Module_1: *Alzheimer's*

Team Members:

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Project Title:

Computational Analysis of Alzheimer's Disease and APOE Genotype ABETA 40/42 Ratio

Disease Background:

Fill in information about 11 bullets:

- Prevalence: Prevalence of Alzheimer's is 2.06% for all Americans and is 11% for those 65 and older. The incidence of Alzheimer's is 3.47% and is expected to rise to 12.7 million cases by 2050.
- Economic Burden: 12 million Americans provide unpaid care for those with dimentia estimating $413.5 billion in cost. Health and longterm care is estimated at $384 billion.
- Risk Factors: Genetic risk factors for Alzheimer's in the U.S. include being female, being a Black American or a Hispanic. The APOE gene is also influences Alzheimer's prevalelance along with APP on chromosome 21, PSEN1 on chromosome 14, and PSEN2 on chromosome 1. Age is the best known risk factor for Alzheimer's. Other risk factors include: unmanaged chronic health issues, physical inactivity, unhealthy diet, alcohol and smoking, solical isolation, and lack of mental stimulation.
- Societal determinants: Lower educational level is associated with poorer brain heath which could lead to Alzheimer's in the long run. Access to healthcare that prevents chronic illnesses. Due to chronic illness being a factor for Alzheimer's managing chronic health conditions is important to prevent Alzheimer's. Communities that are more physically active and engaged can impact brain health positively. Those who are socially isolated are at a greater risk of developing dimentia.

- Symptoms
- Early-Stage (Mild) Memory loss, especially for recent events or conversations, difficulty finding the right words, trouble performing familiar tasks, misplacing items more often, confusion about time or place
- Middle-Stage (Moderate) Increasing confusion and memory loss (forgetting personal history), wandering or becoming lost, suspiciousness or paranoia,agitation, aggression, or inappropriate behavior
- Late-Stage (Severe) Loss of ability to communicate coherently, loss of awareness of surroundings and recent experiences, needing full-time assistance with personal care, severe physical decline (trouble swallowing, walking, and controlling bladder/bowels)
- Diagnosis

Clinical Evaluation Detailed medical history (including family history of dementia), Physical and neurological exams (reflexes, balance, coordination, sensory function), Cognitive and Neuropsychological Tests, Memory, problem-solving, attention, language, and calculation skills are assessed,

Laboratory Tests (Blood and urine tests to rule out vitamin deficiencies, thyroid disease, infection, or other causes of cognitive impairment, Brain Imaging, Magnetic resonance imaging (MRI) or Computed tomography (CT): to detect brain shrinkage and rule out strokes, tumors, or trauma, Positron emission tomography (PET) scans: to look for patterns of reduced brain activity or detect amyloid/tau buildup)

Biomarker Tests (Cerebrospinal fluid analysis: measures beta-amyloid and tau protein levels, Emerging blood tests for amyloid/tau)

- Standard of care treatments (& reimbursement) Two types of medicines for treating symptoms:

  Cholinerastarase inhibitors -- Boost levels of cell to cell communication, improve symptoms related to behaviour such as agitation of depression

  Memantime (Nameda) -- works in another brain cell communicatio network and slows down the progression of symptoms with moderate to severe Alzheimer's

https://www.mayoclinic.org/diseases-conditions/alzheimers-disease/diagnosis-treatment/drc-20350453#:~:text=Alzheimer's%20medicines%20can%20help%20wit
Medicare covers most of the necessary costs, paying for abuot 80% of approved costs after deductible

- Disease progression & prognosis

1. Preclinical: No symptoms, usually only identified in research settings by brain imaging
2. Mild Cognitive Impairment: Aren't enough to affect work or relationships -- usually have memory lapses. "They may have trouble figuring out the number or order of steps needed to complete a task. The ability to make good decisions also may become harder."
3. Mild dementia: Usually when it becomes clear there's a problem with memory and thinking. -Memory Loss of recent events - Trouble with problem solving and complex tasks - Changes in personality - Trouble organizing and expressing thought - Getting lost or misplacing belongings
4. Moderate Dementia: More confused and forgetful. Might need help with daily tasks - Increasingly poor judgement -- Lose track of where they are, time of week, season, etc - Even greater memory loss -- forget details of personal history such as phone numbers - Need help with daily tasks -- Choosing proper clothing for weather - Significant changes in personality and behavior -- Develop unfounded suspicions
5. Severe Dementia: Mental functions continue to decline, more issues with movement - Loss of the ability to communicate - Require daily assistance with personal care -- eating, bathroom, dressing, etc - Decline in physical abilities -- May need assistance walking or even sitting straight Prognosis: Varies wildly: Most people live about 3-11 years after diagnosis, but some have lived 20 years or more. Untreated vascular disease factors also contribute to faster progression of alzheimers

https://www.mayoclinic.org/diseases-conditions/alzheimers-disease/in-depth/alzheimers-stages/art-20048448

- Continuum of care providers -It is first recognized by a PCP, which then refers the patient to specialists. Then, the following specialists play

different roles in care:

Neurologists: Evaluate and diagnose cognitive impairment, manage disease progression.

