Module 1: Alzheimer's Analysis

Team Members:

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Project Title:

Identifying relationships in health data in Alzheimer's disease

Project Goal:

This project seeks to understand: 1) if a patient's pTau/tTau ratio is higher in dementia patients than non-dementia patients, and 2) if there is a significant difference in pTau/tTau ratios between cognitive status groups.

Disease Background:

Fill in information about 11 bullets:

- Prevalence & incidence
    - Prevalence in the United States: approximately 7.2 million adults aged 65+, about 11% of this population

      https://www.alz.org/alzheimers-dementia/facts-figures#:~:text=Over%207%20million%20Americans%20have,
    - Incidence in the United States: approximately 500,000 new cases every year

      https://www.alzsd.org/resources/facts-stats/#:~:text=Prevalence,Alzheimer's%20disease%20and%20
- Economic burden
    - The total economic burden of Alzheimer's disease and related dementias for direct healthcare costs exceeded $321 billion in 2022 with projections to reach $1 trillion annually by 2050. Approximately two-thirds of this cost includes insurance coverage payments, with the remaining

cost being covered by out-of-pocket payments and other sources.

https://www.ajmc.com/view/the-economic-and-societal-burden-of-alzheimer-disease-managed-care-considerations

- Risk factors (genetic, lifestyle)
    - Genetic risk factors of Alzheimer's disease include age, family history, and the presence of the APOE-e4 allele (associated with earlier disease onset in some populations). Other gene variants can influence Alzheimer's risk, like the Amyloid precursor protein and Presenilin 1 and 2. Lifestyle factors that increase risk of Alzheimer's disease include chronic health issues like high blood pressure, lack of physical activity, unhealthy diet, excessive alcohol and drug use, and social isolation or lack of mental stimulation.

  https://www.nia.nih.gov/health/alzheimers-causes-and-risk-factors/what-causes-alzheimers-disease

- Societal determinants
    - Some societal determinants that influence progression of Alzheimer's disease include education level, healthcare access, and social environment. Education research in particular suggest a relationship between lower education level and poorer brain health (progressing memory loss, frequent confusion). Additionally, lack of quality health care access in some communities removes opportunities for consistent checkups, which is imperative for maintaining not only general health, but brain health as well. A person's social environment will also contribute to their risk of dementia diseases due to a lack of mental stimulation and interaction.

  https://www.cdc.gov/alzheimers-dementia/php/sdoh/index.html

- Symptoms
    - One of the main symptoms of Alzheimer's disease is memory loss, especially in forgetting important dates, events, and more recently learned information. Additionally, Alzheimer's can present as experiencing challengers in

planning and problem solving, difficulty completeing normal, familiar tasks, general confusion and difficulty understanding images, mood and personality changes, and decreased judgement.

https://www.alz.org/alzheimers-dementia/10_signs

- Diagnosis
    - Diagnosis of Alzheimer's diease normally consists of biomarker tests that can detect plaques and tangles in the brain. PET scans can help identify the presence of these, and blood and spinal fluid tests can detect levels of amyloid and tau proteins, both of which can be strong indicators for dementia diseases. Other physical and neurological exams like reflexes, muscle strength, balance, lab testing for other diseases, mental status examination, and brain imaging are also tools used by professionals in the diagnosis of Alzheimer's.

  https://www.mayoclinic.org/diseases-conditions/alzheimers-disease/diagnosis-treatment/drc-20350453

- Standard of care treatments (& reimbursement)
    - Medication to support with Alzheimer's during early to middle stage of Alzheimer's includes medication that helps lower Amyloid-Beta level and Cholinesterase inhibitors are also used to increase memory and thinking capabilities.

  https://www.nia.nih.gov/health/alzheimers-treatment/how-alzheimers-disease-treated

- Disease progression & prognosis
    - Start of disease is, little to no complications other than some little cognitive difficulties. During the middle stage of Alzheimer's, usually lasts for the longest, the individual starts to show more intense symptoms of dementia, becoming more frustrated easily and confusing words more often. During late stage Alzheimer's, an individual become incompetent of taking care of themselves and need a caregiver to be with them at all times due to losing the ability to communicate and unaware of recent experiences and their surrondings.

https://www.alz.org/alzheimers-dementia/stages#:~:text=Being%20forgetful%20of%20events%20or,care%20in%20

- Continuum of care providers
    - Primary Care Doctor, Neurologist, Geriatric psychiatrists, Neuropsychologists, Speech, Physical, and Occupational therapists, and Nurses.

