Educational Differences in Risk of Cognitive Impairment Through Adulthood

BIOSTAT 699 Project 5

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Abstract

In this study we investigated the Americans' Changing Lives (ACL) Study, a longitudinal cohort study conducted from 1986-2011, focusing on the Telephone Instrument for Cognitive Status (TICS). We wished to determine whether cohort differences in cognitive status trajectories over the 25 year study period are attributable to educational differences, with four cohorts being defined based on age at baseline. Using a Generalized Estimating Equation (GEE) approach, we modeled the probability of cognitive impairment, defined as a TICS score of three or less. Increases in education over time did not significantly explain cohort differences in age trajectories of CI. In addition, we found that weight, minority status, household income, comorbid health concerns, and education are significantly associated with cognitive impairment.

Introduction

Mild cognitive impairment (MCI) is a term used to describe a set of symptoms based on a deficit in memory and normal cognitive and functional abilities. This definition of MCI has been used widely in the US since 1999, and MCI is seen as a transition state from normal cognitive ability to dementia.[1] For the study, we define cognitive impairment (CI) as either MCI or dementia. Risk factors for CI include heart disease, obesity, smoking, physical activity, diet, and years of formal education. As the US population ages, the economic burden of cognitive impairment, especially dementia, is estimated to grow four-fold in the next 40 years.[2]

The Americans' Changing Lives (ACL) Study is a longitudinal cohort study featuring a nationally representative sample followed from 1986-2011, based at the University of Michigan Interuniversity Consortium for Political and Social Research.[3] The ACL started in 1986 with 3,617 adults who were representative of the above 25 and non-institutionalized adult population, and the survey oversampled minorities and elderly. These individuals were followed for 25 years in five waves, in 1986, 1989, 1994, 2001, and 2011. The Telephone Instrument for Cognitive Status (TICS) was used to measure cognitive impairment at each wave. The TICS instructs individuals to answer five questions via telephone, including providing the day, date, name of the US president, name of the previous US president, and performing serial subtraction.[2]

The study also split individuals into four cohorts, based on their age in 1986, as shown in Table 1. Using these data, we will test whether there are cohort-based differences in the trajectory of cognitive impairment across age. We posit that this may be the case because of different life circumstances specific to each cohort. In particular, prior studies have found that a low educational level is a risk factor for dementia.[1] Education can be protective against dementia and CI though many different pathways, including health behaviors, wealth, leisure activity, as well as the cognitive reserve theory – the brains of higher educated individuals are more able to adapt to disruptions in their neural networks. We will examine education, in particular, as a potential factor explaining cohort-level differences in CI risk over time.

Statistical Methods

Study Population and Variables

ACL study participants were recruited in 1986 from the population of non-institutionalized adults older than 25 in the United States. African Americans and persons aged over 60 were sampled at twice the rate of non-African-Americans and younger people. Investigators conducted five waves of interviews with these participants over the course of 25 years. The first wave in 1986 included 3,617 participants, and this number declined steadily over the course of the study due to death and loss to follow-up until the final wave in 2011, which included only 1427 participants. In addition to TICS score, many demographic, lifestyle, and health-related variables were collected in this study, including gender, race, marriage status, household income, weight, age, and number of comorbid health problems. For our purposes, we defined a binary cognitive impairment variable that takes value 1 (impairment) for a TICS score of 3 or below and 0 (no impairment) for a TICS score of 4 or 5. We defined education level as an ordinal variable with three categories: 0 (Less than high school, 0-11 years), 1 (high school but less than college, 12-15 years), and 2 (some college or more, 16+ years). Baseline characteristics are summarized in Table 2, and an education by cohort bar plot is shown in Figure 1. Many observations are missing from drop-out or loss-to-follow-up at specific waves; Table 3 summarizes the missing data in the cognitive impairment score.

Analysis

We used the generalized estimating equations (GEE) method to fit three logistic regression models using cognitive impairment as the outcome variable. The GEE approach was used in this case because it allows us to account for correlated observations on an individual across time. We used an independent correlation structure to allow us to estimate effects for time-varying variables such as age, marriage status, weight, household income, and number of health problems. Each of the three models includes the potentially relevant demographic and health variables described above.