Psychiatrists: Treat behavioral and mood changes.

Geriatricians: Focus on older adults with complex health needs.

Neuropsychologists: Provide cognitive assessments and functional evaluations.

There are other services that assist the patient with living easier, such as Community-Based Services, Home-Based Care Providers, and Residential and Long-Term Care.

- Biological mechanisms (anatomy, organ physiology, cell & molecular physiology) The disease begins with molecular changes (Aβ accumulation, tau phosphorylation), leading to cellular dysfunction (synaptic loss, inflammation), progressing to tissue/organ damage (hippocampal and cortical atrophy), and ultimately manifesting as clinical symptoms (memory loss, cognitive decline, functional impairment).
- Clinical Trials/next-gen therapies What's approved (U.S.)

Lecanemab (Leqembi®) – anti-amyloid mAb with full FDA approval (for early AD). Medicare provides broader coverage after the 2023 traditional approval. In Aug 2025 the FDA also cleared a weekly subcutaneous autoinjector for maintenance dosing, offering an at-home option. Centers for Medicare & Medicaid Services +2 Eisai +2

Donanemab (Kisunla™) – anti-amyloid mAb with FDA approval (July 2, 2024) for early symptomatic AD; label carries ARIA warnings. Finite dosing possible once amyloid clears. Reuters +1

Aducanumab (Aduhelm®) – discontinued by Biogen (Jan 2024 announcement).

Near-term/"next-gen" directions

1. Anti-amyloid, next iterations

Subcutaneous lecanemab (now approved for maintenance; PDUFA Aug 31, 2025—met). Eisai +1

Remternetug (Lilly) – next-gen amyloid mAb in Phase 3 for early AD.

ClinicalTrials.gov +1

Oral amyloid-oligomer blocker (ALZ-801 / valiltramiprosate, Alzheon) – Phase 3; April 2025 topline in APOE ε4/ε4 showed promising signals; broader program ongoing. Alzheon | Preserving Future Memories +2 NeurologyLive +2

2. Anti-tau approaches (addressing tangles)

BIIB080 (IONIS-MAPTRx; Biogen) – tau-targeting antisense oligonucleotide; reduced tau biomarkers in early trials; now in global Phase 2 with FDA Fast Track. JAMA Network +2 Alzheimer's Journals +2

Antibody programs against tau (e.g., semorinemab) have not shown meaningful clinical benefit to date in Phase 2. JAMA Network

- sources: https://www.alz.org/alzheimers-dementia/facts-figures#costToNation, https://www.nia.nih.gov/health/alzheimers-causes-and-risk-factors/what-causes-alzheimers-disease, https://www.cdc.gov/alzheimers-dementia/php/sdoh/index.html

Data-Set:

We have been provided two sets of data from an article published in Nature Neuroscience titled "Integrated Multimodal Cell Atlas of Alzheirmer's Disease". The first data set gives patient information including general factors such as age, gender, race, etc. and included other relevant information including APOE genotype, if there are known head injuries, CASI score, brain weight, brain pH, MMSE score, and other cognitive markers and data. The second data set provided is from the same article with the same patients and gives ABETA 40 amount, ABETA 42 amount, tTAU amount, and pTAU amount.

citation: Gabitto, M.I., Travaglini, K.J., Rachleff, V.M. et al. Integrated multimodal cell atlas of Alzheimer’s disease. Nat Neurosci 27, 2366–2383 (2024). https://doi.org/10.1038/s41593-024-01774-5

Data Analyis:

Using pandas, we loaded both CSV files (UpdatedLuminex.csv and UpdatedMetaData.csv) and merged them on the shared Donor ID column so that each donor’s biomarker values could be linked with their APOE genotype and other metadata.

