

# Critical Path for Alzheimer's Disease (CPAD) consortium's vision for an aggregated, standardized, and actionable global Alzheimer disease clinical trial database

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## Background

Integrated and standardized clinical research data can catalyze biomedical discoveries and optimize clinical drug development. In 2011, the Critical Path for Alzheimer's Disease (CPAD) consortium (formerly the Coalition Against Major Diseases, CAMD) developed the first publicly-available Alzheimer disease (AD) database of CDISC-standardized clinical trial data ([Critical Path Institute Online Data Repository](#), CODR [Ref. 1]). This regulatory-compliant standardization of data provides a basis for the continued evolution of this unique AD database, which in turn supports the continuous development of solutions for drug development.

The Global Alzheimer's Association Integrated Network (GAAIN; [Ref. 2]), funded by the Alzheimer's Association, facilitated the creation of a portal enabling the sharing of key metadata (derived from roughly 500,000 subjects), enabling qualified researchers to apply for access to individual AD databases across 43 study repositories. Since 2016, the [Critical Path Institute Online Data Repository](#) (Ref. 1) is linked to the GAAIN portal together with 42 other individual partners; additional important repositories are hosted individually:

- National Alzheimer's Coordinating Center (NACC; [Ref. 3])
- Dementias Platform UK (Ref. 4)
- National Institute on Aging Genetics of Alzheimer's Disease Data Storage Site (NIAGADS; [Ref. 5])
- National Cell Repository for Alzheimer's Disease (NCRAD; [Ref. 6])
- Oregon Health & Science University Brain Institute's Layton Aging & Alzheimer's Disease Center database (Ref. 7).

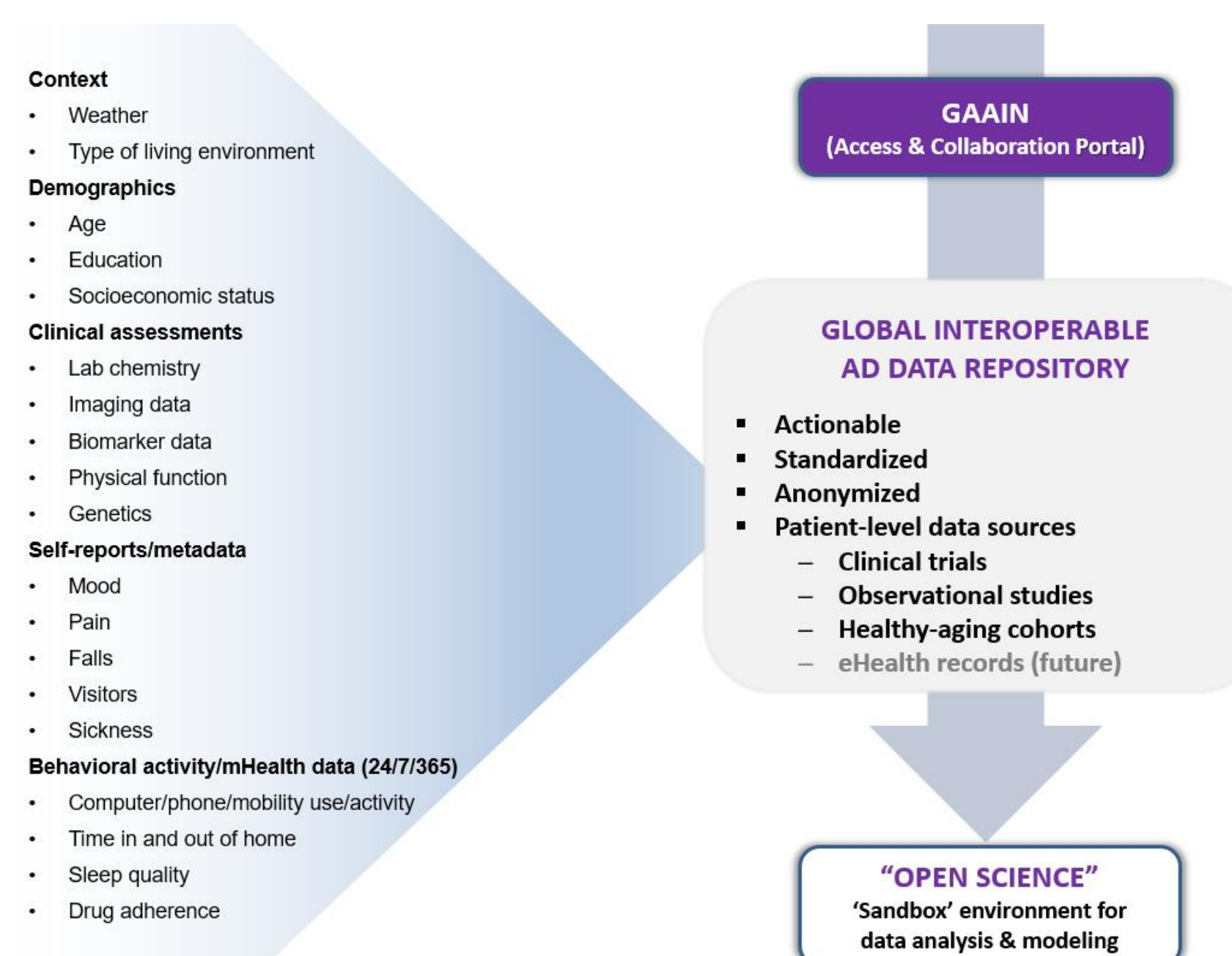
The majority of these databases have not been curated to CDISC standards, a critical limiting step in aggregating data across different study sources and a requirement for regulatory submittal.

