Module_1:

Team Members:

Diya and Marco

Project Title:

Determine whether the APOE gene correlates with age of death

Project Goal:

This project seeks to determine whether APOE gene correlates with age of death for patients by analyzing data sets and learning more about Alzheimers.

Disease Background:

Fill in information about 11 bullets:

- Prevalence & incidence
  - Prevalence: 7.2 million Americans live with Alzheimers in 2025 (https://www.alz.org/getmedia/ef8f48f9-ad36-48ea-87f9-b74034635c1e/alzheimers-facts-and-figures.pdf)
  - Incidence: 910,000 people per year (https://pmc.ncbi.nlm.nih.gov/articles/PMC12040760/)
- Economic burden: https://www.nature.com/articles/s41514-024-00136-6
  - Cost of formal care is $28,078 per person
  - Americans spend 196 billion in direct medical costs and another 254 billion in caregiver time for Alzheimers
- Risk factors (genetic, lifestyle) (https://www.alz.org/alzheimers-dementia/what-is-alzheimers/causes-and-risk-factors)
  - genetic: age (65+ risk doubles every 5 years), family history (having a family member with the disease increases risk), hypertension, diabetes,
  - lifestyle: short sleep, smoking, head injury, sugar intake, lack of physical activity, high cholestrol, alchohol, air polution.
- Societal determinants
  - education: twice as high for people without highschool diploma (https://www.cdc.gov/alzheimers-dementia/php/sdoh/index.html)
  - manual labor is associated with higher risk of Alzheimers (https://pubmed.ncbi.nlm.nih.gov/34103175/)
  - early adversity in childhood relates to increased risk (https://pubmed.ncbi.nlm.nih.gov/34103175/)
- Symptoms (https://www.alz.org/alzheimers-dementia/10_signs)
  - memory loss that disrupts daily life

  - challenges in planning or solving problems
  - difficulty completing familiar tasks
  - confusion with time or place
  - trouble understanding images and spatial relationships
  - new problmes with words in speaking or writing
  - misplacing things and losing the ability to retrace steps
  - decrease in judgement
  - withdrawal from work or social activities
  - changes in mood and personality
- Diagnosis (https://www.alz.org/alzheimers-dementia/diagnosis/medical_tests)
  a. Medical history: during workup doctor will look at medical history and know about medical concerns and talk about family history.
  b. Physcial exam and diagnostic tests: Physician will ask about diet, use of alcohol, review all mediciations, check blood pressure, temperature and pulse, listen to heart and lungs, perform other procedures to assess overall health, and collect blood or urine.
  c. Neurological exam: evauluate reflexes, coordination, muscle tone/strenght, eye movement, speech, sensation, and maybe brain imaging.
  d. Cognitive, functional and behavioral tests: evaluate memory thinking and simple problem solving skills. Many different kinds of these
  e. Computerized cognitive tests and devicesL measure individuals performance on a variety of cognitive or functional tasks.
  f. Depression screen and mood assessment: mental status and sense of well being to detect depression or mood disorders that could also cause the memory loss.
  g. Brain imaging: structural imaging with MRI or CT to rule out other conditions.
  h. Cerebrospinal fluid tests: check for tau and beta amyloid the two markers for Alzheimers.
  i. Blood tests: Additional test to check for tau and beta amyloid.
- Standard of care treatments (& reimbursement) https://www.alz.org/alzheimers-dementia/treatments/cms-medicare-coverage
  - Medicare covers FDA approved monoclonal antibody treatments that recieved traditional approval
  - They also cover braim amyloid PET imaging for the diagnosis for Alzheimers.
- Disease progression & prognosis (https://www.alzinfo.org/understand-alzheimers/clinical-stages-of-alzheimers/)
  - Stage 1. No dementia seen
  - Stage 2. Subjective memory loss
  - Stage 3. Mild cognitive impairment
  - Stage 4. Moderate cognitive decline
  - Stage 5. Moderately severe cognitive decline
  - Stage 6. Severe cognitive decline
  - Stage 7. Very severe cognitive decline
- Continuum of care providers Primary care providers --> Neurologists/Neuropsychologists Other caretakers include home nurses and respite care providers, assisted living facilities, hospice organizations.

- Biological mechanisms (anatomy, organ physiology, cell & molecular physiology) (https://medical.lilly.com/us/diseases/disease-education-resources/neuroscience/alzheimers-disease/answers/alzheimer-s-disease-pathology-includes-both-macroscopic-and-microscopic-changes-155846) Beta amyloid and tau are two hallmark pathologies in Alzheimer's disease that accumulate through various stages of disease progression. Early diagnosis of Alzheimer's disease is possible with improved understanding of disease progression.
- Clinical Trials/next-gen therapies:
  - next generation therapies include removing amyloid plaques, targeting tau tangles through inhibitors, developing oral medications, CRISPR-Cas9, and drugs including semaglutide and benetamine.
  - Clinical trial: https://www.leqembihcp.com/about-leqembi/study-2-clarity-ad
    - Clarity AD is an 18-month global, placebo-controlled, double-blind, parallel-group randomized study

Data-Set:

- Updated Luminex.csv:
  - What are the column headers: Donor ID, ABeta40 pg/ug, ABeta42 pg/ug, tTAU pg/ug, pTAU pg/ug
  - What are the rows: The different pateints or brains and than in each row they give the values for the columns
  - How many rows are there: 84
- UpdatedMetaData.csv:
  - What are the column headers: Donor ID, Primary Study Name, Secondary Study Name, Age at Death, Sex, Race (choice=White), Race (choice=Black/ African American), Race (choice=Asian), Race (choice=American Indian/ Alaska Native), Race (choice=Native Hawaiian or Pacific Islander), Race (choice=Unknown or unreported), Race (choice=Other), specify other race, Hispanic/Latino, Highest level of education, Years of education, APOE Genotype, Cognitive Status, Age of onset cognitive symptoms, Age of Dementia diagnosis, Known head injury, Have they had neuroimaging, Consensus Clinical Dx (choice=Alzheimers disease), Consensus Clinical Dx (choice=Alzheimers Possible/ Probable), Consensus Clinical Dx (choice=Ataxia), Consensus Clinical Dx (choice=Corticobasal Degeneration), Consensus Clinical Dx (choice=Control), Consensus Clinical Dx (choice=Dementia with Lewy Bodies/ Lewy Body Disease), Consensus Clinical Dx (choice=Frontotemporal lobar degeneration), Consensus Clinical Dx (choice=Huntingtons disease), Consensus Clinical Dx (choice=Motor Neuron disease), Consensus Clinical Dx (choice=Multiple System Atrophy), Consensus Clinical Dx (choice=Parkinsons disease), Consensus Clinical Dx (choice=Parkinsons Cognitive Impairment - no dementia), Consensus Clinical Dx (choice=Parkinsons Disease Dementia), 'Consensus Clinical Dx (choice=Prion), Consensus Clinical Dx (choice=Progressive Supranuclear Palsy), Consensus Clinical Dx (choice=Taupathy), Consensus Clinical Dx (choice=Vascular Dementia), Consensus Clinical Dx (choice=Unknown), Consensus Clinical Dx (choice=Other), If other Consensus dx, describe, Last CASI Score, Interval from last CASI in months, Last MMSE Score, Interval from last MMSE in months, Last MOCA Score, Interval from last MOCA in months, PMI, Rapid Frozen Tissue Type, Ex Vivo