https://www.alzheimers.gov/professionals/health-care-providers

- Biological mechanisms (anatomy, organ physiology, cell & molecular physiology)
    - Tau proteins deattach from microtubules and aggregate to form tangles within neurons, this makes information propagation as the tangles clogs up the ability for information to be delivered to neurons. Amyloid-Beta forms plaques on the outside of neurons which interferes with communication between brain cells and inflammation of them.

https://www.nia.nih.gov/health/alzheimers-causes-and-risk-factors/what-happens-brain-alzheimers-disease#:~:text=Neurofibrillary%20tangles&text=In%20healthy%20neuro

- Clinical Trials/next-gen therapies
    - There has been many different kinds of clinical trials that are being done currently to either identify and prevent Alzheimer's before it starts to develop and also some that aim to stop/slow progression of Alzheimer's during the early stages. A recent study of note focused on testing a novel therapeutic approach aimed at modulating neuroinflammation in Alzheimer’s disease. Specifically, it evaluated whether targeting the NLRP3 inflammasome pathway could reduce pathological inflammation and improve cognitive outcomes. The trials assessed the safety, biological activity, and clinical efficacy of this strategy across different stages, suggesting that dampening this inflammatory cascade may offer a new avenue for disease-modifying treatment. Clinical trials of this nature are paving the way for the future of Alzheimer's research.

https://www.nature.com/articles/s41392-024-01911-3

Possible Experimental Questions:

- Does increase levels of Amyloid-Beta 40 affect proportion of pTAU to tTAU
- Does highest level of education have a factor in age of death?
- Does CASI score play a factor in death of patients? (Can we predict using CASI score, how much longer a patient can live for)
- Does having an head injury increase your chances of having Alzheimer's?
- How does brain weight affect CASI, MMSE, OR MOCA scores?

Data-Set:

The datasets include molecular, cellular, and clinical data from human brain donors as part of the Seattle Alzheimer’s Disease Brain Cell Atlas (SEA-AD). Researchers measured things like memory scores, genetic risk factors, and levels of key amyloid-beta and tau proteins that are linked to the disease. They also looked closely at brain cells and tissue using advanced lab techniques and imaging tools. The data is organized in clear units like protein levels per microgram and scores from memory tests, and it helps researchers understand how Alzheimer’s develops and affects the brain. A limitiation of the data is the fact that the dataset is relaitvely small for in-depth research. A potential bias in the dataset is the possibility of instrumentation bias, as some readings of proteins and other quantitative variables could include measurement inaccuracies. There are outliers in the dataset, providing evidence for potential instrumentation bias.

Data Analyis:

In [1]:
```
#conda install -c conda-forge termcolor
```

In [2]:
```
import csv
import warnings
import matplotlib.pyplot as plt
import numpy as np
from scipy import stats

# ranks education order for later use (no longer relevant, our group changed c
EDUCATION_ORDER = {
    "No formal education": 0,
    "Elementary": 1,
    "Middle School": 2,
    "High School": 3,
    "Some College": 4,
    "Associate": 5,
```

```
    "Bachelor": 6,
    "Master": 7,
    "PhD": 8,
    "Unknown": -1
}

 # creates Patient class
class Patient:
    all_patients = []

    def __init__(self, DonorID, ABeta40: float , ABeta42: float, tTau: float,
        self.DonorID = DonorID
        self.ABeta40 = ABeta40
        self.ABeta42 = ABeta42
        self.tTau = tTau
        self.pTau = pTau
        self.sex = None
        self.death_age = None
        self.education_level = None
        self.cog_status = None
        self.age_symptom_onset = None
        self.age_diagnosis = None
        self.head_injury = None
        Patient.all_patients.append(self)

    # creates function definition to gather the tau ratios
    def get_ptau_ratio(self):
        return self.pTau / self.tTau if self.tTau else None

    # method for Patient class to combine the data from the two csv files
    @classmethod
    def combine_data(cls, filename: str):
        with open(filename, encoding="utf8") as f:
            reader = csv.DictReader(f)
            rows = list(reader)
            patient_map = {p.DonorID: p for p in cls.all_patients}

            for row in rows:
                donor_id = row["Donor ID"].strip()
                if donor_id in patient_map:
                    patient = patient_map[donor_id]
                    patient.sex = row["Sex"].strip() if row["Sex"] else None
                    patient.death_age = int(row["Age at Death"]) if row["Age a
                    patient.education_level = row["Highest level of education"
                    patient.cog_status = row["Cognitive Status"].strip() if ro
                else:
                    warnings.warn(f"Donor ID {donor_id} not found in Tau data.

    @classmethod
    def instantiate_from_csv(cls, tau_file: str, meta_file: str):
        with open(tau_file, encoding="utf8") as f:
            reader = csv.DictReader(f)
            for row in reader:
```

