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Temporal trends in cognitive function of older US adults associated with population changes in demographic and cardiovascular profiles

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Abstract

Background—Recent estimates suggest that dementia incidence is decreasing in the US possibly due to better management of cardiovascular disease (CVD) risk factors, but these studies lack repeated cross-sectional assessment among a representative US sample. Our objective was to assess temporal trends in cognitive performance in relation to CVD risk factors among older National Health and Nutrition Examination Survey (NHANES) participants.

Methods—We used repeated cross-sectional assessment of 5711 participants ≥60 years of age from four NHANES cycles: 1999–2000, 2001–2002, 2011–2012 and 2013–2014. Cognitive function was assessed during each cycle with the Digit Symbol Substitution Test (DSST). We estimated mean DSST score at each cycle and annual trend in DSST before and after adjustment

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Contributors

MB had full access to the data in this analysis. As such, he is the guarantor of this work, takes responsibility for the integrity of the data and the accuracy of the data analysis and affirms that the manuscript is an honest, accurate and transparent account of the study being reported. All authors made substantial intellectual contributions participating in creating and designing the study, analysing and interpreting the data and reviewing this manuscript.

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Competing interests

None declared.

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for age, sex, race/ethnicity, education, smoking status, blood pressure, glucose status and body mass index.

Results—DSST scores was significantly higher for 2011–2012 (difference: 6.7, 95% CI 4.4 to 9.0) and 2013–2014 (difference: 6.2, 95% CI 4.0 to 8.5), but not 2001–2002 (difference: 2.3, 95% CI −0.01 to 4.6) as compared with 1999–2000 before adjustment. We observed a linear trend for higher annual DSST score before adjustment (DSST/year: 0.44, 95% CI 0.31 to 0.57) and after adjustment for age, sex, race/ethnicity, educational attainment and CVD risk factors (DSST/year: 0.17, 95% CI 0.08 to 0.26). Educational attainment was most strongly associated with the attenuation in the trend in cognitive function (77% of trend attenuation and 20% of variance in DSST).

Conclusion—Cognitive function is improving over time for US adults aged ≥60 years. These improvements are strongly associated with greater educational attainment and irrespective of the changing US demographic and cardiovascular health profiles.

INTRODUCTION

Recent estimates suggest that cognitive impairment, dementia incidence and prevalence may be decreasing or stable in the US and other nations.[1–8] It is estimated that upwards of 30% of Alzheimer's disease is preventable by improving modifiable risk factor profiles including diabetes, hypertension, obesity, smoking and education.[9] Longitudinal cohort studies observe better cognitive function and less steep cognitive decline among recent birth cohorts, but are mixed with regard to which modifiable factors explain these encouraging temporal trends.[10–12] Establishing whether temporal changes in these cardiovascular disease (CVD) risk factors are associated with temporal improvements in cognitive function in dementia-free adults has important implications for population-wide dementia prevention strategies. Rigorous assessment of CVD risk factors and cognitive function among representative samples of the population over multiple years provides the critical methodological frame-work needed to support population-wide inferences about temporal trends. Our objective was to assess trends in cognitive performance among National Health and Nutrition Examination Survey (NHANES) adults ≥60 years of age in relation to CVD risk factors previously associated with cognitive function.

METHODS

Study sample

NHANES is a continuous, ongoing annual survey of the non-institutionalised civilian resident population of the USA (source: https://www.cdc.gov/nchs/nhanes/index.htm).[13] The survey data are collected in two phases including an in-home face-to-face interview and a physical examination occurring in the mobile examination centre (MEC). Signed informed consent was obtained from every participant for both phases of the interview. This study was conducted according to the principles embodied in the Declaration of Helsinki.

Measures

Cognitive function was assessed using the Digit Symbol Substitution Test (DSST) for a subset of participants aged 60 years and older at NHANES survey cycles 1999–2000, 2001–2002, 2011–2012 and 2013–2014.[13] The DSST is the only objective instrument used in NHANES to assess cognitive function. The DSST is used to assess executive function and processing speed where participants are asked to write and translate a sheet of numerals (1–9) to symbols.[14] Using the provided key, the participant draws the symbol under the corresponding number. The score is the total number of correct symbols drawn during 120 s, with one point given for a correct response and a maximum possible score of 133.

