Module_1:

Team Members:

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Project Title: Does Education Buffer the Brain? Exploring Cognitive Reserve Against AD Biomarkers

Module #1: Alzheimer's Disease

- Does level of education (or years of education) affect resilience to AD biomarkers (cognitive reserve hypothesis)?

Disease Background:

- Prevalence & incidence:
    a. 7.2 million Americans
    b. 11% of people 65+
    c. younger onset (30-64yrs) = 200,000 (0.11%).
    d. Source: https://www.alz.org/getmedia/ef8f48f9-ad36-48ea-87f9b74034635c1e/alzheimers-facts-and-figures.pdf
- Economic burden:
    a. 305 billion (2020), costs mostly from nursing care, home healthcare, and hospice care.
    b. Source: https://pubmed.ncbi.nlm.nih.gov/32840331/
- Risk factors (genetic, lifestyle):
    a. Age is highest risk factor
    b. genetics (APOE-e4 gene, genetic mutations)
    c. midlife obesity, low activity, Cardiovascular Health. ((Physical activity in mid- or late life may reduce risk of dementia)
    d. low education
    e. Source: https://www.alz.org/getmedia/ef8f48f9-ad36-48ea-87f9-b74034635c1e/alzheimers-facts-and-figures.pdf
- Societal determinants
    a. A lower level of education is associated with poorer brain health
    b. Consistent access to health care services can help prevent chronic diseases and manage conditions to avoid complications.
        - Aid in early diagnosis of many health conditions, such as diabetes, heart disease, and dementia.
        - Help diagnose dementia earlier to allow for better care coordination and support
    c. Loneliness and social isolation

        - People experiencing social isolation or loneliness are at a higher risk for dementia
        - Source: https://www.sciencedirect.com/science/article/pii/S156816371500046X?via%3Dihub
- Symptoms
    a. Memory loss that disrupts daily life
        - Repeat statements and questions over and over.
        - Forget conversations, appointments or events.
        - Misplacing items in places that don't make sense.
    b. Challenges in planning or solving problems
    c. Difficulty completing familiar tasks
    d. Confusion, trouble understanding, new problems with words
    e. Decreased judgment, changes in mood or personality
    f. Source: https://www.cdc.gov/alzheimers-dementia/signs-symptoms/alzheimers.html
- Diagnosis
    – Neurologist or geriatrician conduct tests to measure memory impariment and thinking skills.
    – They review medical history and medicine history
    – They judge functional abilities and identify behavioral changes, sometimes a close family member is interviewed.
    – Lab tests, brain imaging, detailed memory tests may be needed.
        - Brain imaging: MRI, CT, PET
        - Memory tests: mental status testing (evaluates cognitive impariment), neuropsychological testing.
    – Various tests also rule out other possible causes or symptoms Source: https://www.mayoclinic.org/diseases-conditions/alzheimers-disease/in-depth/alzheimers/art-20048075
- Standard of care treatments (& reimbursement)
- Treatments:
    a. Cholinesterase Inhibitors, this blocks an enzyme responsible for breaking down the neurotransmitter acetylcholine, slowing down neuron damage.
    b. Lecanemab or Donanemab: IV infusions containing monoclonal antibodies which help the immune system target and destroy amyloid proteins.
    c. NMDA antagonists: these antagonists block the NMDA receptor from excess glutamate and prevent the release of too much calcium into the neurons which activates destructive enzymes.
    d. Symptom management: antidepressants, antipsychotics (neuroleptics), antiseizure medications.
- Source: https://my.clevelandclinic.org/health/diseases/9164-alzheimers-disease
- Disease progression & prognosis: There are generally five stages associated with Alzheimer's disease:
    a. Preclinical Alzheimer's disease.
    b. Mild cognitive impairment due to Alzheimer's disease.

    c. Mild dementia due to Alzheimer's disease.
    d. Moderate dementia due to Alzheimer's disease.
    e. Severe dementia due to Alzheimer's disease.
    – Prognosis: Average 4-8 years after diagnosis, but can range from 3-20 depending on individual factors
    – Source: https://www.mayoclinic.org/diseases-conditions/alzheimers-disease/in-depth/alzheimers-stages/art-20048448
- Continuum of care providers
    a. Primary care physicians: initial screening and referral.
    b. Neurologists / geriatric psychiatrists: diagnosis and management.
    c. Neuropsychologists: cognitive testing.
    d. Nurses / nurse practitioners: care coordination, patient/family education.
    e. Social workers & case managers: link families to resources, support services.
    f. Long-term care facilities: nursing homes, memory care units.
    g. Hospice & palliative care: end-of-life support.
- Biological mechanisms (anatomy, organ physiology, cell & molecular physiology)
    a. Anatomy: Shrinkage of the hippocampus and cortex, areas important for memory and thinking.
    b. Organ physiology: Gradual loss of the brain's ability to send signals between nerve cells, leading to memory and functional decline.
    c. Cell & molecular physiology:
    – Amyloid plaques form outside nerve cells (clumps of sticky protein).
    – Tau tangles build up inside cells (twisted protein fibers).
    – These changes block communication between neurons, trigger inflammation, and cause nerve cell death.
    – Source: https://pmc.ncbi.nlm.nih.gov/articles/PMC5290713/
- Clinical Trials/next-gen therapies Key Next-Generation Therapies
    a. Anti-amyloid antibodies: Lecanemab (Leqembi) and donanemab (Kisunla) are now FDA-approved for mild Alzheimer's. They work by removing amyloid plaques and have demonstrated a slowing of cognitive decline by several months. Combination anti-amyloid therapies and early intervention are ongoing trial strategies.
    b. Tau-targeted therapies: Drugs like posdinemab and others in clinical trials aim to reduce tau phosphorylation and aggregation, addressing another pathological hallmark of Alzheimer's. Anti-tau therapies for genetically at-risk individuals are also in late-stage studies.
    c. Neuroinflammation/modulation: Agents targeting the SHIP1/INPP5D gene to enhance microglial plaque clearance are in preclinical and early-phase trials. Immunomodulators such as baricitinib (repurposed from COVID-19 treatment) are being studied for brain function improvement in Alzheimer's populations.
    d. Repurposed and adjunctive pharmacotherapies: Semaglutide (diabetes drug) has shown an association with reduced Alzheimer's risk in real-world studies. Trials using lithium, metformin, and certain statins for cognitive protection are ongoing.
    e. Symptom-targeted therapies: AXS-05 (dextromethorphan/bupropion) and other agents are being trialed for managing agitation and neuropsychiatric symptoms.

f. Novel technologies: Breakthroughs include ultra-thin graphene brain implants (InBrain), which could modulate neural activity and improve outcomes in clinical studies.
g. Focused ultrasound: Early-stage trials are testing non-invasive brain stimulation as a potential disease-modifying approach.
– Source: https://www.nia.nih.gov/research/ongoing-AD-trials

- # Data-Set:

(Describe the data set(s) you will analyze. Cite the source(s) of the data.)