Imaging, Fresh Brain Weight, Brain pH, Overall AD neuropathological Change, Thal, Braak, CERAD score, Overall CAA Score, Highest Lewy Body Disease, Total Microinfarcts (not observed grossly), Total microinfarcts in screening sections, Atherosclerosis, Arteriolosclerosis, LATE, RIN, Severely Affected Donor

- What are the rows: The rows represent a patient and have the values based on the patient for each column
- How many rows are there: 84

```
#This is the code for the updated luminex csv file
import csv
with open("UpdatedLuminex.csv", "r", newline="", encoding="utf-8") as
f:
    reader = csv.reader(f)

    headers = next(reader)
    print("Column headers:", headers)

    rows = list(reader)
    print("Rows:", rows)

    print("Number of rows:", len(rows))

#This is for the Updated Meta data file
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    print("Number of rows:", len(rows))
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V', 'Moderate', 'Not identified', 'Not Identified (olfactory bulb not
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(olfactory bulb not assessed)', '1', '1', 'Moderate', 'Moderate', 'Not
Identified', '8.67', ''], ['H21.33.027', 'ACT', '', '92', 'Male',
'Checked', 'Unchecked', 'Unchecked', 'Unchecked', 'Unchecked',
'Unchecked', 'Unchecked', '', 'No', 'Graduate (PhD/Masters)', '18',
'3/4', 'Dementia', '', '', '', 'Yes', 'Checked', 'Unchecked',
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'Unchecked', 'Unchecked', '', '71', '28.2', '22', '28.2', '', '',
'6.30', 'Precision Slices', 'Yes', '1214.00', '6.40', 'High', 'Thal
5', 'Braak V', 'Moderate', 'Moderate', 'Not Identified (olfactory bulb
not assessed)', '0', '0', 'Moderate', 'Mild', 'LATE Stage 1', '7.93',
''], ['H21.33.028', 'ACT', '', '72', 'Male', 'Checked', 'Unchecked',
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'No', 'Bachelors', '16', '3/3', 'No dementia', '', '', '', 'Yes',
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'29', '22.3', '', '', '8.30', 'Precision Slices', 'Yes', '1350.00',
'6.40', 'Low', 'Thal 1', 'Braak II', 'Absent', 'Moderate', 'Not
Identified (olfactory bulb assessed)', '0', '0', 'Moderate', 'Mild',
'Not Identified', '6.73', ''], ['H21.33.029', 'ACT', '', '89', 'Male',
'Checked', 'Unchecked', 'Unchecked', 'Unchecked', 'Unchecked',
'Unchecked', 'Unchecked', 'Unchecked', '', 'No', 'Graduate (PhD/Masters)', '18',
'2/4', 'Dementia', '82', '83', '', 'Yes', 'Checked', 'Unchecked',
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'11.03', 'Precision Slices', 'Yes', '1009.00', '6.40', 'High', 'Thal
5', 'Braak V', 'Frequent', 'Moderate', 'Amygdala-predominant', '11',
'4', 'Severe', 'Moderate', 'LATE Stage 1', '7.2', ''], ['H21.33.030',

'ACT', '', '89', 'Male', 'Checked', 'Unchecked', 'Unchecked',
'Unchecked', 'Unchecked', 'Unchecked', 'Unchecked', '', 'No',
'Bachelors', '17', '3/4', 'No dementia', '', '', '', 'Yes',
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'27', '55.2', '', '', '5.50', 'Precision Slices', 'Yes', '1290.00',
'6.70', 'Intermediate', 'Thal 3', 'Braak III', 'Moderate', 'Mild',
'Brainstem-predominant', '3', '2', 'Moderate', 'Mild', 'LATE Stage 1',
'8.67', ''], ['H21.33.031', 'ADRC Clinical Core', '', '84', 'Male',
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'Unchecked', 'Unchecked', '', 'No', 'Graduate (PhD/Masters)', '18',
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'8.90', 'Precision Slices', 'Yes', '1165.00', '6.40', 'High', 'Thal
5', 'Braak V', 'Moderate', 'Moderate', 'Limbic (Transitional)', '1',
'1', 'Moderate', 'Mild', 'LATE Stage 2', '8.43', ''], ['H21.33.032',
'ADRC Clinical Core', '', '98', 'Female', 'Checked', 'Unchecked',
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'1005.00', '6.40', 'Low', 'Thal 2', 'Braak IV', 'Sparse', 'Moderate',
'Not Identified (olfactory bulb not assessed)', '0', '0', 'Mild',
'Mild', 'LATE Stage 2', '8.03', ''], ['H21.33.033', 'ACT', '', '83',
'Female', 'Checked', 'Unchecked', 'Unchecked', 'Unchecked',
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School', '14', '3/4', 'No dementia', '', '', '', 'Unknown',
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'27', '11.4', '', '', '8.20', 'Precision Slices', 'Yes', '1110.00',
'6.00', 'High', 'Thal 5', 'Braak V', 'Moderate', 'Moderate',
'Amygdala-predominant', '2', '0', 'Moderate', 'Mild', 'LATE Stage 1',
'5.6', 'Y'], ['H21.33.034', 'ACT', '', '90', 'Female', 'Checked',
'Unchecked', 'Unchecked', 'Unchecked', 'Unchecked', 'Unchecked',
'Unchecked', '', 'No', 'Bachelors', '16', '3/4', 'Dementia', '', '86',
'', 'Yes', 'Unchecked', 'Unchecked', 'Unchecked', 'Unchecked',
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'66', '47.3', '18', '47.3', '', '', '10.80', 'Precision Slices',
'Yes', '931.00', '4.50', 'High', 'Thal 5', 'Braak VI', 'Frequent',
'Moderate', 'Amygdala-predominant', '0', '0', 'Moderate', 'Moderate',
'LATE Stage 2', '2.9', 'Y'], ['H21.33.035', 'ACT', '', '97', 'Female',
'Checked', 'Unchecked', 'Unchecked', 'Unchecked', 'Unchecked',
'Unchecked', 'Unchecked', '', 'No', 'High School', '14', '3/3', 'No
dementia', '', '', '', 'Yes', 'Unchecked', 'Unchecked', 'Unchecked',
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'Unchecked', '', '97', '30.0', '27', '30.0', '', '', '4.80',
'Precision Slices', 'Yes', '1008.00', '6.40', 'High', 'Thal 5', 'Braak
V', 'Moderate', 'Moderate', 'Not Identified (olfactory bulb
assessed)', '0', '0', 'Moderate', 'Severe', 'LATE Stage 2', '8.27',
''], ['H21.33.036', 'ACT', '', '93', 'Female', 'Checked', 'Unchecked',
'Unchecked', 'Unchecked', 'Unchecked', 'Unchecked', 'Unchecked', '',
'No', 'Trade School/ Tech School', '14', '3/3', 'No dementia', '', '',
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'985.00', '6.80', 'High', 'Thal 4', 'Braak V', 'Frequent', 'Mild',
'Not Identified (olfactory bulb assessed)', '0', '0', 'Moderate',
'Moderate', 'LATE Stage 2', '7.03', ''], ['H21.33.037', 'ACT', '',
'88', 'Female', 'Checked', 'Unchecked', 'Unchecked', 'Unchecked',
'Unchecked', 'Unchecked', 'Unchecked', 'Checked', 'Mixed', 'No', 'Graduate
(PhD/Masters)', '18', '2/3', 'No dementia', '', '', '', 'Yes',
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'26', '29.7', '', '', '6.50', 'Precision Slices', 'Yes', '1239.00',
'7.00', 'Low', 'Thal 2', 'Braak IV', 'Absent', 'Moderate', 'Limbic
(Transitional)', '2', '1', 'None', 'Mild', 'LATE Stage 1', '6.67',
''], ['H21.33.038', 'ACT', '', '84', 'Female', 'Checked', 'Unchecked',
'Unchecked', 'Unchecked', 'Unchecked', 'Unchecked', 'Unchecked', '',
'No', 'High School', '15', '3/3', 'No dementia', '', '', '',
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'97', '21.2', '27', '21.2', '', '', '11.00', 'Precision Slices',
'Yes', '1355.00', '6.20', 'Low', 'Thal 1', 'Braak III', 'Absent', 'Not
identified', 'Not Identified (olfactory bulb assessed)', '1', '0',
'Mild', 'Mild', 'Not Identified', '7.27', ''], ['H21.33.039', 'ACT',
'', '88', 'Female', 'Checked', 'Unchecked', 'Unchecked', 'Unchecked',
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'3/3', 'Dementia', '84', '86', '', 'Yes', 'Checked', 'Unchecked',

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'6.50', 'Precision Slices', 'No', '1035.00', '6.50', 'High', 'Thal 4',
'Braak V', 'Moderate', 'Not identified', 'Not Identified (olfactory
bulb assessed)', '0', '0', 'Mild', 'Mild', 'LATE Stage 3', '7.2',
'Y'], ['H21.33.040', 'ACT', 'ADRC Clinical Core', '83', 'Male',
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dementia', '', '', '', 'Yes', 'Unchecked', 'Unchecked', 'Unchecked',
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'Precision Slices', 'Yes', '1254.00', '6.70', 'High', 'Thal 4', 'Braak
V', 'Frequent', 'Moderate', 'Olfactory bulb only', '3', '1', 'Mild',
'Moderate', 'LATE Stage 1', '7.37', ''], ['H21.33.041', 'ACT', '',
'98', 'Female', 'Checked', 'Unchecked', 'Unchecked', 'Unchecked',
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'2/3', 'No dementia', '', '', '', 'Unknown', 'Unchecked', 'Unchecked',
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0', 'Braak IV', 'Absent', 'Not identified', 'Limbic (Transitional)',
'2', '2', 'Moderate', 'Severe', 'Not Identified', '7.57', ''],
['H21.33.042', 'ACT', '', '91', 'Female', 'Checked', 'Unchecked',
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'89', '', 'No', 'Checked', 'Unchecked', 'Unchecked', 'Unchecked',
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'80', '36.9', '21', '36.9', '', '', '8.10', 'Precision Slices', 'Yes',
'1280.00', '6.40', 'High', 'Thal 5', 'Braak V', 'Moderate',
'Moderate', 'Neocortical (Diffuse)', '2', '0', 'Moderate', 'Moderate',
'LATE Stage 2', '6.23', ''], ['H21.33.043', 'ACT', '', '95', 'Female',
'Checked', 'Unchecked', 'Unchecked', 'Unchecked', 'Unchecked',
'Unchecked', 'Unchecked', '', 'No', 'Bachelors', '16', '3/3',
'Dementia', '93', '94', '', 'Yes', 'Unchecked', 'Unchecked',
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'4.40', 'Precision Slices', 'Yes', '1082.00', '6.60', 'Low', 'Thal 4',
'Braak II', 'Sparse', 'Not identified', 'Not Identified (olfactory
bulb assessed)', '1', '0', 'Moderate', 'Moderate', 'LATE Stage 1',