Standardised questionnaires were used to assess self-reported demographic characteristics including age, sex, race/ethnicity and educational attainment. Cigarette and tobacco use and hypertension awareness, treatment and control were assessed by questionnaire. We used data from both the medication inventory and self-reported use of medications for high blood pressure (BP) and diabetes. With participants in light clothing, standing height was measured using a stadiometer and weight was measured using a digital scale. BP measurements were taken after the participant had been resting quietly for 5 min, sitting with their back and arms supported, feet flat on the floor and legs uncrossed. Three consecutive BP readings were attempted and the average of all BP measurements was used for these analyses. A phlebotomist drew blood for laboratory tests and fasting blood glucose (FG), glycated haemoglobin A1c (HbA1c) and serum lipids were measured with standardised methods and harmonised across examinations where recommended.[15]

Statistical analysis

Educational attainment was categorised as less than high school, high school graduate/general equivalency development (GED equivalent), some college or college graduate and above. We created five categories of BP: normal BP (systolic BP (SBP)/ diastolic BP (DBP) <120/80 mm Hg without BP medication use or physician diagnosis of hypertension (HTN)), prehypertension (SBP/DBP: 120–139/80–89 mm Hg without BP medication use or physician diagnosis of HTN), untreated hypertension (SBP/ DBP ≥140/90 mm Hg or physician diagnosis of HTN without BP medication use), controlled hypertension (SBP/DBP <140/90 mm Hg with BP medication use) and uncontrolled hypertension (SBP/DBP ≥140/90 mm Hg with BP medication use). Smoking status was categorised as never (smoked <100 cigarettes in lifetime), former (smoked ≥100 cigarettes in lifetime and do not smoke at all currently) and current (smoked ≥100 cigarettes in lifetime and smoke any amount currently). Body mass index (BMI) was categorised as normal (<25 kg/m^2), overweight (25–29.9 kg/m^2) or obese (≥30 kg/m^2). In sensitivity analyses, we investigated the impact of finer BMI categories. We created three categories of glucose status: normal (FG <5.6 mmol/L and HbA1c <5.7% without diabetes medication use or physician diagnosis of diabetes), pre-diabetes (FG: 5.6–6.9 mmol/L or HbA1c: 5.7%–6.4% without diabetes medication use or physician diagnosis of diabetes) and diabetes (any of following: FG ≥7.0 mmol/L, HbA1c ≥6.5%, diabetes medication use or physician diagnosis of diabetes). We calculated 10-year predicted risk for atherosclerotic CVD (ASCVD) using the American College of Cardiology/American Heart Association equations and created three categories for stratified analyses (10-year risk <10%, 10%–19.9% and ≥20%).[16]

We assessed the mean DSST score for each NHANES cycle and annual trend in DSST over time linear regression for survey data before and after adjustment for demographics and CVD risk factors. The annual trend in DSST was assessed by including a variable denoting the first year of each NHANES cycle into the model. The first adjusted model included the covariates age, sex and race/ethnicity. To understand whether trends in DSST were driven by population improvements in education, the second model included adjustment for educational attainment. Management of BP and smoking have improved in the USA in recent decades and these are strong risk factors for dementia. As such, our third model included adjustment for BP category and smoking status. Diabetes and obesity prevalence have increased over time and each are risk factors for dementia. Therefore, we assessed the sensitivity of our estimates with adjustment for glucose status and BMI category. We repeated our analysis when modelling systolic BP, HbA1c and BMI as continuous variables rather than the categorical risk factors including adjustment for BP and diabetes medication use and, separately, adjustment for 10-year predicted ASCVD risk. Another sensitivity analysis included adjustment for occupation status (retired, currently working and not retired but looking for work/unable to work), with the assumption that participation to the workforce would be a proxy for current regular cognitive engagement. We performed stratified analyses to further assess the sensitivity of our estimates and to determine whether trends in DSST were occurring for certain subpopulations. These analyses included separate models stratified by sex, race/ethnicity, education and each CVD risk factor, respectively, adjusting for all other covariates.

A total of 40 935 adults (age ≥20 years) participated in the four NHANES cycles. We excluded 33 597 individuals who were <60 years of age, 1367 due to a missing DSST test score and 260 due to a NHANES MEC weight of zero (participant was invited to the MEC but declined to participate). Traditional analyses in NHANES account for the complex, multistage probability sampling design by incorporating survey weights. Because we analysed a subset of NHANES adults 60 years of age and older, we reweighted each cycle sample according to 20 strata of sex, race/ethnicity and age. The new weight was calculated using the following adjustment factor: a numerator consisting of all the NHANES participants in the respective strata and a denominator consisting of all the NHANES participants in the respective strata that had a DSST score. This adjustment factor was then multiplied by the MEC weights. This reweighting method achieves estimates closest to the true model coefficients compared with single and multiple imputation methods and dropping observations.[17] SAS software V.9.4 was used for all analyses and we used proc surveyreg to account for the stratified, cluster sample design with the new survey weight. All data used in this manuscript is de-identified, does not require institutional review and approval and is freely available to the public: https://wwwn.cdc.gov/nchs/nhanes/default.aspx.

