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The Effect of Risk Factors on the Duration of Cognitive Impairment

A Multistate Life Table Analysis of the U.S. Health and Retirement Survey

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The effect of risk factors on the duration of cognitive impairment:

A multistate life table analysis of the U.S. Health and Retirement Survey.

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Abstract

Objectives

Improved health may extend or shorten the duration of cognitive impairment by postponing incidence or death. We assessed the duration of cognitive impairment by BMI, smoking and levels of education.

Methods

Multistate life tables estimated the duration of cognitive impairment. Regression models determine the age specific transition probabilities to disease and death in a both genders and three races of the US population from the Health and Retirement Survey (HRS), 1992-2004. Exposures are self-reported BMI, smoking and education, outcome is cognitive functioning determined by the Telephone Interview Cognitive Screen (TICS).

Results

At age 55, white men and women may expect to live respectively 1.7 (1.5; 1.9) and 2.7 (2.4; 2.9) years with cognitive impairment. Black non-Hispanic males and females live 3.7 [2.8,4.6] and 3.7 [3.0,4.5] years longer with cognitive impairment than whites. BMI makes no difference. (Ever) smoking decreases duration of cognitive impairment among men and women with respectively 0.7 [0.3,1.2] and 0.9 [0.5,1.3] years compared to never smokers. Highly educated men and women expect to live respectively 1.1 [0.7,1.4] and 1.9 [1.4,2.4] years with cognitive impairment, lowly educated men and women 2.7 [2.2,3.1] and 3.8 [3.3,4.3] years with cognitive impairment.

Discussion

Our findings confirm the brain reserve hypothesis. While life extension increases the duration of dementia, higher levels of education compress this cognitive disability. Large differences by race remain after controlling for risk factors.

Introduction

Cognitive impairment is a major cause of disability and care dependence in aging societies. The age specific prevalence of dementia doubles every five years, from approximately 1.5% in persons aged 60-69 to 40% among nonagenarians (Qiu, De Ronchi, & Fratiglioni, 2007). In the absence of effective interventions, numbers of people with dementia will increase as a simple consequence of an increase in the size of the elderly population (Ferri et al., 2005).

Old age and genetic susceptibility are firmly determined as causes of dementia. In European population, incidence rates of dementia among women are higher, often attributed to mortality selection among men (Zhu et al., 2000). Current evidence supports an important role for vascular risk factors in the clinical manifestation of cognitive decline (Qiu et al., 2007). Diabetes, heart disease, cerebrovascular disease and peripheral arterial disease all have been linked to increases in dementia (Biessels, Staekenborg, Brunner, Brayne, & Scheltens, 2006; Hofman, de Jong, van Duijn, & Breteler, 2006). Blood pressure is correlated to dementia, but the relation is more complex and depends on the life course (Qiu, Winblad, & Fratiglioni, 2005). In mid life, high blood pressure plays a causal role, in late life, low blood pressure is related to dementia, maybe as a sign of impending disease, may be as a consequence of hypoperfusion of the brain (Ruitenberg et al., 2005). Obesity shows the same life course dependency. A higher BMI in mid life has been related to an increased risk of dementia, mediated by vascular risk (Gustafson, 2006). Later in life, an accelerated decline of BMI predicts Alzheimer's disease.

There is sufficient evidence that psychosocial factors such as educational attainment, social network and mentally stimulating activities protect against dementia (Qiu et al., 2007). Brain reserve is the overarching hypothesis (Fratiglioni & Wang, 2007). The brain reserve hypothesis posits that a higher cognitive reserve leads to a more plastic and adaptable brain, supporting more neuropathological lesions and vascular damage before expressing clinical dementia. Once clinical

signs of the dementia syndrome appears, the disease is more advanced and the more highly educated progress more rapidly to death. In that process, educational attainment may play several roles: educational attainment is a surrogate of intelligence, an indicator of early life circumstances, and is related to socio-economic status.(Deary, 2008)

Previous papers showed a decreased prevalence of cognitive decline in the Health and Retirement Survey (HRS) (K. M. Langa et al., 2008). Rising levels of education among older adults during the past 15 years in the USA might have influenced prevalence and outcomes of dementia. In the same HRS study, we estimate the incidence and duration of cognitive impairment defined by the Telephone Interview Cognitive Screen (TICS) or proxy-interviews, dependent on the risk factors BMI, smoking and education.

Data and study population

We used the RAND version F of the Health and Retirement Survey (HRS) data file containing the HRS and the Asset and Health Dynamics Among the Oldest Old (AHEAD) which began in 1992 and 1993, respectively, and were merged in 1998. The Children of the Depression cohort and War Baby cohort were included. From now on we will refer to the total survey as HRS. The HRS survey includes a nationally representative sample of initially non-institutionalized individuals, and spouses, who were re-interviewed biannually, with oversampling of minority ethnic groups. We used data from 7 waves from 1992 to 2004. Response was on average 86%. Data on vital status and month and year of death are obtained through the mortality register (the National Death Index) and exit interviews.

