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Investigating environmental risk factors of dementia

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Investigating environmental risk factors of dementia

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An abstract of
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Abstract

Investigating environmental risk factors of dementia

By

Tylor Reynolds

Background: Dementia is a neurodegenerative disease that can commonly associated with cognitive decline and impacts approximately 1 in 10 individuals over the age of 65. There are many known environmental and genetic factors that potentially contribute to the development of dementia. **Objectives:** To examine environmental factors of dementia and determine if the extent of interaction between smoking, exposure to lead, and exposure to organochlorine insecticides. **Methods:** Data was collected from 100 participants over 65 years old from the 2013-2014 NHANES public dataset and analyzed in SAS. Logistic regression models were constructed to determine if smoking, lead exposure or exposure to DDT was correlated with lower signs of cognitive functioning. A multivariate model using environmental exposures was also constructed and analyzed to assess potential interaction. **Results:** Elevated levels of blood lead and DDT were correlated with a lower cognitive score which could indicate that these variables were promoting cognitive decline. Analysis revealed no significant relationship between serum cotinine levels and cognitive scores. **Discussion:** More investigation should be conducted regarding potential interactions between environmental and genetic factors of dementia. Smoking has been linked to dementia and cognitive decline in previous studies, however this data revealed no such relationship.

Investigating environmental risk factors of dementia

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Background

Dementia is a neurodegenerative disease that has a projected global prevalence of about 1-in-10 individuals greater than 65 years old.[1] It is estimated that in 2018 there were 50 million people around the world who were living with dementia.[2] Research has indicated that various metals also potentially contribute to an individual's risk of developing dementia.[2] Dementia causes a cognitive decline among the elderly population, which causes an estimated healthcare cost of $172 billion dollars annually.[3] Currently there is a large amount of research indicating that genetics are important factors towards a person's risk for developing dementia, however there is much less research into the environmental risk factors of dementia, such as pesticides.[4] Little research has indicated that there is likely an interaction between genetics and environmental risk factors of dementia.[5] Further research is needed in order to establish just how important environmental factors are towards the development of dementia.

The main purpose of this study is to investigate potential environmental contributors towards the development of dementia; by investigating potential environmental contributors to dementia it could be possible to develop a better understanding of how to protect populations from becoming future cases of dementia. Three of the main environmental exposures that this study will be focused on are smoking, pesticides, and lead exposure. Reducing cases of dementia would lead to a reduction of healthcare related costs, which could then be allocated elsewhere. Environmental factors play an important role in the development of dementia and should be better understood in order to protect the elderly population. This study aims to investigate the impacts that various

environmental risk factors have on dementia. It is believed that all three variables of interest will be correlated with a higher incidence of dementia.

Literature Review

Dementia is a neurodegenerative disease which can frequently identified by cognitive impairment, it most commonly affects the elderly population.[6] Cognitive impairment can be characterized as cognitive decline that is greater than the expected amount for an individual's age and education level.[7] Cognitive decline can be observed most frequently among the elderly population and results in the loss of neurons.[7] Alzheimer's disease is a form of dementia

There is still much that is unknown about dementia however there is research that suggests potential contributors towards this disease. One notable risk factor for dementia would be an individual's smoking habits.[4] Research has shown that not only have current smokers been found an increase in risk of Alzheimer's including dementia, but people with previous history of smoking have also been found to have a greater risk of developing dementia than people with no history of smoking.[5] Environmental factors are important in understanding dementia, however Alzheimer's disease including dementia is also known to have a big genetic component associated.[8] Two major notable genetic components of Alzheimer's disease are ApoE4 (Apolipoprotein E4) and Trx1 (Thioredoxin-1).[9,10] There have been potential interactions theorized between environmental and genetic risk factors of dementia, however data on these interactions are rare and difficult to obtain.[5]

Effects of smoking on dementia

Smoking status is widely recognized as an important risk factor towards the development of dementia.[11] Mixed results exist among studies that examine relationships between former smoker status and dementia, however there exists a multitude of research that establishes a relationship between current smoker status and development of dementia at a younger age or reduced cognition in general.[11,12,13] Not much is understood about the biological mechanisms that contribute to a higher risk of dementia but a working hypothesis is that oxidative stress generated by smoking is a major contributor.[14] Oxidative stress is created by an imbalance between reactive oxygen species (ROS)and antioxidant defenses.[15] Given the complex composition of cigarettes and their cytotoxic/carcinogenic compounds it is no surprise that combustion of these products is a generator of oxidative stress.[16] The nervous system is extremely sensitive to oxidative stress due to the brains high demand for oxygen to survive.