- How was it acquired?
  - Human brain tissue samples were obtained postmortem from participants in the Adult Changes in Thought (ACT) study and the University of Washington Alzheimer's Disease Research Center (ADRC).
  - The brains were processed using modern, highly optimized methods for single-nucleus RNA sequencing (snRNA-seq), single-nucleus ATAC sequencing (snATAC-seq), combined multiome assays, and spatial transcriptomics (MERFISH), all focused on the middle temporal gyrus (MTG).
  - Extensive quality control checks ensured high sample integrity, including measures like postmortem interval (mean ≈ 7 hours), RNA integrity, and sequencing metrics.
  - The collection strategy was designed to comprehensively span the spectrum of Alzheimer's pathology using a continuous progression score (not just case control or dichotomous groups).
  - Full demographic, genetic (e.g., APOE status), clinical, and neuropathologic characterization was performed for all donors, incorporating cognitive testing, neuropathological staging (Braak, Thal, CERAD), and comorbidity assessment.
- When was the dataset acquired?
  - The cohort comprises 84 donors whose tissue was collected during an explicit time window starting with the launch of the SEA-AD project, continuing through until at least August 2024 (the date of paper acceptance), with collection dates dependent on donor death and available tissues.
  - The dates of tissue collection therefore range primarily from recent years up to 2024, with sequencing and molecular profiling performed before and during
  - The corresponding publication date is December 2024, with the data acquired and finalized in the months preceding this.
- Who acquired the dataset?
  - Primary collection was performed by the University of Washington BioRepository and Integrated Neuropathology (BRaIN) lab and was coordinated with the Adult Changes in Thought (ACT) study and the UW ADRC.
  - The project and primary analyses were carried out by the Seattle Alzheimer's Disease Brain Cell Atlas (SEA-AD) consortium, based at the Allen Institute for Brain Science and the University of Washington, with dozens of authors and contributors listed (including principal investigators Michael Hawrylycz, C. Dirk Keene, and Ed S. Lein).
- What questions about Alzheimer's disease are you curious about answering, given the data you have available in these data sets?

- How does highest level of education affect onset of Alzhiemer's?
  - does it cause earlier onset? not affect at all?