In [4]:
```
!pip install scipy
import pandas as pd
import matplotlib.pyplot as plt
from scipy.stats import ttest_ind
from scipy.stats import linregress
import numpy as np
from scipy.stats import f_oneway
from scipy.stats import f_oneway, ttest_ind

# Load the two CSV files
luminex = pd.read_csv("UpdatedLuminex.csv")
metadata = pd.read_csv("UpdatedMetaData.csv")

# Merge on Donor ID
merged = pd.merge(luminex, metadata, on="Donor ID")
```

```
161.79s - pydevd: Sending message related to process being replaced timed-out a
fter 5 seconds
Collecting scipy
  Downloading scipy-1.16.2-cp311-cp311-macosx_14_0_arm64.whl.metadata (62 kB)
Requirement already satisfied: numpy<2.6,>=1.25.2 in ./.conda/lib/python3.11/si
te-packages (from scipy) (2.0.1)
Downloading scipy-1.16.2-cp311-cp311-macosx_14_0_arm64.whl (20.9 MB)
   ━━━━━━━━━━━━━━━━━━━━━━━━━━━━━━━━━━━━━━━━ 20.9/20.9 MB 26.7 MB/s  0:00:00 eta
0:00:01
Installing collected packages: scipy
Successfully installed scipy-1.16.2
```

From this merged dataset, we created a new column for the Aβ40/42 ratio, since this ratio is an important biomarker in Alzheimer's research (a higher ratio often indicates reduced Aβ42 availability due to plaque formation).

In [5]:
```
#Adds a new columns of ABeta40 divided by Abeta42
merged["ABeta_ratio"] = merged["ABeta40 pg/ug"] / merged["ABeta42 pg/ug"]
```

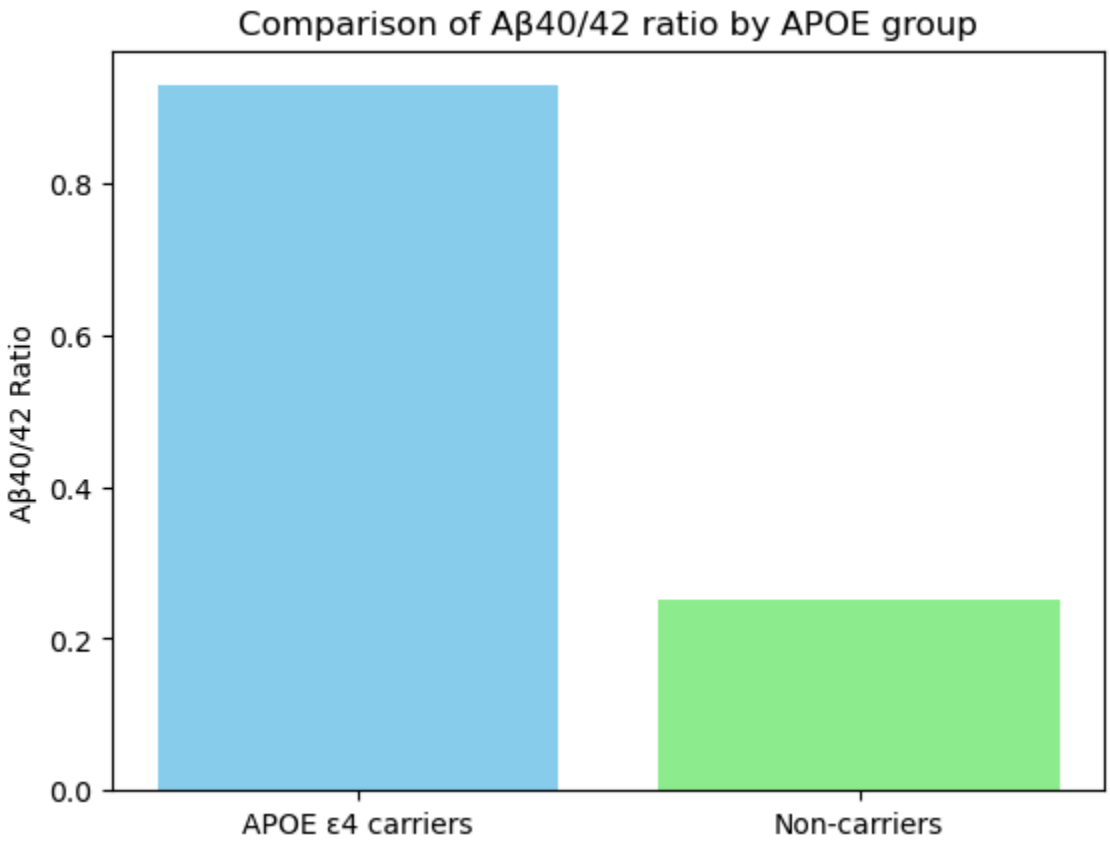
We then divided the donors into two groups: APOE ε4 carriers (any genotype containing a "4"), who are at increased risk for Alzheimer's disease, and Non-carriers, who lack the ε4 allele.