Outcomes

Cognitive impairment (CI) in the AHEAD93 and HRS98 was measured by a modified version of the TICS (The Telephone Interview Cognitive Screen) instrument, a telephone interview adapted

from the MMSE (mini mental state examination)(Brandt, Spencer, & Folstein, 1988) (Folstein, Robins, & Helzer, 1983). There were six tasks yielding a maximum of 35 points, with higher scores implying better functioning. The tasks included immediate and delayed recall test; a serial seven subtraction test; a counting backwards test; an object naming test and recall of date, the president and the vice-president. For those who refused an entire task, we assigned those who refused the immediate recall task a score of 2 out of 10, and those who refused the serial 7s a score of 1 out of 5 (Herzog & Wallace, 1997). For the other questions assessing cognitive impairment we assigned 0 points for refusal. As suggested elsewhere,(Herzog & Wallace, 1997) we adopted a cutoff of 8 out of 35 to identify the population with severe cognitive impairment. We explored the sensitivity of cut off points 7 and 9, which did not result in meaningful changes (data not shown). Recovery is defined as scoring 10 points or more after having been identified as cognitively impaired.

When a proxy represented the respondent (about 10% of the sample in each wave), he was asked: "How would you rate the respondent's memory at the present time?" and "How would you rate the respondent in making judgments and decisions?" Respondents whose memory and judgment were assessed as poor were considered to be cognitively impaired. Our definitions and cut points were based on prior studies using HRS data (K. M. Langa et al., 2008; Suthers, Kim, & Crimmins, 2003).

Exposure measures

Exposures assessed are BMI, smoking and levels of education. We studied differences by sex and race/ethnicity categorized as non-Hispanic white, non-Hispanic black and Hispanic. Self-reported weight and height at the first report defines BMI (kg/m2), classified as low normal weight (18.5-22.9), high normal weight (23-24.9), overweight (25-29.9), mildly obese (30-34.9) and severely obese (35+). Weight loss at older ages may be a sign of impending disease. To avoid reverse causation, we excluded persons with a BMI less than 18.5. Smoking status is included as 'never

smoked', 'stopped smoking' and 'currently smoking' based on the first reported information on smoking status. We distinguish three groups of educational attainment: Less than high-school or General Educational Development (GED), High-School graduate and some college, and College graduate and above. We did not include self reported hypertension or alcohol use (see discussion).

Methods

We estimated Cox proportional hazard model for proportional hazard ratios for the studied determinants, including sampling weights to account for the oversampling of minority ethnic groups. We use age as the time scale for the baseline hazard because we are interested in age at onset of cognitive impairment and years with impairment. In Cox models, age is used less frequently than time since diagnosis or time-on-study. The choice of time scale depends on the research question and the methodological considerations (Chueng et al., 2003; Thiébaut and Bénichou, 2004). The use of age as the time scale is also consistent with the life table structure. The implication of using age instead of another time measure in the Cox proportional hazard model is that the effects of the studied determinants do not vary with age. We used Schoenfeld residuals test to verify proportionality over age. Because the effect of the risk factors was not proportional for the transitions healthy to death or cognitive impairment, we ran the Cox analysis separately for ages 55 to 75 under and age 75+ We defined multistate life tables by the estimated transition rates to cognitive impairment, recovery and death. For cognitive impairment we assume transitions halfway between two waves. We estimated the hazard rates of transitions to death and cognitive impairment by age for each determinant of interest and for males and females and smoothed these by Poisson regression. The life table model is thus piece-wise constant, with rates increasing exponentially with age (Qiu et al., 2007). The main outcome is duration at age x in the life table cohort: total residual life expectancy, life expectancy with and life expectancy without cognitive impairment. Because of large heterogeneity between ethnic groups and gender, we stratified the life tables by race and sex. Life expectancies by risk factor are only shown for the

white population, as the sample of individuals of ethnic minorities by risk factor was too small. Confidence intervals for the multistate life table outcomes were calculated using bootstrapping with 250 replicates.

Results

From the HRS sample (N=30207), we selected individuals who participated at least 2 waves (N=24586), reported information on BMI, smoking and education (23817), and had a BMI>18.5 (23408) and were aged 55 or over, resulting in a sample of 22388, 9834 males and 12554 females. Table 1 shows the characteristics of the study population.

[Table 1 about here]

Incidence and recovery

861 men and 1332 women experienced the onset of cognitive impairment during observation, of which 39% and 35% reported by proxy. A total of 557 individuals experienced recovery, 28% and 23% for males and females respectively. We ignored recovery in relapse/recovery/relapse episodes as these were rare (N=26). Table 2 shows the exposure and incidence by age and sex.

