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Introduction

The purpose of this analysis is to observe the differential effects of Alzheimer's Disease (AD) on the various strata within a given population. In particular, this research endeavour segments the data based on the age of onset of the disease. This is operationalized based on whether a patient is 75 or older at disease onset and observing the associated variation in Mini-Mental State Exam (MMSE) scores. The Mini-Mental State Exam (MMSE) is used to evaluate cognitive function among the elderly; it includes tests of orientation, attention, memory, language and visual-spatial skills. The MMSE score is a measure of mental acuity with a maximum score of 30 points. A score of 20 to 24 suggests mild dementia, 13 to 20 suggests moderate dementia, and less than 12 indicates severe dementia.[1] The data used in this study comes largely from encounter data which is data generated when a patient interacts with a healthcare provider. The most prevalent claim is for general examination with the average number of general examinations per patient being roughly seven. For strokes, there are 1170 encounters with an average of 1.06 encounters per patient. Likewise, for myocardial infarction (MI), the average number of encounters per patient is 1.06. It appears as though encounters that are considered emergencies have this average, or something similar. However, wellness encounters are far more prevalent. When applying encounter data in tandem with other patient specific information, it is possible to derive additional insights on the initial diagnosis of individual patients. The data can be filtered to discern the prevalence of AD across the populations of interest. The analysis is longitudinal in nature, and the variable of interest is the age at the time of diagnosis. Given the characteristics of longitudinal data, time-series methods utilizing various multivariate models are relied upon in the analysis.

Descriptive Analysis

In terms of the prevalence, there were 658 patients with AD with an additional 153 patients with early onset.When observing the distribution of AD more generally, the distribution of the data is right-skewed. This is significant in that it poses challenges to using linear models. For instance, OLS will no longer be BLUE under the Gauss Markov assumptions with the violation of the normality assumption. Thus, there is a greater trade-off that must be made in this

[1] Medical Tests for Diagnosing Alzheimer's https://www.alz.org/alzheimers-dementia/diagnosis/medical_tests

study: having a parsimonious model that may be understood or using a less efficient estimator with weaker confidence.

Figure 1

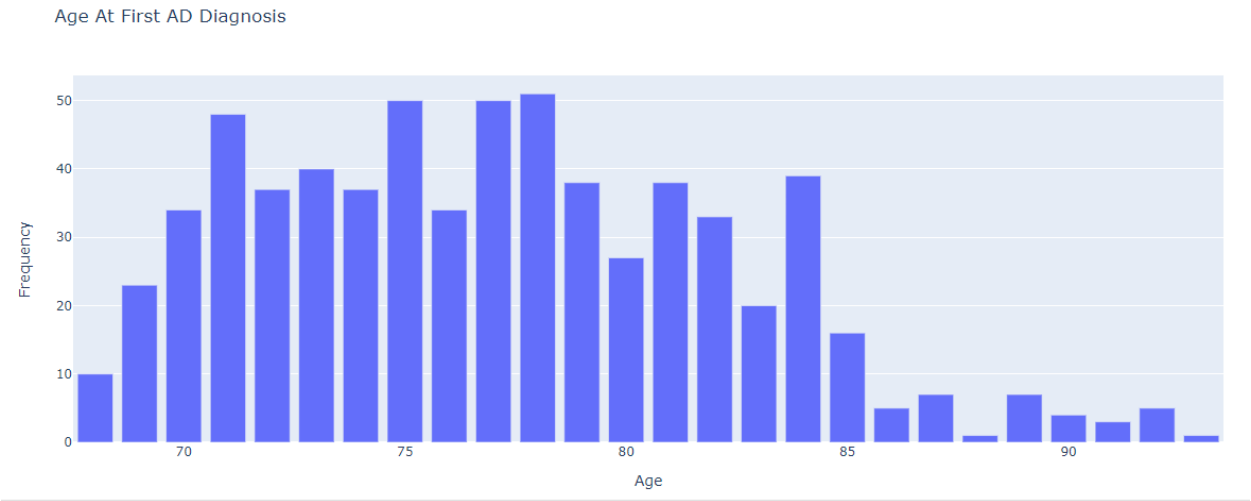


Figure 1 demonstrates that the mean of the distribution appears to be about 78 , and the median value being about 75. One facet of the distribution that is noteworthy is the characteristic of the tail. The expectation is that there would be monotonicity while decreasing to create smoothness. This possibly relates to the dispersion of the distribution; the standard deviation of 5.26 which is somewhat high.