In [6]:
```
# --- Define groups ---
# Group 1: APOE ε4 carriers (any genotype containing "4")
group1 = merged[merged["APOE Genotype"].str.contains("4")]["ABeta_ratio"]

# Group 2: Non-carriers (no "4" in genotype)
group2 = merged[~merged["APOE Genotype"].str.contains("4")]["ABeta_ratio"]
```

Using these groups, we constructed a bar graph showing the mean Aβ40/42 ratio for carriers versus non-carriers. Finally, we performed a Student's t-test to statistically compare the two groups. We reported both the t-value and p-value, and determined whether the difference was statistically significant at the standard

significance level of α = 0.05.

In [7]:
```python
# --- Bar plot (2 bars) ---
means = [group1.mean(), group2.mean()]
labels = ["APOE ε4 carriers", "Non-carriers"]

plt.bar(labels, means, color=["skyblue", "lightgreen"])
plt.ylabel("Aβ40/42 Ratio")
plt.title("Comparison of Aβ40/42 ratio by APOE group")
plt.show()

# --- T-test ---
t_stat, p_val = ttest_ind(group1, group2, nan_policy="omit")
print("t-statistic:", t_stat)
print("p-value:", p_val)

# --- Interpretation ---
if p_val < 0.05:
    print("Result: Statistically significant difference (p < 0.05)")
else:
    print("Result: No significant difference (p >= 0.05)")
```



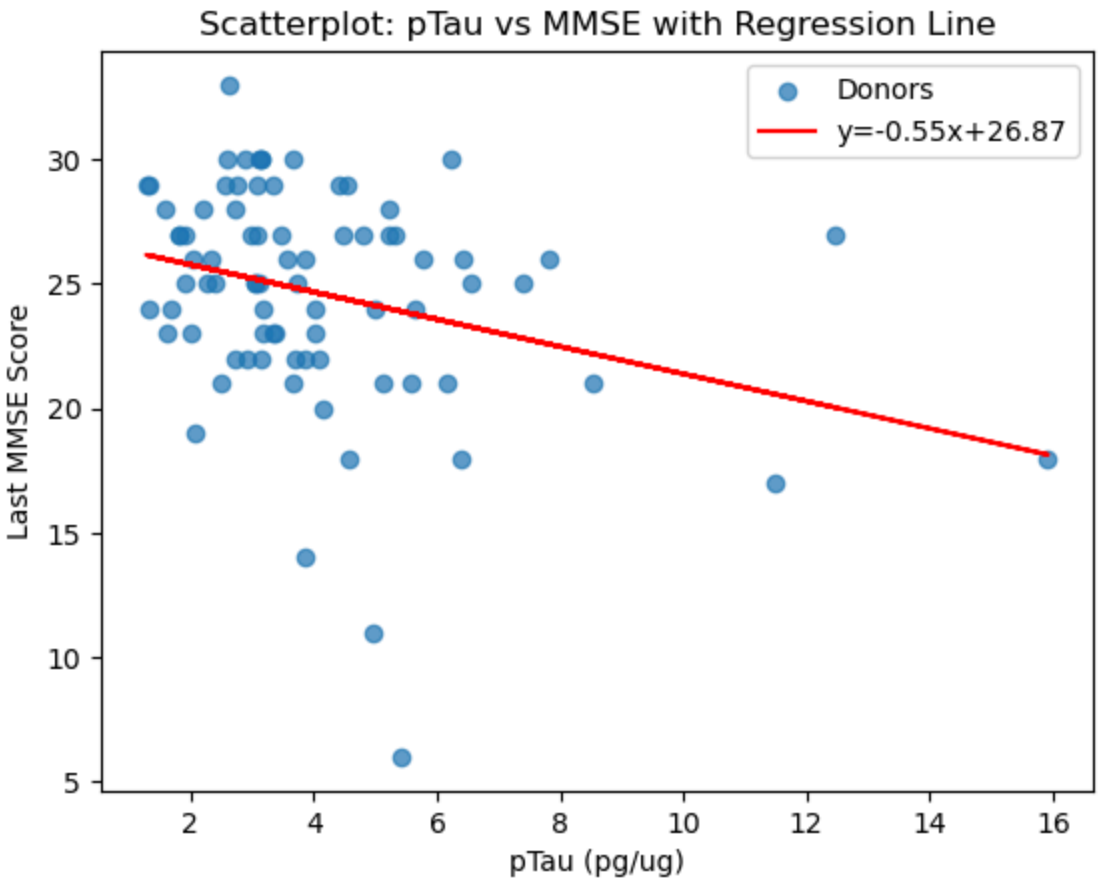

```
t-statistic: 2.8354314236707343
p-value: 0.00576191472426646
Result: Statistically significant difference (p < 0.05)
```