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.)

```
import csv
import warnings
import matplotlib.pyplot as plt
#Patient class
class Patient:

    all_patients = []

    death_age = []

    education_lvl = {}

    def __init__(self, DonorID, ABeta40: float , ABeta42: float, tTau:
float, pTau: float):

        self.DonorID = DonorID
        self.ABeta40 = ABeta40
        self.ABeta42 = ABeta42
        self.tTau = tTau
        self.pTau = pTau
        self.sex = None
        self.death_age = None
        self.ed_lvl = None
        self.ed_length = None
        self.cog_stat = None
        self.age_symp_on = None
        self.age_diag = None
        self.head_inj = None
        self.thal_score = None
        Patient.all_patients.append(self)

    def __repr__(self):
        return f"{self.DonorID} | sex: {self.sex} | ABeta42
{self.ABeta42} | ABeta40 {self.ABeta40} | tTau {self.tTau} | pTau
{self.pTau} | Death Age {self.death_age} | Thal Score
{self.thal_score}"

    def get_id(self):
        return self.DonorID

    def get_ABeta42(self):
```

```
        return self.ABeta42

    def get_thal(self):
        return self.thal_score

    def get_death_age(self):
        return self.death_age
    @classmethod
    def combine_data(cls, filename: str):
            with open(filename, encoding="utf8") as f:
                reader = csv.DictReader(f)
                rows_of_patients = list(reader)
                #for line in csv create object
                for row in range(len(rows_of_patients)):
                    if Patient.all_patients[row].DonorID ==
rows_of_patients[row]["Donor ID"]:
                        if rows_of_patients[row]["Sex"] != "":
                            Patient.all_patients[row].sex =
rows_of_patients[row]["Sex"]

                        if rows_of_patients[row]["Age at Death"] !=
"":
                            Patient.all_patients[row].death_age =
int(rows_of_patients[row]["Age at Death"])

                        if rows_of_patients[row]["Highest level of
education"] != "":
                            Patient.all_patients[row].ed_lvl =
rows_of_patients[row]["Highest level of education"]

                        if rows_of_patients[row]["Years of education"]
!= "":
                            Patient.all_patients[row].ed_length =
int(rows_of_patients[row]["Years of education"])

                        if rows_of_patients[row]["Cognitive Status"] !
= "":
                            Patient.all_patients[row].cog_stat =
rows_of_patients[row]["Cognitive Status"]

                        if rows_of_patients[row]["Age of onset
cognitive symptoms"] != "":
                            Patient.all_patients[row].age_symp_on =
int(rows_of_patients[row]["Age of onset cognitive symptoms"])

                        if rows_of_patients[row]["Age of Dementia
diagnosis"] != "":
                            Patient.all_patients[row].age_diag =
int(rows_of_patients[row]["Age of Dementia diagnosis"])
```

```
                        if rows_of_patients[row]["Known head injury"]
!= "":
                            Patient.all_patients[row].head_inj =
rows_of_patients[row]["Known head injury"]

                        if rows_of_patients[row]["Thal"] != "":
                            Patient.all_patients[row].thal_score =
int(rows_of_patients[row]["Thal"].split()[1])

                    else:
                        warnings.warn("IDs do not match.")

    @classmethod
    def instantiate_from_csv(cls, filename: str, other_file: str):
    #open csv and create list of all rows
        with open(filename, encoding="utf8") as f:
            reader = csv.DictReader(f)
            rows_of_patients = list(reader)
            #for line in csv create object
            for row in rows_of_patients:
                Patient(
                    DonorID = row['Donor ID'],
                    ABeta40 = float(row['ABeta40 pg/ug']),
                    ABeta42 = float(row['ABeta42 pg/ug']),
                    tTau = float(row['tTAU pg/ug']),
                    pTau = float(row['pTAU pg/ug'])
                )
            Patient.all_patients.sort(key = Patient.get_id)
            Patient.combine_data(other_file)

    @classmethod
    def sort_ed(cls):
        # Reset education_lvl dictionary with two groups as keys
        cls.education_lvl = {"High School": [], "Higher Education":
[]}

        for patient in cls.all_patients:
            if patient.ed_lvl is None:
                continue  # Skip patients with no education data
            elif patient.ed_lvl.strip().lower() == "high school":
                cls.education_lvl["High School"].append(patient)
            else:
                cls.education_lvl["Higher Education"].append(patient)

    @classmethod
    def subsort_thal(cls):
        for key in Patient.education_lvl:
            values = Patient.education_lvl.get(key)
            values.sort(key = Patient.get_thal)
```

```
            Patient.education_lvl.update({key: values})

    @classmethod
    def remove_abeta42_outliers(cls, threshold=300):
        filtered_patients = []
        for p in cls.all_patients:
            try:
                val = float(p.ABeta42)
                if val <= threshold:
                    filtered_patients.append(p)
            except (ValueError, TypeError):
                # Skip patients with invalid or missing ABeta42
                continue
        cls.all_patients = filtered_patients

#Load all data into the all_patients object
Patient.instantiate_from_csv('UpdatedLuminex.csv',
'UpdatedMetaData.csv')
Patient.remove_abeta42_outliers() #Removes the 1400 Abeta42 outlier to
make our data more uniform

for patient in Patient.all_patients:
    print(patient)
```

```
H19.33.004 | sex: Female | ABeta42 0.971578947 | ABeta40 0.019621053 |
tTau 1552.414737 | pTau 1.901052632 | Death Age 80 | Thal Score 0
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tTau 756.0905263 | pTau 2.737894737 | Death Age 82 | Thal Score 2
H20.33.002 | sex: Female | ABeta42 0.147157895 | ABeta40 0.000597895 |
tTau 313.5252632 | pTau 2.615789474 | Death Age 97 | Thal Score 0
H20.33.004 | sex: Male | ABeta42 80.26631579 | ABeta40 60.76631579 |
tTau 318.5284211 | pTau 7.412631579 | Death Age 86 | Thal Score 5
H20.33.005 | sex: Female | ABeta42 16.15684211 | ABeta40 5.136842105 |
tTau 107.3484211 | pTau 1.327368421 | Death Age 99 | Thal Score 3
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tTau 125.9336842 | pTau 2.569473684 | Death Age 92 | Thal Score 4
H20.33.011 | sex: Female | ABeta42 60.51157895 | ABeta40 11.84526316 |
tTau 1141.492355 | pTau 8.536842105 | Death Age 93 | Thal Score 5
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tTau 272.5084211 | pTau 3.106315789 | Death Age 94 | Thal Score 3
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tTau 393.1831579 | pTau 1.827368421 | Death Age 88 | Thal Score 3
H20.33.016 | sex: Female | ABeta42 21.27368421 | ABeta40 2.671578947 |
tTau 488.8989474 | pTau 2.282105263 | Death Age 93 | Thal Score 4
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tTau 239.3778947 | pTau 5.881052632 | Death Age 69 | Thal Score 4
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H20.33.019 | sex: Female | ABeta42 28.81368421 | ABeta40 1.718947368 | tTau 312.7442105 | pTau 2.884210526 | Death Age 87 | Thal Score 4
H20.33.020 | sex: Male | ABeta42 45.72842105 | ABeta40 145.2547368 | tTau 21.71894737 | pTau 3.873684211 | Death Age 81 | Thal Score 5
H20.33.024 | sex: Male | ABeta42 105.1042105 | ABeta40 5.095789474 | tTau 309.08 | pTau 5.222105263 | Death Age 90 | Thal Score 4
H20.33.025 | sex: Male | ABeta42 95.79263158 | ABeta40 3.532631579 | tTau 384.84 | pTau 3.691578947 | Death Age 94 | Thal Score 4
H20.33.026 | sex: Female | ABeta42 63.37473684 | ABeta40 31.56526316 | tTau 191.0505263 | pTau 12.56736842 | Death Age 75 | Thal Score 4
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H20.33.030 | sex: Female | ABeta42 58.26631579 | ABeta40 17.22105263 | tTau 114.6231579 | pTau 6.56 | Death Age 86 | Thal Score 4
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tTau 452.1894737 | pTau 3.038947368 | Death Age 80 | Thal Score 2
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tTau 200.3842105 | pTau 7.317894737 | Death Age 70 | Thal Score 5
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tTau 160.5831579 | pTau 3.169473684 | Death Age 97 | Thal Score 4
H21.33.007 | sex: Female | ABeta42 287.412 | ABeta40 11.41894737 |
tTau 1179.673684 | pTau 6.410526316 | Death Age 86 | Thal Score 4
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126.1673684 | pTau 6.175789474 | Death Age 91 | Thal Score 4
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H21.33.015 | sex: Male | ABeta42 10.09578947 | ABeta40 0.661052632 |
tTau 322.6021053 | pTau 5.006315789 | Death Age 98 | Thal Score 2
H21.33.016 | sex: Female | ABeta42 0.525263158 | ABeta40 0.009426737 |
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H21.33.017 | sex: Female | ABeta42 20.18210526 | ABeta40 1.412631579 |
tTau 164.9431579 | pTau 2.075789474 | Death Age 92 | Thal Score 5
H21.33.018 | sex: Female | ABeta42 10.98842105 | ABeta40 0.263157895 |
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H21.33.020 | sex: Male | ABeta42 38.15894737 | ABeta40 1.547368421 |
tTau 202.5905263 | pTau 3.328421053 | Death Age 82 | Thal Score 4
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tTau 58.70105263 | pTau 1.324210526 | Death Age 99 | Thal Score 4
H21.33.022 | sex: Female | ABeta42 7.666315789 | ABeta40 0.000130411 |
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H21.33.023 | sex: Male | ABeta42 0.114736842 | ABeta40 0.000597684 |
tTau 188.3642105 | pTau 1.683157895 | Death Age 102 | Thal Score 0
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tTau 738.4673684 | pTau 2.74 | Death Age 88 | Thal Score 3
H21.33.026 | sex: Female | ABeta42 263.5368421 | ABeta40 76.91789474 |
tTau 386.6842105 | pTau 6.217894737 | Death Age 90 | Thal Score 4

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tTau 222.8189474 | pTau 2.709473684 | Death Age 92 | Thal Score 5
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tTau 391.1515789 | pTau 3.065263158 | Death Age 72 | Thal Score 1
H21.33.029 | sex: Male | ABeta42 146.8621053 | ABeta40 17.82736842 |
tTau 953.1326316 | pTau 2.04 | Death Age 89 | Thal Score 5
H21.33.030 | sex: Male | ABeta42 18.54736842 | ABeta40 1.827368421 |
tTau 948.1368421 | pTau 5.212631579 | Death Age 89 | Thal Score 3
H21.33.031 | sex: Male | ABeta42 124.4347368 | ABeta40 34.42947368 |
tTau 860.3778947 | pTau 4.793684211 | Death Age 84 | Thal Score 5
H21.33.032 | sex: Female | ABeta42 6.777894737 | ABeta40 1.375789474 |
tTau 359.58 | pTau 3.14 | Death Age 98 | Thal Score 2
H21.33.033 | sex: Female | ABeta42 31.76315789 | ABeta40 3.967368421 |
tTau 667.3905263 | pTau 4.462105263 | Death Age 83 | Thal Score 5
H21.33.034 | sex: Female | ABeta42 161.0947368 | ABeta40 12.15368421 |
tTau 393.3484211 | pTau 6.388421053 | Death Age 90 | Thal Score 5
H21.33.035 | sex: Female | ABeta42 143.4642105 | ABeta40 7.491578947 |
tTau 903.6189474 | pTau 5.306315789 | Death Age 97 | Thal Score 5
H21.33.036 | sex: Female | ABeta42 75.78947368 | ABeta40 5.302105263 |
tTau 238.4989474 | pTau 5.577894737 | Death Age 93 | Thal Score 4
H21.33.037 | sex: Female | ABeta42 0.449649126 | ABeta40 0.036216842 |
tTau 558.1957895 | pTau 2.334736842 | Death Age 88 | Thal Score 2
H21.33.038 | sex: Female | ABeta42 0.122631579 | ABeta40 0.079678842 |
tTau 131.0326316 | pTau 2.977894737 | Death Age 84 | Thal Score 1
H21.33.039 | sex: Female | ABeta42 76.22631579 | ABeta40 1.450526316 |
tTau 704.8010526 | pTau 4.146315789 | Death Age 88 | Thal Score 4
H21.33.040 | sex: Male | ABeta42 0.490526316 | ABeta40 0.065191789 |
tTau 894.1368421 | pTau 3.850526316 | Death Age 83 | Thal Score 4
H21.33.041 | sex: Female | ABeta42 88.16947368 | ABeta40 5.010526316 |
tTau 740.5831579 | pTau 3.327368421 | Death Age 98 | Thal Score 0
H21.33.042 | sex: Female | ABeta42 47.93263158 | ABeta40 20.53894737 |
tTau 531.6515789 | pTau 2.507368421 | Death Age 91 | Thal Score 5
H21.33.043 | sex: Female | ABeta42 29.89263158 | ABeta40 1.593684211 |
tTau 611.0 | pTau 4.404210526 | Death Age 95 | Thal Score 4
H21.33.044 | sex: Female | ABeta42 33.63789474 | ABeta40 7.130526316 |
tTau 417.8947368 | pTau 3.662105263 | Death Age 88 | Thal Score 3
H21.33.045 | sex: Female | ABeta42 53.87894737 | ABeta40 21.42315789 |
tTau 147.5652632 | pTau 11.48947368 | Death Age 94 | Thal Score 4
H21.33.046 | sex: Male | ABeta42 19.19578947 | ABeta40 2.421052632 |
tTau 1124.777383 | pTau 3.129473684 | Death Age 97 | Thal Score 4
H21.33.047 | sex: Male | ABeta42 0.049052632 | ABeta40 0.000981053 |
tTau 212.9031579 | pTau 3.575789474 | Death Age 90 | Thal Score 2
```

```
#Sorting by education level
from termcolor import colored


Patient.sort_ed()
Patient.subsort_thal()
```

```
for key in Patient.education_lvl:
    print(colored(key,"red"))
    for patient in Patient.education_lvl.get(key):
        print(patient)
    print()
```

```
High School
H20.33.002 | sex: Female | ABeta42 0.147157895 | ABeta40 0.000597895 |
tTau 313.5252632 | pTau 2.615789474 | Death Age 97 | Thal Score 0
H21.33.023 | sex: Male | ABeta42 0.114736842 | ABeta40 0.000597684 |
tTau 188.3642105 | pTau 1.683157895 | Death Age 102 | Thal Score 0
H21.33.041 | sex: Female | ABeta42 88.16947368 | ABeta40 5.010526316 |
tTau 740.5831579 | pTau 3.327368421 | Death Age 98 | Thal Score 0
H21.33.019 | sex: Male | ABeta42 0.019621053 | ABeta40 0.001077758 |
tTau 122.2210526 | pTau 2.208421053 | Death Age 75 | Thal Score 1
H21.33.038 | sex: Female | ABeta42 0.122631579 | ABeta40 0.079678842 |
tTau 131.0326316 | pTau 2.977894737 | Death Age 84 | Thal Score 1
H21.33.015 | sex: Male | ABeta42 10.09578947 | ABeta40 0.661052632 |
tTau 322.6021053 | pTau 5.006315789 | Death Age 98 | Thal Score 2
H21.33.022 | sex: Female | ABeta42 7.666315789 | ABeta40 0.000130411 |
tTau 270.3010526 | pTau 3.095789474 | Death Age 82 | Thal Score 2
H20.33.005 | sex: Female | ABeta42 16.15684211 | ABeta40 5.136842105 |
tTau 107.3484211 | pTau 1.327368421 | Death Age 99 | Thal Score 3
H20.33.027 | sex: Female | ABeta42 29.95578947 | ABeta40 1.843157895 |
tTau 224.2431579 | pTau 3.365263158 | Death Age 99 | Thal Score 3
H20.33.025 | sex: Male | ABeta42 95.79263158 | ABeta40 3.532631579 |
tTau 384.84 | pTau 3.691578947 | Death Age 94 | Thal Score 4
H20.33.026 | sex: Female | ABeta42 63.37473684 | ABeta40 31.56526316 |
tTau 191.0505263 | pTau 12.56736842 | Death Age 75 | Thal Score 4
H20.33.029 | sex: Female | ABeta42 28.85473684 | ABeta40 1.633684211 |
tTau 302.2315789 | pTau 3.191578947 | Death Age 91 | Thal Score 4
H20.33.031 | sex: Female | ABeta42 42.51368421 | ABeta40 2.004210526 |
tTau 335.7452632 | pTau 7.827368421 | Death Age 87 | Thal Score 4
H21.33.039 | sex: Female | ABeta42 76.22631579 | ABeta40 1.450526316 |
tTau 704.8010526 | pTau 4.146315789 | Death Age 88 | Thal Score 4
H21.33.045 | sex: Female | ABeta42 53.87894737 | ABeta40 21.42315789 |
tTau 147.5652632 | pTau 11.48947368 | Death Age 94 | Thal Score 4
H20.33.020 | sex: Male | ABeta42 45.72842105 | ABeta40 145.2547368 |
tTau 21.71894737 | pTau 3.873684211 | Death Age 81 | Thal Score 5
H21.33.010 | sex: Female | ABeta42 24.63789474 | ABeta40 66.77578947 |
tTau 290.8684211 | pTau 1.922105263 | Death Age 93 | Thal Score 5
H21.33.035 | sex: Female | ABeta42 143.4642105 | ABeta40 7.491578947 |
tTau 903.6189474 | pTau 5.306315789 | Death Age 97 | Thal Score 5

Higher Education
H19.33.004 | sex: Female | ABeta42 0.971578947 | ABeta40 0.019621053 |
tTau 1552.414737 | pTau 1.901052632 | Death Age 80 | Thal Score 0
H20.33.035 | sex: Female | ABeta42 0.525263158 | ABeta40 0.030147368 |
tTau 533.5926316 | pTau 4.036842105 | Death Age 99 | Thal Score 0
H20.33.044 | sex: Male | ABeta42 0.245263158 | ABeta40 0.007088421 |
```