RESULTS

The unweighted sample included 5711 NHANES participants. The number of NHANES participants who completed the DSST increased over time from 1289 (1999–2000) to 1590 (2013–2014). The percentage of minority race/ethnicities and educational attainment exceeding high school was higher in 2013–2014 (table 1) compared with 1999–2002. The 10-year ASCVD predicted risk, prevalence of smoking and untreated hypertension and level

of SBP and DBP decreased over time. In contrast, the prevalence of controlled hypertension, BP-lowering medication use, BMI, obesity, HbA1c, diabetes and diabetes medication use all increased over time.

In an unadjusted model, the mean (SE) DSST score was 44.7 (0.8) in 1999–2000, 47.0 (0.8) in 2001–2002, 51.4 (0.8) in 2011–2012 and 51.0 (0.8) in 2013–2014 (table 2). The DSST population mean score was significantly higher in 2011–2012 (difference: 6.7, 95% CI 4.4 to 9.0) and 2013–2014 (difference: 6.2, 95% CI 4.0 to 8.5) as compared with 1999–2000 in an unadjusted model. The DSST population mean score in 2001– 2002 was higher, though not statistically significantly different from 1999 to 2000 (difference: 2.3, 95% CI −0.01 to 4.6). There was a significant linear trend for higher DSST score per annum before adjustment (per annum DSST score: 0.44, 95% CI 0.31 to 0.57). The increasing trend in the DSST score over time was modestly attenuated, yet remained significant, after adjustment for age, sex and race/ethnicity (per annum: 0.37, 95% CI 0.25 to 0.48). We observed considerable attenuation in DSST trend estimate (per annum: 0.13, 95% CI 0.05 to 0.22) after adjustment for educational attainment (Model 3). The adjustment for educational attainment was associated with the greatest attenuation in the per annum change in DSST from the unadjusted to demographics and education adjusted estimate (77% of attenuation in per annum trend estimate and 20% of the variance in DSST, change in R-squared: 0.195). We then assessed whether including adjustment for the four CVD risk factors, without including adjustment for education, was associated with attenuation in the DSST (Models 4 and 5). From an age-adjusted, sex-adjusted and race-adjusted model, we observed minor attenuation after further adjustment for BP category and smoking status (per annum: 0.40, 95% CI 0.28 to 0.51). Additional adjustment for glucose status and BMI category did not appreciably alter these estimates and the population mean score in the DSST was significantly higher in 2001–2002, 2011–2012 and 2013–2014 compared with 1999–2000 (table 2) after adjustment for demographics and all CVD risk factors. Estimates for mean DSST score and per annum trend in DSST did not differ materially when risk factors were modelled continuously rather than categorically (Model 6), after adjustment for 10-year ASCVD predicted risk rather than the four risk factor groups combined (Model 7) or the inclusion of occupation status to the final model (Model 8).

Stratified models

Women had higher DSST scores than men at each cycle. The trend of higher DSST score over time was observed for both women (per annum: 0.19, 95% CI 0.08 to 0.31) and men (per annum: 0.12, 95% CI 0.003 to 0.24). Non-Hispanic blacks, Hispanics and multiethnic individuals all had lower DSST scores compared with non-Hispanic whites (online supplementary figure 1). Before adjustment for education, the trend in DSST score was 0.57/year (95% CI 0.37 to 0.79) for non-Hispanic blacks, 0.32/year (95% CI 0.07 to 0.57) for Hispanics, 0.36/year (95% CI 0.22 to 0.49) for non-Hispanic whites and 0.27/year (95% CI −0.26 to 0.79) for multiethnic individuals. The trend in DSST score was present for non-Hispanic blacks (per annum: 0.30, 95% CI 0.13 to 0.47), Hispanics (per annum: 0.20, 95% CI 0.01 to 0.40) and non-Hispanic whites (per annum: 0.17, 95% CI 0.06 to 0.27), but not multiethnic individuals (per annum: −0.05, 95% CI −0.43 to 0.33), before and after adjustment for education. We did not observe evidence for effect modification by sex (p for

interaction: 0.58) or race/ethnicity (p for interaction: 0.07). Education level was associated with higher DSST at each cycle. We observed an increasing trend in DSST score within each strata of education. However, the magnitude of effect for the trend was largest for the lowest educational level and smallest for the highest educational level (figure 1). We did not observe evidence for effect modification by education level (p for interaction: 0.54).