```
'7.27', ''], ['H21.33.044', 'ACT', '', '88', 'Female', 'Checked',
'Unchecked', 'Unchecked', 'Unchecked', 'Unchecked', 'Unchecked',
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'Dementia', '87', '88', 'Yes', 'Yes', 'Checked', 'Unchecked',
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'7.00', 'Precision Slices', 'Yes', '1168.00', '6.60', 'Intermediate',
'Thal 3', 'Braak VI', 'Frequent', 'Moderate', 'Not Identified
(olfactory bulb not assessed)', '9', '9', 'Mild', 'Severe', 'LATE
Stage 1', '8.63', ''], ['H21.33.045', 'ADRC Clinical Core', '', '94',
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'3/4', 'Dementia', '78', '78', '', 'Unknown', 'Unchecked', 'Checked',
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VI', 'Frequent', 'Moderate', 'Limbic (Transitional)', '0', '0',
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'ACT', '', '97', 'Male', 'Checked', 'Unchecked', 'Unchecked',
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'6.40', 'High', 'Thal 4', 'Braak V', 'Moderate', 'Moderate',
'Neocortical (Diffuse)', '0', '0', 'Mild', 'Severe', 'LATE Stage 2',
'7.28', ''], ['H21.33.047', 'ACT', '', '90', 'Male', 'Checked',
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'', '', 'Unknown', 'Unchecked', 'Unchecked', 'Unchecked', 'Unchecked',
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'Unchecked', 'Unchecked', 'Unchecked', 'Unchecked', 'Unchecked', '',
'90', '7.4', '26', '7.4', '', '', '4.40', 'Precision Slices', 'Yes',
'1168.00', '7.20', 'Intermediate', 'Thal 2', 'Braak V', 'Frequent',
'Not identified', 'Neocortical (Diffuse)', '1', '1', 'Moderate',
'Moderate', 'LATE Stage 2', '8.7', '']]
Number of rows: 84
```

Data Analyis:

(Describe how you analyzed the data. This is where you should intersperse your Python code so that anyone reading this can run your code to perform the analysis that you did, generate your figures, etc.)