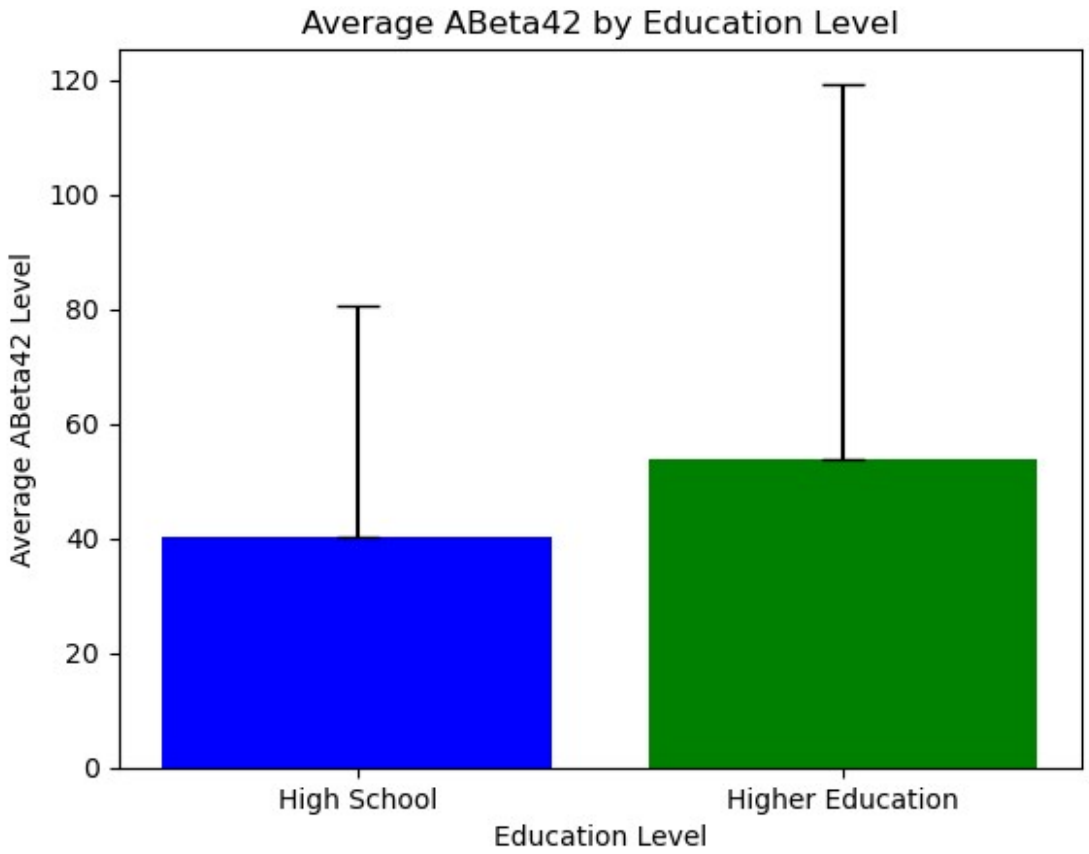
tTau 7005.543158 | pTau 5.630526316 | Death Age 81 | Thal Score 0
H21.33.003 | sex: Male | ABeta42 0.405263158 | ABeta40 0.000804526 |
tTau 393.8768421 | pTau 3.092631579 | Death Age 78 | Thal Score 0
H21.33.004 | sex: Male | ABeta42 0.670526316 | ABeta40 0.001155368 |
tTau 324.3410526 | pTau 3.475789474 | Death Age 93 | Thal Score 0
H21.33.011 | sex: Female | ABeta42 0.137347368 | ABeta40 0.000688421 |
tTau 276.5368421 | pTau 3.052631579 | Death Age 83 | Thal Score 0
H20.33.012 | sex: Female | ABeta42 47.70947368 | ABeta40 2.529473684 |
tTau 950.7410526 | pTau 4.545263158 | Death Age 91 | Thal Score 1
H21.33.016 | sex: Female | ABeta42 0.525263158 | ABeta40 0.009426737 |
tTau 303.0031579 | pTau 4.090526316 | Death Age 94 | Thal Score 1
H21.33.028 | sex: Male | ABeta42 0.204385895 | ABeta40 0.072506632 |
tTau 391.1515789 | pTau 3.065263158 | Death Age 72 | Thal Score 1
H20.33.001 | sex: Male | ABeta42 2.744210526 | ABeta40 0.215789474 |
tTau 756.0905263 | pTau 2.737894737 | Death Age 82 | Thal Score 2
H21.33.001 | sex: Male | ABeta42 0.405263158 | ABeta40 0.000882947 |
tTau 452.1894737 | pTau 3.038947368 | Death Age 80 | Thal Score 2
H21.33.032 | sex: Female | ABeta42 6.777894737 | ABeta40 1.375789474 |
tTau 359.58 | pTau 3.14 | Death Age 98 | Thal Score 2
H21.33.037 | sex: Female | ABeta42 0.449649126 | ABeta40 0.036216842 |
tTau 558.1957895 | pTau 2.334736842 | Death Age 88 | Thal Score 2
H21.33.047 | sex: Male | ABeta42 0.049052632 | ABeta40 0.000981053 |
tTau 212.9031579 | pTau 3.575789474 | Death Age 90 | Thal Score 2
H20.33.013 | sex: Male | ABeta42 24.78105263 | ABeta40 1.127368421 |
tTau 272.5084211 | pTau 3.106315789 | Death Age 94 | Thal Score 3
H20.33.014 | sex: Female | ABeta42 16.13789474 | ABeta40 0.526168105 |
tTau 258.6242105 | pTau 3.398947368 | Death Age 82 | Thal Score 3
H20.33.015 | sex: Male | ABeta42 27.60947368 | ABeta40 1.944210526 |
tTau 393.1831579 | pTau 1.827368421 | Death Age 88 | Thal Score 3
H20.33.034 | sex: Female | ABeta42 4.96 | ABeta40 4.794736842 | tTau
569.2336842 | pTau 2.593684211 | Death Age 85 | Thal Score 3
H21.33.005 | sex: Male | ABeta42 6.554736842 | ABeta40 1.655789474 |
tTau 549.82 | pTau 3.131578947 | Death Age 95 | Thal Score 3
H21.33.012 | sex: Female | ABeta42 3.502105263 | ABeta40 0.215789474 |
tTau 238.6705263 | pTau 3.669473684 | Death Age 93 | Thal Score 3
H21.33.018 | sex: Female | ABeta42 10.98842105 | ABeta40 0.263157895 |
tTau 170.9052632 | pTau 1.995789474 | Death Age 89 | Thal Score 3
H21.33.025 | sex: Female | ABeta42 8.842105263 | ABeta40 21.20947368 |
tTau 738.4673684 | pTau 2.74 | Death Age 88 | Thal Score 3
H21.33.030 | sex: Male | ABeta42 18.54736842 | ABeta40 1.827368421 |
tTau 948.1368421 | pTau 5.212631579 | Death Age 89 | Thal Score 3
H21.33.044 | sex: Female | ABeta42 33.63789474 | ABeta40 7.130526316 |
tTau 417.8947368 | pTau 3.662105263 | Death Age 88 | Thal Score 3
H20.33.008 | sex: Female | ABeta42 101.8305263 | ABeta40 3.991578947 |
tTau 125.9336842 | pTau 2.569473684 | Death Age 92 | Thal Score 4
H20.33.016 | sex: Female | ABeta42 21.27368421 | ABeta40 2.671578947 |
tTau 488.8989474 | pTau 2.282105263 | Death Age 93 | Thal Score 4
H20.33.017 | sex: Male | ABeta42 209.4347368 | ABeta40 52.64210526 |
tTau 239.3778947 | pTau 5.881052632 | Death Age 69 | Thal Score 4

