Principal Investigator

First Name: Suzanne
Last Name: Hendrix
Degree: PhD
Primary Affiliation: Pentara Corporation
E-mail: shendrix@pentara.com
State or Province: UT
Country: United States

General Information

Key Personnel (other than PI):
First Name: Caleb
Last name: Dayley
Degree: MSc
Primary Affiliation: Pentara Corporation
SCOPUS ID:
Requires Data Access? Yes

First Name: Daniel
Last name: Smith
Degree: MS, BS
Primary Affiliation: Pentara Corporation
SCOPUS ID:
Requires Data Access? Yes

First Name: Garrett
Last name: Duncan
Degree: MS
Primary Affiliation: Pentara Corporation
SCOPUS ID:
Requires Data Access? Yes

First Name: Katelyn
Last name: Miller
Degree: MS
Primary Affiliation: Pentara Corporation
SCOPUS ID:
Requires Data Access? Yes

First Name: Jason
Last name: Cook
Degree: MS
Primary Affiliation: Pentara Corporation
SCOPUS ID:
Requires Data Access? Yes

First Name: Caitlin
Last name: McHugh
Degree: PhD
Primary Affiliation: Alzheimer's Disease Data Initiative
SCOPUS ID:
Requires Data Access? Yes

Are external grants or funds being used to support this research?: External grants or funds are being used to support this research.
Project Funding Source: Alzheimer's Disease Data Initiative
How did you learn about the YODA Project?: Colleague

Conflict of Interest

https://yoda.yale.edu/wp-content/uploads/2025/06/Conflict-of-interest-for-Suzanne-Hendrix.pdf
https://yoda.yale.edu/wp-content/uploads/2025/06/Conflict-of-interest-for-Caleb-Dayley.pdf
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https://yoda.yale.edu/wp-content/uploads/2025/06/COI-FORM-CM.pdf

Certification

Certification: All information is complete; I (PI) am responsible for the research; data will not be used to support litigious/commercial aims.
Data Use Agreement Training: As the Principal Investigator of this study, I certify that I have completed the YODA Project Data Use Agreement Training

1. NCT00574132 - ELN115727-301 - A Phase 3, Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group, Efficacy and Safety Trial of Bapineuzumab (AAB-001, ELN115727) In Patients With Mild to Moderate Alzheimer's Disease Who Are Apolipoprotein E4 Non-Carriers
2. NCT00575055 - ELN115727-302 - A Phase 3, Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group, Efficacy and Safety Trial of Bapineuzumab (AAB-001, ELN115727) In Patients With Mild to Moderate Alzheimer's Disease Who Are Apolipoprotein E4 Carriers

What type of data are you looking for?: Individual Participant-Level Data, which includes Full CSR and all supporting documentation

Research Proposal

Project Title

Alzheimer's Disease (AD) Placebo Data Harmonization for Future AD Data Initiative/Vivli Challenge

Narrative Summary:

The proposed project will combine and standardize data from the placebo groups of several Phase 3 clinical trials focused on Alzheimer's disease (AD). These efforts will involve working with two types of standardized datasets commonly used in clinical research: Study Data Tabulation Model (SDTM) files, which organize raw clinical trial data, and Analysis Data Model (ADaM) files, which are prepared to support statistical analysis. Both formats are used to meet FDA requirements. The project will include harmonizing the structure and content of these datasets by standardizing variables such as demographic information and disease-specific measurements. The end goal is to make the data from different studies stackable, meaning they can be merged into a single, consistent file. The resulting harmonized dataset, will be available to researchers.

Scientific Abstract:

Background: Alzheimer's disease (AD) is a progressive brain disorder that affects memory, thinking, and behavior in desperate of new treatment. A harmonized and analysis-ready placebo participant dataset would provide valuable information such as disease progression to researchers to inform their clinical trial design.
Objectives: To generate a single analyzable dataset comprised of placebo-arm data from a number of Alzheimer's
Study Design: Harmonizing and standardizing placebo participant data across different phase 3 AD clinical trials.
Participants: The placebo participants across difference Phase 3 AD trials
Primary and Secondary Outcome Measure(s): As the proposed research aims to generate an analyzable, aggregate dataset, we will focus on standardizing several commonly used primary outcomes. These elements will be standardized to SDTM, but otherwise not altered. The primary clinical outcomes we are interested in including are: ADAS-Cog, ADCS-ADL, MMSE, NPI, CDR-sb
Statistical Analysis: All studies will then have their data stacked into a singular ADaM dataset. Specifically, the following will be standardized across all visits to help facilitate analysis of the data. 1. Visit Windowing, 2. Standardization of Outcome Labels, 3. Standardization of Outcome Measurements, 4. Categorization of Related Outcomes, 5. Redefinition of Baseline Measurements, 6. Standardization of Analysis Day (Reference Day)