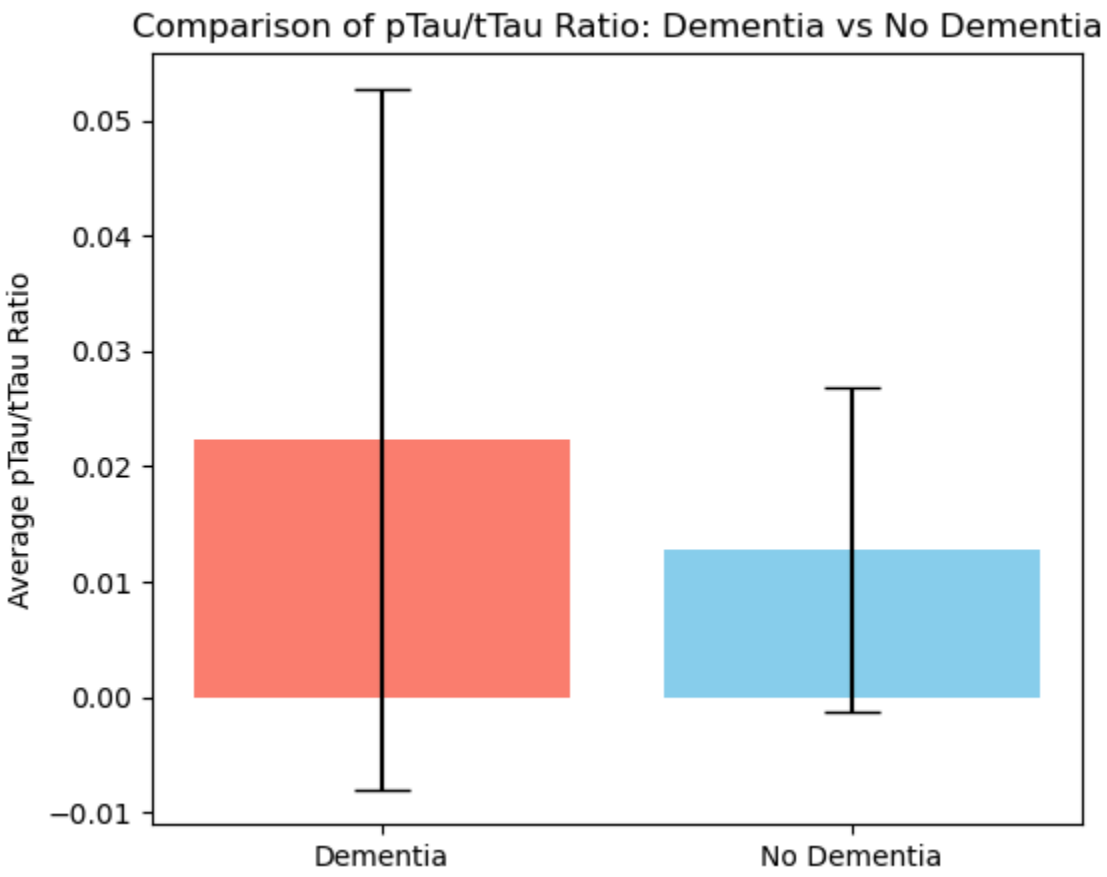
```
                Patient(
                    DonorID = row['Donor ID'].strip(),
                    ABeta40 = float(row['ABeta40 pg/ug']),
                    ABeta42 = float(row['ABeta42 pg/ug']),
                    tTau = float(row['tTAU pg/ug']),
                    pTau = float(row['pTAU pg/ug'])
                )
        cls.combine_data(meta_file)

    #filters patients based on cognitive status
    @classmethod
    def filter_by_dementia(cls, dementia: bool = True):
        if dementia:
            return [p for p in cls.all_patients if p.cog_status and p.cog_stat
        else:
            return [p for p in cls.all_patients if p.cog_status and p.cog_stat

    # NO LONGER USE THE NEXT TWO CLASS METHODS, WAS FROM PREVIOUS RESEARCH QUE
    @classmethod
    def group_by_education(cls, patient_list):
        groups = {}
        for p in patient_list:
            ed = p.education_level if p.education_level else "Unknown"
            if ed not in groups:
                groups[ed] = []
            groups[ed].append(p)
        return groups

    @classmethod
    def plot_age_and_ratio_by_education(cls):

        dementia_patients = cls.filter_by_dementia(True)
        non_dementia_patients = cls.filter_by_dementia(False)

        def stats_by_edu(patient_list, attr="death_age"):
            groups = cls.group_by_education(patient_list)
            averages = {}
            for ed, patients in groups.items():
                if attr == "death_age":
                    values = [p.death_age for p in patients if p.death_age is
                elif attr == "ptau_ratio":
                    values = [p.get_ptau_ratio() for p in patients if p.get_pt
                else:
                    values = []
                averages[ed] = sum(values)/len(values) if values else 0
            return averages

        # Computing stats of desired variables
        avg_age_dementia = stats_by_edu(dementia_patients, "death_age")
        avg_age_non_dementia = stats_by_edu(non_dementia_patients, "death_age"
        avg_ratio_dementia = stats_by_edu(dementia_patients, "ptau_ratio")
        avg_ratio_non_dementia = stats_by_edu(non_dementia_patients, "ptau_rat
```

```
        print(dementia_patients)

        # sorting education levels
        edu_levels = sorted(
            set(list(avg_age_dementia.keys()) + list(avg_age_non_dementia.keys
            key=lambda x: EDUCATION_ORDER.get(x, -1)
        )

        x = np.arange(len(edu_levels))
        width = 0.35

        # plot
        fig, axs = plt.subplots(1, 2, figsize=(16, 6))

        # avg age of death
        dementia_values_age = [avg_age_dementia.get(ed, 0) for ed in edu_level
        non_dementia_values_age = [avg_age_non_dementia.get(ed, 0) for ed in e

        axs[0].bar(x - width/2, dementia_values_age, width, label="Dementia",
        axs[0].bar(x + width/2, non_dementia_values_age, width, label="No Deme
        axs[0].set_ylabel("Average Age of Death")
        axs[0].set_xlabel("Education Level")
        axs[0].set_title("Age of Death by Education Level")
        axs[0].set_xticks(x)
        axs[0].set_xticklabels(edu_levels, rotation=45, ha="right")
        axs[0].legend()

        # avg pTau/tTau ratio
        dementia_values_ratio = [avg_ratio_dementia.get(ed, 0) for ed in edu_l
        non_dementia_values_ratio = [avg_ratio_non_dementia.get(ed, 0) for ed

        axs[1].bar(x - width/2, dementia_values_ratio, width, label="Dementia"
        axs[1].bar(x + width/2, non_dementia_values_ratio, width, label="No De
        axs[1].set_ylabel("Average pTau/tTau Ratio")
        axs[1].set_xlabel("Education Level")
        axs[1].set_title("pTau/tTau Ratio by Education Level")
        axs[1].set_xticks(x)
        axs[1].set_xticklabels(edu_levels, rotation=45, ha="right")
        axs[1].legend()

        plt.tight_layout()
        plt.show()

Patient.instantiate_from_csv('UpdatedLuminex.csv', 'UpdatedMetaData.csv')
```