H20.33.019 | sex: Female | ABeta42 28.81368421 | ABeta40 1.718947368 | tTau 312.7442105 | pTau 2.884210526 | Death Age 87 | Thal Score 4
H20.33.024 | sex: Male | ABeta42 105.1042105 | ABeta40 5.095789474 | tTau 309.08 | pTau 5.222105263 | Death Age 90 | Thal Score 4
H20.33.028 | sex: Female | ABeta42 18.94736842 | ABeta40 1.127368421 | tTau 192.0284211 | pTau 2.927368421 | Death Age 94 | Thal Score 4
H20.33.030 | sex: Female | ABeta42 58.26631579 | ABeta40 17.22105263 | tTau 114.6231579 | pTau 6.56 | Death Age 86 | Thal Score 4
H20.33.038 | sex: Female | ABeta42 81.13789474 | ABeta40 5.176842105 | tTau 121.4084211 | pTau 4.016842105 | Death Age 90 | Thal Score 4
H20.33.039 | sex: Female | ABeta42 27.33473684 | ABeta40 2.062105263 | tTau 482.5421053 | pTau 3.865263158 | Death Age 96 | Thal Score 4
H20.33.040 | sex: Male | ABeta42 12.69789474 | ABeta40 1.412631579 | tTau 401.9305263 | pTau 1.809473684 | Death Age 98 | Thal Score 4
H20.33.041 | sex: Female | ABeta42 242.5863158 | ABeta40 5.522105263 | tTau 196.9957895 | pTau 2.406315789 | Death Age 91 | Thal Score 4
H20.33.043 | sex: Male | ABeta42 60.95368421 | ABeta40 97.8 | tTau 709.8136842 | pTau 5.782105263 | Death Age 85 | Thal Score 4
H21.33.006 | sex: Male | ABeta42 82.97263158 | ABeta40 12.87684211 | tTau 160.5831579 | pTau 3.169473684 | Death Age 97 | Thal Score 4
H21.33.007 | sex: Female | ABeta42 287.412 | ABeta40 11.41894737 | tTau 1179.673684 | pTau 6.410526316 | Death Age 86 | Thal Score 4
H21.33.008 | sex: Female | ABeta42 18.994 | ABeta40 18.994 | tTau 126.1673684 | pTau 6.175789474 | Death Age 91 | Thal Score 4
H21.33.013 | sex: Female | ABeta42 68.36631579 | ABeta40 43.23368421 | tTau 599.8652632 | pTau 1.630526316 | Death Age 94 | Thal Score 4
H21.33.014 | sex: Male | ABeta42 35.27578947 | ABeta40 4.864210526 | tTau 197.3589474 | pTau 1.598947368 | Death Age 92 | Thal Score 4
H21.33.020 | sex: Male | ABeta42 38.15894737 | ABeta40 1.547368421 | tTau 202.5905263 | pTau 3.328421053 | Death Age 82 | Thal Score 4
H21.33.021 | sex: Male | ABeta42 2.672631579 | ABeta40 0.001261053 | tTau 58.70105263 | pTau 1.324210526 | Death Age 99 | Thal Score 4
H21.33.026 | sex: Female | ABeta42 263.5368421 | ABeta40 76.91789474 | tTau 386.6842105 | pTau 6.217894737 | Death Age 90 | Thal Score 4
H21.33.036 | sex: Female | ABeta42 75.78947368 | ABeta40 5.302105263 | tTau 238.4989474 | pTau 5.577894737 | Death Age 93 | Thal Score 4
H21.33.040 | sex: Male | ABeta42 0.490526316 | ABeta40 0.065191789 | tTau 894.1368421 | pTau 3.850526316 | Death Age 83 | Thal Score 4
H21.33.043 | sex: Female | ABeta42 29.89263158 | ABeta40 1.593684211 | tTau 611.0 | pTau 4.404210526 | Death Age 95 | Thal Score 4
H21.33.046 | sex: Male | ABeta42 19.19578947 | ABeta40 2.421052632 | tTau 1124.777383 | pTau 3.129473684 | Death Age 97 | Thal Score 4
H20.33.004 | sex: Male | ABeta42 80.26631579 | ABeta40 60.76631579 | tTau 318.5284211 | pTau 7.412631579 | Death Age 86 | Thal Score 5
H20.33.011 | sex: Female | ABeta42 60.51157895 | ABeta40 11.84526316 | tTau 1141.492355 | pTau 8.536842105 | Death Age 93 | Thal Score 5
H20.33.032 | sex: Male | ABeta42 44.25684211 | ABeta40 91.74842105 | tTau 156.6284211 | pTau 12.47052632 | Death Age 98 | Thal Score 5
H20.33.033 | sex: Male | ABeta42 123.3684211 | ABeta40 20.21157895 |

```
tTau 92.80210526 | pTau 3.712631579 | Death Age 68 | Thal Score 5
H20.33.036 | sex: Female | ABeta42 102.4557895 | ABeta40 3.594736842 |
tTau 345.8894737 | pTau 1.28 | Death Age 100 | Thal Score 5
H20.33.037 | sex: Female | ABeta42 67.65473684 | ABeta40 53.01263158 |
tTau 283.24 | pTau 4.569473684 | Death Age 96 | Thal Score 5
H20.33.045 | sex: Female | ABeta42 142.778 | ABeta40 981.444 | tTau
1122.432229 | pTau 5.415789474 | Death Age 77 | Thal Score 5
H20.33.046 | sex: Male | ABeta42 69.98842105 | ABeta40 25.29578947 |
tTau 283.4368421 | pTau 15.91789474 | Death Age 94 | Thal Score 5
H21.33.002 | sex: Female | ABeta42 74.77684211 | ABeta40 93.67684211 |
tTau 200.3842105 | pTau 7.317894737 | Death Age 70 | Thal Score 5
H21.33.009 | sex: Female | ABeta42 40.19894737 | ABeta40 189.2905263 |
tTau 130.4147368 | pTau 4.948421053 | Death Age 65 | Thal Score 5
H21.33.017 | sex: Female | ABeta42 20.18210526 | ABeta40 1.412631579 |
tTau 164.9431579 | pTau 2.075789474 | Death Age 92 | Thal Score 5
H21.33.027 | sex: Male | ABeta42 39.83789474 | ABeta40 31.71157895 |
tTau 222.8189474 | pTau 2.709473684 | Death Age 92 | Thal Score 5
H21.33.029 | sex: Male | ABeta42 146.8621053 | ABeta40 17.82736842 |
tTau 953.1326316 | pTau 2.04 | Death Age 89 | Thal Score 5
H21.33.031 | sex: Male | ABeta42 124.4347368 | ABeta40 34.42947368 |
tTau 860.3778947 | pTau 4.793684211 | Death Age 84 | Thal Score 5
H21.33.033 | sex: Female | ABeta42 31.76315789 | ABeta40 3.967368421 |
tTau 667.3905263 | pTau 4.462105263 | Death Age 83 | Thal Score 5
H21.33.034 | sex: Female | ABeta42 161.0947368 | ABeta40 12.15368421 |
tTau 393.3484211 | pTau 6.388421053 | Death Age 90 | Thal Score 5
H21.33.042 | sex: Female | ABeta42 47.93263158 | ABeta40 20.53894737 |
tTau 531.6515789 | pTau 2.507368421 | Death Age 91 | Thal Score 5


#Bar graph of Education level (HS or Higher education) vs ABeta42
levels
import numpy as np
import matplotlib.pyplot as plt
from scipy.stats import ttest_ind

def plot_abeta42_by_education():
    groups = ["High School", "Higher Education"]
    means = []
    stds = []

    for group in groups:
        patients = Patient.education_lvl.get(group, [])
        if patients:
            abeta42_values = [p.get_ABeta42() for p in patients if
p.get_ABeta42() is not None]
            mean_val = np.mean(abeta42_values) if abeta42_values else
0
            std_val = np.std(abeta42_values, ddof=1) if
len(abeta42_values) > 1 else 0
            means.append(mean_val)
```

```
            stds.append(std_val)
        else:
            means.append(0)
            stds.append(0)

    # Asymmetric error bars: only upper error shown
    lower_error = np.zeros_like(stds)
    upper_error = np.array(stds)
    asymmetric_error = [lower_error, upper_error]

    plt.bar(groups, means, yerr=asymmetric_error, capsize=8,
color=['blue', 'green'])
    plt.xlabel('Education Level')
    plt.ylabel('Average ABeta42 Level')
    plt.title('Average ABeta42 by Education Level')
    plt.show()

def print_ttest_for_abeta42_by_education():
    high_school_patients = Patient.education_lvl.get("High School",
[])
    higher_edu_patients = Patient.education_lvl.get("Higher
Education", [])

    high_school_abeta42 = [p.ABeta42 for p in high_school_patients if
p.ABeta42 is not None]
    higher_edu_abeta42 = [p.ABeta42 for p in higher_edu_patients if
p.ABeta42 is not None]

    t_stat, p_val = ttest_ind(high_school_abeta42, higher_edu_abeta42,
equal_var=False)  # Welch's t-test

    print(f"T-statistic: {t_stat:.4f}")
    print(f"P-value: {p_val:.4e}")

# Example usage
print_ttest_for_abeta42_by_education()
plot_abeta42_by_education()
```

