AlzPED: A New Data Resource for Improving the Rigor, Transparency, Reproducibility and Translation of Alzheimer's Disease Preclinical Research

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BACKGROUND

One of the major challenges to the successful development of therapies for Alzheimer's disease (AD) is the poor translation of preclinical efficacy from animal models to the clinic. A number of key factors have been identified as contributors to the unsuccessful translation of therapeutic efficacy, these include:

- the failure of the models to fully recapitulate human AD,
- poor rigor, study design and data analysis, insufficient attention given to using a standard set of "best practices",
- failure to match outcome measures used in preclinical animal studies and clinical studies,
- poor reproducibility of published data, and
- publication bias in favor of reporting positive findings.

To address this challenge and ameliorate some of the factors contributing to the preclinical to clinical gap in the development of AD therapies, several advisory meetings and workshops including the National Institutes of Health (NIH) AD Summits in 2012 and 2015 were held. In response to expert recommendations from these meetings, the National Institute on Aging (NIA) and the NIH Library have created an open science knowledge portal – the **Alzheimer's Preclinical Efficacy Database** or **AlzPED**. Through the following capabilities, AlzPED is intended to guide the development and implementation of strategies and recommendations for standardized best practices for the rigorous preclinical testing of AD candidate therapeutics:

1 Publicly available database of preclinical efficacy studies that houses experimental designs and analyses of **positive and negative data** to overcome publication bias.

2 Knowledge platform for data sharing, mining and analysis of experimental details, designs, data and methods relating to the preclinical testing of candidate therapeutic agents in AD animal models.

3 Database identifying critical experimental design elements and methodology missing from studies, making them susceptible to misinterpretation and reducing their reproducibility and translational value.

CAPABILITIES AND SCOPE

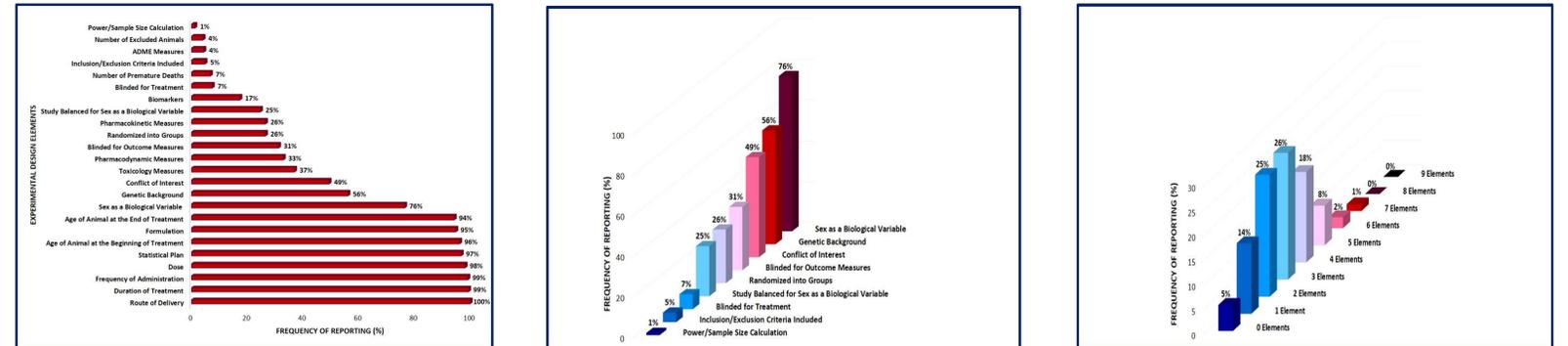**AlzPED** has the following capabilities:

- Provides researchers and information scientists with a facile way to survey existing AD preclinical therapy development literature and raise awareness about the elements of rigorous study design and requirements for transparent reporting.

- Currently hosts curated summaries from **720** preclinical efficacy studies published between 2000 and 2018.

- Influences the development and implementation of reproducibility strategies including guidelines for standardized best practices for the rigorous preclinical testing of AD candidate therapeutics.

- Provides search capability across relevant translational criteria data sets and external databases:
  - Therapy Type
  - Therapeutic Agent
  - Therapeutic Target
  - Animal Model
  - Principal Investigator
  - Funding Source
  - Related Publications (PubMed)
  - Therapeutic Agents (PubChem and Drug Bank)
  - Therapeutic Targets (Open Targets and Pharos)
  - Animal Model (Alzforum)
  - Related Clinical Trials (ClinicalTrials.gov)
  - Related Patents (Google Patents and USTPO)

- Provides funding agencies with a tool for enforcement of requirements for transparent reporting and rigorous study design.

- Provides a platform for creating **citable reports/preprints** of **unpublished studies**, including studies with **negative data**.