The first model includes the main effects of participant age at interview and cohort and the interaction effect of cohort and age. The second model includes these effects and the main effect of education, and the final model additionally includes the interaction effect between cohort and education. We use these models to establish that there exist cohort differences in cognitive impairment across age and to determine whether these differences are attributable to education level. We also calculate Tjur's R used to determine how much variation in CI is explained by variables in each of our models.[5] The significance threshold in our models is set at

$\alpha = 0.05$. All data management and analysis was performed using the SAS statistical software package.

Results

Table 4 shows the results of the logistic regression models. A model including only age as a predictor is included for comparison. The results of the model 1 indicate that weight, minority status, household income, and comorbid health concerns are significantly associated with cognitive impairment. We observe significant main effects of age and cohort and a significant age-cohort interaction. The significance of the interaction term in particular indicates that the trajectory of cognitive impairment across age differs by cohort. Figures 2 and 3 demonstrates this difference visually – the trajectory lines of each cohort are clearly different.

In model 2, the demographic and health variables identified by the first model remain significant in this model, as do cohort, age, and age-cohort interaction ($p < 0.01$ in all cases). Education itself is also significant in the second model ($p < 0.0001$). However, adding education in the model does not lower the cohort nor age-cohort interactions, suggesting that education does not significantly explain the difference in cohort trajectories of CI. The only covariate that decreased with the addition of education was the effect of cohort 2, from 0.323 to -0.030.

In the final model, all variables previously identified as significant remain significant in this model ($p < 0.01$ in all cases). However, the education-cohort interaction is not significant in the model. The age-cohort interactions are unchanged from model 2.

Looking at Tjur's R, we see that the age-only comparison model explains about 4% of the variation, the variables without education explain about 12% of the variation, and the variables with education explain about 13% of the variation. This result agrees with previous studies suggesting that more education decreases the risk of CI.

Discussion

The results we obtained above indicate that neither individual nor cohort-level differences in education substantially account for the cohort differences in cognitive impairment trajectory. The main (individual) effect of education was significantly associated with cognitive impairment in the second and third models, but its inclusion in the model did not eliminate the significance of the age-cohort interaction term. This result, along with the reduction in risk of cognitive impairment associated with higher levels of education, supports the cognitive reserve theory of cognitive impairment. It also indicates that individual differences in level of education are not sufficient to completely account for the cohort differences in cognitive impairment by age that we observe in our data. The cohort-education interaction effect was not significant in the third regression model, indicating that cohort-level differences in education are not significantly associated with the risk of cognitive impairment. Since this interaction term had no impact on the significance of the age-cohort interaction, we also conclude that cohort differences in education do not explain cohort differences in cognitive impairment across age.

The results of our study indicate that, though individual differences in education impact the risk of cognitive impairment, other factors influence the cohort differences in cognitive impairment across age that we observe in our data. These factors are likely to differ by cohort and may be related to differences in the environments and experiences of different generations of Americans. As noted in a paper by Clarke using ACL data to study mental health over adult life, the framework of this paper is based on a structural model that views health outcomes as highly deterministic. Clarke cites the work of recent scholars in including political and economic interests as explanatory variables.[6] It is possible that differences in psychological stressors such as wartime experiences and military service can partially explain generational differences. The twentieth century was also a period of public health transition in the United States. Many preventive measures, such as vaccines, that were common later in the century were not available to or frequently used by older generations. It is therefore possible that improved public health and infectious disease prevention later in the century can explain the cohort differences.

Our study had some important advantages. First, our sample size was very large, which allowed us to estimate all main and some interaction effects of nine variables without sacrificing much power. We also used the robust GEE approach to fit our regression models. This method was advantageous since it allowed us to use all available data and did not require observations at each wave for a person's data to be included in estimating effects.

However, there were also drawbacks to our approach. We did not use survey weights in our model fit. As the ACL was conducted with an oversampling of African Americans and the elderly, excluding the weights in our analysis may have caused our results to not be generalizable to the population of the United States, and explained some of the coefficients in our model. The healthy-survivor effect may also explain some of our results, and is compounded by the larger loss to follow-up in the older cohorts. In addition, use of the TICS instrument came with some limitations. In a review of using telephone tests to test for CI, researchers had difficulties contacting people, some because they did not have the correct phone numbers. After establishing contact, refusal rates ranges from 7% to 35% in studies, and telephone interviews can be compromised by illness, deafness, and dementia.[4] We also used a linear age effect in our models, and the effect of age is likely to be nonlinear.