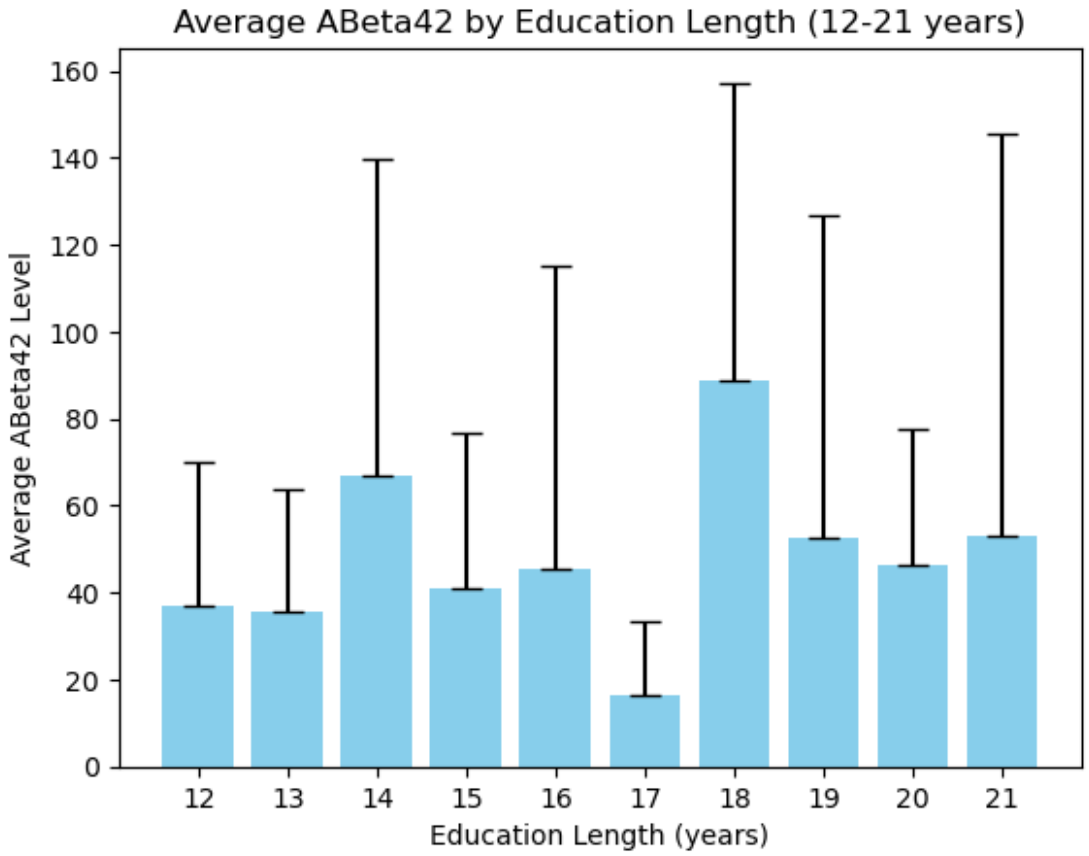
```
T-statistic: -1.0603
P-value: 2.9469e-01
```



Our p-value: 0.29469 > alpha: 0.05 thus we fail to reject the null hypothesis that there is no significant difference of Abeta42 levels from differing education level.