At each cycle, better profile for each CVD risk factor was associated with higher DSST score except for BMI category (figure 1). We observed an increasing trend in DSST score over time within each CVD risk factor stratum. While we did not observe evidence for effect modification of the increasing temporal trend in DSST by any of the CVD risk factors (all p for interaction >0.25), we did observe qualitative differences in the trend in DSST over time between CVD risk factor categories. For BP, the positive trend in DSST over time was strongest for prehypertension (per annum: 0.19; 95% CI 0.04 to 0.35) and controlled hypertension groups (per annum: 0.18; 95% CI 0.04 to 0.32). Among smoking categories, the positive trend in DSST was greatest in never smokers (per annum: 0.15; 95% CI 0.02 to 0.28) and former smokers (per annum: 0.19; 95% CI 0.06 to 0.31). The trend in DSST was greatest among obese individuals (per annum: 0.28; 95% CI 0.15 to 0.40) per BMI category.

On assessment of finer BMI categories, this trend was strongest among individuals with a BMI of 27.5–29.9, 30.0–32.4 and 32.5–34.9 kg/m^2 (online supplementary figure 2). For glucose status, the trend in DSST was greatest in the pre-diabetes category (per annum: 0.19; 95% CI 0.07 to 0.31). We observed an increasing temporal trend in DSST for all strata of 10-year ASCVD predicted risk; the trend was greatest for the <10% 10-year risk stratum (per annum: 0.31; 95% CI 0.13 to 0.50).

DISCUSSION

Results from this nationally representative sample of US adults showed a trend in increasing cognitive function between 1999 and 2014. This temporal trend was in parallel with improvements in educational attainment and cardiovascular risk factors including management of BP and never smoking. Population increases in educational attainment were most strongly associated with the trend in cognitive function. Cognitive function improved over time within every demographic and CVD risk factor stratum. The primary finding of this study is that scores for this test of processing speed and executive function appear to be improving over time. This improvement is strongly related to better educational attainment and irrespective of the changing demographic and cardiovascular health profile of US adults 60 years of age and older.

Recent reports from longitudinal cohort studies suggest that the incidence and prevalence of dementia in the US is on the decline, in contrast to earlier data reporting no temporal trends in incidence or prevalence.[1267] No temporal trend in Alzheimer's disease incidence was observed among a community-based cohort of black and white Chicago residents from 1997 to 2008.[7] Similarly, no difference in the prevalence of dementia was observed between 1992 and 2001 among a community-based sample of African Americans living in Indianapolis.[6] In contrast, Rocca observed a 3% annual decline in dementia incidence in the Rochester Epidemiology Cohort from 1985 to 1994, though no decline was observed in the 10 years

before 1985.[6] More recently, among a nationally representative sample of older adults, the prevalence of cognitive impairment declined between 1993 and 2002[8] and the prevalence of dementia declined between 2000 and 2012.[3] Among participants of the Framingham Heart Study (FHS), the 5-year incidence of dementia decreased from 3.6 per 100 persons to 2.0 per 100 persons from the 1970s to 2010s.[1] The strongest risk reduction was observed for those with a high school education or greater in the FHS. This is somewhat in contrast to our observation that the strongest positive temporal trend in DSST score over time occurred among individuals with less than a high school education. Given the earlier birth cohorts of FHS and more contemporary cycles in NHANES, temporal differences in quality of education within level of attainment may explain our disparate findings. Between 1993 and 2015, the incidence of dementia decreased for successive birth cohorts for a population-based sample of Bronx County, New York, residents independent of changes in cardiovascular profiles.[2] Higher baseline DSST is shown to be associated with lower risk for incident dementia across race and age group in the Atherosclerosis Risk in Communities (ARIC) study and the Cardiovascular Health Cognition Study.[1819] In ARIC, within-individual decline of the DSST on average of 2.4 symbols over a 6-year period was strongly associated with greater risk for incident dementia hospitalisation.[20] We observed change in the DSST of an additional .4 symbols over a 14-year period on a national level, which would suggest that population-level declines in dementia in the USA are forthcoming.

We observed a graded association between healthier levels for each CVD risk factor with higher DSST score, except for BMI. This higher BMI–higher DSST score was previously observed in NHANES.[21] This paradoxical association is proposed to be the result of reverse causation due to weight loss during the preclinical dementia phase, demonstrated by Kivimaki.[22] In our sample, BMI was strongly and inversely associated with age, suggesting that age-related weight loss may be occurring among the oldest of NHANES participants. Coupled with our finding that within the higher stratum of BMI, continuous BMI was associated with lower DSST score suggests that reverse causation is explaining these unexpected higher BMI–higher DSST findings.

