# Alzheimer's Preclinical Efficacy Database (AlzPED): Optimizing the Scientific Rigor and Translatability of Preclinical Research in Alzheimer's Disease

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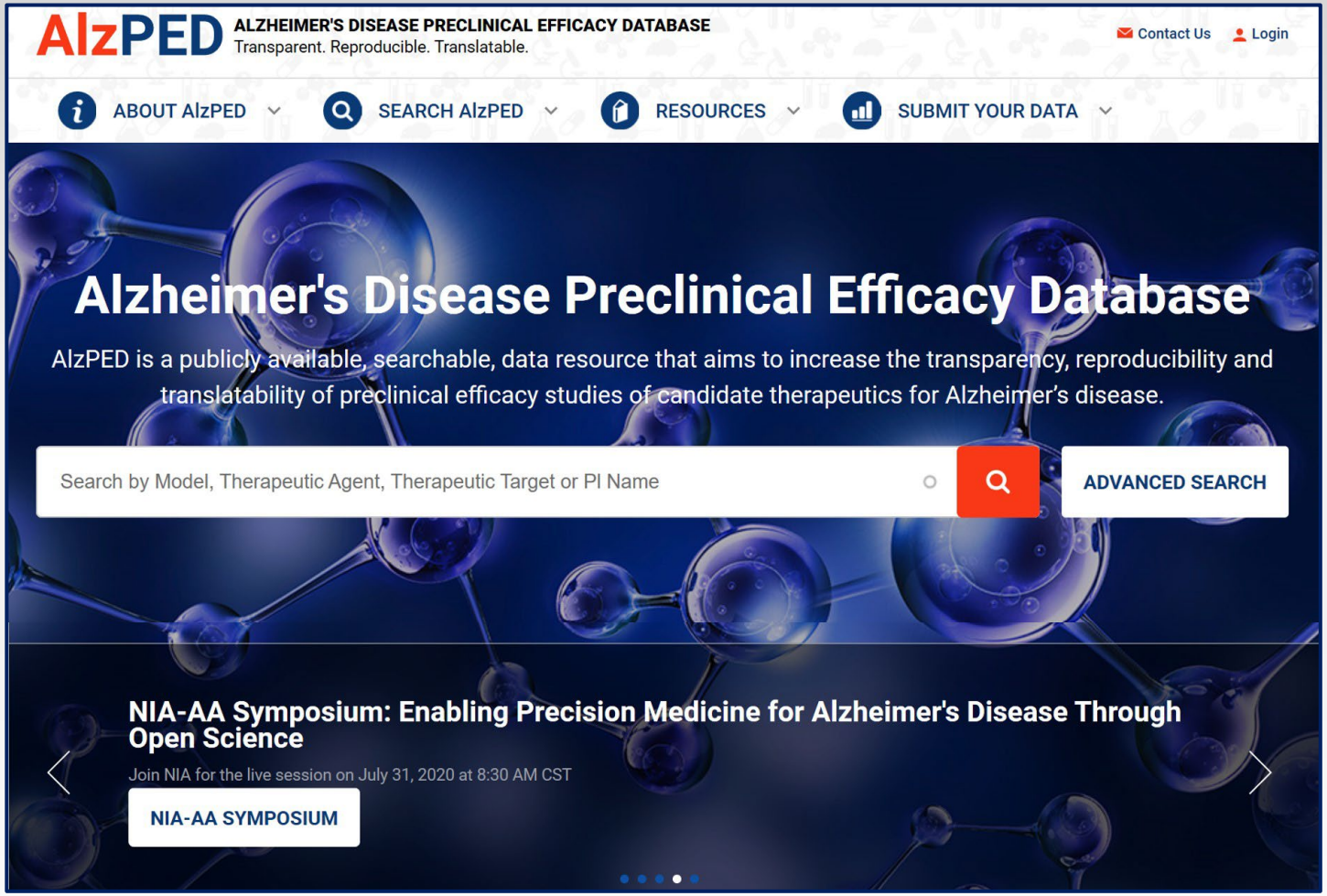
# Background: Recommendations from 2015 NIA AD Summit

## Increasing the Predictive Value and Enabling Transparent and Reproducible Preclinical Efficacy Testing in AD Animal Models

- ❑ Develop a publicly available database of preclinical therapeutic studies that incorporates experimental details of positive and negative data for the AD scientific community




https://alzped.nia.nih.gov/

- Hosts curated summaries of ~1200 published studies (1996-2020) and provides easy access to information on study design methods, animal models, therapeutic agents, therapeutic targets, outcomes, patents and related clinical trials.
- Provides a platform for creating citable reports/preprints of unpublished studies, including studies with negative findings.
- Report on the rigor of each curated study by summarizing the elements of experimental design and identifying critical elements of experimental design missing from the study.