Figure 2

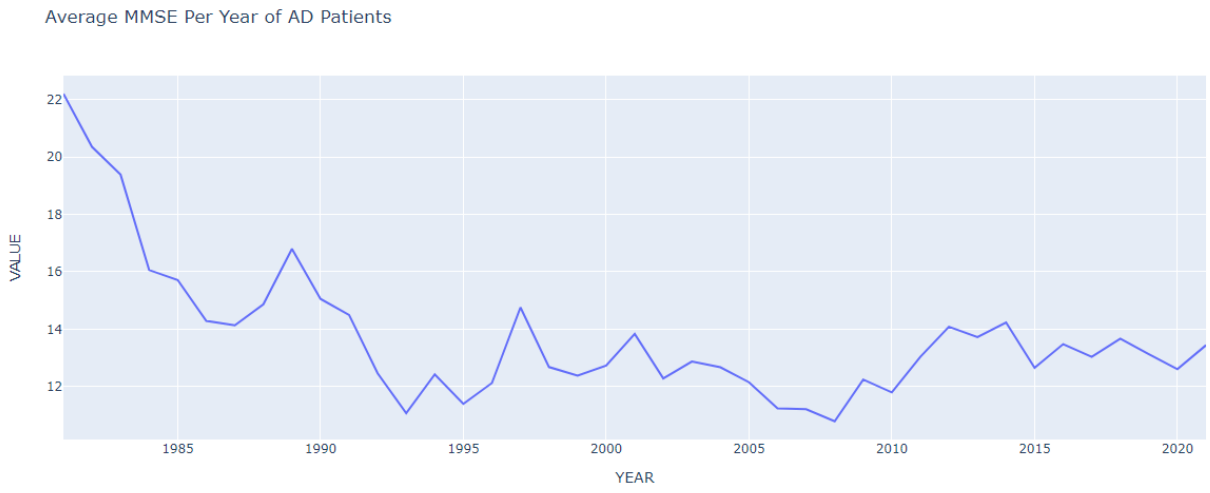
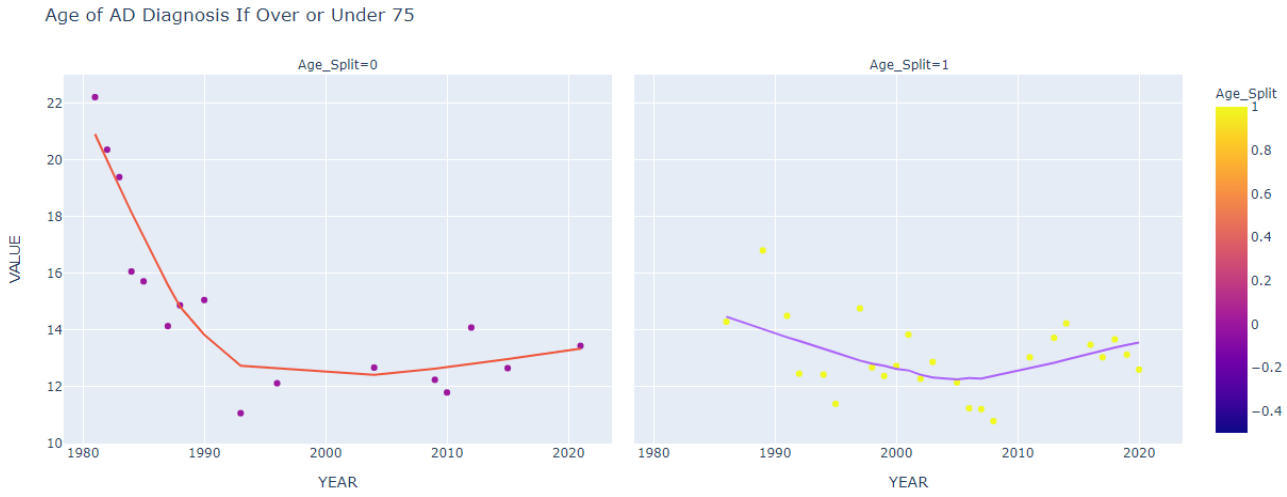


Figure 2 depicts the variation in the average MMSE score per year for patients. The general trend is negative which follows expectations. As one ages, the expectation is that there is

a gradual erosion of mental facilities. There are some interesting forces that are being captured in this graph. There is a relatively large decline in the age of diagnosis during the earlier years. The trend's minimum is around 2008. After which, the MSSE scores begin to increase gradually. What is being reflected is likely variation in the cohort. As time progresses, those with comorbidities are more likely to succumb to disease. These patients also likely have lower MSSE scores that are lowering the average. As more time passes, the more likely it is that these patients are to exit the cohort and will elevate the average. There is essentially survivorship bias. Also, this effect is likely distributed through multiple periods given the nature of patients with AD. They are not all located within the same location, but they are spread amongst various contexts.