In [3]:

```
#get patients by group
dementia = Patient.filter_by_dementia(True)
non_dementia = Patient.filter_by_dementia(False)

#ratios for each group
dementia_ratios = [p.get_ptau_ratio() for p in dementia if p.get_ptau_ratio()
non_dementia_ratios = [p.get_ptau_ratio() for p in non_dementia if p.get_ptau_
```

```
#means of each group
avg_ratio_dementia = np.mean(dementia_ratios)
avg_ratio_non_dementia = np.mean(non_dementia_ratios)

#standard deviations of each group
std_dementia = np.std(dementia_ratios, ddof=1)
std_non_dementia = np.std(non_dementia_ratios, ddof=1)

# create plot with error bars
plt.figure(figsize=(6,5))
plt.bar(
    ["Dementia", "No Dementia"],
    [avg_ratio_dementia, avg_ratio_non_dementia],
    yerr=[std_dementia, std_non_dementia],
    capsize=10,
    color=["salmon","skyblue"]
)
plt.ylabel("Average pTau/tTau Ratio")
plt.title("Comparison of pTau/tTau Ratio: Dementia vs No Dementia")
plt.show()

#runs t-test on pTau/tTau ratio and dementia status
t_stat, p_val = stats.ttest_ind(dementia_ratios, non_dementia_ratios, equal_va
print("t-statistic:", t_stat)
print("p-value:", p_val)
```




```
t-statistic: 1.8535072442018263
p-value: 0.06892230088908319
```