There exists a huge stigma towards smokers in our society and this can potentially affect studies that utilize self-reporting of smoking status to determine actual smoker status, this can make a better argument to utilize biomarkers for assessing an objective marker of smoking status.[17] Presence of nicotine can also serve as a good biomarker for determining smoker status however it has a relatively short half-life which makes it difficult to assess lifetime exposure.[18]

Lead exposure effects on cognitive decline

Heavy metals have been widely considered as an extreme environmental concern and have been observed to demonstrate an effect on cognitive decline and development of dementia.[19] One of the most widely recognized and studied heavy metals that affects cognition is lead.[20-23] Exposure to lead has been demonstrated to negatively impact cognition of mammalian species and increase the risk of developing dementia in later stages of life.[20-23] Lead exposure is a complicated issue and is primarily tied to occupational exposures among workers.[24] Lead exposure used to be a lot more common in the past however its widespread use has been discontinued in many countries. Lead is a poisonous heavy metal that affects nearly every organ in the body, but it especially impacts the nervous system.[23] Lead toxicity induces oxidative stress and intensifies oxidative stress.[25]

There are many potential biomarkers available to assess lead exposure but the most commonly measured option is blood lead.[26] One of the issues with using blood lead is that it has a relatively short half-life, which makes it potentially difficult to assess a long time exposure. Bone lead is a possible biomarker that would get a better sense of a chronic exposure; however, it is rarer to see bone lead being measured due to its high cost.

Effects of pesticide exposure on cognitive impairment

Currently there is some data available that suggests that lifetime exposure to copious amounts of pesticides can likely lead to a higher risk of developing Alzheimer's including dementia in later life.[26] Epidemiological studies suggest that organochlorines and organophosphate insecticides are associated with an increased risk of cognitive decline in later life.[26] Currently the biological mechanisms are not well understood on what contributes to the higher risk of cognitive decline due to insecticide exposure.[26] A pesticide is defined as "any substance or mixture of substances intended for the preventing, destroying or controlling any pest.[27] DDT is an organochlorine pesticide that was primarily used between 1940-1972, after which the EPA banned the use of this pesticide for residential use.[28] Levels of DDT in the United States have decreased significantly, however there still remains some levels of this pesticide in the environment.[28] DDT has been shown to disrupt the nervous system and it has been shown to generate oxidative stress which can potentially lead to apoptosis of neurons.[29]

Methods

Data was gathered from the National Health and Nutrition Examination Survey (NHANES) public dataset from 2013 - 2014 to assess environmental exposures and their relationship with cognitive impairment. 100 individuals were selected from the NHANES database after removing all participants who had missing data from any of the variables of interest. Individuals under 65 years of age were also removed from the study as dementia is a disease that primarily affects the elderly population. This study utilized statistical analysis via SAS and data was analyzed using a logistic regression

model. The key variables of interest of this study include smoking, pesticides, and lead blood levels. Smoking status was assessed via serum cotinine levels in order to reduce the potential effects of self-reporting bias. Exposure to lead was assessed via blood lead levels. It would have been preferable to obtain bone lead levels due to the significantly longer half-life, however that data was not available.[28] Lastly pesticide exposure was assessed via dichlorodiphenyltrichloroethane(DDT) serum levels, this variable was chosen due to previous literature indicating a possibility that exposure to DDT is possibly an indicator of dementia.[30] The main outcome of interest in this study is cognitive impairment, which is widely accepted as an early symptom of dementia.[31] One of the more widely used biomarkers for assessing pesticide exposure is through blood serum levels, depending on the substance of interest the half-life could be relatively short however data on blood serum pesticide levels usually are collected more often.[32]

Laboratory methods

Serum samples from NHANES 2013-2014 were stored frozen before analysis. Organochlorine pesticides and metabolites were measured in serum using automated liquid/liquid extraction and subsequent sample clean-up. Final determination of target analytes was performed by isotope dilution gas chromatography high-resolution mass spectrometry GC/IDHRMS. Whole blood specimens were processed, stored, and shipped to the National Center for Environmental Health, and Centers for Disease Control and Prevention for analysis.

Analysis

Data was inserted into SAS and analyzed using logistic regression modeling. All three independent variables were assessed as continuous variables, exposure to smoking was analyzed as a continuous variable due to its ability to give a better picture of the effects of smoking than a simple yes or no. Blood lead levels and serum DDT levels were also assessed as continuous variables to determine a positive or negative association with dementia.