In addition, we created a scatterplot of pTau (pg/ug) levels versus MMSE cognitive scores to visualize the relationship between tau pathology and cognition. A linear

regression line was fit to the data, and we reported the slope, intercept, correlation coefficient (r), coefficient of determination (R^2), and the p-value for the regression. This allowed us to evaluate whether higher tau levels were significantly associated with lower cognitive performance.

In [18]:

```
# --- Scatterplot with regression line and R^2 ------------------------
# Pick variables: pTau vs MMSE
x = merged["pTAU pg/ug"]
y = merged["Last MMSE Score"]

# Remove missing values
mask = ~x.isna() & ~y.isna()
x = x[mask]
y = y[mask]

# --- Linear regression using scipy ---
slope, intercept, r_value, p_value, std_err = linregress(x, y)

# --- Scatterplot ---
plt.scatter(x, y, alpha=0.7, label="Donors")

# Regression line
plt.plot(x, slope*x + intercept, color="red", label=f"y={slope:.2f}x+{intercep

plt.xlabel("pTau (pg/ug)")
plt.ylabel("Last MMSE Score")
plt.title("Scatterplot: pTau vs MMSE with Regression Line")
plt.legend()
plt.show()

# --- Stats ---
print("Slope:", slope)
print("Intercept:", intercept)
print("R-squared:", r_value**2)
print("Correlation coefficient (r):", r_value)
print("r-squared: ", r_value ** 2)
print("p-value:", p_value)
```




```
Slope: -0.5485501724264154
Intercept: 26.873050098136243
R-squared: 0.09006738701916535
Correlation coefficient (r): -0.30011229068327966
r-squared:  0.09006738701916535
p-value: 0.006836845538766106
```

We also ran an ANOVA test to determine if being a non-carrier, heterozygous, or homozygous with the epsilon 4 allele had an effect on the participants AB40/42 ratio. This first portion of code maps the month number label to the allele number.

In [9]:
```python
# Map month label to allele number
month_to_num = {"Feb": 2, "Mar": 3, "Apr": 4}

def parse_apoe_label(label):
    """Return (allele1, allele2) as ints from labels like '4-Mar', '3-Feb', '4
    if pd.isna(label):
        return (pd.NA, pd.NA)
    try:
        first, month = str(label).split("-")
        a1 = int(first)
        a2 = month_to_num.get(month, pd.NA)
        return (a1, a2)
    except Exception:
        # Fallback: extract any digits present
        s = str(label)
```

```
        digits = [int(ch) for ch in s if ch.isdigit()]
        if len(digits) == 2:
            return (digits[0], digits[1])
        elif len(digits) == 1:
            return (digits[0], pd.NA)
        return (pd.NA, pd.NA)
```

This portion of the code counts the epsilon 4 copies and builds the groups to be analzyed in the bar graph.