[Table 2 about here]

Proportional hazard analysis

Table 3 shows the proportional hazard ratios for transitions to death and to cognitive impairment by race, BMI, smoking status and levels of education. The effects of risk factors on recovery from cognitive impairment to healthy were not significant (data not shown). The risk to cognitive impairment is about twice as high for blacks and Hispanics as for whites (not significant for

Hispanics aged 75+). BMI has little effect on the incidence of cognitive impairment or on survival of the impaired. BMI over 35 increases the risk of cognitive impairment for males, maybe due to an increased risk of vascular dementia in the severely obese. This effect disappears when we control for interaction effects with race, smoking and education. The evidence for an effect of smoking is mixed and also disappears after including interaction effects (data not shown). Higher education postpones incidence of cognitive decline in both males and females. The mortality risks of higher educated individuals, once cognitively impaired, tend to be higher compared to the lower educated, although this is only significant for medium educated females. The protective effect of higher education against cognitive impairment is much stronger between age 55 and 75 than at 75 and over. High education is even more protective for blacks than for whites: relative risks to cognitive impairment for black men and women are 0.09 [0.01,1.48] and 0.10 [0.01,0.73] compared to 0.28 [0.16,0.48] and 0.25 [0.11,0.58] for whites.

[Table 3 about here]

Life expectancy with cognitive impairment

Translating age, sex and risk factor-specific transition rates into life expectancies at age 55 defines the stratified life expectancy with and without cognitive impairment for each risk group. The life expectancy of the USA population in 2003 was 24.6 and 28.1 for white men and women and 21.2 and 25.9 for black men and women at age 55 (Centers for Disease Control and Prevention, 2006). The life expectancy of our study population, slightly selected for good health (there are no persons in institutions at entry and low BMI was excluded), was respectively 25.4 and 30.0 years for whites and 22.9 and 26.5 for blacks. In the white non-hispanic population, 55 year old males and females spend respectively 1.7 [1.5,1.9] years and 2.7 [2.4,2.9] years with cognitive impairment. Average lifespan with cognitive impairment differs remarkably between the ethnic groups, as demonstrated in figure 1.

[Figure 1 about here]

Male and Female blacks live on average 3.7 [2.8,4.6] and 3.7 [3.0,4.5] years longer with cognitive impairment than whites. Hispanic men and women live 3.2 [1.9,4.6] and 5.8 [4.2,7.5] years more with cognitive impairment compared to white non-Hispanic men and women.

The number of years lived with cognitive impairment varies among risk factors, as shown for the white non-Hispanic population in table 4.

[Table 4 about here]

BMI does not change duration of life with cognitive impairment. Smoking shortens the duration of cognitive impairment. Ever and current smokers live significantly shorter than never smokers with cognitive impairment: -0.7 years [-1.2,-0.3] for men and -0.9 [-1.3,-0.5] for women. The high mortality of smoking compresses both morbidity and a healthy life (Barendregt, Bonneux, & van der Maas, 1997; Mamun et al., 2004; Reuser, Bonneux, & Willekens, 2009). A high education effectively and seriously compresses cognitive impairment. Highly educated men live 1.1 [0.7,1.4] years with cognitive impairment, which is 1.6 [1.1,2.2] years shorter than lowly educated men. Highly educated women, live 1.9 [1.4,2.4] years with cognitive impairment, which is 1.9 [1.6,2.6] years shorter than lowly educated women. For black men and women, low education doubles the number of years with cognitive impairment from 3.2[2.1,4.4] and 4.0[3.0,5.1] for medium or high education to 6.8[5.6,7.9] and 8.2[7.1,9.3] for lowly educated. Factors that extend lifespan to older ages, like being a woman or a non-smoker, increase the duration of cognitive impairment. Only higher levels of education increase life in good cognitive health while decreasing the duration of cognitive impairment. Ironically, lifespan with cognitive impairment is most compressed in the highly educated smokers. Figure 2 shows the gains and

losses in years lived with and without cognitive impairment by risk factors for non-Hispanic whites, illustrating the distinctive effect of smoking and education. Smoking shortens life with and without cognitive impairment. Higher education extends life in cognitive health and compresses cognitive impairment to a short period at the end of life.