- **Reports on the rigor of each study by summarizing the elements of experimental design.**

ANALYTICS

A CURATED RECORD IN AlzPED


ELEMENTS OF EXPERIMENTAL DESIGN

LEFT: Frequency of reporting the 24 recommended elements of experimental design that improve the reproducibility and translational value of preclinical efficacy research. **CENTER:** Frequency of reporting the 9 core elements of experimental design that are critical for ensuring scientific rigor of preclinical efficacy research. **RIGHT:** Trends in the reporting of the 9 core elements of experimental design. Data are presented as percentages calculated from 720 published preclinical efficacy studies curated in AlzPED. The studies were published between 2000 and 2018.
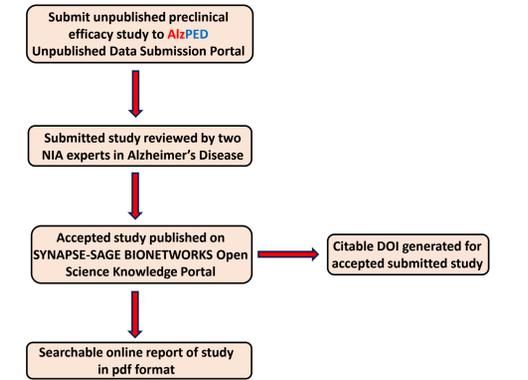
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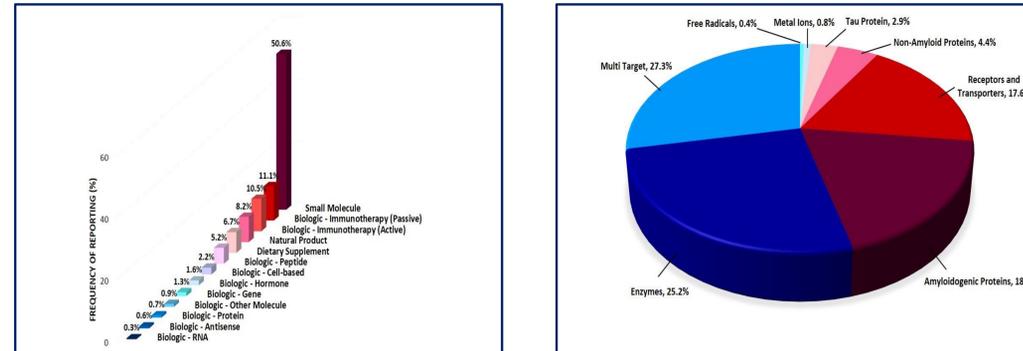
LEFT: 640 therapeutic agents are catalogued in 13 categories. **RIGHT:** 145 therapeutic targets are catalogued in 7 categories. Data are presented as percentages calculated from 720 published preclinical efficacy studies curated in AlzPED.

OUTCOME MEASURES
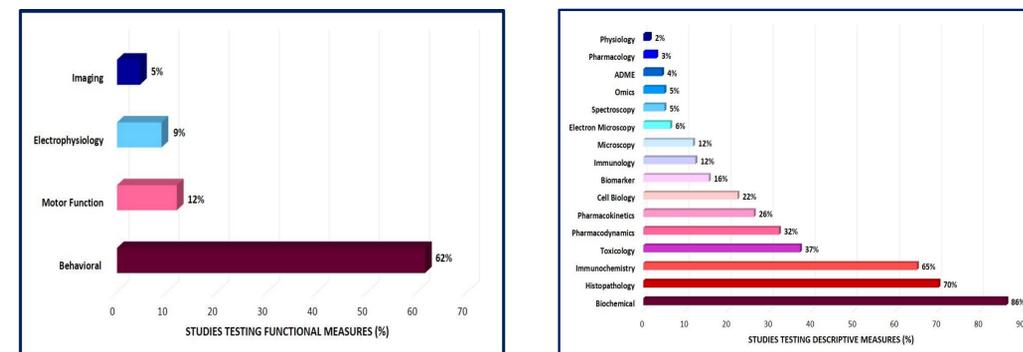
LEFT: Frequency of reporting functional outcome measures. **RIGHT:** Frequency of reporting descriptive outcome measures. Data are presented as percentages calculated from 720 published preclinical efficacy studies curated in AlzPED.

UNPUBLISHED STUDY SUBMISSION PORTAL

Submit unpublished preclinical efficacy study to **AlzPED** Unpublished Data Submission Portal

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Submitted study reviewed by two NIA experts in Alzheimer's Disease

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Accepted study published on SYNAPSE-SAGE BIONETWORKS Open Science Knowledge Portal → Citable DOI generated for accepted submitted study

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Searchable online report of study in pdf format

Overview of the submission process for unpublished data. The DOI provided is citable in grant applications and peer-reviewed publications

SUMMARY

In summary, **AlzPED**:

- Provides free access to information pertaining to experimental designs, AD animal models, therapeutic agents and targets, outcome measures, and principal findings from preclinical studies.

- Serves as a platform for reporting unpublished negative findings to mitigate publication bias that favors reporting of positive findings.

- Is a resource for researchers to survey existing preclinical therapy developments, understand the requirements of rigorous study design, transparent reporting, and plan preclinical intervention studies.

- Provides funding agencies with a tool for the enforcement of requirements for transparent reporting and rigorous study design.