```
#This is the code for the patient class and printing the table: the
table has donor id, sex, age of death, and apoe genotype
import csv

class Patient:
    all_patients = {}

    def __init__(self, DonorID, sex, death_age, apoe):
        self.DonorID = DonorID
        self.sex = sex
        self.death_age = death_age
        self.apoe = apoe
        Patient.all_patients[self.DonorID] = self

def load_data_from_metadata(filename):
    with open(filename, "r", newline="", encoding="utf-8-sig") as f:
        reader = csv.DictReader(f)
        for row in reader:
            Patient(
                DonorID=row['Donor ID'],
                sex=row['Sex'],
                death_age=int(row["Age at Death"]) if row["Age at
Death"] else None,
                apoe=row['APOE Genotype']
            )

# Main execution
load_data_from_metadata("Metadata.csv")

# Find the maximum width for each column
donor_id_width = max(len("Donor ID"), max(len(p.DonorID) for p in
Patient.all_patients.values()))
sex_width = max(len("Sex"), max(len(p.sex) if p.sex else 0 for p in
Patient.all_patients.values()))
age_width = max(len("Age at Death"), max(len(str(p.death_age)) if
p.death_age else 0 for p in Patient.all_patients.values()))
apoe_width = max(len("APOE Genotype"), max(len(p.apoe) if p.apoe else
0 for p in Patient.all_patients.values()))

# Print the final table with formatted alignment
header = f"{'Donor ID':<{donor_id_width}}  {'Sex':<{sex_width}}  {'Age
at Death':<{age_width}}  {'APOE Genotype':<{apoe_width}}"
print(header)
print("-" * len(header))
```

```
for patient in Patient.all_patients.values():
    print(f"{patient.DonorID:<{donor_id_width}}
{patient.sex:<{sex_width}}  {str(patient.death_age) if
patient.death_age is not None else 'N/A':<{age_width}}
{patient.apoe:<{apoe_width}}")
```

```
Donor ID    Sex     Age at Death  APOE Genotype
-----------------------------------------------
H19.33.004  Female  80            3/3
H20.33.001  Male    82            3/3
H20.33.002  Female  97            2/3
H20.33.004  Male    86            3/4
H20.33.005  Female  99            2/3
H20.33.008  Female  92            3/4
H20.33.011  Female  93            3/4
H20.33.012  Female  91            3/3
H20.33.013  Male    94            3/3
H20.33.014  Female  82            3/3
H20.33.015  Male    88            3/3
H20.33.016  Female  93            2/3
H20.33.017  Male    69            3/3
H20.33.018  Female  81            3/4
H20.33.019  Female  87            3/4
H20.33.020  Male    81            4/4
H20.33.024  Male    90            3/3
H20.33.025  Male    94            3/3
H20.33.026  Female  75            4/4
H20.33.027  Female  99            3/3
H20.33.028  Female  94            3/3
H20.33.029  Female  91            3/3
H20.33.030  Female  86            3/4
H20.33.031  Female  87            3/3
H20.33.032  Male    98            3/3
H20.33.033  Male    68            3/3
H20.33.034  Female  85            2/2
H20.33.035  Female  99            3/3
H20.33.036  Female  100           2/3
H20.33.037  Female  96            3/3
H20.33.038  Female  90            3/3
H20.33.039  Female  96            3/3
H20.33.040  Male    98            3/3
H20.33.041  Female  91            3/3
H20.33.043  Male    85            4/4
H20.33.044  Male    81            2/3
H20.33.045  Female  77            4/4
H20.33.046  Male    94            3/3
H21.33.001  Male    80            2/3
H21.33.002  Female  70            3/4
H21.33.003  Male    78            3/3
```

```
H21.33.004  Male    93              2/3
H21.33.005  Male    95              3/3
H21.33.006  Male    97              3/4
H21.33.007  Female  86              3/3
H21.33.008  Female  91              3/3
H21.33.009  Female  65              4/4
H21.33.010  Female  93              3/3
H21.33.011  Female  83              3/3
H21.33.012  Female  93              2/4
H21.33.013  Female  94              3/4
H21.33.014  Male    92              2/3
H21.33.015  Male    98              3/3
H21.33.016  Female  94              3/3
H21.33.017  Female  92              3/3
H21.33.018  Female  89              3/3
H21.33.019  Male    75              2/3
H21.33.020  Male    82              3/3
H21.33.021  Male    99              3/3
H21.33.022  Female  82              3/3
H21.33.023  Male    102             3/3
H21.33.025  Female  88              3/3
H21.33.026  Female  90              3/4
H21.33.027  Male    92              3/4
H21.33.028  Male    72              3/3
H21.33.029  Male    89              2/4
H21.33.030  Male    89              3/4
H21.33.031  Male    84              3/4
H21.33.032  Female  98              3/3
H21.33.033  Female  83              3/4
H21.33.034  Female  90              3/4
H21.33.035  Female  97              3/3
H21.33.036  Female  93              3/3
H21.33.037  Female  88              2/3
H21.33.038  Female  84              3/3
H21.33.039  Female  88              3/3
H21.33.040  Male    83              3/4
H21.33.041  Female  98              2/3
H21.33.042  Female  91              4/4
H21.33.043  Female  95              3/3
H21.33.044  Female  88              3/3
H21.33.045  Female  94              3/4
H21.33.046  Male    97              3/3
H21.33.047  Male    90              3/3
```

```
import csv
import matplotlib.pyplot as plt
from collections import defaultdict
from scipy.stats import sem
import numpy as np
```

```
try:
    # Use 'utf-8-sig' encoding to handle the Byte Order Mark (BOM)
    with open("Metadata.csv", "r", newline="", encoding="utf-8-sig")
as f:
        reader = csv.DictReader(f)

        # A dictionary to hold a list of ages for each genotype
        genotype_ages = defaultdict(list)

        for row in reader:
            genotype = row.get("APOE Genotype", "").strip()
            age_str = row.get("Age at Death", "")

            # Check if both genotype and age data exist and are not
empty
            if genotype and age_str:
                try:
                    age = int(age_str)
                    genotype_ages[genotype].append(age)
                except (ValueError, KeyError):
                    # Skip rows with invalid or missing data
                    continue

        # Calculate the average age and standard error of the mean
(SEM) for each genotype
        avg_ages = {}
        sems = {}
        for genotype, ages in genotype_ages.items():
            if ages:
                avg_ages[genotype] = np.mean(ages)
                # Handle cases with a single data point where SEM is
undefined
                if len(ages) > 1:
                    sems[genotype] = sem(ages)
                else:
                    sems[genotype] = 0

        # Sort the data by average age in descending order
        sorted_genotypes = sorted(avg_ages, key=avg_ages.get,
reverse=True)
        sorted_ages = [avg_ages[genotype] for genotype in
sorted_genotypes]
        sorted_sems = [sems[genotype] for genotype in
sorted_genotypes]