[Figure 2 about here]

Lifetime probability and percentage of CI

A measure of interest both for individuals and public health, is the lifetime probability of ever developing cognitive impairment. A high probability is often the prize paid for a long life. In the HRS life table cohort of white individuals at age 55, more than one in three women (36% [0.34%,0.38%]) will experience cognitive impairment compared to close to one in four men (23 % [0.21%,0.24%]). As blacks and Hispanics face higher risks to cognitive impairment at all ages, this lifetime probability raises to very high levels. Black men and women run a risk of respectively 44% [39%,48%] and 53%[49%,57%] to ever become cognitively impaired and Hispanics 46%[39%,54%] and 61%[54%,68]. BMI has little effect on the lifetime probability of cognitive impairment. Smoking, by shortening life, considerably lowers the probability of cognitive impairment at age 55: 28% [23%,0.32%] and 41% [38%,43%] for never smoking white men and women, 18% [15%,22%] and 22% [17%,27%] for male and female white smokers . High education, however, increases life expectancy but decreases the probability of cognitive impairment. The lifetime probability of cognitive impairment is lower in the higher educated men and women (for whites respectively 20% [13%,27%] and 29% [22%,36%]) compared to the lower educated people (30% [26%,33%] among men and 39% [36%,43%] among women). When expressed as relative percentages of total life expectancy, a long life still goes with a relatively long duration of cognitive impairment. White men live on average 6.7% [5.9%,7.4%]of their life after age 55 with cognitive impairment; white women 8.9% [8.2%,9.6%]. Black men and women

can expect to live 23.7% [20.3%,27.1%] and 24.1% [21.6%,26.5%] of their life over age 55 with cognitive impairment, Hispanics 18.3% [13.9%,22.6%] and 26.6% [22.4%,30.8%]. Again education has a significant impact on this share, ranging from 11.2% [9.4%,13.1%] and 3.6% [2.6%,4.7%] for respectively lowly and highly educated white men and from 13.5% [11.8%,15.2%] to 5.9% [4.2%,7.7%] for lowly and highly educated white women.

Discussion

The life table cohort of Americans aged 55 and over from the HRS study shows that white race, male sex, smoking and higher education compress life with cognitive impairment. Blacks and Hispanics have shorter life expectancies and still live more life years with cognitive impairment. Our findings of increased incidence and duration of cognitive disability are consistent with other epidemiologic studies describing higher prevalence and incidence of dementia in racial and ethnic minorities (Tang et al., 2001)(Bachman et al., 2003)(Gurland et al., 1999), while disagreeing with others (Fillenbaum et al., 1998)(Fitzpatrick et al., 2004). These results are to be interpreted with caution, however, as the HRS has not been designed to measure dementia epidemiology. We identified several reasons why the observed occurrence of dementia may appear higher in ethnic minorities than in whites in the HRS. Culturally and educationally sensitive diagnostic ascertainment methods lead to very different estimates of dementia prevalence in low and middle income countries (Llibre Rodriguez et al., 2008). In less educated minority populations, the MMSE (source of the TICS used in the HRS) was less specific, yielder lower scores (Ng et al., 2007)(Fitzpatrick et al., 2004). Differences in learned test-taking strategies, comfort with testing staff, and cultural relevance of test items can explain some of the race differences in baseline test scores (Karlamangla et al., 2009). Differences in levels of education may not fully be accounted for by actual stratification in three classes (Fitzpatrick et al., 2004)(Gurland et al., 1999). A final explanation is that prevalence of uncontrolled hypertension and diabetes and hence risk for

vascular dementia is higher in African Americans, even after controlling for BMI and other risk factors (Natarajan et al., 2009)(Kramer et al., 2004)(Tang et al., 2001)(Maskarinec et al., 2009). In brief, while an ethnic component can not be excluded, part of these higher rates may be explained by uncontrolled high blood pressure and diabetes and part is spurious, explained by residual confounding by levels of education and the culturally less specific TICS.

Women and non-smokers live more years with cognitive impairment than men, simply because they live longer. The same holds for never-smokers compared to (former) smokers. High education increased total lifespan, but increases lifespan free of cognitive decline even more, shortening life with cognitive impairment. Our findings on the effect of education are in line with the cognitive reserve hypothesis as described before (Fratiglioni & Wang, 2007; Y. Stern, 2006; Y. Stern, Tang, Denaro, & Mayeux, 1995). A higher education is related to both a decreased risk of cognitive decline and an increased risk of mortality once cognitively impaired. Brain reserve is accumulated and preserved by mentally stimulating exercise throughout life, with education as most important factor. Brains with larger reserves can sustain and adapt to more damage before reaching the critical threshold of clinical disease. A higher level of neuropathological damage means a more advanced stage of brain disease, resulting in an increased dementia related mortality risk (Witthaus, Ott, Barendregt, Breteler, & Bonneux, 1999). The protective effect of high education among African Americans was stronger.

We found little effect of BMI on the incidence of cognitive impairment. However, weight loss induced by imminent disease mask effects of increased BMI over the life span, a suspected cause of dementia (Gorospe & Dave, 2007; Kivipelto et al., 2005; Qiu et al., 2007). The disentanglement of the intimate relationships of BMI, weigh loss and cognitive impairment is beyond the scope of this study.