Brief Project Background and Statement of Project Significance:

The proposed project will harmonize placebo-patient data from several Alzheimer's disease phase 3 clinical trials. The efforts include parsing SDTM and ADaM files, standardizing demographic and disease-specific variables, and making the files 'stackable' so that a permissioned researcher can perform analysis on a single file that comprises several clinical trials. The combined, harmonized placebo-arm trial data will be made permissibly accessible to
researchers who have applied to participate in a future data challenge. We believe this harmonized file will be a valuable asset to the Alzheimer's research field, enabling scientists to perform analyses quicker, more efficiently, and with higher statistical power to innovate and propel our understanding of Alzheimer's disease and related dementias forward. This analyzable and aggregate dataset generated from this study will also be used to Inform Patient Care Decisions, including: Code, Clinical guidelines, Clinical trial design, Clinical trial patient selection / recruitment, Disease progression.

Specific Aims of the Project:

Aim 1. Map each study into SDTM to ensure standardization. An initial mapping is required so that upon aggregation, data values are formatted and coded in a consistent manner.
Aim 2. Generate a tall format ADaM with one row per participant, per parameter, per visit, with key demographic and baseline characteristics merged into each row. In this format, study data can be stacked together for a single data table including all placebo-arm participants across all harmonized trials.
Aim 3. Transpose the integrated, tall dataset to generate a wide-format file with one row per person per visit. A transposed, wide version of the file is useful for analyses that require one entry per participant. Upon completion of these aims, a harmonized dataset will be made permissibly available via the Vivli platform. To our knowledge, this proposal aims to create one of the largest Alzheimer's disease datasets. The aggregated dataset will enable researchers to perform analyses immediately across trials without having to perform harmonization themselves, and allows them to focus on hypothesis testing, generation, and validation. We believe this dataset will spur innovation and progress in ADRD research.

Study Design:

Other

Study Design Explanation:

all the datasets across different phase 3 AD trails will be standardized into SDTM and ADaM datasets.

What is the purpose of the analysis being proposed? Please select all that apply.

Develop or refine statistical methods

Research on clinical trial methods

Other: To generate a single analyzable dataset comprised of placebo-arm data from a number of Alzheimer's disease phase 3 clinical trials. This dataset will be made available on Vivli platform for qualified researchers to perform analyses immediately across trials without having to perform harmonization themselves, and allows them to focus on hypothesis testing, generation, and validation.

Research Methods

Data Source and Inclusion/Exclusion Criteria to be used to define the patient sample for your study:

Data Source: We are going to pool data (see the following list of phase 3 Alzheimer's disease trails) from Vivli platform with the two phase 3 Alzheimer's disease trial from Yoda, and standardize the data to form an analysis-ready placebo dataset. Trails from Vivli platform including: NCT02245737, NCT02783573, NCT00762411, NCT00905372, NCT00904683, NCT01900665, NCT01035138, NCT02791191, NCT01224106, NCT02670083, NCT03114657, NCT01931566.

Inclusion and exclusion criteria: Only Placebo or control group will be included in this project.

Primary and Secondary Outcome Measure(s) and how they will be categorized/defined for your study:

Since the scope of this project is to make a cross-study, harmonized, placebo participants individual level, analysis ready SDTM and ADaM files, we will not analysis any outcome measures. We will keep the all the key outcomes and their measurement (only standardize the measurements when necessary) for AD clinical research, including:
- Alzheimer's Disease Assessment Scale -- Cognitive Subscale (ADAS-Cog)
- Alzheimer's Disease Cooperative Study -- Activities of Daily Living (ADCS-ADL)
- Mini-Mental State Examination (MMSE)
- Neuropsychiatric Inventory (NPI)
- Clinical Dementia Rating -- Sum of Boxes (CDR-sb)

As assessed at baseline and all relevant post-baseline timepoints, where available. Where available, we request that all individual item level data points are included for each outcome.