# AlzPED Monitors Rigor in Study Design for Each Curated Study

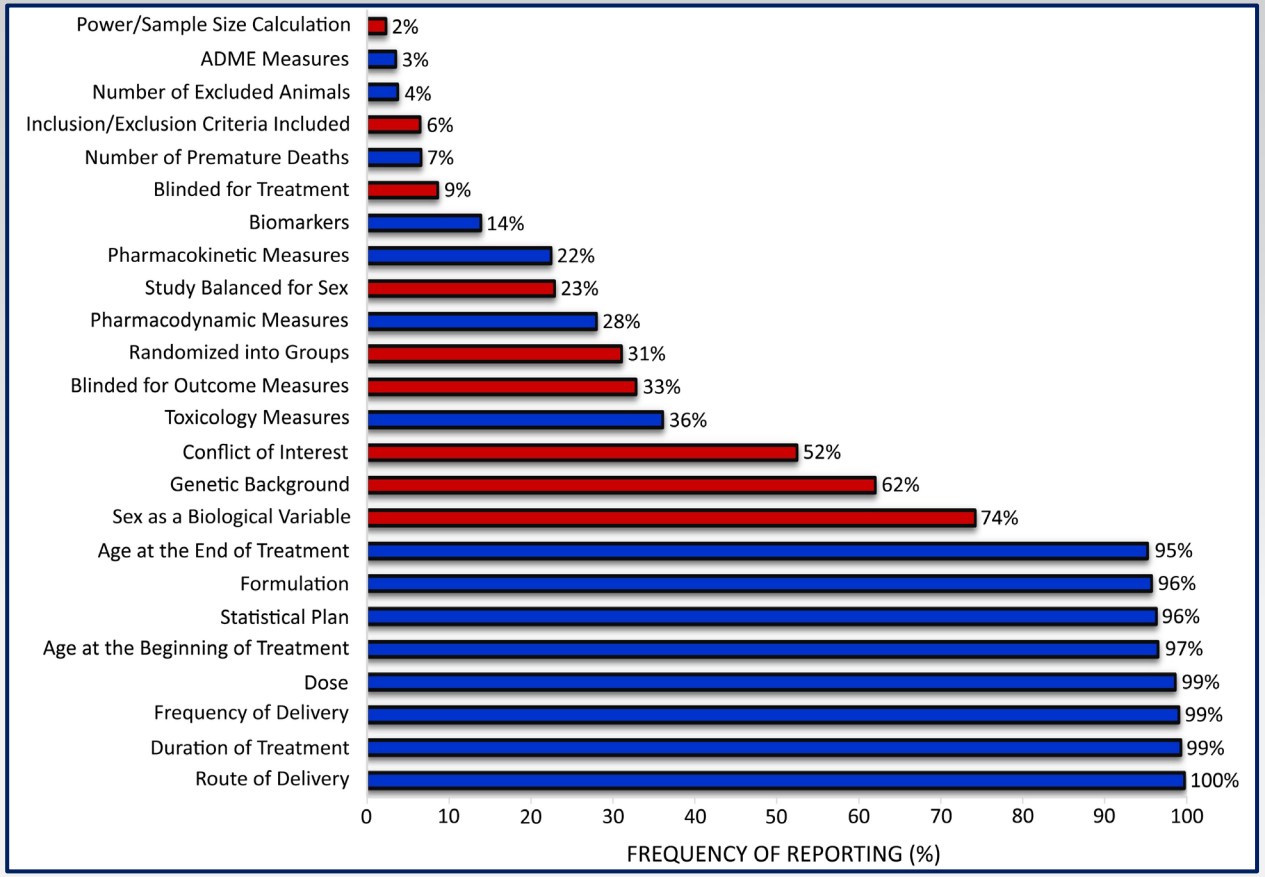
## Experimental Design *Rigor Report Card*