Consistent with a meta-analysis of prospective studies of smoking as risk factor for cognitive impairment (Anstey, Sanden, Salim, & O'Kearney, 2007). we found an increased risk of cognitive impairment for smokers compared to never smokers. But this is largely offset by the high mortality of smokers, shortening life expectancy with cognitive impairment.

The expected lifespan with and without cognitive impairment is higher than the results of the 1980 cohort of the Kaiser Permanente Medical Care Program of North California (Sauvaget, Tsuji, Haan, & Hisamichi, 1999) and AHEAD 1993 (Suthers et al., 2003). The differences are mainly due to higher mortality in those studies, which can be explained by the older period and the inclusion underweight individuals and ethnic minorities in their life expectancy calculations. The study of Suthers et al. uses cross-sectional estimates of prevalence of cognitive impairment (Sullivan's method) representing information of lifetime cognitive impairment rather than recent onset of impairment as measured with incidence rates in the multistate life table approach.

The HRS survey is a comprehensive social study, not a specific epidemiological study that provides a clinical diagnosis of dementia. The definition of cognitive impairment has to be understood as a score of a screening tool, comparable to the MMSE, which is correlated to, but not identical with clinical dementia (K. Langa et al., 2001). A similar limitation is the different measure for cognitive impairment, defined by self-report or proxy respondents. We combined these as in other studies (Suthers et al., 2003).

A certain weakness of this study is the lack of detail of other known causal factors related to the onset of dementia, high blood pressure, moderate and high alcohol consumption and the presence of the APOE4 allele. Information on the APOE4 allele is not available in the HRS. We excluded alcohol use, mistrusting the results. We might have been erroneous, but alcohol in the HRS had a very large protective effect both on dementia and on death. Even drinking 6 glasses or more drinking showed no detrimental effect on incidence of cognitive disability (data not shown).

While moderate alcohol use may protect against dementia, mediated by vascular disease, it is not plausible that this holds for high levels of use (Anttila et al., 2004; Stampfer, Kang, Chen, Cherry, & Grodstein, 2005). We excluded blood pressure, fearing to introduce confounding. The incidence of dementia is related to both a higher blood pressure in mid life and a lower blood pressure at the end of life (Qiu et al., 2005; Ruitenberg et al., 2005). The period life table, stretching a limited follow up over the rest of life after age 55, confounds these opposite effects in a single synthetic cohort. Changes over times and age, such as declining cognitive impairment prevalence or changing effects of blood pressure over the life course can not be taken into account in this relatively simple analysis (K. M. Langa et al., 2008).

The HRS sample includes only non-institutionalized persons at baseline, but follows these into nursing homes. Therefore, our sample at baseline is initially healthier than the total population and estimates of life years with cognitive impairment are underestimated.

As Olshansky put it “Few topics in the world of science are as interesting and personal as the question of how much time will pass between our birth and death, and the status of our health along the way.”(Olshansky, 2008). Cognitive impairment is a major cause of disability and care dependence and nearly all people fear loss of cognition and the ability for self care. Ageing and life extension of the baby boom cohorts will cause numbers of demented people to increase rapidly. The good news is that these findings from the HRS confirm that raising levels of education and mentally stimulating occupations compress cognitive disability by postponing incidence of dementia more than death. Raising education to the highest level attainable is not only a millennium goal for developing countries, but for developed countries, too.

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Table 1: Distribution of sample characteristics at entry into the survey.

		Males	Females
Total		9834	12554
Race/ethnicity	White	7763	9579
	Black	1309	1985
	Hispanic	762	990
Education	Low education	3409	4258
	Medium education	4446	6682
	High education	1979	1614
Smoking	Never smoked	2568	6592
	Stopped smoking	5036	3731
	Currently smoking	2230	2231
BMI	BMI 18.5-22.9	1287	3075
	BMI 23-24.9	1800	2189
	BMI 25-29.9	4804	4357
	BMI 30-34.9	1516	1975
	BMI 35+	427	958
Age at Entry	[55,65]	6045	7013
	(65,75]	2424	3206
	(75,85]	1143	1849
	(85,95]	216	459
	(95,105]	6	27

Table 2: Population size, exposures and events by age and sex.