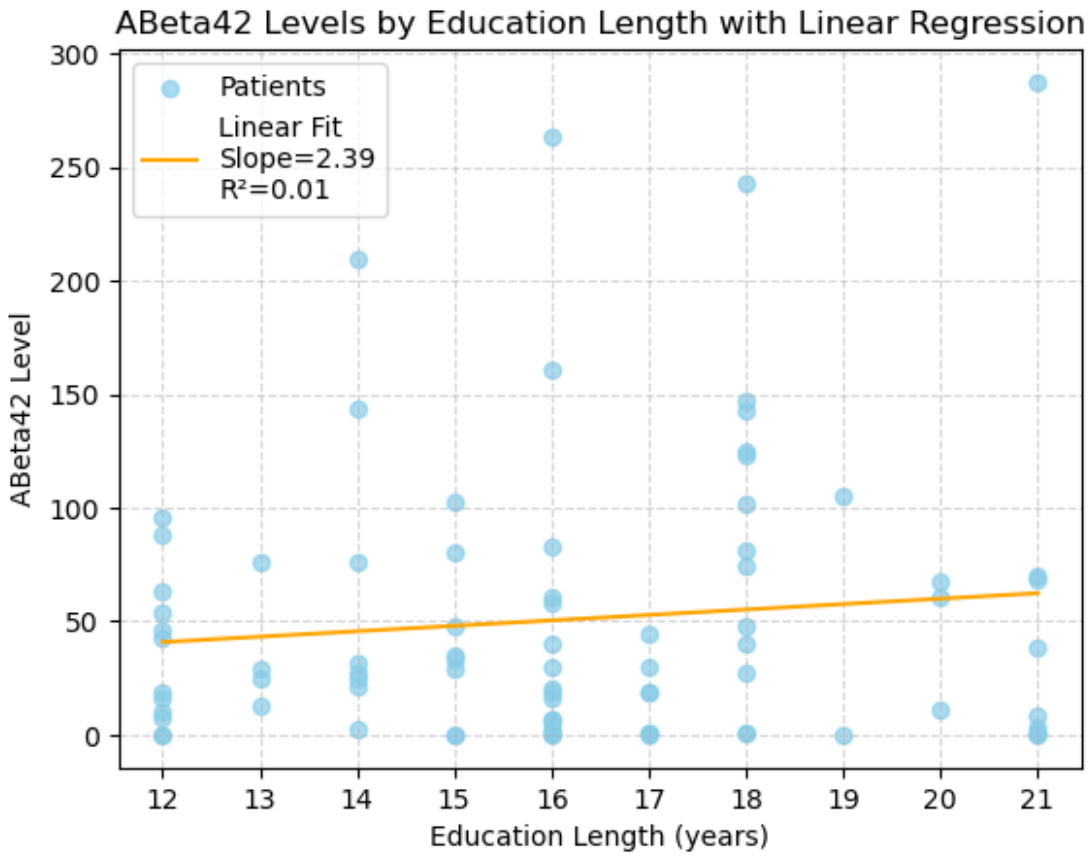
```
#Histogram of Education length vs ABeta42 levels
import numpy as np
import matplotlib.pyplot as plt

def plot_histogram_edlength_vs_abeta42():
    # Define the year range
    years = list(range(12, 22))  # 12 to 21 inclusive

    avg_abeta42_per_year = []
    std_abeta42_per_year = []

    for year in years:
        abeta_values = [p.ABeta42 for p in Patient.all_patients if
p.ed_length == year and p.ABeta42 is not None]
        if abeta_values:
            avg_abeta42_per_year.append(np.mean(abeta_values))
            std_abeta42_per_year.append(np.std(abeta_values, ddof=1)
if len(abeta_values) > 1 else 0)
        else:
            avg_abeta42_per_year.append(0)  # or np.nan if preferred
```

```
            std_abeta42_per_year.append(0)

    # Asymmetric error bars: only upper error shown
    lower_error = np.zeros_like(std_abeta42_per_year)
    upper_error = np.array(std_abeta42_per_year)
    asymmetric_error = [lower_error, upper_error]

    plt.bar(years, avg_abeta42_per_year, yerr=asymmetric_error,
capsize=6, color='skyblue')
    plt.xlabel('Education Length (years)')
    plt.ylabel('Average ABeta42 Level')
    plt.title('Average ABeta42 by Education Length (12-21 years)')
    plt.xticks(years)
    plt.show()

# Call the function
plot_histogram_edlength_vs_abeta42()
```