        # Create the bar graph with error bars
        plt.figure(figsize=(10, 6))

        # Plot the bars with error bars
```

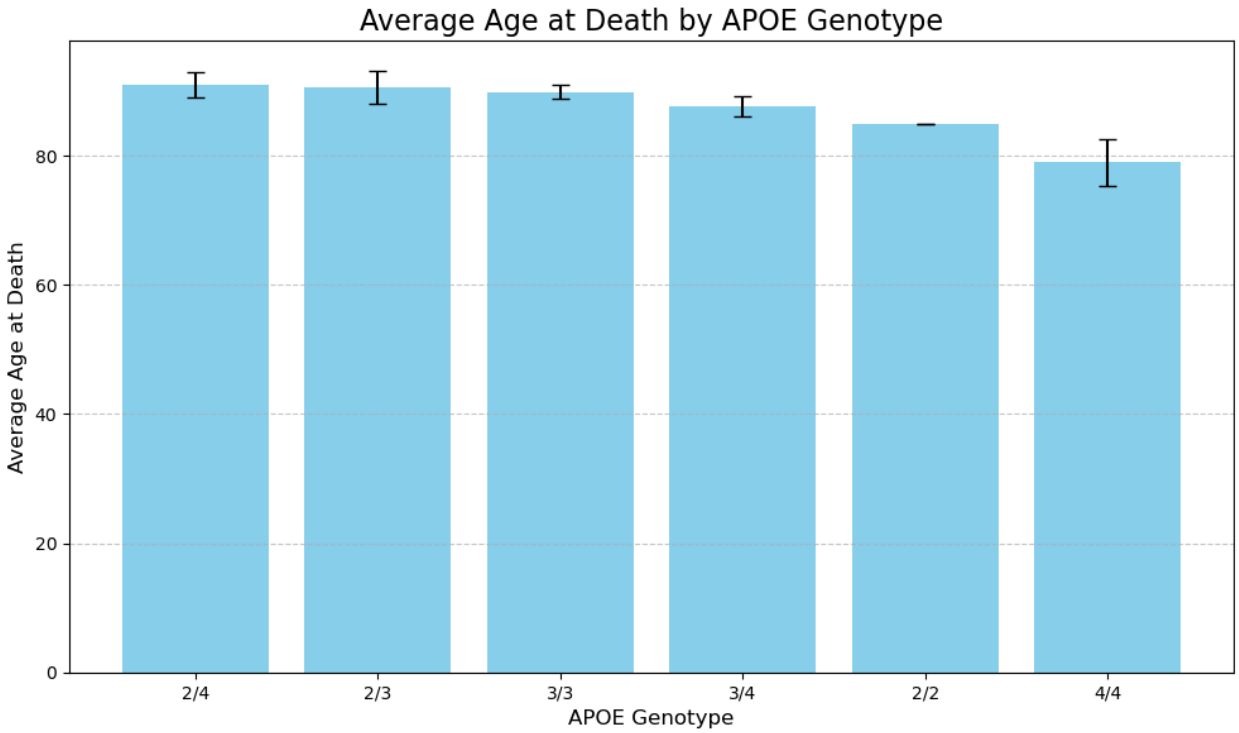
```
        plt.bar(
            sorted_genotypes,
            sorted_ages,
            yerr=sorted_sems,
            color='skyblue',
            capsize=5
        )

        plt.title('Average Age at Death by APOE Genotype',
fontsize=16)
        plt.xlabel('APOE Genotype', fontsize=12)
        plt.ylabel('Average Age at Death', fontsize=12)
        plt.xticks(rotation=0)
        plt.grid(axis='y', linestyle='--', alpha=0.7)
        plt.tight_layout()

        # Save the plot
        plt.savefig('average_age_by_genotype_bar_chart.png')
        print("Bar graph has been saved as
'average_age_by_genotype_bar_chart.png'")

except FileNotFoundError:
    print("Error: The file 'Metadata.csv' was not found.")
except ImportError:
    print("Error: Required libraries 'matplotlib', 'scipy', and
'numpy' not found.")
    print("Please install them by running: pip install matplotlib
scipy numpy")
```

```
Bar graph has been saved as 'average_age_by_genotype_bar_chart.png'
```



After finding the bar graph with all the APOE genotypes we wanted it to be in one bar graph with just two lines, so we divided it up into higher or elevated risk due to the APOE alleles and lower of standard risk. The higher risk consisted of any of them that contained the e4 allele which in the graph above was 2/4, 3/4, and 4/4 and the lower risk are the ones that did not which were 2/3, 3/3, and 2/2. Than below we created a bar graph with average age of death with the lower and higher risk groups

```
import csv
import matplotlib.pyplot as plt
from collections import defaultdict
from scipy.stats import sem
import numpy as np

try:
    # Open CSV with 'utf-8-sig' to handle BOM
    with open("Metadata.csv", "r", newline="", encoding="utf-8-sig")
as f:
        reader = csv.DictReader(f)

        # Dictionary to hold ages for each risk group
        risk_group_ages = defaultdict(list)

        def categorize_genotype(genotype):
            """Put APOE genotypes into risk groups."""
            if "4" in genotype:
                return "Increased Risk"
            return "Standard or Lowered Risk"
```

```
        # Loop through rows
        for row in reader:
            genotype = row.get("APOE Genotype", "").strip()
            age_str = row.get("Age at Death", "")

            if genotype and age_str:
                try:
                    age = float(age_str)  # allow decimals if needed
                    risk_group = categorize_genotype(genotype)
                    risk_group_ages[risk_group].append(age)
                except ValueError:
                    continue  # skip invalid rows

        # Calculate averages and SEMs
        avg_ages = {}
        sems = {}
        for group, ages in risk_group_ages.items():
            if ages:
                avg_ages[group] = np.mean(ages)
                sems[group] = sem(ages) if len(ages) > 1 else 0

        # Sort groups by average age (descending)
        sorted_groups = sorted(avg_ages, key=avg_ages.get,
reverse=True)
        sorted_ages = [avg_ages[g] for g in sorted_groups]
        sorted_sems = [sems[g] for g in sorted_groups]

        # Plot
        plt.figure(figsize=(8, 6))
        bars = plt.bar(
            sorted_groups,
            sorted_ages,
            yerr=sorted_sems,
            color=['lightcoral', 'skyblue'],
            capsize=5
        )

        # Add text labels above bars
        for bar, sem_val in zip(bars, sorted_sems):
            height = bar.get_height()
            plt.text(
                bar.get_x() + bar.get_width() / 2,
                height + sem_val + 0.5,
                f"{height:.2f}",
                ha="center",
                va="bottom"
            )