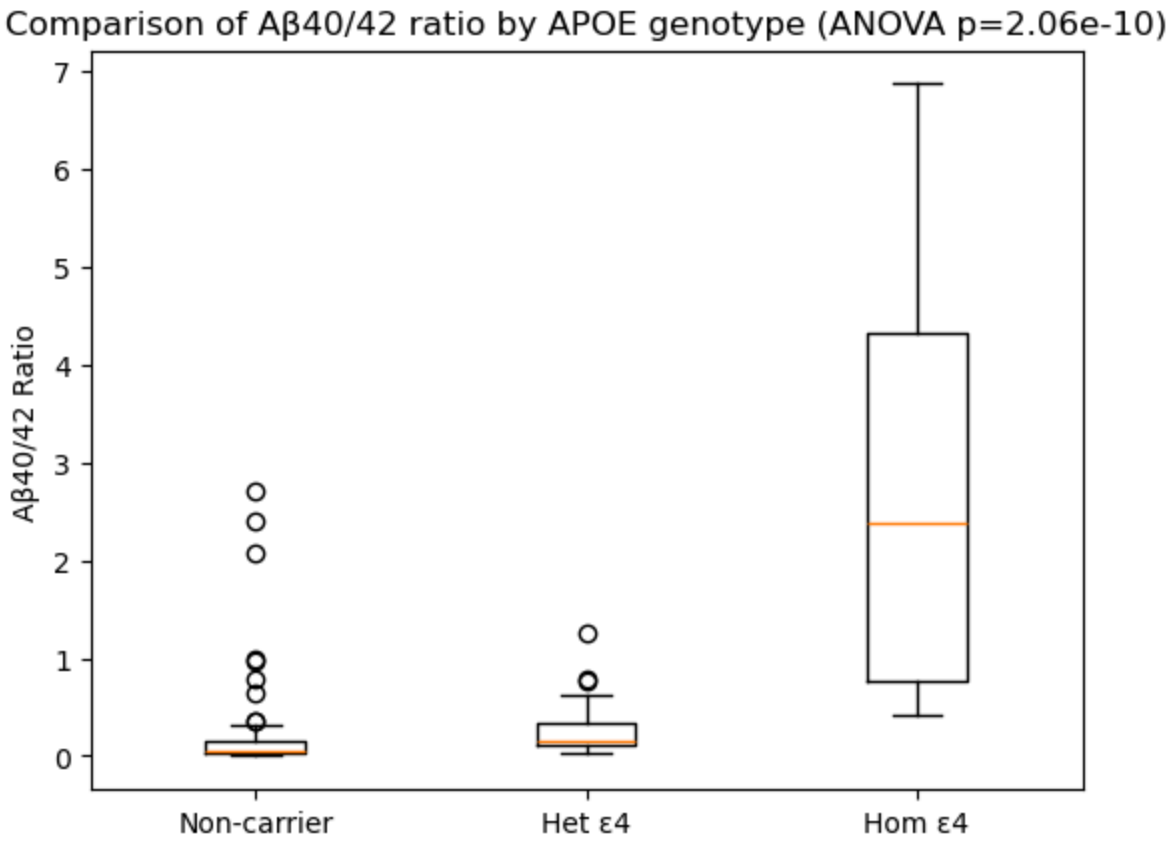
In [10]:
```
# Extract alleles and count ε4 copies
alleles = merged["APOE Genotype"].apply(parse_apoe_label)
merged[["Allele1", "Allele2"]] = pd.DataFrame(alleles.tolist(), index=merged.i

merged["APOE4_copies"] = merged[["Allele1", "Allele2"]].apply(lambda row: (row

def classify_from_copies(c):
    if pd.isna(c):
        return pd.NA
    if c == 0:
        return "Non-carrier"
    elif c == 1:
        return "Heterozygous"
    elif c == 2:
        return "Homozygous"
    return pd.NA

merged["APOE4_status"] = merged["APOE4_copies"].apply(classify_from_copies)

# Show counts
print("\nAPOE genotype counts:")
print(merged["APOE Genotype"].value_counts())
print("\nAPOE4_status counts:")
print(merged["APOE4_status"].value_counts())

# Build groups
non_carriers  = merged.loc[merged["APOE4_status"] == "Non-carrier", "ABeta_rat
heterozygotes = merged.loc[merged["APOE4_status"] == "Heterozygous", "ABeta_ra
homozygotes   = merged.loc[merged["APOE4_status"] == "Homozygous", "ABeta_rati

groups = [non_carriers, heterozygotes, homozygotes]
labels = ["Non-carrier", "Het ε4", "Hom ε4"]
non_empty = [(lab, g) for lab, g in zip(labels, groups) if len(g) > 0]

print("\nGroup sizes:", {lab: len(g) for lab, g in non_empty})
```

```
APOE genotype counts:
APOE Genotype
3-Mar    47
4-Mar    17
3-Feb    11
4-Apr     6
4-Feb     2
2-Feb     1
Name: count, dtype: int64

APOE4_status counts:
APOE4_status
Non-carrier     59
Heterozygous    19
Homozygous       6
Name: count, dtype: int64

Group sizes: {'Non-carrier': 59, 'Het ε4': 19, 'Hom ε4': 6}
```

This code prints the p-value for the ANOVA, checks to ensure there are 3 groups, and prints the graph of our ANOVA statistics.