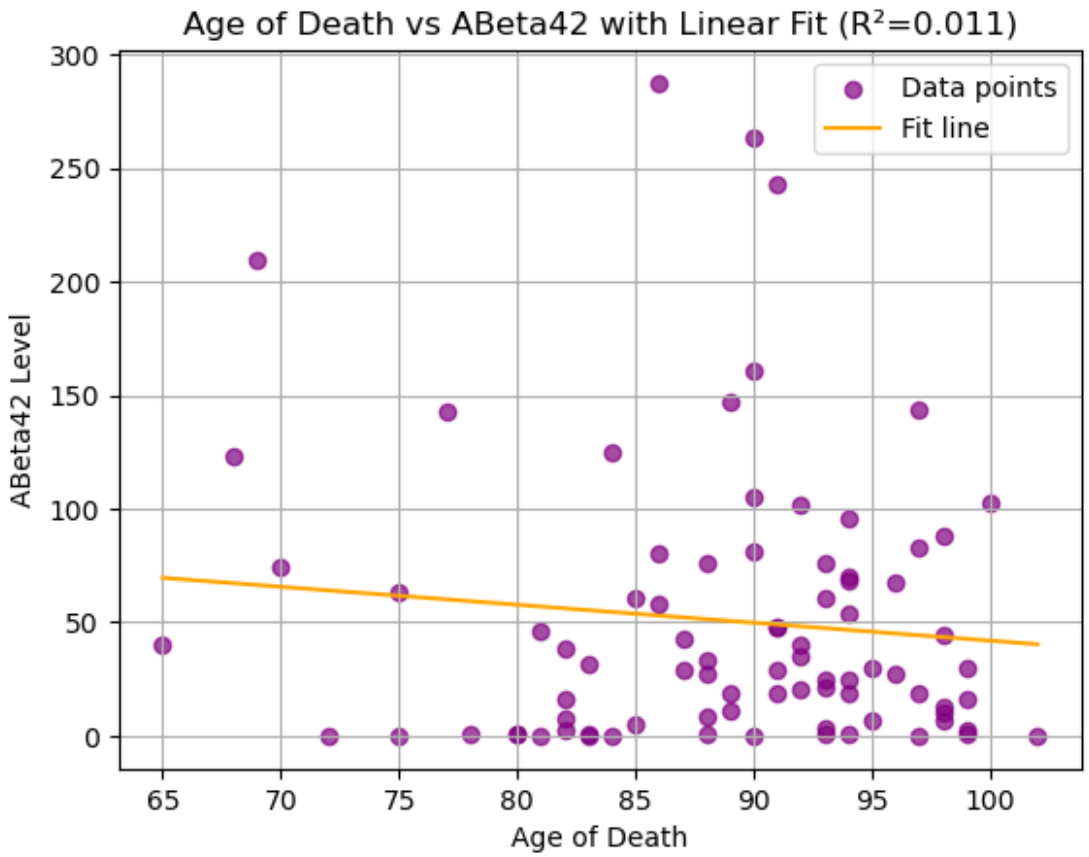

```
#Scatterplot of education length vs ABeta42 levels with a linear
regression
#Our data does not linearize well so we made a death age vs ABeta42
levels after this graph
import numpy as np
```

```
import matplotlib.pyplot as plt
from scipy.stats import linregress

def plot_scatter_with_regression():
    ed_lengths = [p.ed_length for p in Patient.all_patients if
p.ABeta42 is not None]
    abeta_values = [p.ABeta42 for p in Patient.all_patients if
p.ABeta42 is not None]

    plt.scatter(ed_lengths, abeta_values, color='skyblue', alpha=0.7,
label='Patients')

    # Perform linear regression
    slope, intercept, r_value, p_value, std_err =
linregress(ed_lengths, abeta_values)

    # Sorted x-values for plotting the regression line
    x_sorted = sorted(set(ed_lengths))
    regression_line = [slope * x + intercept for x in x_sorted]

    plt.plot(x_sorted, regression_line, color='orange', label=f'Linear
Fit\nSlope={slope:.2f}\nR²={r_value**2:.2f}')
    plt.xlabel('Education Length (years)')
    plt.ylabel('ABeta42 Level')
    plt.title('ABeta42 Levels by Education Length with Linear
Regression')
    plt.xticks(range(12, 22))
    plt.grid(True, linestyle='--', alpha=0.5)
    plt.legend()
    plt.show()

# Call the function
plot_scatter_with_regression()
```




```
#NOT RELATED TO OUR QUESTION JUST FOR PRACTICE
import matplotlib.pyplot as plt
import numpy as np

def plot_death_age_vs_abeta42_with_regression():
    # Extract data, filtering out None values
    ages = np.array([p.death_age for p in Patient.all_patients if
p.death_age is not None and p.ABeta42 is not None])
    abeta42_levels = np.array([p.ABeta42 for p in Patient.all_patients
if p.death_age is not None and p.ABeta42 is not None])

    plt.scatter(ages, abeta42_levels, color='purple', alpha=0.7,
label='Data points')

    # Linear regression (1st degree polynomial fit)
    coefficients = np.polyfit(ages, abeta42_levels, 1)
    poly = np.poly1d(coefficients)

    # Generate x values for the regression line
    x_line = np.linspace(ages.min(), ages.max(), 100)
    y_line = poly(x_line)

    plt.plot(x_line, y_line, color='orange', label='Fit line')
```

```
    # Calculate R-squared
    y_pred = poly(ages)
    ss_res = np.sum((abeta42_levels - y_pred) ** 2)
    ss_tot = np.sum((abeta42_levels - np.mean(abeta42_levels)) ** 2)
    r_squared = 1 - (ss_res / ss_tot)

    plt.xlabel('Age of Death')
    plt.ylabel('ABeta42 Level')
    plt.title(f'Age of Death vs ABeta42 with Linear Fit
(R²={r_squared:.3f})')
    plt.legend()
    plt.grid(True)
    plt.show()

# Call the function
plot_death_age_vs_abeta42_with_regression()
```



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 data quality control was performed by filtering out outliers for ABeta42 (namely, the 1400+ level patient), and confirming that education length was properly categorized. Both t-tests and scatter plot visualization were used. No significant difference in ABeta42 levels was observed between education groups, reflected in the non-significant p-values (e.g., $p = 0.29$) and very low R^2 scores from regression (e.g., $R^2 = 0.01$). The results were reproducible across multiple visualizations and statistical analyses in the Jupyter notebook, using group averages and patient-level scatterplots to rule out both categorical and continuous trends. Following this analysis, we searched for literature that reinforces our conclusion. Multiple meta-analyses and cohort studies report no direct association between educational attainment and ABeta42 levels. For example, Hwangbo et al. (2022) found no significant effect of education on amyloid-positive Alzheimer's Disease, indicating education is not protective against amyloid pathology itself. A systematic review published in 2025 analyzed over 6,000 records and found that, while higher education may affect cognitive reserve and clinical onset, it does not consistently reduce ABeta accumulation in Alzheimer's patients. In addition, a 2020 study found that "[p]resymptomatic mutation carriers of autosomal dominant AD showed no relation between APOE ε4 and Aβ burden, but increasing level of education was associated with reduced Aβ burden", reinforcing the cognitive reserve theory.
- https://pmc.ncbi.nlm.nih.gov/articles/PMC9388911/
- https://pmc.ncbi.nlm.nih.gov/articles/PMC12226377/
- https://pmc.ncbi.nlm.nih.gov/articles/PMC7713743/

Conclusions and Ethical Implications:

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

- The absence of correlation between education and ABeta42 suggests education does not directly prevent or reduce underlying Alzheimer's disease pathology, but rather influences cognitive reserve. This means people with higher education may better compensate for early pathological changes, delaying symptom onset, but do not necessarily have less amyloid buildup in their brains. Studies consistently report that while highly educated individuals may be diagnosed with Alzheimer's later, once cognitive decline begins, they often experience more rapid progression—likely because a greater reserve masked underlying pathology for longer. Ethically, it is crucial to clearly communicate that education does not reduce or prevent Alzheimer's disease pathology—so that patients and families are not misled about the limits of education's protective effects. This transparency helps prevent unrealistic expectations, supports informed decision-making, and avoids inadvertently blaming or stigmatizing individuals with less educational opportunity.
- https://pmc.ncbi.nlm.nih.gov/articles/PMC12263273/

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.

- Limitations of this analysis include reliance on education as a singular proxy for cognitive reserve, which may not capture other influential factors such as occupational complexity, social engagement, or lifestyle, potentially leading to an incomplete representation of cognitive resilience. The sample size, demographic diversity, and small range of education level may also limit the generalizability of the conclusions we made. Future work should incorporate multidimensional measures of cognitive reserve, larger and more diverse cohorts, and gradual biomarker tracking to observe the dynamic interplay between education, pathology, and cognition. Ethically, future research must carefully communicate the distinctions between cognitive reserve and pathology prevention, ensuring clear public understanding to avoid misconceptions that education alone can prevent Alzheimer's disease, thereby promoting equitable access to comprehensive prevention and care strategies across populations.
- NOTES FROM YOUR TEAM: This is where our team is taking notes and recording activity.
  - 9/11 - We worked on our respective bullet points for the Jupyter notebook: Jack (points 1-6) and Nolan (7-11). We also discussed and decided on a question to base our project around: Does level of education (or years of education) affect resilience to AD biomarkers (cognitive reserve hypothesis)?. ACTION ITEMS: finish bullet points and research further into our topic.
  - 9/16 - Used Rizzo notebook in class as inspiration to sort and analyze our patient data. Stored all relevant bio markers as well as gender, education level, death age, donor id, education length. ACTION ITEMS:
  - 9/18 - Presented our bar graphs in class and worked on finding the t statistic and p value for education level vs Abeta42 ACTION ITEMS: Complete 2nd Jupyter Notebook check in
- QUESTIONS FOR YOUR TA: These are questions we have for our TA.
  - 9/11 - For future reference, whenever we list sources, would you like for us to give a real citation (MLA, APA) or just the link?
  - 9/18 - No current questions '''