Given the strong cross-sectional associations between each CVD risk factor with DSST, it is unclear why adjustment for temporal improvements in CVD risk factors was not strongly associated with temporal improvements in DSST, yet education was. We observed striking improvements in educational attainment over time, consistent with national trends.[23] We also observed that adjustment for education was strongly associated with an attenuation in the racial/ethnic disparity in DSST trend. It is possible that greater educational attainment by successive NHANES cycles contributes to better cardiovascular health at these later cycles directly through exposure to higher income and wealth, access to medical care, better health literacy and cognitive reserve.[24] Quality of education has improved over time and is associated with greater economic returns and better long-term health.[2526] Recent birth cohorts score higher on standardised intelligence tests than older cohorts, known as the Flynn effect.[2728] The causes of this related phenomenon are unclear; the Flynn effect cannot be fully attributed to temporal improvements in education and is likely multifactorial in origin.[28] It may be that education is reflective of a long term or multifactorial exposure, originating much in earlier life and of long duration. In contrast, the value for CVD risk

factors measured concurrently with cognitive function are snapshots and may not reflect this prior long-term exposure.

Our study has multiple unique strengths. Few studies can repeatedly assess demographics, cognitive function and CVD risk factors on a broad sample of US adults over time. NHANES is designed to be representative of the US non-institutionalised civilian population and data are collected using comprehensive study protocols and methods. As such, our findings are generalisable to the overwhelming majority of the US population over the age of 60 years. The repeated assessment of independent cross-sectional samples precludes the influence of practice effects in cognitive assessment. We reported our findings stratified according to multiple characteristics including sex, race/ ethnicity, education and traditional CVD risk factors.

Limitations

It is important to also consider potential limitations of this work. The assessment of cognitive function is limited to a single test of executive function during only four NHANES cycles over 15 years. Whether our findings are occurring for other cognitive domains such as memory, language and social cognition and other birth cohorts is unknown. Further, the cross-sectional assessment relies on single measurement for CVD risk factors and prevents assessment of long-term exposure. We could not assess quality of education or specifically inquire about cognitive engagement throughout adulthood. However, our findings persisted after adjustment for current occupational status, a possibly proxy for cognitive reserve. Finally, it is possible that the participants selected to participate in recent NHANES cycles are different from older cycles independent of population changes in education and cardiovascular health. While certain populations are oversampled in NHANES, education is not a specific oversampling factor and the incorporation of sampling weights during analysis should mitigate any potential differences in population sampling.

CONCLUSIONS

Population improvements in educational attainment, but not CVD risk factor profiles, were strongly associated with temporal trends in better cognitive performance of older US adults. Our findings support recent reports that suggest the incidence of dementia is declining. Our observation that cognitive improvements persist within various demographic strata after adjustment for strong modifiable dementia risk factors call for a better understanding of the factors contributing to these population improvements in cognitive health.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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What is already known on this subject?

- The incidence and prevalence of dementia appears to be decreasing or stable in the US and Europe.
- These declines are posited to better management of cardiovascular risk factors and greater educational attainment, but the prior studies lack repeated cross-sectional assessment among representative samples of US or European adults.

What this study adds?

- We show in this work that temporal improvements in cognitive function in older US adults are strongly associated with improvements in educational attainment and less so with improvements in cardiovascular risk factors.
- Our work emphasises the importance of equal access to and equitable quality of education as a lever to enact population improvements in cognitive health and that factors remain that may explain population improvements in cognitive function.