	Population at entry into the survey		mean follow up until CI or death/censoring		Onset of first cognitive decline		Mean follow-up until Death/censoring		Death incidence	
	Males	Females	Males	Females	Males	Females	Males	Females	Males	Females
[55,60]	4850	6122	7.92	7.67	89	114	8.07	7.79	553	395
(60,65]	1195	891	9.51	9.56	155	134	9.72	9.76	262	126
(65,70]	646	1033	7.48	7.10	81	77	7.73	7.35	175	147
(70,75]	1778	2173	6.76	7.32	118	134	7.20	7.75	588	473
(75,80]	686	1089	6.98	7.39	136	183	7.58	8.35	378	427
(80,85]	457	760	6.01	6.02	144	299	7.06	7.51	306	459
(85,90]	181	349	4.64	4.92	88	239	5.59	6.49	147	267
(90,95]	35	110	3.82	3.86	44	110	4.96	5.69	32	92
(95,105]	6	27	3.36	1.90	6	42	4.61	4.49	5	23
Total	9834	12554	7.64	7.45	861	1332	7.95	7.86	2446	2409

Table 3: Cox proportional hazard ratios by risk factor status (95% confidence intervals), adjusted for each other. Significant ratios are printed in bold.

	Males		Females	
	55-74	75+	55-74	75+
Healthy to death				
White	1.00	1.00	1.00	1.00
Black	**1.30 (1.09; 1.55)**	1.16 (0.93; 1.44)	**1.35 (1.10; 1.65)**	**1.23 (1.00; 1.52)**
Hispanic	0.77 (0.53; 1.11)	0.90 (0.59; 1.38)	0.99 (0.66; 1.48)	1.03 (0.63; 1.66)
BMI 18.5-22.9	**1.39 (1.16; 1.67)**	**1.27 (1.07; 1.51)**	0.83 (0.67; 1.02)	1.04 (0.88; 1.22)
BMI 23-24.9	1.00	1.00	1.00	1.00
BMI 25-29.9	0.89 (0.76; 1.03)	0.87 (0.75; 1.01)	0.90 (0.75; 1.09)	0.91 (0.77; 1.07)
BMI 30-34.9	1.14 (0.95; 1.37)	1.01 (0.81; 1.25)	0.98 (0.77; 1.23)	0.93 (0.76; 1.15)
BMI 35+	**1.45 (1.09; 1.91)**	1.23 (0.83; 1.83)	**1.55 (1.21; 1.99)**	1.22 (0.89; 1.66)
Never smoked	1.00	1.00	1.00	1.00
Stopped smoking	**1.42 (1.21; 1.66)**	**1.25 (1.08; 1.44)**	**1.37 (1.17; 1.60)**	**1.21 (1.06; 1.37)**
Currently smoking	**2.67 (2.25; 3.17)**	**1.67 (1.37; 2.03)**	**2.57 (2.18; 3.03)**	**1.85 (1.52; 2.24)**
Low education	1.00	1.00	1.00	1.00
Medium education	0.93 (0.82; 1.05)	0.91 (0.80; 1.03)	**0.70 (0.61; 0.81)**	**0.83 (0.74; 0.94)**
High education	**0.62 (0.52; 0.73)**	**0.65 (0.54; 0.78)**	**0.47 (0.36; 0.61)**	0.85 (0.69; 1.04)
Healthy to CI				
White	1.00	1.00	1.00	1.00
Black	**2.96 (2.27; 3.86)**	**1.83 (1.23; 2.71)**	**2.92 (2.22; 3.84)**	**2.06 (1.55; 2.72)**
Hispanic	**1.85 (1.09; 3.12)**	1.76 (0.88; 3.50)	**2.11 (1.32; 3.36)**	1.50 (0.75; 2.99)
BMI 18.5-22.9	**1.63 (1.07; 2.51)**	1.00 (0.70; 1.44)	1.13 (0.72; 1.77)	1.11 (0.84; 1.47)
BMI 23-24.9	1.00	1.00	1.00	1.00
BMI 25-29.9	1.10 (0.77; 1.58)	**0.70 (0.51; 0.95)**	1.34 (0.90; 1.99)	0.93 (0.71; 1.23)
BMI 30-34.9	1.27 (0.84; 1.92)	0.65 (0.40; 1.07)	1.36 (0.88; 2.10)	0.89 (0.63; 1.26)
BMI 35+	**1.71 (1.00; 2.92)**	0.66 (0.24; 1.82)	1.41 (0.87; 2.28)	0.89 (0.50; 1.58)
Never smoked	1.00	1.00	1.00	1.00
Stopped smoking	**0.69 (0.52; 0.92)**	1.02 (0.76; 1.37)	**1.45 (1.10; 1.90)**	0.86 (0.69; 1.07)
Currently smoking	0.93 (0.69; 1.26)	0.88 (0.55; 1.39)	1.26 (0.93; 1.70)	0.63 (0.39; 1.01)
Low education	1.00	1.00	1.00	1.00
Medium education	**0.50 (0.39; 0.64)**	**0.53 (0.40; 0.70)**	**0.36 (0.28; 0.46)**	**0.65 (0.53; 0.79)**
High education	**0.14 (0.09; 0.24)**	**0.42 (0.28; 0.63)**	**0.25 (0.15; 0.40)**	**0.49 (0.33; 0.73)**
CI to death				
White	1.00	1.00	1.00	1.00