In [11]:
```python
# --- ANOVA p-value only ---
anova_p = np.nan
if len(non_empty) >= 3:
    _, anova_p = f_oneway(*(g for _, g in non_empty))
    print(f"ANOVA p-value: {anova_p:.6g}")
else:
    print("ANOVA p-value: N/A (need ≥3 non-empty groups)")

# Plot only the groups that exist
plt.figure()
plt.boxplot([g for _, g in non_empty], labels=[lab for lab, _ in non_empty])
plt.ylabel("Aβ40/42 Ratio")
title = "Comparison of Aβ40/42 ratio by APOE genotype"
if np.isfinite(anova_p):
    title += f" (ANOVA p={anova_p:.3g})"
plt.title(title)
plt.show()

# Print anova statistics
f_stat, p_val = f_oneway(*(g for _, g in non_empty))
print("\nANOVA (≥3 groups)")
print("F-statistic:", f_stat)
print("p-value:", p_val)
```

```
ANOVA p-value: 2.06315e-10
/var/folders/sn/8kd2cfwx7cg1h3tmpxbjfz5h0000gn/T/ipykernel_54290/214847562.py:1
1: MatplotlibDeprecationWarning: The 'labels' parameter of boxplot() has been r
enamed 'tick_labels' since Matplotlib 3.9; support for the old name will be dro
pped in 3.11.
  plt.boxplot([g for _, g in non_empty], labels=[lab for lab, _ in non_empty])
```




```
ANOVA (≥3 groups)
F-statistic: 29.74289395106097
p-value: 2.0631528691826475e-10
```

Finally, becuase we saw statisical significance, we ran a Tukey HSD post-hoc test to determine where the significant differences were among our data.

In [13]:
```python
# --- Tukey HSD post-hoc ---
!pip install statsmodels
from statsmodels.stats.multicomp import pairwise_tukeyhsd

# Flatten data for Tukey
data = np.concatenate([np.asarray(g) for _, g in non_empty])
group_labels = np.concatenate([[lab]*len(g) for lab, g in non_empty])

tukey = pairwise_tukeyhsd(data, group_labels, alpha=0.05)

print("\nTukey HSD Post-hoc Results (α = 0.05):")
print(tukey.summary())
```

```
289.54s - pydevd: Sending message related to process being replaced timed-out a
fter 5 seconds
```

```
Collecting statsmodels
  Downloading statsmodels-0.14.5-cp311-cp311-macosx_11_0_arm64.whl.metadata
(9.5 kB)
Requirement already satisfied: numpy<3,>=1.22.3 in ./.conda/lib/python3.11/sit
e-packages (from statsmodels) (2.0.1)
Requirement already satisfied: scipy!=1.9.2,>=1.8 in ./.conda/lib/python3.11/si
te-packages (from statsmodels) (1.16.2)
Requirement already satisfied: pandas!=2.1.0,>=1.4 in ./.conda/lib/python3.11/s
ite-packages (from statsmodels) (2.3.2)
Collecting patsy>=0.5.6 (from statsmodels)
  Downloading patsy-1.0.1-py2.py3-none-any.whl.metadata (3.3 kB)
Requirement already satisfied: packaging>=21.3 in ./.conda/lib/python3.11/site-
packages (from statsmodels) (25.0)
Requirement already satisfied: python-dateutil>=2.8.2 in ./.conda/lib/python3.1
1/site-packages (from pandas!=2.1.0,>=1.4->statsmodels) (2.9.0.post0)
Requirement already satisfied: pytz>=2020.1 in ./.conda/lib/python3.11/site-pac
kages (from pandas!=2.1.0,>=1.4->statsmodels) (2025.2)
Requirement already satisfied: tzdata>=2022.7 in ./.conda/lib/python3.11/site-p
ackages (from pandas!=2.1.0,>=1.4->statsmodels) (2025.2)
Requirement already satisfied: six>=1.5 in ./.conda/lib/python3.11/site-package
s (from python-dateutil>=2.8.2->pandas!=2.1.0,>=1.4->statsmodels) (1.17.0)
Downloading statsmodels-0.14.5-cp311-cp311-macosx_11_0_arm64.whl (9.7 MB)
   ━━━━━━━━━━━━━━━━━━━━━━━━━━━━━━━━━━━━━━━━ 9.7/9.7 MB 47.0 MB/s  0:00:00 eta
0:00:01
Downloading patsy-1.0.1-py2.py3-none-any.whl (232 kB)
Installing collected packages: patsy, statsmodels
   ━━━━━━━━━━━━━━━━━━━━━━━━━━━━━━━━━━━━━━━━ 2/2 [statsmodels] [statsmodels]
Successfully installed patsy-1.0.1 statsmodels-0.14.5

Tukey HSD Post-hoc Results (α = 0.05):
   Multiple Comparison of Means - Tukey HSD, FWER=0.05
=============================================================
group1    group2   meandiff p-adj   lower   upper  reject
-------------------------------------------------------------
Het ε4      Hom ε4    2.571    0.0  1.6751  3.4669   True
Het ε4 Non-carrier  -0.0602 0.9562 -0.5649  0.4444  False
Hom ε4 Non-carrier  -2.6312    0.0  -3.451 -1.8114   True
-------------------------------------------------------------
```