Results

All the analyses were performed as an individual variable and as a multivariate model as well because dementia is known to be a complex disease with multiple influential factors. Exposure to lead was revealed to have a statistically significant negative impact on the digit symbol score (Figure 1), which was the variable that researchers for NHANES used to measure cognitive scores.

Presence of DDT levels in blood was also significantly correlated with a lower digit symbol score on cognition among subjects (Figure 2). Analysis between serum cotinine levels and digital symbol score were not statistically significant, nor did they reveal any relationship between serum cotinine levels and their impact on digit symbol scores of cognition (Figure 3). Figure 3 also had a relatively low r-squared value of 0.001 which indicates that the observations did not necessarily fit this model well.

The multivariate model was also possibly skewed by the presence of low serum cotinine levels because it revealed no statistically significant relationship between any of the variables and digit symbol score. The multivariate model was not successful in revealing

interaction between these DDT, serum cotinine and blood lead levels among the participants (Figure 4). The findings of figure 4 suggest that there did not exist an interaction between any of the variables of interest and cognitive decline however this does not guarantee that a relationship does not exist outside of this study.

As suspected the analyses between DDT levels in blood and lower cognitive scores. It is potentially interesting that serum cotinine levels in participants were not correlated with lower cognitive scores, especially given the fact that there is a significant amount of previous literature that has shown a correlation between these two variables. One potential explanation for this observation is that there were so few participants with serum cotinine levels above zero present in their system. There were approximately only 8 participants with serum cotinine levels above 0 ng/mL, this potentially heavily skews the results presented by the data. Analysis of the data revealed that levels of DDT in blood was related to a lower digit score, seemingly indicating that DDT does in fact have an influence on lower cognitive functioning in later life. Figure 5 details the distribution of race and ethnicity of the participants. The distribution of participants by race is relatively distributed considering the diversity of race/ethnicity of the United States. Figure 6 details the distribution of participants by age, the age of participants is not evenly distributed due to the NHANES database coding all ages above 80+ to be set to 80.

Figure 1 Regression model for the relationship between cognitive scores and blood lead levels.