Future studies should focus on collecting data regarding environmental exposures, as cohort differences in environment may explain a significant amount of the cohort-level variation we observed in CI risk. Future studies should also try to account for hereditary factors that may be associated with CI by collecting genetic data from participants. Future investigators should consider using a more sensitive tool for CI than TICS, since a more sensitive assessment can provide information not only on CI, but also its severity. Future study of CI and its causal factors is crucial – as the population of the United States ages, the economic and social impact of late life health problems will only continue to increase.

Tables and Figures

Table 1: Cohort Assignment by age at baseline.

Cohort	Age at baseline
1	$Age_1 \leq 39$
2	$40 \leq Age_1 \leq 54$
3	$55 \leq Age_1 \leq 69$
4	$70 \leq Age_1$

Table 2: Baseline characteristics of the population split into continuous and categorical

Continuous Variables at Baseline

Variable	**Statistic**	**Cohort 1**	**Cohort 2**	**Cohort 3**	**Cohort 4**
Age	**Mean**	31.8	46.3	62.9	76.6
	SD	4.3	4.3	3.9	5.3
Years of Education	**Mean**	13.1	12.2	10.7	9.7
	SD	2.5	3.0	3.5	3.8
Household Income	**Mean**	25,707.54	29,115.31	20,723.00	12,614.16
	SD	18,387.46	21,659.21	18,529.93	12,266.25
Number of Comorbidities	**Mean**	0.34	0.75	1.52	1.81
	SD	0.64	0.99	3.54	1.19

Categorical Variables at Baseline

Variable	**Cohort 1**	**Cohort 2**	**Cohort 3**	**Cohort 4**
% Cognitively Impaired	14.1	20.7	23.2	34.0
% Less Than High School Education	16.3	29.5	46.6	59.4
% High School Graduates Only	62.1	54.3	43.7	33.5
% College Graduates	21.5	16.2	9.7	7.1
% Married	54.1	61.4	61.4	39.9
% Normal Weight	55.5	40.7	37.5	46.0
% Female	56.6	59.4	64.2	70.5
% Minority	44.3	43.5	35.8	32.7

Table 3: Missing Cognitive Impairment Variables (N=3,617)

Variable	**Number Missing**
Cognitive Impairment Wave 1	0
Cognitive Impairment Wave 2	750
Cognitive Impairment Wave 3	1,222
Cognitive Impairment Wave 4	1,927
Cognitive Impairment Wave 5	2,298

Figure 1: Educational Attainment by Cohort. For education status, we have that 0 indicates 0-11 years of education, 1 indicates 12-15 years of education, and 2 indicates 16+ years of education. The 1st cohort was youngest at baseline (25-39), the 4th cohort oldest (70+).