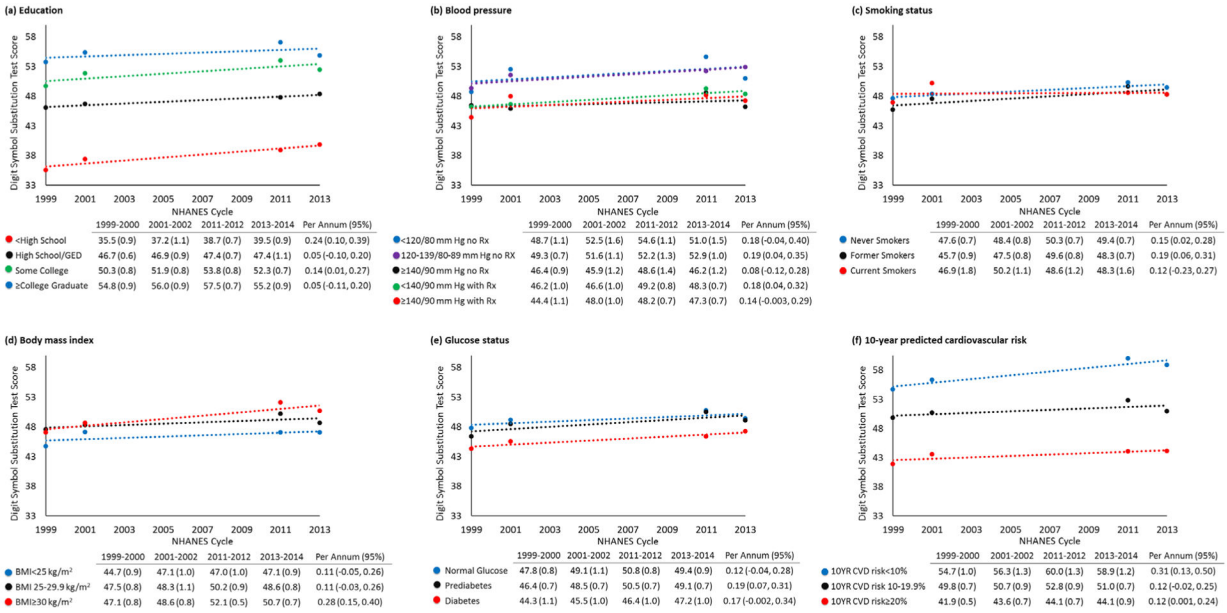

Figure 1.

National Health and Nutrition Examination Survey (NHANES) cycle mean Digit Symbol Substitution Test (DSST) score from 1999 to 2014 stratified by (A) education, (B) blood pressure, (C) smoking status, (D) body mass index (BMI), (E) glucose status and (F) 10-year predicted cardiovascular risk. All figures are adjusted for age, sex and race/ethnicity. Panels (A)–(E) are further adjusted for educational attainment, blood pressure, smoking status, BMI and glucose status when not stratified by these respective factors. Panel (F) is further adjusted for educational attainment. The dashed line represents the linear estimated change in mean DSST score across NHANES cycle. The table below each figure includes the weighted mean DSST score (SE) at each NHANES cycle (represented by solid dots in the figure) and the per annum change in score (95% CI) within each respective risk factor stratum. No cognitive test data is available for NHANES cycles 2003 through 2010. Glucose status was categorised as normal (fasting glucose (FG): <5.6 mmol/L and glycated haemoglobin (HbA1c): <5.7% without diabetes medication use or physician diagnosis of diabetes), pre-diabetes (FG: 5.6–6.9 mmol/L or HbA1c: 5.7%–6.4% without diabetes medication use or physician diagnosis of diabetes) and diabetes (any of following: FG: ≥7.0 mmol/L, HbA1c: ≥6.5%, diabetes medication use or physician diagnosis of diabetes).

Table 1

Characteristics of NHANES participants with valid cognitive test scores at examinations 1999–2000, 2001–2002, 2011–2012, 2013–2014

Cycle	1999–2000	2001–2002	2011–2012	2013–2014
N	1289	1412	1420	1590
Demographics				
Age, years	70.4 (0.4)	71.1 (0.4)	69.7 (0.3)	69.6 (0.3)
Female, n (%)	55.4 (0.9)	57.1 (1.1)	54.8 (1.4)	54.5 (1.0)
Non-Hispanic white, n (%)	79.9 (2.6)	81.4 (3.4)	77.1 (3.0)	77.4 (2.6)
Non-Hispanic black, n (%)	8.0 (1.8)	8.5 (1.9)	8.6 (2.0)	9.1 (1.5)
Hispanic, n (%)	9.5 (3.2)	6.9 (2.8)	7.7 (1.8)	7.8 (1.7)
Multiethnic, other, n (%)	2.7 (0.7)	3.3 (1.2)	6.5 (1.3)	5.7 (0.8)
Less than high school education, n (%)	34.1 (2.6)	28.3 (1.6)	18.6 (2.1)	15.3 (2.1)
High school graduate/general equivalency development, n (%)	29.9 (2.3)	27.4 (1.6)	21.9 (2.5)	22.3 (1.4)
Some college, n (%)	21.0 (1.3)	22.3 (1.5)	30.2 (2.3)	31.9 (1.3)
College graduate and above, n (%)	15.0 (1.9)	22.0 (1.6)	29.3 (3.4)	30.5 (2.0)
Never smoker, n (%)	46.2 (1.7)	47.9 (2.1)	49.6 (2.0)	50.3 (2.2)
Former smoker, n (%)	41.0 (1.7)	40.3 (1.6)	39.1 (2.0)	39.5 (2.1)
Current smoker, n (%)	12.9 (1.2)	11.7 (1.1)	11.3 (1.1)	10.2 (0.9)
SBP (mm Hg)	138.7 (0.8)	137.5 (1.0)	130.9 (0.8)	131.2 (0.7)
DBP (mm Hg)	70.3 (0.6)	69.8 (0.5)	68.7 (0.7)	67.6 (0.6)
BP-lowering medication use, n (%)	41.6 (2.2)	45.6 (1.7)	63.0 (1.8)	66.6 (2.5)
Normal BP, n (%) *	11.2 (0.7)	11.2 (1.2)	12.7 (1.6)	9.6 (1.0)
Prehypertension, n (%) *	22.6 (1.3)	18.7 (0.9)	14.0 (1.5)	12.8 (1.3)
Untreated hypertension, n (%) *	22.0 (2.2)	21.3 (1.6)	7.9 (0.8)	7.2 (0.9)
Controlled hypertension, n (%) *	21.8 (1.4)	28.4 (1.3)	43.3 (1.6)	49.7 (1.6)
Uncontrolled hypertension, n (%) *	22.5 (1.4)	20.4 (0.8)	22.1 (1.6)	20.7 (1.5)
BMI, kg/m^2	28.2 (0.2)	28.4 (0.2)	28.9 (0.3)	29.1 (0.2)
Underweight (BMI <18.5 kg/m^2), n (%)	1.5 (0.4)	1.8 (0.3)	1.3 (0.3)	1.6 (0.4)
Normal weight (BMI: 18.5–24.9 kg/m^2), n (%)	27.9 (1.6)	26.8 (1.8)	26.0 (1.9)	24.2 (1.3)
Overweight (BMI: 25–29.9 kg/m^2), n (%)	37.4 (1.4)	38.7 (1.8)	36.3 (1.7)	36.0 (1.5)