Black	0.72 (0.37; 1.40)	0.74 (0.49; 1.12)	1.37 (0.73; 2.57)	0.80 (0.55; 1.15)
Hispanic	0.90 (0.32; 2.56)	0.42 (0.16; 1.14)	0.91 (0.22; 3.72)	0.76 (0.35; 1.65)
BMI 18.5-22.9	1.56 (0.66; 3.67)	0.99 (0.65; 1.52)	0.97 (0.42; 2.21)	1.25 (0.86; 1.81)
BMI 23-24.9	1.00	1.00	1.00	1.00
BMI 25-29.9	0.82 (0.36; 1.83)	0.79 (0.53; 1.17)	0.62 (0.27; 1.41)	0.95 (0.63; 1.43)
BMI 30-34.9	1.89 (0.71; 5.01)	0.94 (0.50; 1.79)	0.60 (0.24; 1.51)	1.24 (0.76; 2.01)
BMI 35+	**3.33 (1.22; 9.07)**	1.26 (0.50; 3.17)	0.48 (0.14; 1.60)	1.60 (0.73; 3.51)
Never smoked	1.00	1.00	1.00	1.00
Stopped smoking	1.23 (0.60; 2.53)	1.06 (0.74; 1.53)	1.14 (0.59; 2.19)	1.16 (0.84; 1.60)
Currently smoking	**2.04 (1.01; 4.10)**	1.28 (0.76; 2.17)	1.10 (0.55; 2.18)	1.38 (0.76; 2.51)
Low education	1.00	1.00	1.00	1.00
Medium education	1.17 (0.62; 2.21)	1.22 (0.85; 1.75)	**3.36 (1.83; 6.17)**	**1.44 (1.08; 1.92)**
High education	2.08 (0.84; 5.17)	1.29 (0.68; 2.43)	1.33 (0.40; 4.45)	1.40 (0.77; 2.56)

Table 4: Life years to live at age 55 with cognitive impairment (CI), by risk factor for non-Hispanic whites. In brackets 95% confidence limits.

	Males		Females	
	Life years with CI at age 55	Life years with CI at age 80	Life years with CI at age 55	Life years with CI at age 80
BMI 18.5-22.9	1.82 (1.35; 2.28)	1.74 (1.29; 2.19)	2.82 (2.13; 3.51)	2.66 (2.31; 3.01)
BMI 23-24.9	1.59 (1.25; 1.92)	1.43 (1.04; 1.81)	2.45 (2.01; 2.88)	2.43 (1.92; 2.94)
BMI 25-29.9	1.73 (1.43; 2.03)	1.63 (1.27; 1.99)	2.82 (2.36; 3.28)	2.95 (2.43; 3.47)
BMI 30-34.9	1.71 (1.01; 2.41)	1.55 (0.52; 2.58)	2.58 (1.93; 3.23)	2.14 (1.60; 2.68)
BMI 35+	1.63 (0.06; 3.20)	1.81 (0.00; 4.41)	2.21 (1.30; 3.13)	2.45 (1.03; 3.87)
Never smoked	2.25 (1.81; 2.70)	1.77 (1.33; 2.21)	3.00 (2.72; 3.29)	2.90 (2.61; 3.20)
Stopped smoking	1.54 (1.35; 1.73)	1.44 (1.21; 1.66)	2.16 (1.85; 2.46)	1.97 (1.59; 2.34)
Currently smoking	1.52 (1.09; 1.95)	1.85 (1.01; 2.70)	1.85 (1.34; 2.35)	1.49 (0.74; 2.24)
Low education	2.65 (2.20; 3.11)	2.37 (1.97; 2.76)	3.78 (3.28; 4.29)	3.55 (3.05; 4.05)
Medium education	1.32 (1.05; 1.59)	1.20 (0.92; 1.47)	2.24 (2.00; 2.48)	2.34 (2.04; 2.64)
High education	1.05 (0.73; 1.36)	1.04 (0.63; 1.46)	1.89 (1.36; 2.42)	1.67 (1.16; 2.18)
Total	1.69 (1.50; 1.89)	1.58 (1.37; 1.78)	2.66 (2.44; 2.88)	2.63 (2.41; 2.86)
	Life years free of CI at age 55	Life years free of CI at age 80	Life years free of CI at age 55	Life years free of CI at age 80
BMI 18.5-22.9	21.13 (20.10; 22.16)	5.72 (5.11; 6.34)	27.40 (26.71; 28.09)	7.54 (7.11; 7.97)
BMI 23-24.9	23.97 (23.07; 24.87)	6.96 (6.38; 7.53)	27.68 (26.86; 28.49)	7.70 (7.17; 8.23)
BMI 25-29.9	24.81 (24.19; 25.42)	7.31 (6.85; 7.77)	27.88 (27.20; 28.56)	8.45 (8.00; 8.90)
BMI 30-34.9	23.22 (22.18; 24.27)	6.97 (6.00; 7.95)	27.29 (26.25; 28.33)	7.59 (6.83; 8.35)
BMI 35+	21.39 (19.58; 23.21)	4.99 (3.58; 6.41)	23.69 (22.08; 25.30)	6.42 (5.10; 7.73)
Never smoked	26.87 (26.02; 27.72)	7.60 (6.94; 8.25)	28.89 (28.43; 29.34)	8.10 (7.79; 8.41)
Stopped smoking	24.62 (24.09; 25.16)	6.84 (6.48; 7.19)	27.46 (26.77; 28.14)	7.83 (7.37; 8.30)
Currently smoking	18.82 (18.04; 19.60)	5.05 (4.37; 5.73)	23.06 (22.13; 23.98)	6.21 (5.45; 6.97)
Low education	20.95 (20.22; 21.67)	5.56 (5.13; 5.99)	24.23 (23.48; 24.97)	6.34 (5.92; 6.75)
Medium education	23.84 (23.27; 24.42)	7.20 (6.72; 7.68)	28.36 (27.87; 28.86)	8.57 (8.20; 8.95)
High education	27.80 (26.88; 28.72)	8.60 (7.77; 9.42)	29.99 (29.09; 30.90)	8.64 (7.93; 9.35)
Total	23.75 (23.34; 24.15)	6.84 (6.56; 7.12)	27.35 (26.97; 27.74)	7.82 (7.56; 8.07)