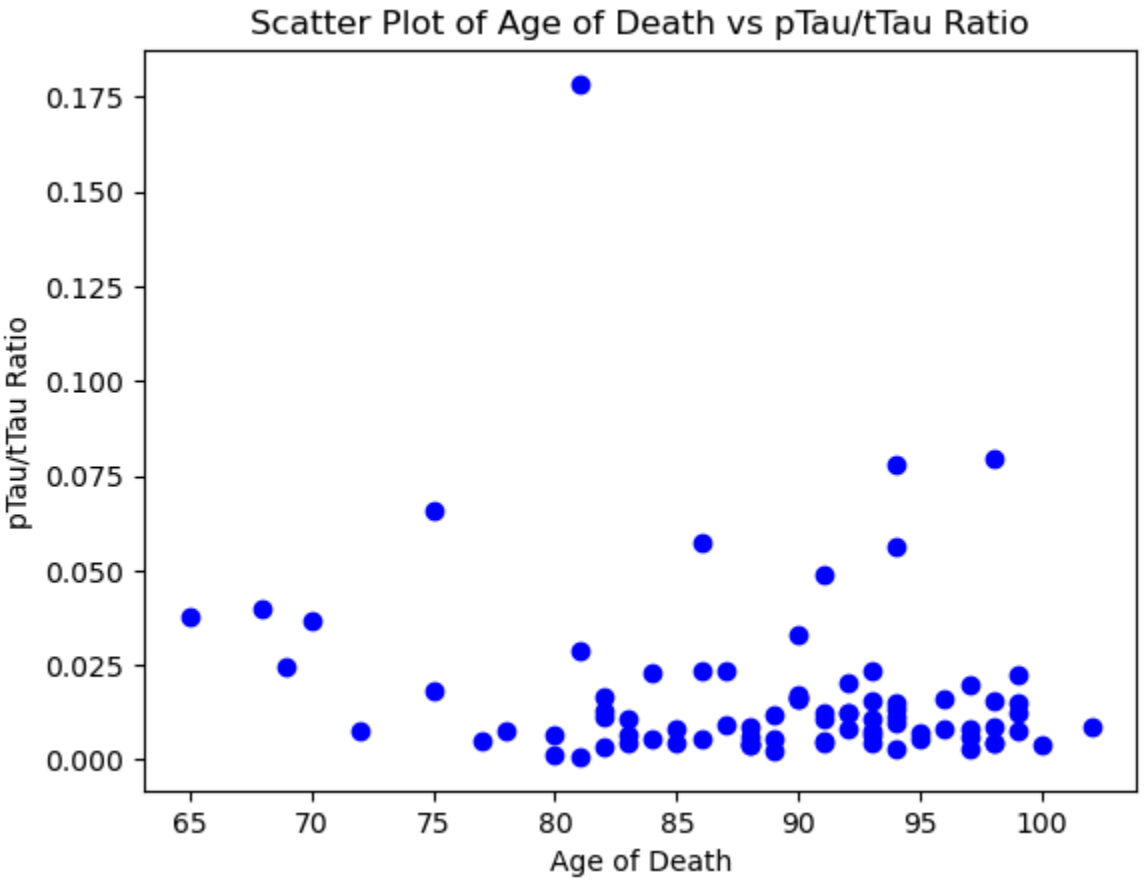
After running the Student's T-test in order to test if the difference in pTau/tTau ratio between dementia and non-dementia patients, the t-statistic was found to be 1.85. This correlates with a p-value of 0.0689, which is greater than the significance level of 0.05. Because of this, we fail to reject the null hypothesis and cannot conclude that there is a statistically significant difference between pTau/tTau ratios in dementia and non-dementia patients.