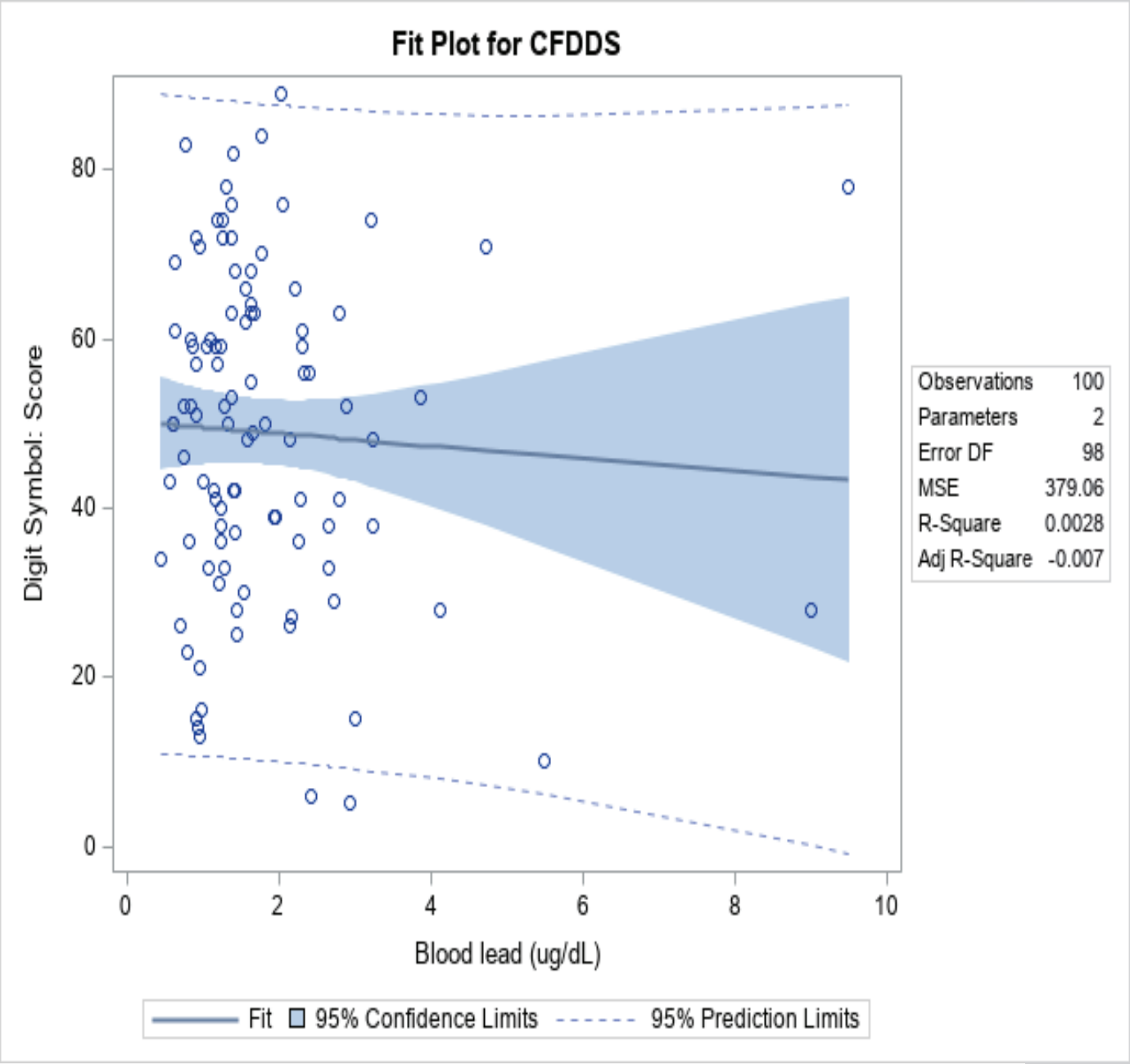


Figure 2 Regression model for the relationship between cognitive score and levels of DDT in blood samples.