**Is the following information reported in the study?:**

| | |
|---|---|
| ✓ Power/Sample Size Calculation | ✓ Randomized into Groups |
| ✓ Blinded for Treatment | ✓ Blinded for Outcome Measures |
| ✗ Pharmacokinetic Measures | ✗ Pharmacodynamic Measures |
| ✗ Toxicology Measures | ✗ ADME Measures |
| ✗ Biomarkers | ✓ Dose |
| ✓ Formulation | ✓ Route of Delivery |
| ✓ Duration of Treatment | ✓ Frequency of Administration |
| ✓ Age of Animal at the Beginning of Treatment | ✓ Age of Animal at the End of Treatment |
| ✓ Sex as a Biological Variable | ✓ Study Balanced for Sex as a Biological Variable |
| ✗ Number of Premature Deaths | ✓ Number of Excluded Animals |
| ✓ Statistical Plan | ✓ Genetic Background |
| ✓ Inclusion/Exclusion Criteria Included | ✓ Conflict of Interest |

AlzPED is designed to monitor the scientific rigor of curated studies with a "Rigor Report Card" consisting of a standardized set of 24 experimental design elements recommended by expert advisory groups.

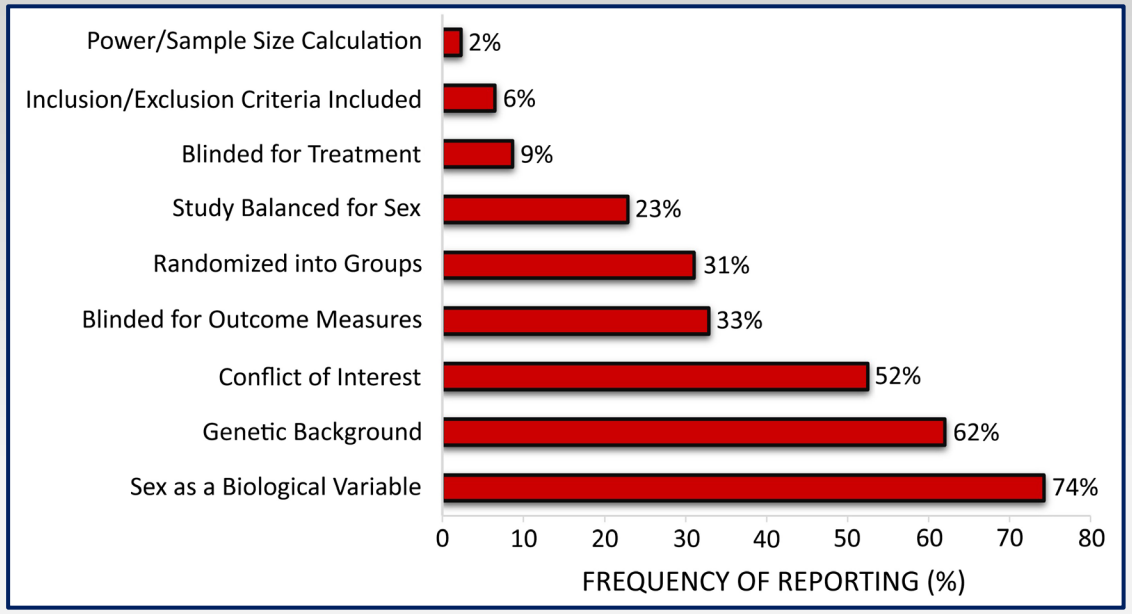
# Critical Elements of Experimental Design are Under-Reported