In [4]:
```
"Creates lists of patient death ages and their corresponding pTau/tTau ratios"

death_age_list = []
ratio = []
for patient in Patient.all_patients:
    death_age_list.append(patient.death_age)
print(death_age_list)
for p in Patient.all_patients:
    ratio.append(p.get_ptau_ratio())
print(ratio)
X = [death_age_list] # Independent variable
y = [ratio] # Dependent variable
```

```
[77, 81, 94, 94, 82, 97, 90, 93, 80, 95, 80, 90, 86, 91, 94, 86, 69, 94, 88, 8
1, 92, 99, 75, 91, 99, 91, 87, 82, 97, 94, 97, 91, 86, 87, 81, 98, 68, 85, 99,
100, 96, 85, 93, 93, 83, 90, 93, 96, 65, 92, 94, 98, 98, 70, 78, 92, 94, 99, 8
2, 93, 82, 75, 89, 102, 88, 88, 90, 92, 72, 89, 89, 84, 98, 83, 90, 97, 93, 88,
84, 88, 83, 98, 91, 95]
[0.004825048082257089, 0.0008037244491985185, 0.07786028656641192, 0.0561602882
0411417, 0.013142417569603368, 0.002782304953228242, 0.016795380159084057, 0.00
747866778748597, 0.001224577805589332, 0.005695643932559746, 0.0067205177138116
12, 0.0168956427559208, 0.0054341521752552715, 0.0047807582785765156, 0.0095925
03240307661, 0.023271491923393707, 0.024568068991376254, 0.011398971732547314,
0.004647626390611478, 0.02878094470212576, 0.020403386912109415, 0.012365048385
420548, 0.06578033917721796, 0.012215062033089799, 0.015007205524195839, 0.0489
49181966135076, 0.00922226672522208, 0.0036211202782795667, 0.00834315374557669
8, 0.015244453941927454, 0.01973727335698385, 0.0105600445810992, 0.05723101788
665692, 0.023313414302251277, 0.17835506228771714, 0.0796185406991886, 0.040005
89823472718, 0.004556448929485189, 0.007565400768176574, 0.003700604086929171,
0.016132868535517583, 0.008145947861679728, 0.004667846546073378, 0.01537464110
4145418, 0.0110387880176057, 0.03308536647298513, 0.0066081606787392845, 0.0080
1020908962325, 0.03794372610350581, 0.012584877726534664, 0.01349994615353149,
0.01551854655239908, 0.004501956347175813, 0.03651931815755513, 0.0078517730631
5161, 0.008101722212569927, 0.002718154252343112, 0.022558548214572285, 0.01642
9302563098186, 0.010716464801902786, 0.011453116605436409, 0.01806907243899812
5, 0.011677753140138518, 0.008935656569430952, 0.0037103873742405434, 0.0087632
24181865313, 0.016080032667897103, 0.01215997883311067, 0.007836509740341994,
0.002140310731545832, 0.005497762925713021, 0.005571603176382724, 0.00873241003
3928472, 0.0066858984165355535, 0.016241125450903712, 0.005872293630260812, 0.0
23387502535367585, 0.004182648608100975, 0.022726359843634553, 0.00588295913251
5915, 0.004306417244765939, 0.004492903174351273, 0.004716187293542522, 0.00720
8200533551555]
```

In [5]:
```
"Creates scatterplot of age of death and pTau/tTau ratio using previously crea
```

```
plt.scatter(X, y, color='blue')
plt.xlabel('Age of Death')
plt.ylabel('pTau/tTau Ratio')
plt.title('Scatter Plot of Age of Death vs pTau/tTau Ratio')
plt.show()
```