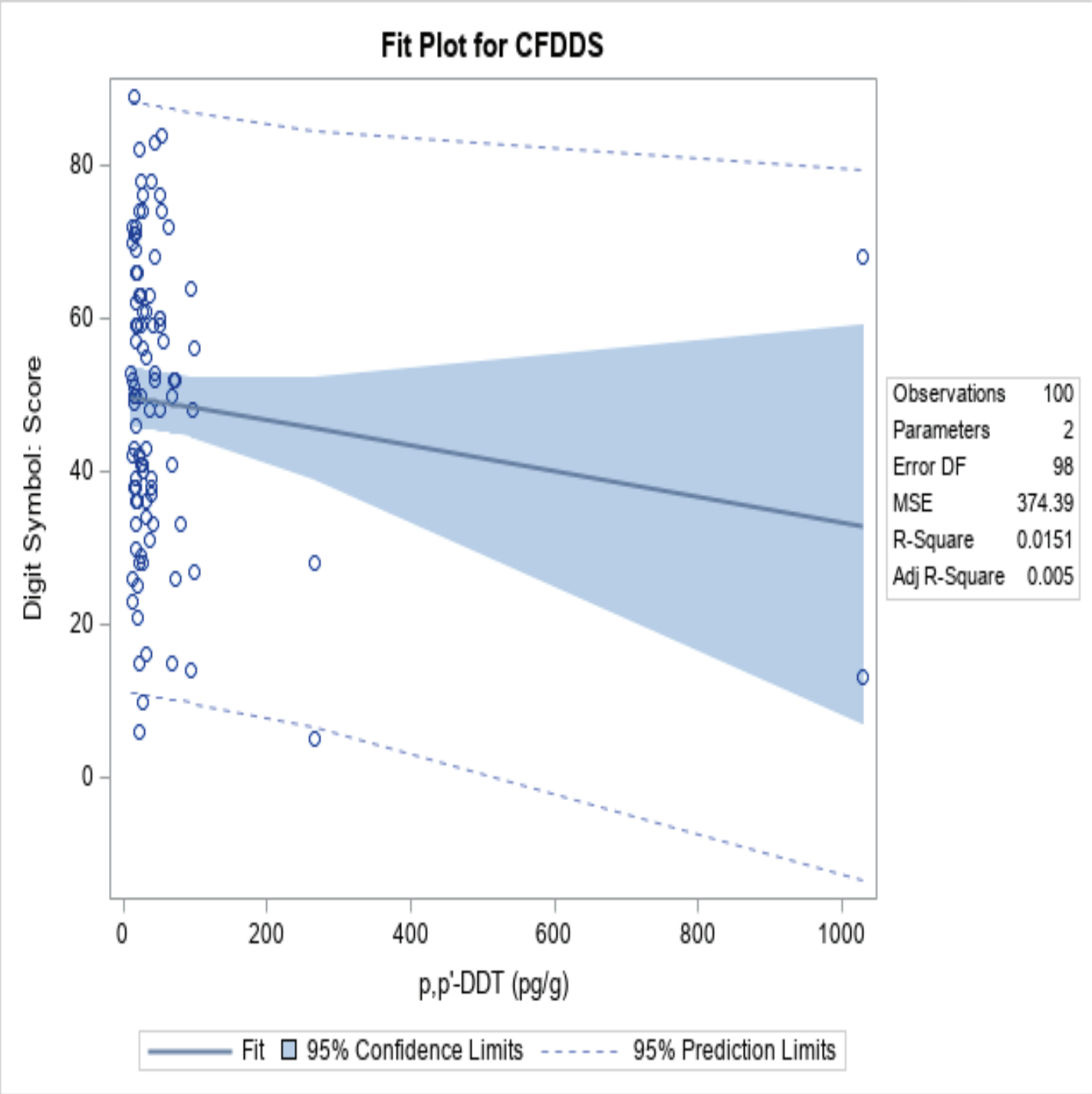


Figure 3 Regression model for the relationship between cognitive score and serum cotinine levels.