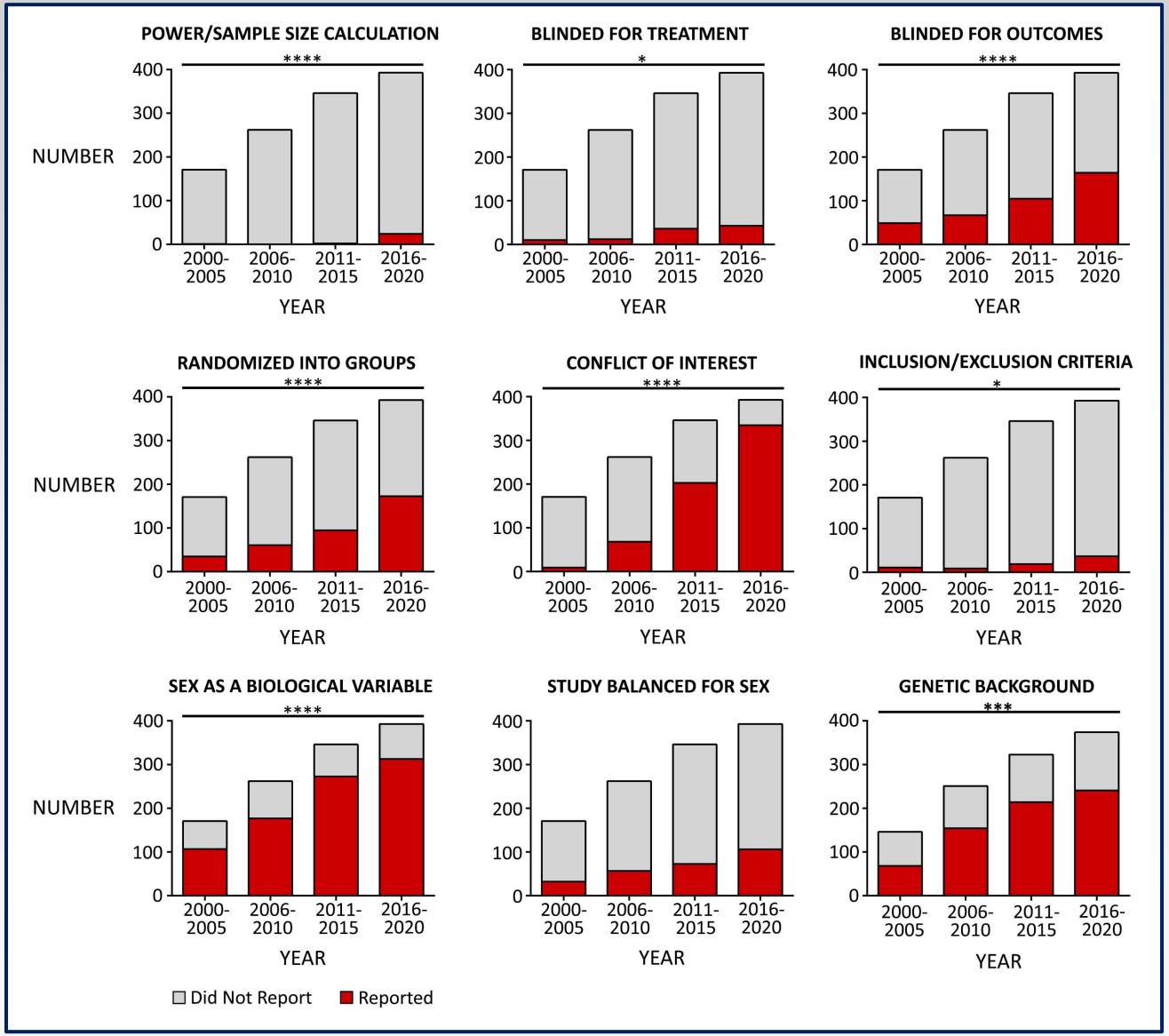

Graph shows the percentage of studies reporting the standardized set of 24 experimental design elements, calculated from 1172 published preclinical studies curated to AlzPED. The red bars represent the 9 core design elements critical for scientific rigor and reproducibility. Detailed Analytics Summary is available on the AlzPED Analytics page.

# Reporting Trends In The 9 Core Design Elements

9 core design elements are derived from Shineman et al., 2011, Landis et al., 2012, Snyder et al., 2016 and ARRIVE guidelines.




Graphs show reporting trends for the 9 critical core experimental design elements evaluated over 5-year spans from 2000 to 2020. Data analyzed using Chi square test; *p<0.05, ***p<0.001, ****p<0.0001. Data presented as number that reported Vs number that did not report core experimental design elements, calculated from 171, 262, 346 and 393 curated studies published between 2000-2005, 2006-2010, 2011-2015 and 2016-2020 respectively.



# Conclusions

- Analysis of ~1200 curated studies demonstrates serious deficiencies in reporting critical elements of study design and methodology which 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 effective translation of preclinical drug testing data to the clinic.

- Federal funding agencies, private foundations and scientific journal publishers must continue to collaborate on this issue and enforce a standardized set of best practices, so that funded and published research are sufficiently rigorous, transparent and reproducible.

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