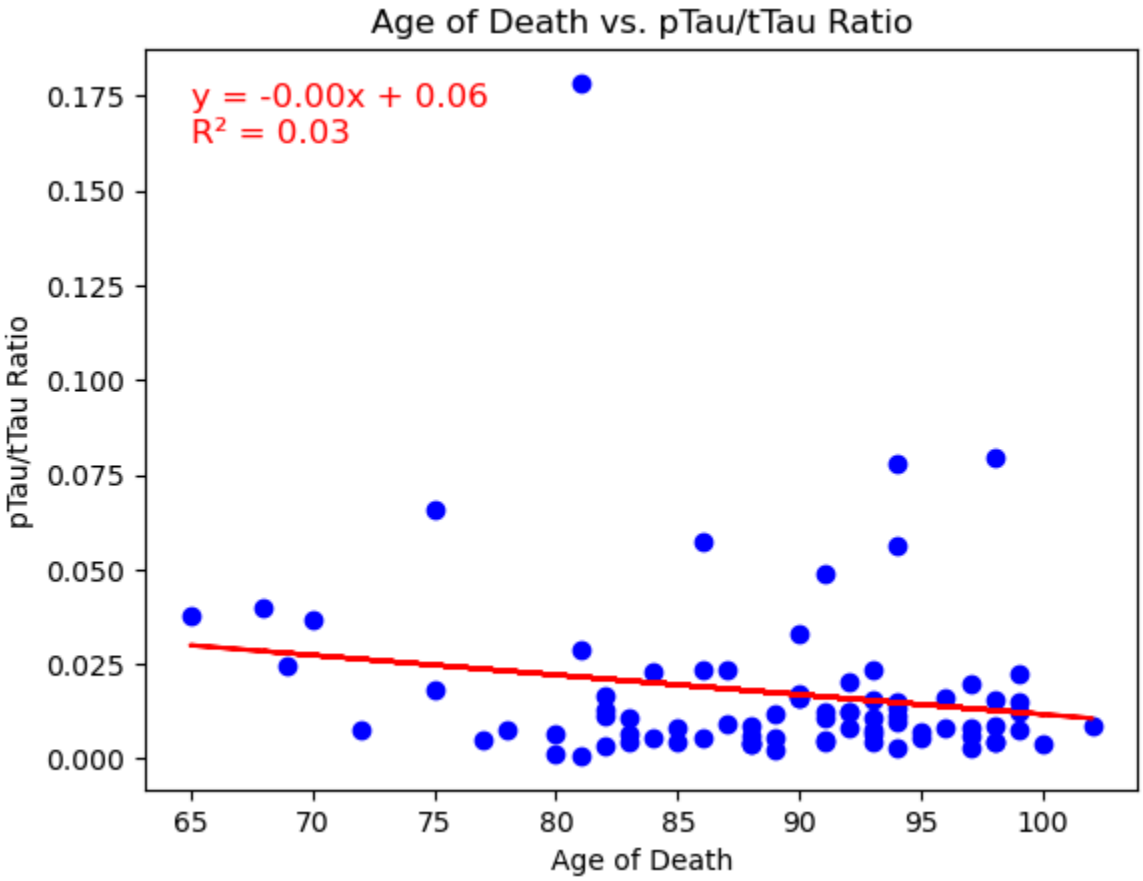
In [6]:
```
import pandas as pd
print(death_age_list)
print(ratio)

# Creates a DataFrame to write the data to a csv file

df = pd.DataFrame({
'Age of Death': death_age_list,
'pTau/tTau Ratio': ratio
})

# writes data to csv file
df.to_csv('patient_data.csv', index=False)
print("CSV file 'patient_data.csv' has been created.")
```

```
[77, 81, 94, 94, 82, 97, 90, 93, 80, 95, 80, 90, 86, 91, 94, 86, 69, 94, 88, 8
1, 92, 99, 75, 91, 99, 91, 87, 82, 97, 94, 97, 91, 86, 87, 81, 98, 68, 85, 99,
100, 96, 85, 93, 93, 83, 90, 93, 96, 65, 92, 94, 98, 98, 70, 78, 92, 94, 99, 8
2, 93, 82, 75, 89, 102, 88, 88, 90, 92, 72, 89, 89, 84, 98, 83, 90, 97, 93, 88,
84, 88, 83, 98, 91, 95]
[0.004825048082257089, 0.0008037244491985185, 0.07786028656641192, 0.0561602882
0411417, 0.013142417569603368, 0.002782304953228242, 0.016795380159084057, 0.00
747866778748597, 0.001224577805589332, 0.005695643932559746, 0.0067205177138116
12, 0.0168956427559208, 0.0054341521752552715, 0.0047807582785765156, 0.0095925
03240307661, 0.023271491923393707, 0.024568068991376254, 0.011398971732547314,
0.004647626390611478, 0.02878094470212576, 0.020403386912109415, 0.012365048385
420548, 0.06578033917721796, 0.012215062033089799, 0.015007205524195839, 0.0489
49181966135076, 0.00922226672522208, 0.0036211202782795667, 0.00834315374557669
8, 0.015244453941927454, 0.01973727335698385, 0.0105600445810992, 0.05723101788
665692, 0.023313414302251277, 0.17835506228771714, 0.0796185406991886, 0.040005
89823472718, 0.004556448929485189, 0.007565400768176574, 0.003700604086929171,
0.016132868535517583, 0.008145947861679728, 0.004667846546073378, 0.01537464110
4145418, 0.0110387880176057, 0.03308536647298513, 0.0066081606787392845, 0.0080
1020908962325, 0.03794372610350581, 0.012584877726534664, 0.01349994615353149,
0.01551854655239908, 0.004501956347175813, 0.03651931815755513, 0.0078517730631
5161, 0.008101722212569927, 0.002718154252343112, 0.022558548214572285, 0.01642
9302563098186, 0.010716464801902786, 0.011453116605436409, 0.01806907243899812
5, 0.011677753140138518, 0.008935656569430952, 0.0037103873742405434, 0.0087632
24181865313, 0.016080032667897103, 0.01215997883311067, 0.007836509740341994,
0.002140310731545832, 0.005497762925713021, 0.005571603176382724, 0.00873241003
3928472, 0.0066858984165355535, 0.016241125450903712, 0.005872293630260812, 0.0
23387502535367585, 0.004182648608100975, 0.022726359843634553, 0.00588295913251
5915, 0.004306417244765939, 0.004492903174351273, 0.004716187293542522, 0.00720
8200533551555]
CSV file 'patient_data.csv' has been created.
```