## Objectives

Foment integration within the community of data centers and consortia by facilitating the creation of a fully-integrated, and actionable (CDISC standardized) [Global Interoperable AD Data Repository](#) (Figure 1).

- Ensure that studies used to support our understanding of AD progression have informed consents that do not inhibit data sharing in compliance with applicable local regulations
- Collect data using CDISC standards to ensure that all data can be integrated into a standardized, actionable database, minimizing the need for remapping
- Reinforce data/sample sharing principles established by the Collaboration for Alzheimer's Prevention (CAP) (Ref. 8)
- Provide a mechanism to enable qualified researchers an "Open Science" environment for data analysis and modeling

**Figure 1** Vision of a fully-integrated, actionable, and CDISC standardized Global Interoperable AD Data Repository



## Methods

As a nonprofit, pre-competitive consortium of the Critical Path Institute (<https://c-path.org/>), CPAD convenes diverse stakeholders (e.g., academia, advocacy groups, industry, and regulators) to create new Drug Development Tools (DDTs) accelerating the delivery of treatments for AD. The FDA, in particular the Center for Drug Evaluation and Research (CDER), is engaged in providing input to CPAD's strategy. CPAD has aligned around a new vision with focus on:

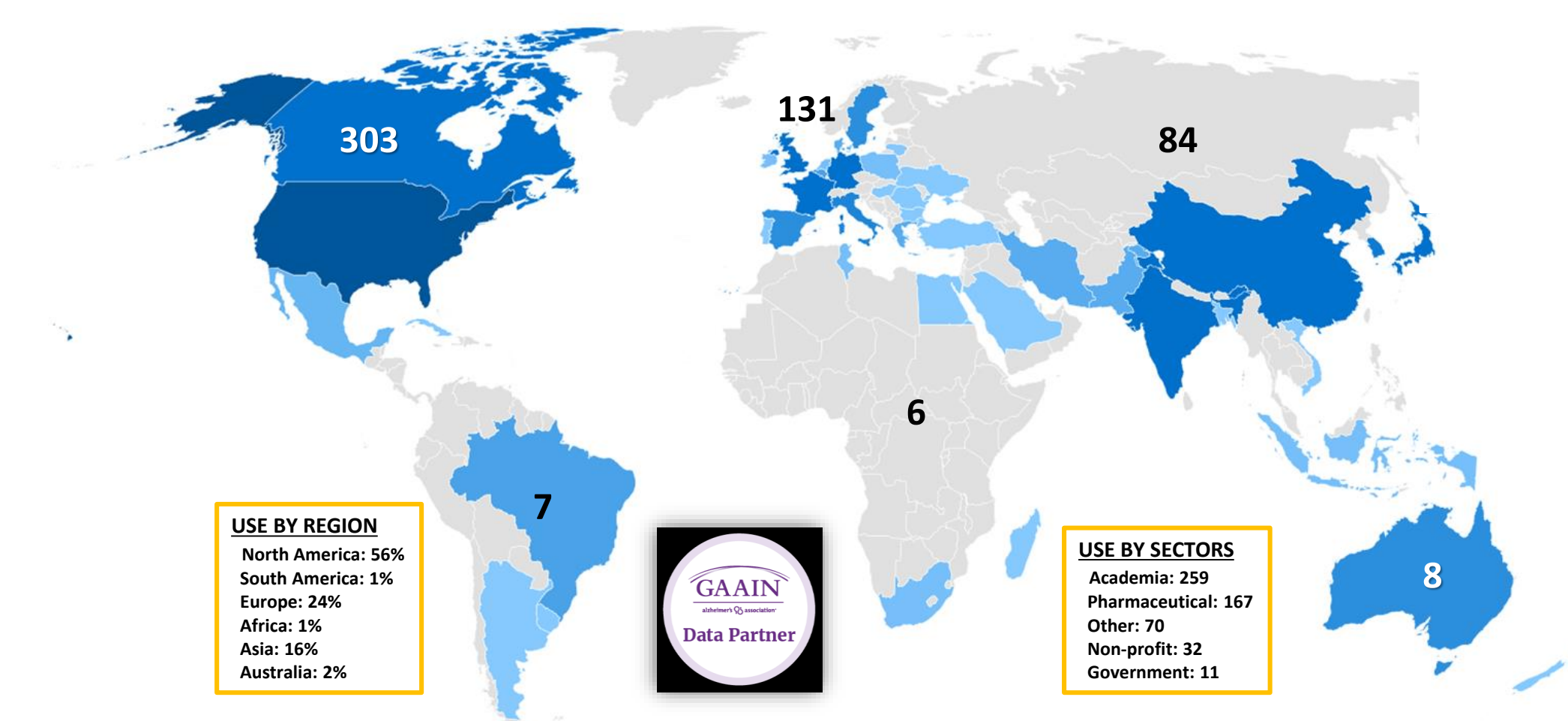
- The creation of a sustainable, interoperable, curated data repository for AD trials that is linked to GAAIN (Ref. 2)
- Expansion of the CPAD database to include earlier stages of the disease, and to augment the existing regulatory-accepted models with contemporary studies that include relevant biomarker dimensions to support the quantitative development of the *NIA-AA AD Research Framework* (Ref. 9)
- Development of comprehensive quantitative descriptions of disease progression as regulatory-accepted Drug Development Tools for clinical trial execution
- Continued planning and collection of data, sharing of information and tools, etc., which can inform appropriate regulatory science-based strategies in support of drug development
- Creation of infrastructure for handling integration of data from newer technologies that use biometric monitoring measurements (e.g., medication adherence, computer use, mobility and sleep analysis) as potential metrics related to activities of daily living (Ref. 10).