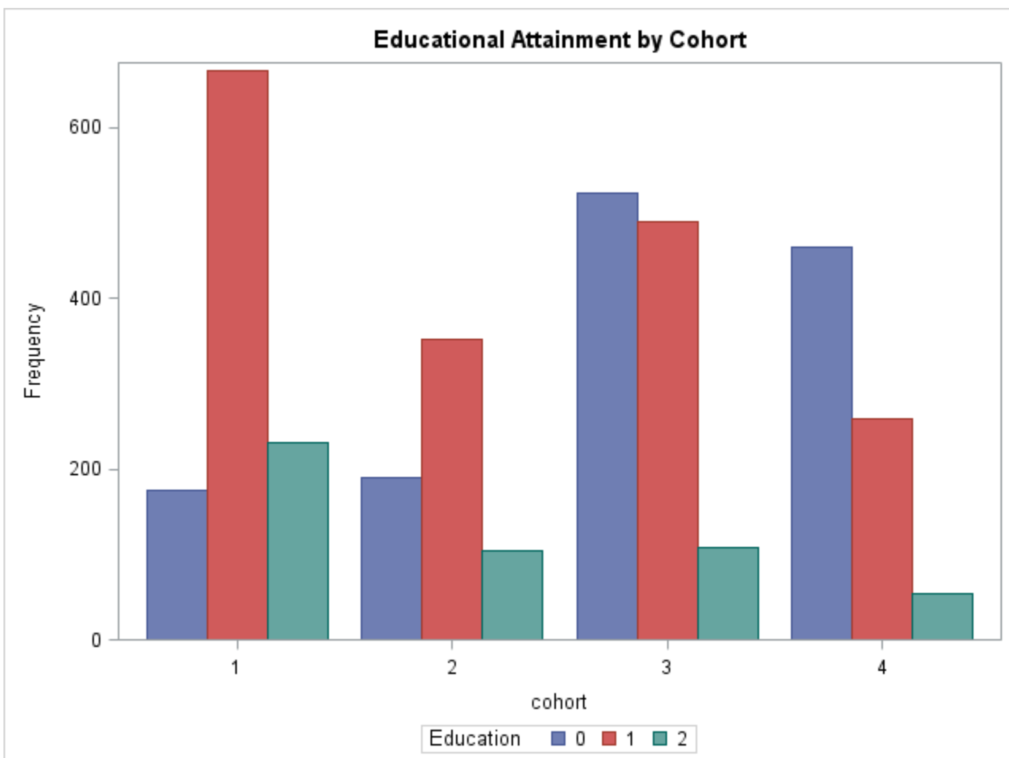

Figure 2: Mean Cognitive Impairment Scores by Cohort.

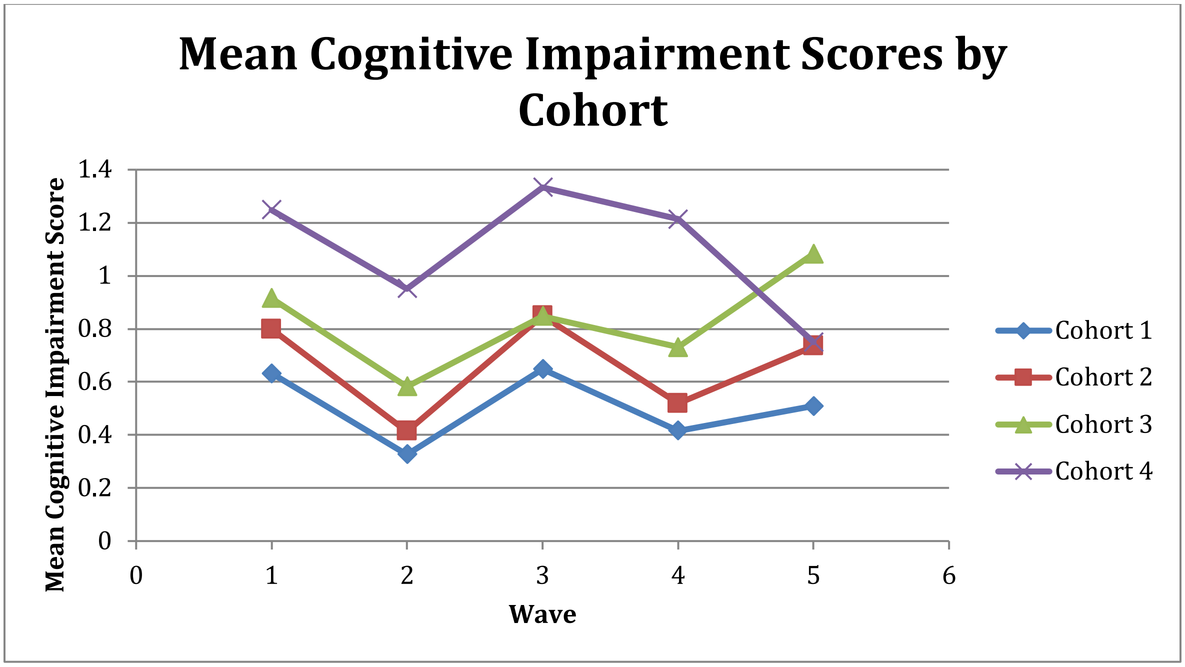

Figure 3: Percent cognitively impaired in the data, with 95% confidence intervals around the mean.