In [7]:
```
from sklearn.linear_model import LinearRegression
from sklearn.metrics import r2_score

"reads from dataframe and creates linear regression computational model to plc

df = pd.read_csv("patient_data.csv")

x = df["Age of Death"].values.reshape(-1, 1)
y = df["pTau/tTau Ratio"].values

model = LinearRegression()
model.fit(x, y)
slope = model.coef_[0]
intercept = model.intercept_
r2 = model.score(x, y)
```

In [8]:
```
"Plots scatterplot of age of death vs pTau/tTau ratio and adds linear regressi

plt.scatter(x, y, color='blue')
plt.plot(x, model.predict(x), color="red")

# Annotate equation
```

```
equation = f"y = {slope:.2f}x + {intercept:.2f}\nR² = {r2:.2f}"
plt.text(x.min(), y.max(), equation, color="red", fontsize=12, verticalalignme

# Annotate scatterplot with labels and title

plt.xlabel("Age of Death")
plt.ylabel("pTau/tTau Ratio")
plt.title("Age of Death vs. pTau/tTau Ratio")
plt.show()
```



Verify and validate your analysis:

Our results show a weak statistical relationship between pTau/tTau ratio and age of death, with higher ratios occuring in patients who died at a younger age. Though our results were not found to be statistically significant, this finding is consistent with prior literature. The regression of age of death on the pTau/tTau ratio shows that the ratio is a very poor predictor of lifespan. The nearly flat regression line and low r-squared value (0.03) indicate that the ratio explains only about 3% of the variance in age at death. This suggests that the pTau/tTau ratio does not meaningfully predict how long individuals live with this sample. Prior studies support this interpretation as while tau biomarkers can be associated with

neurodegeneration, disease progression, or cognitive decline, they are not typically direct predictors of age of death. Instead, mortality is influenced by a larger set of factors, including cardiovascular health and other non-neurological conditions. The pTau/tTau ratio is more often utilized in differentiating between other forms of neurodegeneration. Conversely, though our tests do not suggest a statistically significant relationship between pTau/tTau ratio and dementia status due to a p-value of 0.0689, other research suggests that the pTau/tTau ratio may have some predictive value for disease status. In this sample, individuals with dementia show a higher average ratio than those without, consistent with biomarker research showing elevated pTau in dementia. Although the variability is large, the group-level difference aligns with the literature that assigns pTau as a biomarker for Alzheimer's disease and related dementias. The ratio itself is less commonly studied than absolute pTau, but its elevation in dementia cases suggests it could serve as a weak predictor of disease presence rather than of age at death.

https://www.sciencedirect.com/science/article/pii/S2352872915000858

https://pmc.ncbi.nlm.nih.gov/articles/PMC2815003/

Conclusions and Ethical Implications:

Our results indicate that we failed to reject the null hypothesis that there is no correlation between the pTau/tTau ratio and dementia status. The statistical test produced a p-value greater than the alpha significance level of 0.05, suggesting that, within our sample, the ratio does not significantly differentiate between patients with and without dementia. However, this does not mean that the ratio has no relationship to dementia risk. Other factors such as genetic predisposition or measurement variability could influence the observed outcomes and may conceal potential associations. From an ethical standpoint, it is important to avoid overstating our conclusions: the absence of statistical significance in this dataset does not rule out the possibility that the pTau/tTau ratio could still hold diagnostic or predictive value in other contexts or larger studies. Therefore, clinicians should be cautious not to disregard the ratio entirely, as premature dismissal of potentially informative biomarkers could hinder the development of more comprehensive diagnostic approaches for Alzheimer's disease and related dementias.

Limitations and Future Work:

A key limitation of our study is that it was conducted using only a single patient sample. As a result, our findings cannot be generalized, and a larger sample size would be necessary to draw stronger conclusions about the relationship between

the pTau/tTau ratio and dementia risk. Future research should include additional patient groups and larger cohorts to better assess whether specific pTau/tTau ratios are consistently associated with dementia. It may also be more informative to focus on absolute pTau concentrations or the pTau/Amyloid-Beta ratio, as prior studies suggest these biomarkers show stronger and more consistent associations with Alzheimer’s disease and related dementias. Finally, incorporating tTau measures directly could provide further insight, not only into disease risk but also into potential links between tau biomarkers and age of death.

Notes from our team

- used ChatGPT to help debug some coding of class methods

Questions for our TA

We have no questions at this point in time.