Eleanor Cotton

BIOS 6623-Project 3

**Introduction**

The primary aim of this project is to measure trajectories of memory and cognitive loss in individuals at risk for developing mild cognitive impairment (MCI) or dementia. Specifically, we want to see the how the trajectories differ for non-dementia individuals compared to individuals diagnosed with dementia or MCI. We also want to see if there is a period before diagnosis that the memory and cognitive loss trajectory changes in the dementia individuals.

For this study, 216 healthy, community dwelling, cognitively intact elders were enrolled and examined annually for an average of 15.7 years. Age, gender, and SES were recorded on each individual. The category fluency for animals test (Animal Score) was performed during each examination to measure memory and cognitive abilities. Individuals who had at least two consecutive clinical Dementia Ratings of 0.5 were categorized as having developed MCI.

**Methods**

RStudio version 3.4.2 was used for all statistical analysis

Initially, 216 individuals were enrolled in the study. A priori, it was decided that only individuals that had 3 or more time points recorded would be involved in analysis. Therefore, only 187 individuals were included in the analysis.

Categorical data was presented using percents and group sizes. Numerical variables were presented using means and standard deviations.

Based on likelihood maximization over 0.1 day intervals across the period prior to dementia diagnosis, a change point of -3.9 was identified. This value represents a change in trajectory of the animal score over time. On average, at 3.9 years prior to diagnosis, the relationship between animal score and time changed. Bootstrapping (of 1000 iterations) was used to find a confidence interval around this estimate. This change point was included in modeling later in analysis.

A mixed model with a random intercept for each individual and an AR(1) covariance structure on time points was run with animal score as the outcome. Age, dementia status, the interaction between age and dementia status, SES, gender, and the identified change point were all included in the model. Proper standard error estimates for each coefficient were generated from the same bootstrapping mentioned above. These standard errors and the coefficient estimates from the model were used to test each coefficient. For the model, men were used as the reference group for gender and non-dementia patients were used as the reference group for dementia. Finally, an adjusted age variable (age – 59) was used in modelling in order for the intercept to have a more interpretable value.

**Results**

Table One shows the demographics for the entire cohort (column 1), those diagnosed with dementia (column 2), and those not diagnosed with dementia (column 3). There were slightly more females involved in the study than males. Nearly two-thirds of individuals diagnosed with dementia were female. The average SES was about 49 for demented and non-demented individuals. The average age for demented individuals was higher than that of non-demented individuals (84.8 vs. 77.72 year old respectively). The age of onset of dementia was 90.7.

The change point identified was -3.9, with a 95% confidence interval of -5.30 to -2.60.

Table Two shows the results of the mixed modelling. The intercept represents the predicted animal score for a male without dementia at age 59. There was not a significant difference in trajectories between men and women (p = 0.0916), when controlling for the other variables. There was also not a significant difference in average animal score for those with dementia and those without (p = 0.0916). Finally, there was not a significant difference in the relationship between age and animal score for those with dementia and those without (p = 0.9486). SES had a statistically significant impact on animal score (p = 0.0314). For everyone 1 unit increase in SES, there was a 0.039 point increase in animal score on average (95% CI: 0.003 to 0.074). There was also a significant relationship between age and animal score (p < 0.0001). For everyone 1 year increase in age, there is on average a 0.183 point decrease in animal score (95% CI: -0.232 to -0.134). This value represents the estimated slope for all non-dementia patients and dementia patients 4+ years prior to their diagnosis. Finally, the change point was also significant (p < 0.0001). This value shows how the relationship between age and animal score changes for those diagnosed with dementia approximately 4 years prior to their diagnoses and onward. For individuals diagnosed with dementia after four years prior to their diagnosis, a 1 year increase in age is now associated with a 1.112 point decrease on average in animal score.

Graph one visually shows the relationship between animal score and age for non-dementia individuals (blue lines) and those diagnosed with dementia (yellow lines). Each line represents a single individual’s animal score as an individual ages.

Graph two visually shows the relationship between animal score and time before diagnosis for individuals diagnosed with dementia. The red line denotes when the dementia diagnoses was made. The blue dashed line denotes the change point estimate.

**Conclusions**

The cognitive loss trajectory was the same for dementia and non-dementia individuals up to four years prior to dementia diagnoses. At this point, dementia individuals developed a more negative relationship between age and animal score. A one year increase in age was associated with a great drop in animal score than those who have not been diagnosed with dementia (-1.112 vs. -0.183 respectively). It appears that four years before diagnosis is a critical time for those developing cognitive loss. Using these results, individuals may be able to be identified sooner if they have dementia and therefore get help and treatment sooner.

This study had several limitations. First, 29 individuals had to be dropped from analysis due to missingness, nearly 15% of the entire cohort. Second, the change point was fixed for every individual. This forced individuals all individuals to have a change in the animal score and time relationship at 4 years prior to dementia diagnosis. This may not be a very accurate estimate for everyone. MORE LIMITATIONS!?!

**GitHub Link**

Full Code to generate the above analysis can be found at:

<https://github.com/BIOS6623-UCD/bios6623-elcotton>

**Tables and Graphs**

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| **Table One: Demographics** | | | |
| **Variable** | **All Patients** | **Dementia Diagnosis** | **No Dementia Diagnosis** |
| **N** | 216 | 71 | 145 |
| **# Obs** (mean ± sd) | 15.67 ± 8.42 | 18.73 ± 6.18 | 14.17 ± 8.97 |
| **Sex** (n (%)) |  |  |  |
| Male | 42.13 (91) | 33.8 (24) | 46.21 (67) |
| Female | 57.87 (125) | 66.2 (47) | 53.79 (78) |
| **SES-Baseline** (mean ± sd) | 49.1 ± 11.54 (NA = 1) | 49.01 ± 12.89 | 49.15 ± 10.86 |
| **Age-Baseline** (mean ± sd) | 80.05 ± 9.22 | 84.8 ± 6.07 | 77.72 ± 9.62 |
| **Age at onset** (mean ± sd) | 90.7 ± 4.93 (NA = 145) | 90.7 ± 4.93 | NA |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Table Two: Model Results** | | | | |
| **Variable** | **Estimate** | **SE** | **95% CI** | **P-value** |
| **Intercept** | 24.59 | 1.3593 | (21.926,27.255) | <0.0001 |
| **Age** | -0.183 | 0.0251 | (-0.232,-0.134) | <0.0001 |
| **Change Point** | -0.929 | 0.1503 | (-1.223,-0.634) | <0.0001 |
| **Gender** | -0.562 | 0.4649 | (-1.473,0.349) | 0.2269 |
| **SES** | 0.039 | 0.0181 | (0.003,0.074) | 0.0314 |
| **Dementia** | -4.348 | 2.5773 | (-9.4,0.703) | 0.0916 |
| **Interaction**  (Dementia and Age) | 0.005 | 0.0816 | (-0.155,0.165) | 0.9486 |