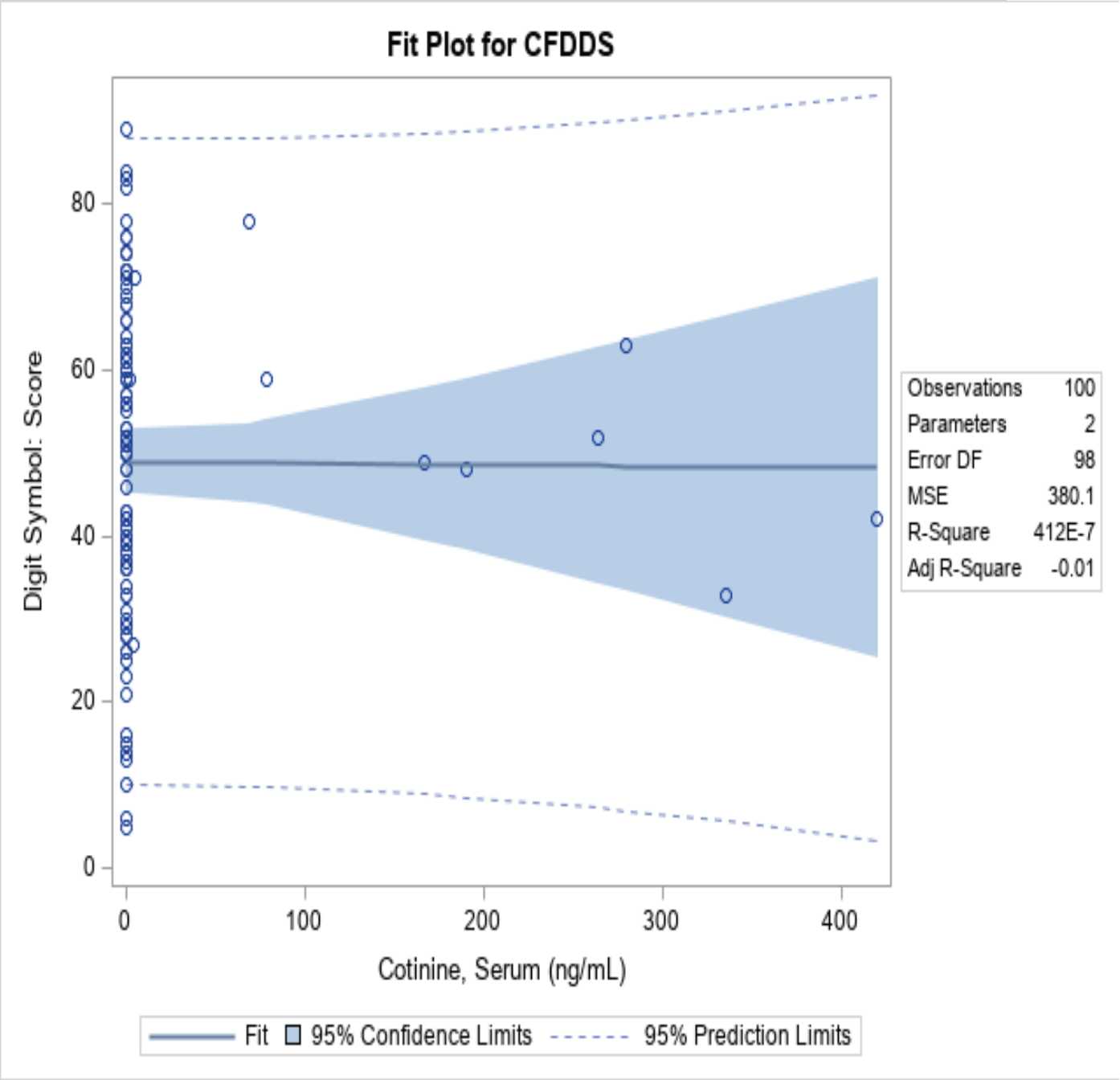


Figure 4 Regression models for the relationship between cognitive scores serum cotinine, blood lead levels, and DDT levels among participants.