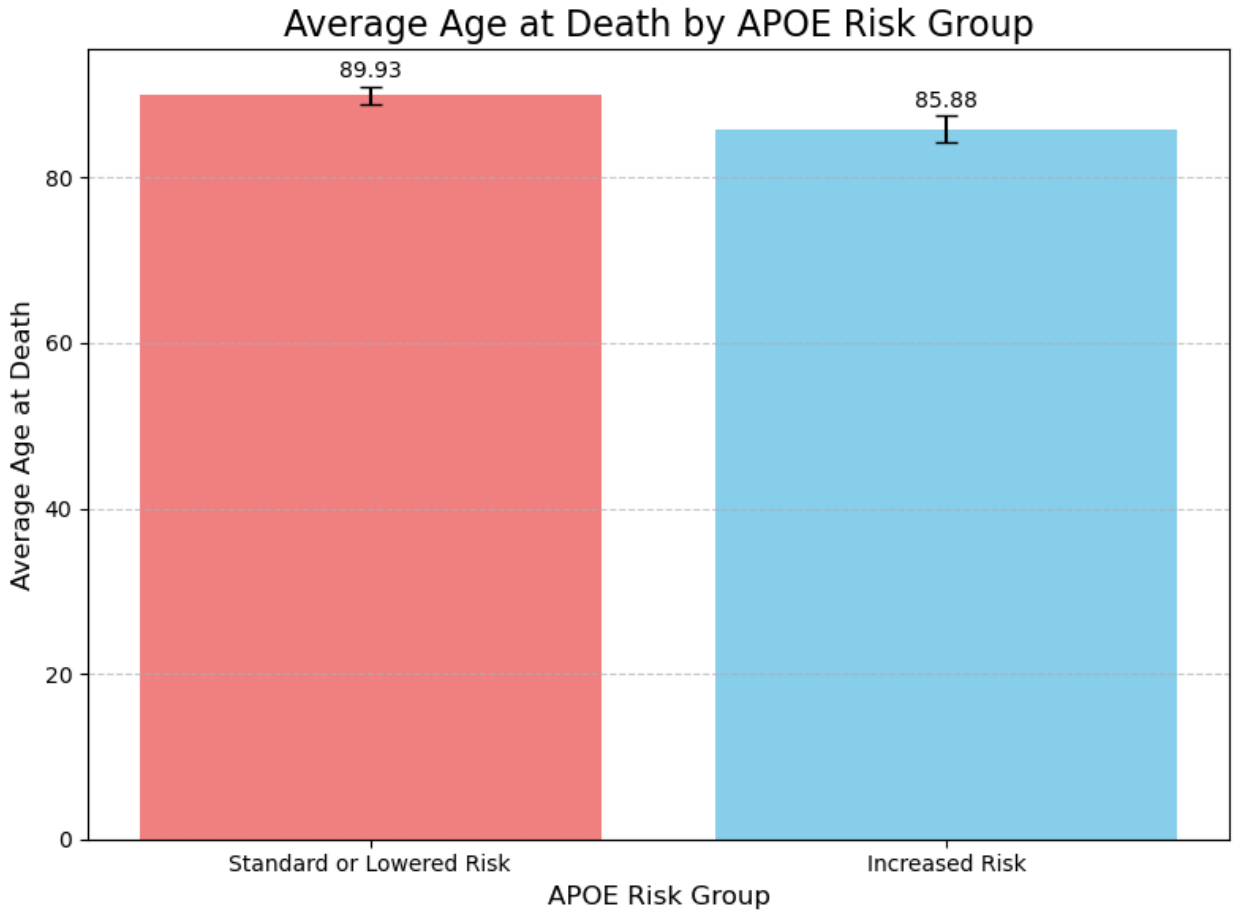
        plt.title("Average Age at Death by APOE Risk Group",
```

```
fontsize=16)
        plt.xlabel("APOE Risk Group", fontsize=12)
        plt.ylabel("Average Age at Death", fontsize=12)
        plt.xticks(rotation=0)
        plt.grid(axis="y", linestyle="--", alpha=0.7)
        plt.tight_layout()

        # Save figure
        plt.savefig("average_age_by_risk_group_bar_chart.png")
        print("Bar graph has been saved as
'average_age_by_risk_group_bar_chart.png'")

except FileNotFoundError:
    print("Error: The file 'Metadata.csv' was not found.")
except ImportError:
    print("Error: Missing required libraries. Run: pip install
matplotlib scipy numpy")
```

```
Bar graph has been saved as 'average_age_by_risk_group_bar_chart.png'
```



Lastly we created a t-test to figure out if there is a significant difference between the increased risk and the lowered risk

```
import pandas as pd
from scipy import stats
import numpy as np

try:
    # Load the data from the 'Metadata.csv' file
    df = pd.read_csv("Metadata.csv", encoding="utf-8-sig")

    # Clean the 'APOE Genotype' column by removing whitespace
    df['APOE Genotype'] = df['APOE Genotype'].str.strip()

    # Categorize the genotypes into risk groups
    def categorize_genotype(genotype):
        if '4' in str(genotype):
            return 'Increased Risk'
        else:
            return 'Standard or Lowered Risk'

    df['Risk Group'] = df['APOE Genotype'].apply(categorize_genotype)

    # Convert 'Age at Death' to numeric, dropping invalid values
    df['Age at Death'] = pd.to_numeric(df['Age at Death'],
errors='coerce')

    # Filter out rows with missing 'Age at Death' values
    df.dropna(subset=['Age at Death'], inplace=True)

    # Separate the data into two groups based on the 'Risk Group'
    increased_risk_ages = df[df['Risk Group'] == 'Increased Risk']
['Age at Death'].values
    standard_risk_ages = df[df['Risk Group'] == 'Standard or Lowered
Risk']['Age at Death'].values

    # Perform a one-sided independent t-test (Welch's T-test)
    # The alternative='less' parameter tests the hypothesis that the
mean of the first sample (increased_risk_ages)
    # is less than the mean of the second sample (standard_risk_ages).
    t_statistic, p_value = stats.ttest_ind(increased_risk_ages,
standard_risk_ages, equal_var=False, alternative='less')

    # Print the results of the t-test
    print("--- One-Sided T-Test Results for APOE Risk Groups and Age
at Death ---")
    print(f"Number of patients in 'Increased Risk' group:
{len(increased_risk_ages)}")
    print(f"Average age of death for 'Increased Risk' group:
{np.mean(increased_risk_ages):.2f} years")
    print("-" * 50)
    print(f"Number of patients in 'Standard or Lowered Risk' group:
{len(standard_risk_ages)}")
    print(f"Average age of death for 'Standard or Lowered Risk' group:
```

```
{np.mean(standard_risk_ages):.2f} years")
    print("-" * 50)
    print(f"T-Statistic: {t_statistic:.4f}")
    print(f"P-Value: {p_value:.4f}")