## Results

CPAD's anonymized, patient-level database consists of 28 standardized studies across all stages of the disease integrated into a single dataset of 6,955 individual subjects. As of September 30, 2018, CPAD's patient-level database has been utilized by 569 qualified applicants (Figure 2).

A concise addendum to standard informed consent forms has been created to enable patients to share their data and samples for future research (Ref. 11).

**Figure 2** CPAD database utilization (as of September 30, 2018)



## Results (continued)

In association with Alzheimer's Association, philanthropic organizations, and other stakeholders, a framework is being developed (*AD Data Initiative*) to create a repository of clinical data brought together in a standardized format to enable "open science" data analysis and modeling of fully-anonymized patient-level data, accessible by qualified researchers.

## Conclusions

A [Global Interoperable AD Data Repository](#) that is standardized and actionable, together with the potential to link to other observational studies and healthy aging cohorts, will allow the development of a quantitative understanding of disease progression and biomarker dynamics across the AD continuum. Quantitative medicine approaches applied to the AD continuum in an "Open Science" environment, will be a catalyst for AD research and optimize drug development.

1. Critical Path Institute Online Data Repository (CODR): <https://codr.c-path.org/>
2. Global Alzheimer's Association Integrated Network (GAAIN): <http://www.gaain.org/>
3. National Alzheimer's Coordinating Center (NACC): <https://www.alz.washington.edu/>
4. Dementias Platform UK: <https://www.dementiasplatform.uk/>
5. National Institute on Aging Genetics of Alzheimer's Disease Data Storage Site (NIAGADS): <https://www.niagads.org/>
6. National Cell Repository for Alzheimer's Disease (NCRAD): <https://ncrad.iu.edu/>
7. Oregon Health & Science University (OHSU) Brain Institute's Layton Aging & Alzheimer's Disease Center database: <https://www.ohsu.edu/xd/health/services/brain/getting-treatment/diagnosis/alzheimers-aging-dementia/research-for-researchers/clinical-data-resources.cfm>
8. Wenginger S *et al.* (2016) Collaboration for Alzheimer's Prevention: Principles to guide data and sample sharing in preclinical Alzheimer's disease trials. *Alzheimer's & Dementia* 2016; 12: 631-632. doi: 10.1016/j.jalz.2016.04.001.
9. Jack Jr. *et al.* (2018) NIA-AA Research Framework: Toward a biological definition of Alzheimer's disease. *Alzheimer's & Dementia* 2018; 14: 535-562. doi: 10.1016/j.jalz.2018.02.018.
10. Arnerić SP *et al.* (2017) Biometric monitoring devices for assessing end points in clinical trials: developing an ecosystem. *Nat Rev Drug Discov* 2017 Oct, 16(10): 736. doi: 10.1038/nrd.2017.153
11. Hake AM, *et al.* (2017) Concise informed consent to increase data and biospecimen access may accelerate innovative Alzheimer's disease treatments. *Alzheimer's Dement Transl Res Clin Interv.* 2017 Nov;3(4):536-41.