Cycle	1999–2000	2001–2002	2011–2012	2013–2014
Obese (BMI: ≥30 kg/m^2), n (%)	33.2 (2.0)	32.7 (1.6)	36.4 (1.7)	38.2 (1.8)
FG (mmol/L)	6.22 (0.10)	6.33 (0.06)	6.37 (0.06)	6.27 (0.05)
HbAlc (%)	5.77 (0.05)	5.83 (0.03)	5.97 (0.05)	5.95 (0.02)
Normal glucose, n(%)[†]	36.1 (2.4)	30.6 (1.8)	20.3 (1.7)	26.2 (1.7)
Pre-diabetes, n (%)[†]	47.5 (1.9)	52.3 (1.9)	61.3 (2.3)	54.9 (1.9)
Diabetes, n (%)[†]	16.4 (1.4)	17.0 (0.8)	18.3 (1.6)	18.9 (1.1)
Diabetes medication use, n (%)	12.2 (1.0)	13.1 (0.8)	18.6 (1.6)	18.3 (1.3)
10-year predicted cardiovascular risk, n (%)	24.4 (0.9)	25.0 (0.7)	21.5 (0.7)	20.9 (0.5)

Means and proportions are presented with SEs in order to account for the complex survey design and weighting for Digit Symbol Substitution Test subsample.

[*] BP categories are defined as: normal BP (SBP/DBP: <120/80 mm Hg without BP medication use or physician diagnosis of HTN), prehypertension (SBP/DBP: 120–139/80–89 mm Hg without BP medication use or physician diagnosis of HTN), untreated hypertension (SBP/DBP: ≥140/90 mm Hg or physician diagnosis of HTN without BP medication use), controlled hypertension (SBP/DBP: <140/90 mm Hg with BP medication use) and uncontrolled hypertension (SBP/DBP: ≥140/90 mm Hg with BP medication use).

[†] Glucose categories are defined as: normal glucose (FG: <5.6 mmol/L and HbA1c: <5.7% without diabetes medication use or physician diagnosis of diabetes), pre-diabetes (FG: 5.6–6.9 mmol/L or HbA1c: 5.7%–6.4% without diabetes medication use or physician diagnosis of diabetes) and diabetes (any of following: FG: ≥7.0 mmol/L, HbA1c: ≥6.5%, diabetes medication use or physician diagnosis of diabetes).

BP, blood pressure; DBP, diastolic BP; FG, fasting glucose; FG, fasting glucose; HTN, hypertension; HbA1c, glycated haemoglobin; NHANES, National Health and Nutrition Examination Survey; SBP, systolic BP.

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Table 2

Adjusted mean and annual change in DSST score for NHANES 1999–2000, 2001–2002, 2011–2012 and 2013–2014