    # Interpret the p-value for the one-sided test
    if p_value < 0.05:
        print("\nConclusion: The difference in average age of death is
statistically significant, with the 'Increased Risk' group having a
significantly lower average age of death (p < 0.05).")
    else:
        print("\nConclusion: The difference in average age of death is
NOT statistically significant. We do not have sufficient evidence to
conclude that the 'Increased Risk' group has a significantly lower
average age of death (p >= 0.05).")

except FileNotFoundError:
    print("Error: The file 'Metadata.csv' was not found. Please ensure
it is in the same directory as your script.")
except KeyError as e:
    print(f"Error: A required column was not found. Please check your
CSV headers. Missing column: {e}")
except ImportError:
    print("Error: Required libraries 'pandas' and 'scipy' not found.")
    print("Please install them by running: pip install pandas scipy")
```

```
--- One-Sided T-Test Results for APOE Risk Groups and Age at Death ---
Number of patients in 'Increased Risk' group: 25
Average age of death for 'Increased Risk' group: 85.88 years
--------------------------------------------------
Number of patients in 'Standard or Lowered Risk' group: 59
Average age of death for 'Standard or Lowered Risk' group: 89.93 years
--------------------------------------------------
T-Statistic: -2.1675
P-Value: 0.0177

Conclusion: The difference in average age of death is statistically
significant, with the 'Increased Risk' group having a significantly
lower average age of death (p < 0.05).
```

```
import pandas as pd
import matplotlib.pyplot as plt
import numpy as np
from scipy.stats import linregress

# Load datasets
metadata = pd.read_csv("Metadata.csv", encoding="utf-8-sig")
tau_data = pd.read_csv("UpdatedLuminex.csv", encoding="utf-8-sig")

# Clean column names
```

```
metadata.columns = metadata.columns.str.strip()
tau_data.columns = tau_data.columns.str.strip()

# Change "ID" if your datasets use a different shared key
merged = pd.merge(metadata, tau_data, on="Donor ID")

# Convert to numeric
merged["Age at Death"] = pd.to_numeric(merged["Age at Death"],
errors="coerce")
merged["tTAU pg/ug"] = pd.to_numeric(merged["tTAU pg/ug"],
errors="coerce")

# Drop missing
merged = merged.dropna(subset=["Age at Death", "tTAU pg/ug"])

# Extract values
x = merged["Age at Death"].values   # independent variable
y = merged["tTAU pg/ug"].values     # dependent variable

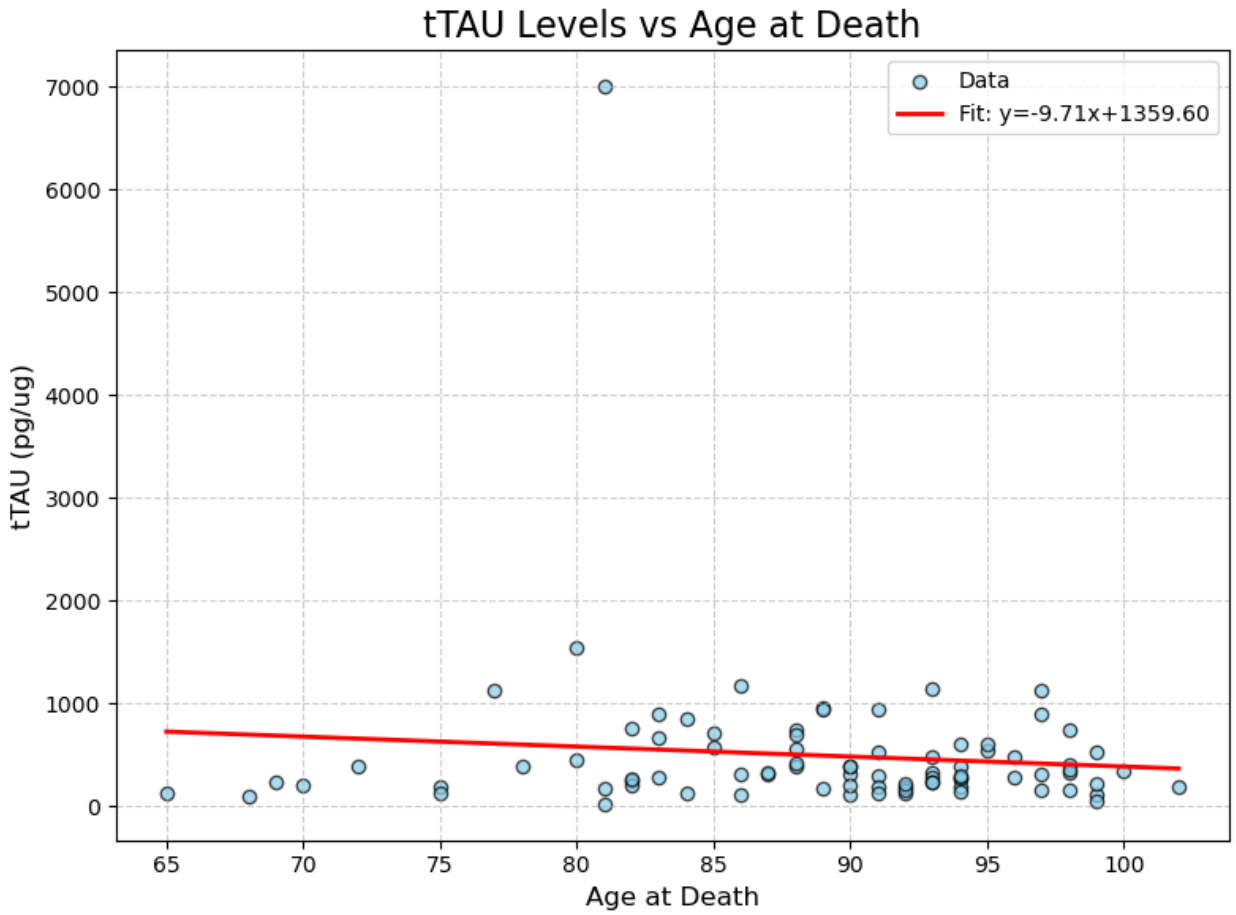
# Linear regression (x = Age, y = Tau)
slope, intercept, r_value, p_value, std_err = linregress(x, y)

# Regression line
x_vals = np.linspace(x.min(), x.max(), 100)
y_vals = slope * x_vals + intercept

# Plot
plt.figure(figsize=(8, 6))
plt.scatter(x, y, alpha=0.7, color="skyblue", edgecolor="black",
label="Data")
plt.plot(x_vals, y_vals, color="red", linewidth=2,
         label=f"Fit: y={slope:.2f}x+{intercept:.2f}")
plt.xlabel("Age at Death", fontsize=12)
plt.ylabel("tTAU (pg/ug)", fontsize=12)
plt.title("tTAU Levels vs Age at Death", fontsize=16)
plt.grid(linestyle="--", alpha=0.6)
plt.legend()
plt.tight_layout()