Figure 3.



When segmenting this data based on the age of the initial diagnosis, this point was further emphasized. There is substantially more curvature in the graph of patients who had an AD diagnosis prior to age 75 than those diagnosed later in life. For those diagnosed at 75 or later, the decline in MMSE score is far more gradual.

Modeling

To further elucidate this variation in demographic groups, several models are applied to investigate. An initial exploratory model is applied with MMSE scores as the dependent variable with years as an independent variable. The beta-coefficient of years is -.011. The interpretation of this coefficient is that for each year that passes, there is a .011 associated drop in MMSE. An autoregressive model (ARIMA) is fit to observe the variation amongst difference years with lag factors as model parameters.

$$\widehat{MMSE} = \beta_{t0} + \beta_1 \widehat{MMSE}_{t-1} + B_2 \widehat{MMSE}_{t-5} + \beta_3 \widehat{MMSE}_{t-10} + \epsilon$$

The table in the below summarizes the results of the lag terms with the associated p-values. The first term is the intercept term followed by the lag years in their respective order.

Beta_Coefficients	P_Value
12.95608342283647	4.3943008107420767e-150
-0.014138717359519994	0.5067860143293506
-0.0026491359103272714	0.9009787903241229
0.015818138979765153	0.45733527250640127

The base MMSE score is about 13. This is the intercept term. It suggests that the average patient does not have severe dementia. The one year lag has a negative association. This suggests that the effects that dampen MMSE scores may linger for prolonged periods. This is substantiated with the negative coefficient for the five-year lag period. While the p-value for this lag is 0.9, it still is valuable in arguing for the duration of the effects, while the effect size itself is a bit more difficult to support. As for the ten-year lag period, it has a positive association. This suggests that the dampening effects tend to dissipate over the period of a decade.

An alternative model this is explored includes age and gender. Gender is encoded in a binary fashion while age is centered. Additionally, a dummy variable is introduced to create a discrete split for those initially diagnosed before or after age 75. The main reservation in this respect is with multicollinearity. However, the inclusion of the variable enables for a more parsimonious analysis when attempting to investigate the threshold of disease onset.

$$\widehat{MMSE} = \beta_0 + \beta_1 \widehat{Gender} + \beta_2 \widehat{Age} + \beta_3 \widehat{Age\,Split} + \epsilon$$

Both gender and age have a beta-coefficient of -04. Age has a significant p-value, while gender is nearly significant and should have some weight on the analysis. The way to interpret these cofficents is to consider a man and a woman that are identical in all factors except the woman is a year older. This model suggests that the woman and man would have the same MMSE scores holding all factors equal as a year of aging is about equivalent to the effect of gender.

	coef	std err	t	P>|t|	[0.025	0.975]
const	12.6796	0.375	33.850	0.000	11.945	13.414
Gender_Indicator	-0.0444	0.298	-0.149	0.882	-0.630	0.541
Age	-0.0429	0.044	-0.970	0.332	-0.129	0.044
Age_Split	0.4928	0.491	1.005	0.315	-0.469	1.455

As for answering whether or not there is a significant difference between if a patient has their diagnosis at age 75 or below, the age split variable targets this. If a patient has their first diagnosis after or at 75, they should be on average half a MMSE point higher holding all factors equal than their earlier onset counterparts. Also, given that the p-value of the split is under 0.5, it suggests that this measure is statistically significant.

An additional model is also tested with an interaction term with age split and gender. The coefficient of the interaction term is negative, but the p-value is only significant with 90% confidence. This suggests that there may be a differentiation in how the segmentation along age of diagnosis may vary across gender.

Conclusion

One of the guiding questions motivating this analysis is to explore how patients that received their first AD diagnosis at age 75 or later differed in terms of their MMSE scores when compared to patients that received a diagnosis of early onset AD. In this analysis, it is confirmed that there is a statistically significant difference amongst these groups. However, some of the exploratory analysis with interaction effects suggests that male patients may be affected negatively by later onsets. Future analysis may utilize multilevel models to explore how gender specific effects impact MMSE scores with further gerontological analysis of AD. Additionally, a piece-weise regression model with a partition to split the groups by threshold may also be advisable to further investigate the relationships presented in this endeavour.