Main Predictor/Independent Variable and how it will be categorized/defined for your study:

Wherever available, we aim to have the following baseline/demographic characteristics as independent variables. As with the primary outcomes, these variables will only be altered to adhere to the SDTM format (if not already in SDTM) but otherwise remain unaltered:
- Smoking/Alcohol History
- Cerebrospinal Fluid (CSF) Biomarkers (Amyloid-Beta40, Amyloid-Beta42, Total Tau, Ptau) and Assay Types for each
- Plasma Biomarkers (Amyloid-Beta40, Amyloid-Beta42, Total Tau, Ptau) and Assay Types for each
- Magnetic Resonance Imaging (MRI) Volumes (Hippocampal, Whole Brain, Ventricular Volume) corrected for intracranial volume (or just include intracranial volume as a variable)
- Cholinesterase Inhibitor/Memantine Use at Baseline

- APOE4 Status
- Education
- Race
- Sex
- Ethnicity
- Baseline Clinical Outcome Scores
- Baseline NPI (item level)
- Baseline MMSE

Where relevant and available, we will consider baseline and post-baseline measurements.

Other Variables of Interest that will be used in your analysis and how they will be categorized/defined for your study:

Other Variables of Interest
Other variables that we would like to have included in the data are:

- Study ID
- Subject Number
- Assigned Treatment (should be placebo for all data but we would still like to have it as a reference)
- Visit
- Visit Date
- Treatment Start Date

Statistical Analysis Plan:

As studies become available, each study will have the data of interest be standardized into an SDTM format strictly following Clinical Data Interchange Standards Consortium (CDISC) standards using the most recent SDTM implementation guide. These datasets will contain all data as given in the raw data or SDTM datasets as provided by each study. All studies selected are phase 3 trials completed after 2010.

All studies will then have their data stacked into a singular ADaM dataset. Specifically, the following will be standardized across all visits to help facilitate analysis of the data:

1. Visit Windowing
A harmonized visit windowing strategy will be applied across all studies. Study protocols will be reviewed to define visit windows that align with the timing and structure of the data in each trial, ensuring comparability across datasets.

2. Standardization of Outcome Labels
Clinical outcome labels will be standardized to ensure that identical outcomes across studies are consistently named and can be accurately grouped for analysis. This step facilitates cross-study comparisons and pooled analyses.

3. Standardization of Outcome Measurements
In addition to standardize the labels of different outcomes within the final ADaM datset, work will be done to help standardize the outcomes themselves to make the studies as comparable as possible. For example, the ADAS-Cog13 might be imputed using the results from the ADAS-Cog11 within studies in which not all 13 items for the ADAS-Cog13 are available.

4. Categorization of Related Outcomes
Outcomes that are similar but not identical (e.g., ADAS-Cog11 vs. ADAS-Cog13) will be grouped into broader parameter categories. This allows for meaningful classification while preserving the distinctions between closely related measurements.

5. Redefinition of Baseline Measurements
A consistent approach to defining baseline values will be implemented across studies. Each protocol will be examined to determine the most appropriate and comparable method for deriving baseline

measurements for key outcomes.

6. Standardization of Analysis Day (Reference Day)
The definition of "Day 1" or the reference day for baseline will be standardized across all studies to ensure uniformity in the calculation of analysis days. This is critical for accurate temporal alignment of data during longitudinal analyses.

Many of these decisions will be finalized after seeing the availability of different visits and outcomes within each study.

Software Used:

I am not analyzing participant-level data / plan to use another secure data sharing platform

Project Timeline:

Target Analysis Start Date
10/29/25
Estimated Analysis Completion Date
10/29/26

Dissemination Plan:

After standardization, the data will be made requestable to all those participating in the Future AD Data Initiative/Vivli data challenge. The governance for making the harmonized data available would be governed by the IRP. Data Contributor review would be skipped in this instance as that preferred approach. The findings and results from the future data challenge will be published according to the publication requirements outlined in the Data Use Agreements.