# Save + show
plt.savefig("ttau_vs_age_regression.png", dpi=300)
plt.show()

# Print regression stats
print("Regression results:")
print(f"Slope = {slope:.4f}")
print(f"Intercept = {intercept:.4f}")
print(f"R² = {r_value**2:.4f}")
print(f"P-value = {p_value:.4e}")
print(f"Std Err = {std_err:.4f}")
```




```
Regression results:
Slope = -9.7081
Intercept = 1359.6014
R² = 0.0099
P-value = 3.6701e-01
Std Err = 10.7024
```

Verify and validate your analysis:

Describe how you checked to see that your analysis gave you an answer that you believe (verify). Describe how your determined if your analysis gave you an answer that is supported by other evidence (e.g., a published paper).*

- Our analysis of Higher Risk vs Lower Risk and Age of death showed that there was a statistical difference between APOE gene whether it is in the Higher risk or standard and lower risk and age of death as the p-value was 0.0177 which is lower than the statistical significant value of 0.05. As the alternative hypothesis was that higher risk will have a lower age of death due to the p-value we can conclude that we have enough evidence to suggest that this is true. We verified this analysis and statisitcal test with different peer reviewed published papers. One article we found was titled "APOE Alleles and Extreme Human Longevity" and it concluded that carrying the E4

gene has substantially decreased odds for extreme longevity, and increased risk for death. This supports what we concluded as our "Higher Risk" group were the patients that carried atleast one of the E4 alelle. Another article was titled "Mortality differences by APOE genotype estimated from demographic synthesis" and in this it concludes that "The 4 allele of apolipoprotein E (APOE) is associated with increased risk of two major causes of death in low-mortality populations: ischemic heart disease and Alzheimer's disease." This also supports our conclusion that the higher risk (E4) leads lower age of death.

- Sources:
  - https://onlinelibrary.wiley.com/doi/abs/10.1002/gepi.0164
  - https://academic.oup.com/biomedgerontology/article/74/1/44/5060332

Conclusions and Ethical Implications:

Our main conclusions was that there is a statistical difference between APOE gene and age of death and that the group with higher risk (contains the e4 allele) has a lower age of death than the lower or standard risk group.

This conclusion was drawn based on 84 patients and one data set, so to have our conclusion be able to be generalized across more people we would need to combine or look at this at other data sets so we have more than 84 people in our study. Additionally we only tested the gene on age of death we did not really keep much constant across and other factors do affect Alzheimers not only genetics it could be prior family history and lifestyle choices so this conclusion needs to be taken with a bit of caution as even though the results were significant there are other factors that could also play into the difference. Additionally this conclusion could make people more scared if they do have the alelle however the age of deaths across the groups were 89 and 95 which are pretty old in general which means there could also be an old age factor and not the ALzheimers that caused the death.

Limitations and Future Work:

(Think about the answer your analysis generated, draw conclusions related to your overarching question, and discuss the ethical implications of your conclusions.

The answer concludes that we were correct about our initial assumption the the higher risk APOE gene will have a lower age of death. The implications are that some with these genes have a lower life expectancy than those who do not possess the traits caused by this gene. This could lead to increased testing in people who are known to have the allele earlier for Alzheimers. However, looking at our ethical implication this data cannot be generalized and more tests need to be done to prove this as this data set only had 84 participants. The limitations would be the amount of data and that there were not much that was controlled we did not filter by previous family history or even age of onset. Maybe in the future look at the difference between age of onset vs age of death because that would be more standardized because some people could have developed the disease at 30 vs 60 which could have also played a factor in age of death. However, with our limitations other research articles with more people do support our data and conclusions including the two linked above in the verify and validate your analysis section. For

future work we try verifying our results with other data sets and we can keep more things controlled if we have more data values. Additionally we could look at other proteins and age of death like ABeta42 or tTau levels compared to age of death.

Check in 1 Notes

- Did the data-set section
- Questions about the data set:
  - How was it aquired: generated quantititive neuropathology single nucleus omics datasets on all donors with available tissues that were obtained with updated postmortem processing procedures. This tissue were specfically from middle temporal gyrus, quantitiative neuropathology, multiomics, spatial transcriptiomics, and precision rapid procedure.
  - When was it aquired: April 24, 2024 (when the paper was last updated)
  - Who was it aquired by: Michael Hawrylcz and Dirk Keene, Ed Lein
  - Donors: 84 donors with varios Alzheimers disease pathologies
  - Physiological/pathological: Alzheimers disease and proteins like amyloid beta and pTau.
  - Bias: Gender was a bias as there were 51 females and 33 males.
  - Limtations: The sample size of 84 is very small to generalize the conclusions.
- 6 questions to decide between:
  - Does Alzheimers cause an earlier death compared to the people without Alzheimers?
  - Does education level change affect Alzheimers disease progression?
  - Are the ABeta42 ratios differ between people with Alzheimers and without?
  - If you have the APOE genotype does it correlate to tTau levels?
  - Is APOE gene more common in some racial groups?
  - Does APOE correlate with age of death for patients?
- Question we decided:Does APOE correlate with age of death for patients?
- We do not have any questions for the TA

Check in 2 Notes

- We did two bar graphs
  - Bar graph 1: APOE genotype versus average age of death. This led us to see 5 different bars of genotypes when we needed two so we had to create the second bar graph.
  - Bar graph 2: we split the APOE genotype into high risk and low risk. The high risk was anything that contained the e4 allele while the lower or standard risk did not and we ended up getting two bars with the average age of death in the y.
  - these two bars can be seen above in the data analysis section.
- We than did a two sample one sided independent t-test for the second bar graph.
  - null hypothesis: The higher and standard or lower risk have the same age of death

  - alternative hypothesis: The higher risk has a lower age of death than the lower risk group
  - Increased Risk group (n = 25, average age of death = 85.88 years)
  - Standard/Lower risk group (n = 59, average age of death = 89.93 years)
  - The t-test was than run
  - t-statistic = -2.1675
  - p-value = 0.0177
  - Since the p-value of 0.0.0177 is lower than the statistical significance level of 0.05 we reject the null hypothesis which means there is a statistical difference and the 'Increased Risk' group having a significantly lower average age of death.
- We have no questions for the TA

Check in 3 Notes

- Did the regression for tTau levels and age of death -- not part of our question but just did it to learn how to do a regression graph
  - found the slope was -9.7081
  - and R^2 was 0.0099 (since this is so low it means that the line really is not a good representation of the points, we want the R^2 to be around 1 not 0)
  - This R^2 is showing that there is not a linear correlation between these levels and this can be seen in the graph by the high outliers which will disrupt the correlation.
- Finished the Validation section - found two articles to support our conclusion that the e4 allele leads to lower age of death
- Finished the conclusions and limitations sections