Our results were as follows:

In [ ]:
```
# Tukey HSD Post-hoc Results (α = 0.05):
# Multiple Comparison of Means - Tukey HSD, FWER=0.05
# =============================================================
# group1    group2   meandiff p-adj   lower   upper  reject
# -------------------------------------------------------------
# Het ε4      Hom ε4    2.571    0.0  1.6751  3.4669   True
# Het ε4 Non-carrier  -0.0602 0.9562 -0.5649  0.4444  False
# Hom ε4 Non-carrier  -2.6312    0.0  -3.451 -1.8114   True
# -------------------------------------------------------------
```

Verify and validate your analysis:

To verify the analysis, we first ensured that the datasets were merged correctly on the donor identifier so that each biomarker value corresponded to the right clinical and genetic information. We checked for missing or extreme values in the ABeta40 and ABeta42 measures, then created the Aβ40/Aβ42 ratio. Grouping individuals by APOE genotype was also double-checked to confirm that carriers and non-carriers were assigned appropriately. The statistical methods used (t-tests and ANOVA) were chosen because they are standard approaches for comparing group means, and we verified that the results were consistent when using different but related tests. Together, these steps gave us confidence that the analysis pipeline was functioning as intended and not producing skewed/biased results.

To validate the analysis, we compared the findings against what is known from published Alzheimer's research. Numerous studies (e.g., Corder et al., 1993; Reiman et al., 2009; Belloy et al., 2019) show that APOE ε4 carriers tend to have higher amyloid burden and altered Aβ40/Aβ42 ratios compared with non-carriers. The fact that our analysis produced patterns in line with these published results supports the validity of the conclusions.

Conclusions and Ethical Implications:

Our team used the idea that a higher AB40/42 ratio and a higher pTAU value is a stronger indiciation of having Alzheimer's Disease and dimentia symptoms. We then compared AB40/42 to different APOE-4 geneotypes and pTAU to MMSE score. Based on our data we can conclude that there is no significant correlation between last MMSE score and pTAU accumulation in the brain. The r-squared value for this statistic was only 0.09 which does not suggest a strong correlation between the two variables. From these statistics we can conclude that 9% of the variability of last MMSE score is due to pTAU score. Similarly, we can conclude that there is a statistically significant difference in AB40/42 ratio between carrier of ε4 alleles and non-carriers. This is shown by a p-value of 0.00576 which is less than 0.05. We then took this data a step further and analyzed homozygous APOE-4 carriers, heterozygous APOE-4 carriers, and non-carries and their respective AB40/42 ratios. Using an ANOVA test we were able to determine that there was a statistically signficiant differece between the groups and their associated AB40/42 ratios (p-value of 2.063e-10). To understand where this statistically significant difference was, we then ran a Tukey post-hoc test and were able to determine a difference was between the homozygous ε4 carriers and the heterozygous ε4 carriers and there was a difference between the homozygous ε4 carriers and non-carriers, but

there was no difference between heterozygous ε4 carriers and non-carriers.

Ethical implications include doctors and medical physicans being aware of how a homozygous carrier of the APOE-4 genotype is more likely to have a higher AB40/42 ratio and thus is at more risk for Alzheimer's disease. It is also useful for doctors to be able to communicate to patients that even if they are a carrier of the ε4 allele, they are not at a higher risk of having Alzheimer's disease due to a higher AB40/42 ratio. Lastly, carriers of these allels should be responsible at informing their relatives of the associated risks of possible having 2 copies of the allele or passing the allele down through generations.

Limitations and Future Work:

The limitations of this analysis was the small sample size. Once split into groups, the sample sizes became even smaller with only 6 homozygous carriers being present. Expanding this data set would provide more difinitive results. Similarly, tracking patients over time to determine if having 1 or 2 copies of the allele causes Alheimer's disease to progress faster and further. Future work and anaysis could be done to look at ε4 allele and age of onset, age of death, and other cognitive scores to determine if the ε4 allele is what should be focused on by doctors when determining risk factors of Alzheimer's.

Questions for Consideration

- Is there a correlation between APOE genotype and higher levels of pTAU, tTAU, or ABETA 42?
- Is the ABETA 40/42 ratio different between different APOE groups?
- Are higher tTAU or pTAU levels associated with lower cognitive scores?
- Which biomarker best predicts cognitive decline?

Notes from the team:

- Notes here

Questions for TAs

- None yet, we are good so far!