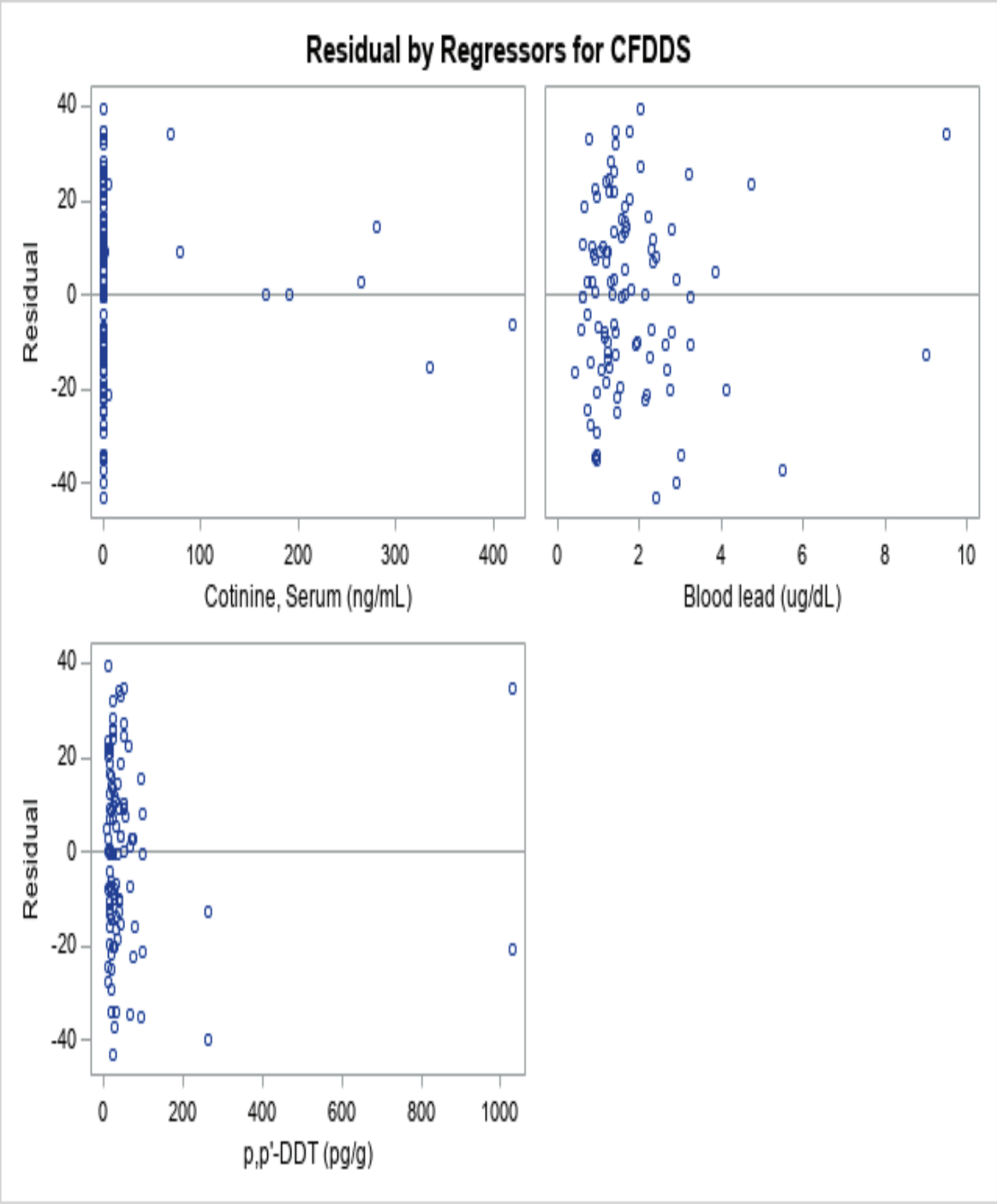


Figure 5 Demographics of participants by race/ethnicity n=100

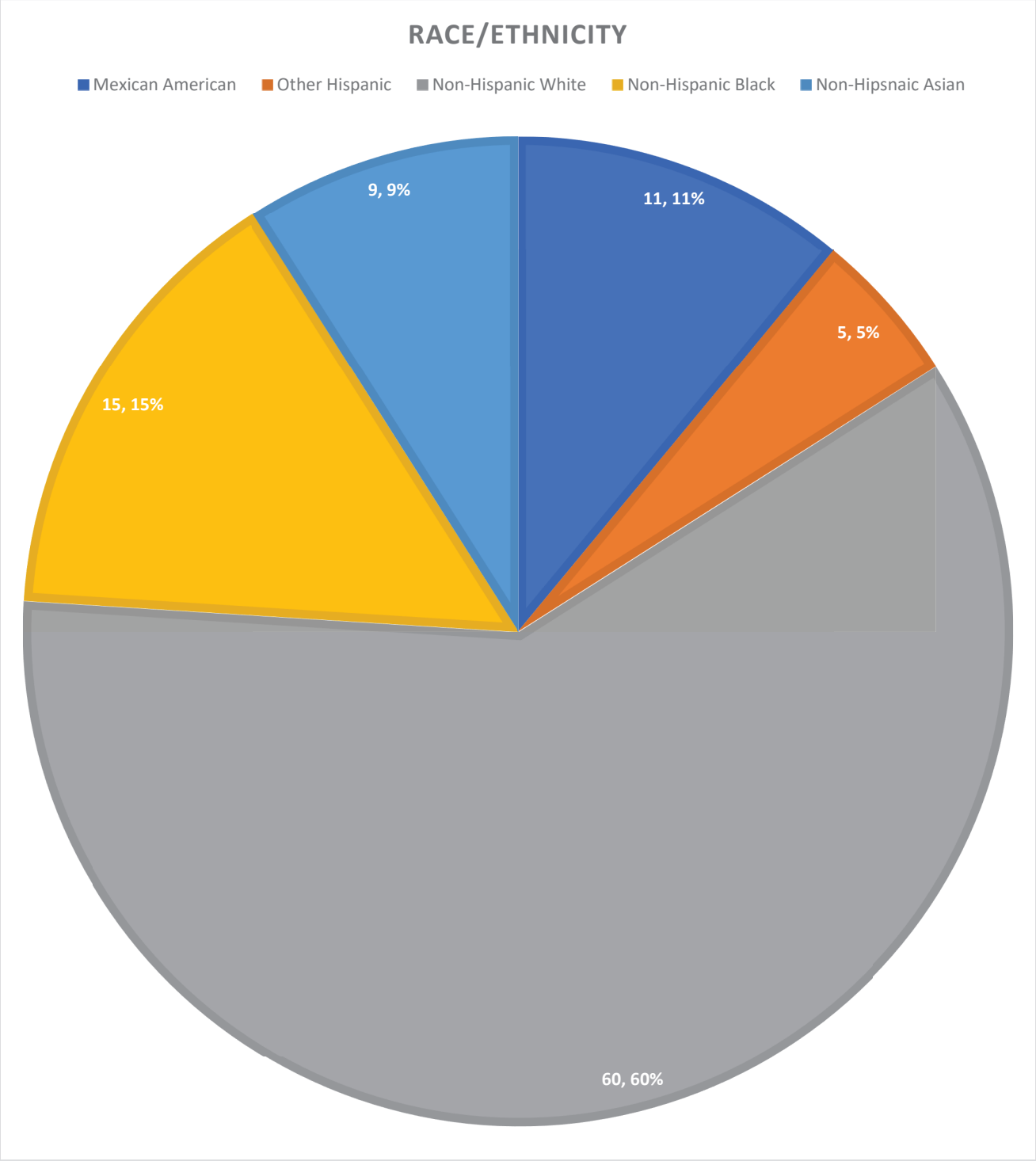
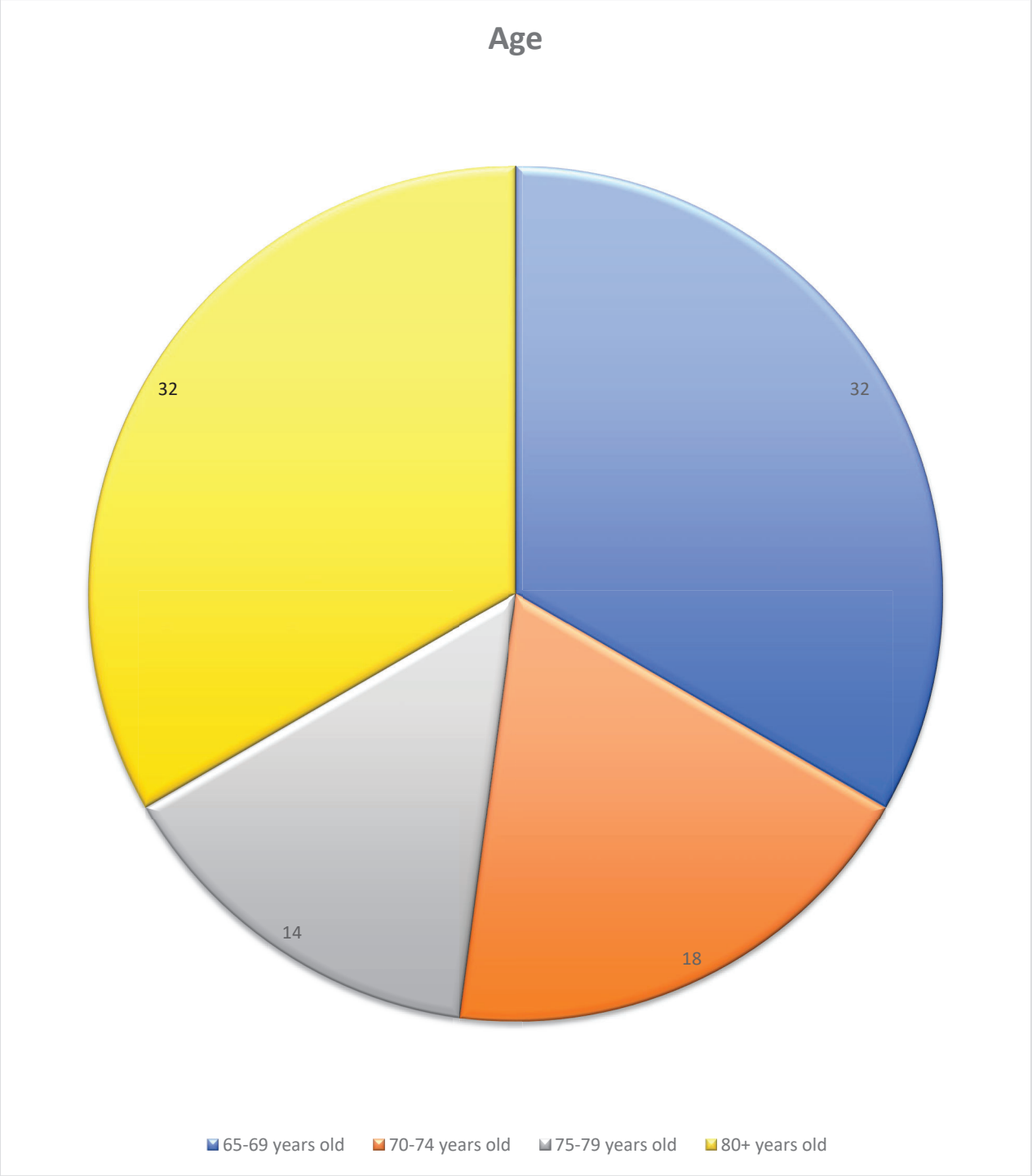


Figure 6 Demographics of participants by age n=100



Discussion:

There are a few limitations with this data, the most notable being that only two of the variables of interest were statistically significant, however just because the fact that this data was not able to identify a relationship does not mean one doesn't necessarily exist. It is entirely possible that the data or confounding variables influenced the collected data, making it look like a relationship does not exist despite a relationship being identified in previous literature. One notable strength of this study is the fact that it controlled for age as a confounding variable, age is such an important factor and should always be considered when studying the effects of diminishing cognition. Future investigations into this topic should consider more confounding variables such as race, gender and genetic risk factors however those areas were beyond the scope of this research.

The findings of this study indicate that lead and DDT levels both had statistically significant relationships with lower cognitive scores individually. A multivariate model was constructed and indicated that the variables of this studies interest did not appear to have an interactive relationship among this studies population, however this does not guarantee that these variables do not interact with each other outside of this study.

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