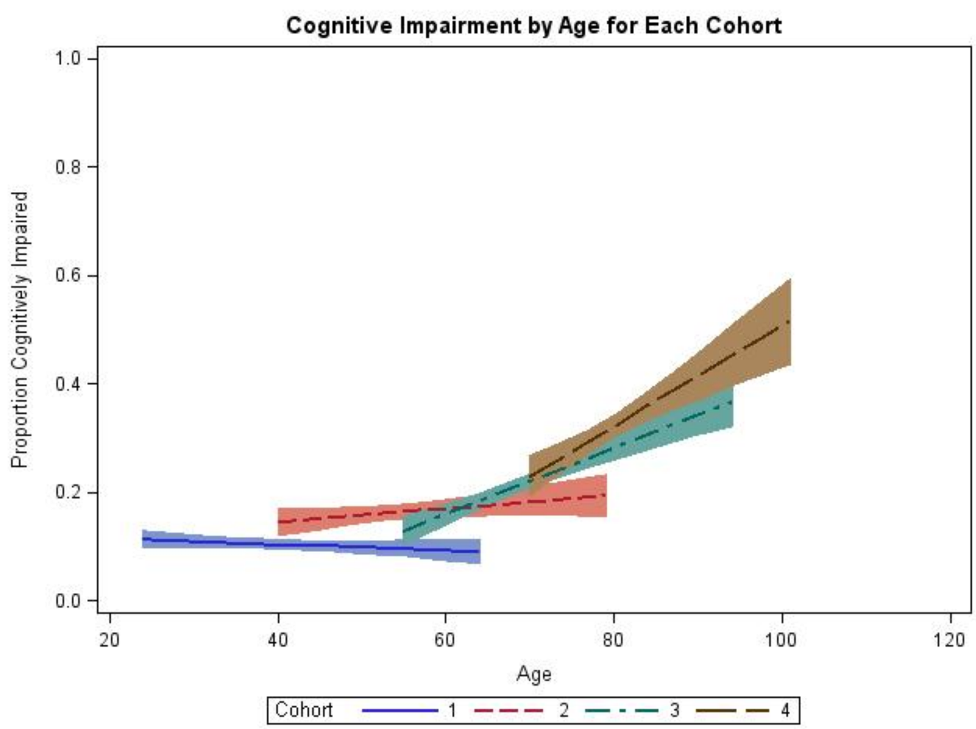

Table 4: Model fits for the comparison model with only age, the comparison model including covariates without education, the comparison models with covariates and education, and the comparison model with education and an education-cohort interaction.

	Only Age	+ Variables without education	+ Education	+ Education-cohort interaction
Effects	**Comparison Model**	**Model 1**	**Model 2**	**Model 3**
Intercept	-3.289 *	-2.063 *	-1.561 *	-1.527 *
Age	0.029 *	-0.002	-0.002	-0.002 *
Birth Cohort 1 (25-39)		0	0	0
2 (40-54)		0.323	-0.030	-0.075
3 (55-69)		-1.904 *	-2.571 *	-2.574 *
4 (70 and above)		-2.548 *	-3.167 *	-3.143 *
Female		-0.025	0.027	0.027
Married		0.006	-0.049	-0.050
Normal Weight		0.186 *	0.218 *	0.219 *
Minority		0.948 *	0.795 *	0.790 *
Household income		0.000 *	0.000 *	0.000 *
Number of Health Conditions		0.119 *	0.088 *	0.0873 *
Birth Cohort*age 1 (25-39)*age		0	0	0
2 (40-54)*age		0.003	0.008	0.077
3 (55-69)*age		0.037 *	0.044 *	0.044 *
4 (70 and above)*age		0.030 *	0.051 *	0.050 *
Education 0 (0-11 years)			0	0
1 (12-15 years)			-0.792 *	-0.824 *
2 (16+ years)			-1.498 *	-1.688 *
Education*cohort 2(16+ years)*1				0
2(16+ years)*2				-0.221
2(16+ years)*3				0.423
2(16+ years)*4				0.570
1(12-15 years)*1				0
1(12-15 years)*2				0.083
1(12-15 years)*3				-0.049
1(12-15 years)*4				0.100
0(0-11 years)*1				0
0(0-11 years)*2				0

0(0-11 years)*3				0
0(0-11 years)*4				0
Goodness of Fit				
Tjur's R	0.0346	0.1143	0.1373	0.1372

References

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