A major challenge to the successful development of therapies for Alzheimer's disease (AD) is the poor translation of preclinical efficacy from animal models to the clinic. Key contributing factors to the unsuccessful translation of therapeutic efficacy include:

- the failure of animal models to fully recapitulate human AD
- poor rigor in study design, methodology and data analysis
- 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 and under reporting negative findings.

To address key factors contributing to the unsuccessful translation of preclinical efficacy from animal models to the clinic, several recent meetings and workshops held between 1996 and 2019. 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 Disease Preclinical Efficacy Database (AlzPED) – to improve the scientific rigor of preclinical AD research.

AlzPED provides a platform for creating reports/preprints for Alzheimer's Disease Preclinical Efficacy Database identifying critical experimental design elements critical for scientific rigor, and reproducibility. AlzPED serves as a platform for reporting unpublished studies. A Rigor Report Card consisting of a standardized set of 24 experimental design elements recommended by expert advisory groups. Right: Graph shows the percentage of studies reporting the standardized set of 24 experimental design elements. The bars represent values for each design element reporting of positive findings.

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 critical experimental design elements and outcomes achieved in response to the therapeutic agent tested.
- Includes a database categorizing 1019 novel therapeutic agents into 16 distinct categories – therapeutics, animal model, therapeutic target, principal investigator, related clinical trials, and funding source.
- Influences the development and implementation of reproducibility strategies by providing 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.

Therapeutic Target (225 targets)

Therapeutic Agent (1019 agents)

Animal Model (Alzforum)

Animal Model (195 models)

Therapeutic Therapeutics (225 targets)

Funding Source (662 sources)

Related Patents (Google Patents and USPTO)

Published and Unpublished Data Submission Platform

Published data is extracted from the scientific literature and curated in 14 categories – bibliographic, pharmacological, animal model, experimental design and methodology missing, and outcomes. Unpublished data (positive and negative) will be obtained directly from researchers. Aitable (DOL) will be generated for an accepted study. A downloadable PDF will be available on the NIA Knowledge Portal. A diverse array of therapeutic agents and targets are cataloged in AlzPED. Curated studies provide an individual snapshot of the measures tested and outcomes achieved in response to the therapeutic agent tested. AlzPED provides a 24-element outcome measure that is categorized either functional or descriptive. Data is presented as percentage reported, calculated from 1172 published preclinical studies curated to AlzPED.

Current hosts curated summaries from 1172 preclinical studies published between 1996 and 2019. Analysis of more than 1100 curated studies demonstrates serious discrepancies in reporting critical elements of study design and methodology that diminish the scientific rigor, reproducibility and predictive value of preclinical therapeutic studies done in AD animal models.

CONCLUSIONS

- Analysis of more than 1200 curated studies demonstrated serious discrepancies in reporting critical elements of study design and methodology that diminish the scientific rigor, reproducibility and predictive value of preclinical therapeutic studies done in AD animal models.
- Adoption of a standardized set of best practices is very likely to improve the predictive validity of preclinical studies done in AD animal models. This measure is likely to promote the effectiveness of translation of preclinical drug testing data to the clinic.
- AlzPED serves as a platform for reporting unpublished negative findings to mitigate publication bias that favors reporting of positive findings.