Figure 1: Years lived with cognitive impairment at age 55 by race, error bars are 95% confidence intervals.

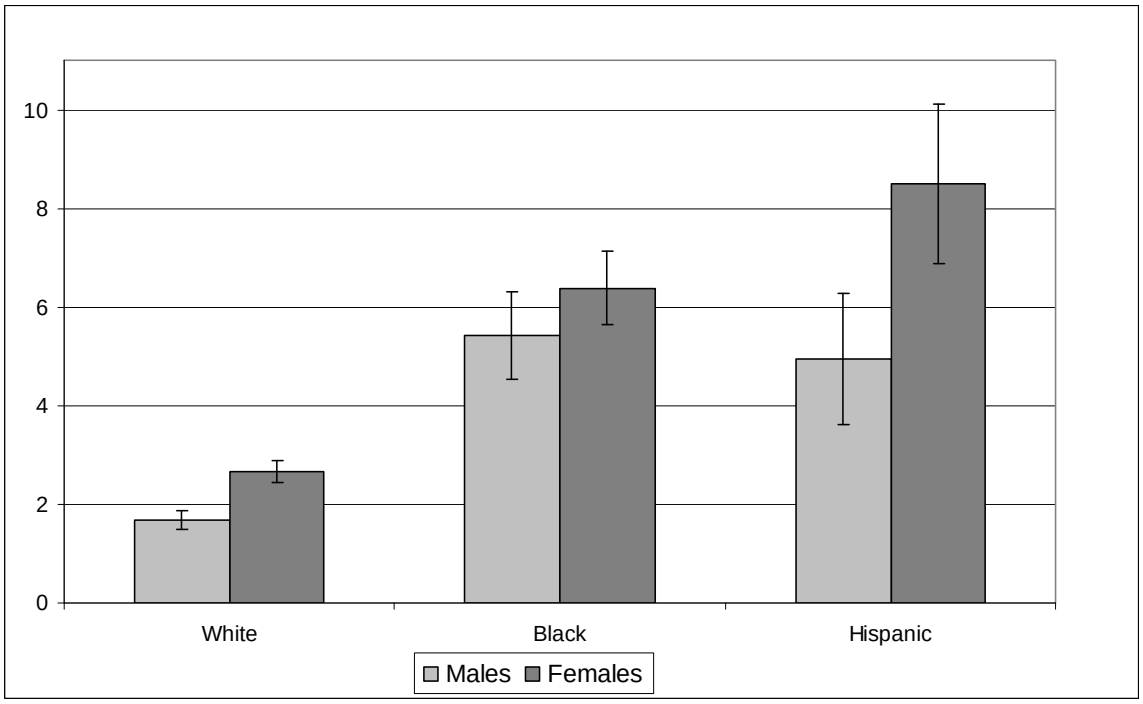

Figure 2: Gains and losses in years lived with and without cognitive impairment by risk factors for non-Hispanic whites, errors bars are 95% confidence intervals.