NHANES cycle	1999–2000	2001–2002	2011–2012	2013–2014	
N	1289	1412	1420	1590	
Model	**Mean (SE)**	**Mean (SE)**	**Mean (SE)**	**Mean (SE)**	**Per annum (95% CI)**
Model 1: unadjusted	44.7 (0.8)	47.0 (0.8)	51.4 (0.8)	51.0 (0.8)	0.44 (0.31 to 0.57)
Difference (95% CI)	Reference	2.3 (−0.01 to 4.6)	6.7 (4.4 to 9.0)	6.2 (4.0 to 8.5)	
Model 2 (M2): age, sex and race/ethnicity	44.8 (0.7)	47.3 (0.8)	50.7 (0.7)	50.1 (0.6)	0.37 (0.25 to 0.48)
Difference (95% CI)	Reference	2.5 (0.4 to 4.7)	6 (3.9 to 8)	5.4 (3.4 to 7.3)	
Model 3: M2+educational attainment *	47.0 (0.4)	48.3 (0.6)	49.9 (0.4)	48.8 (0.6)	0.13 (0.05 to 0.22)
Difference (95% CI)	Reference	1.3 (−0.2 to 2.9)	2.9 (1.8 to 4.1)	1.8 (0.4 to 3.2)	
Model 4 (M4): M2+categorical BP † and smoking ‡	44.5 (0.7)	47.2 (0.8)	50.8 (0.6)	50.4 (0.6)	0.40 (0.28 to 0.51)
Difference (95% CI)	Reference	2.6 (0.6 to 4.7)	6.3 (4.4 to 8.2)	5.8 (3.9 to 7.8)	
Model 5 (M5): M4+categorical glucose § and BMI ¶	44.5 (0.7)	47.2 (0.8)	50.9 (0.6)	50.3 (0.7)	0.40 (0.29 to 0.51)
Difference (95% CI)	Reference	2.7 (0.7 to 4.7)	6.4 (4.6 to 8.2)	5.9 (4.0 to 7.7)	
Model 6: M2+smoking and continuous ** BP, BMI and glucose	44.2 (0.6)	46.9 (0.7)	50.6 (0.6)	50.0 (0.7)	0.39 (0.28 to 0.51)
Difference (95% CI)	Reference	2.6 (0.7 to 4.7)	6.4 (4.6 to 8.1)	5.8 (4.0 to 7.7)	
Model 7: M2+10-year predicted cardiovascular risk	44.8 (0.7)	47.3 (0.8)	50.4 (0.7)	49.7 (0.6)	0.33 (0.22 to 0.45)
Difference (95% CI)	Reference	2.5 (0.4 to 4.5)	5.6 (3.6 to 7.5)	4.9 (3.0 to 6.8)	
Model 8: M5+occupation status ††	44.7 (0.6)	47.2 (0.7)	50.8 (0.6)	50.2 (0.7)	0.47 (0.26 to 0.48)
Difference (95% CI)	Reference	2.5 (0.6 to 4.4)	6.1 (4.4 to 7.7)	5.5 (3.6 to 7.3)	
Model 9: M5+educational attainment *	46.6 (0.4)	48.2 (0.6)	50.0 (0.4)	49.0 (0.6)	0.17 (0.08 to 0.26)
Difference (95% CI)	Reference	1.6 (0.0 to 3.1)	3.3 (2.2 to 4.5)	2.4 (0.9 to 3.8)	

* Educational attainment: less than high school, high school/general equivalency development, some college and college graduate and above.

† BP: normal BP (SBP/DBP: <120/80 mm Hg without BP medication use or physician diagnosis of HTN), prehypertension (SBP/DBP: 120–139/80–89 mm Hg without BP medication use or physician diagnosis of HTN), untreated hypertension (SBP/DBP: ≥140/90 mm Hg or physician diagnosis of HTN without BP medication use), controlled hypertension (SBP/DBP: <140/90 mm Hg with BP medication use) and uncontrolled hypertension (SBP/DBP: ≥140/90 mm Hg with BP medication use).

‡ Smoking status: never (smoked <100 cigarettes in lifetime), former (smoked ≥100 cigarettes in lifetime and do not smoke at all currently) and current (smoked ≥100 cigarettes in lifetime and smoke any amount currently).

[§] Glucose status: normal (FG: <5.6 mmol/L and HbA1c: <5.7% without diabetes medication use or physician diagnosis of diabetes), pre-diabetes (FG: 5.6–6.9 mmol/L or HbA1c: 5.7%–6.4% without diabetes medication use or physician diagnosis of diabetes) and diabetes (any of following: FG: ≥7.0 mmol/L, HbA1c: ≥6.5%, diabetes medication use or physician diagnosis of diabetes).

[¶] BMI: normal (BMI: <25 kg/m^2), overweight (BMI: 25–29.9 kg/m^2) and obese (BMI: ≥30 kg/m^2).

[**] Continuous variables: continuous BP modelled as continuous SBP and use of BP-lowering medications; continuous glucose modelled as continuous HbA1c and use of diabetes medication.

[††] Occupation status (retired, currently working and not retired but looking for work/unable to work).

.BP, blood pressureBMI, body mass index;DBP, diastolic BP; DSST, Digit Symbol Substitution Test; FG, fasting glucose; HTN, hypertension; HbA1c, glycated haemoglobin; NHANES, National Health and Nutrition Examination Survey; SBP, systolic BP.