-year-old women.

Table 4

Adjusted[a] risk ratios (RR) and risk differences[b] (RD) (and 95% confidence intervals) of incident Alzheimer's disease dementia, by race and *APOE ε4* carriership.[c]

	Carriers of at least one ε4 allele	Non-carriers of an ε4 allele	ε4 carriers compared with non-carriers
Black participants	RR[d]: 2.19 (1.29, 3.72)	RR[d]: 2.32 (1.50, 3.58)	RR: 0.95 (0.57, 1.57)
	RD[d]: 62 (13, 112)	RD[d]: 69 (32, 106)	RD: −7 (−66, 53)
White participants	RR[d]: 2.01 (1.22, 3.33)	RR[d]: 1.00 *referent*	RR: 2.01 (1.22, 3.33)
	RD[d]: 53 (7, 99)	RD[d]: 0 *referent*	RD: 53 (7, 99)
Black compared with white participants	RR: 1.09 (0.60, 1.97)	RR: 2.32 (1.50, 3.58)	
	RD: 9 (−56, 75)	RD: 69 (32, 106)	

[a] Adjusted for age and sex.

[b] In cases per 1,000.

[c] Unweighted cases/total and weighted and age- and sex-standardized estimated risk (95% confidence interval), in cases per 1000: black ε4+, 101/537, 115 (69–161); black ε4-, 156/983, 122 (90–153); white ε4+, 62/296, 106 (61–151); white ε4-, 91/874, 53 (35–70).

[d] Referent: white, non-carriers of an ε4 allele. Estimates are predicted values marginally standardized to the distribution of age and sex in the CHAP population.

Table 5

Mediation by education of the associations of race with cognitive score and Alzheimer's dementia risk.

	Adjusted[a] difference (95% CI) between black and white participants' baseline cognitive scores	Adjusted[a] relative risk (95% CI) of incident Alzheimer's dementia among black versus white participants
	N = 7335	N = 2827
Estimated total effect	−0.69 (−0.73, −0.65)	1.49 (1.05, 2.01)
Estimated natural direct effect	−0.45 (−0.49, −0.41)	1.30 (0.91, 1.78)
Estimated controlled direct effect		
Everyone attains 12 years of education	−0.57 (−0.62, −0.53)	1.30 (0.91, 1.78)
Everyone attains 16 years of education	−0.29 (−0.35, −0.24)	
Proportion of effect eliminated by setting years of education to specified level		
Everyone attains 12 years of education	17%	37%
Everyone attains 16 years of education	58%	

[a]Adjusted for age, sex, and childhood socioeconomic resources.

[b]With no interaction between race and education with respect to Alzheimer's dementia risk, the estimated natural direct effect and controlled direct effects are equivalent, and the controlled direct effect and proportion of effect eliminated do not vary by years of education.

[c][(Total Effect - Controlled Direct Effect)/(Total Effect)].

[d][RR(Total Effect) - RR(Controlled Direct Effect)]/[RR(Total Effect)-1]. Excess relative risk is the portion of the relative risk that exceeds 1, i.e., RR − 1.