The Critical Path for Alzheimer's Disease (CPAD) Consortium – Facilitating rapid data and information sharing by establishing a sustainable, integrated, and standardized platform advancing knowledge to enable expedited drug development

CPAD
CRITICAL PATH FOR ALZHEIMER'S DISEASE
CRITICAL PATH INSTITUTE

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Background

In 2008 the Coalition Against Major Diseases (CAMD) was created in response to the U.S. Food and Drug Administration's (FDA) *Critical Path Initiative.* In January 2018, with the consortium's work now exclusively focused on Alzheimer disease (AD), CAMD was rebranded to ***Critical Path for Alzheimer's Disease*** (**CPAD**).

As a nonprofit, pre-competitive consortium of the Critical Path Institute (**Figure 1**), CPAD convenes diverse stakeholders (e.g., academia, advocacy groups, industry, regulators; **Figure 2**) 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.

Figure 1 **Critical Path Institute's (C-Path) consortia in the neurological disorders, drug safety, pediatrics, neonatal health, tuberculosis, and other therapeutic area spaces, as well as Clinical Outcome Assessments, electronic data capture, data standards, and data collaboration**

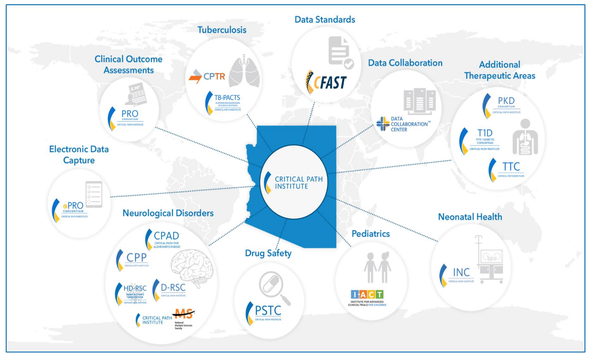
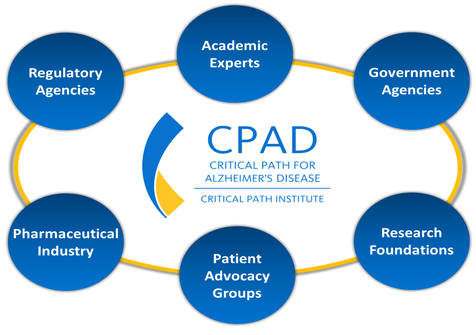
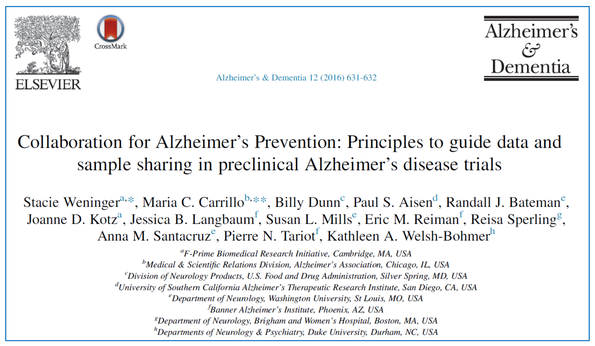


Figure 2 **The CPAD consortium brings together pharmaceutical industry, academia, patient-advocacy groups, government agencies, and regulators**



In 2016, the Collaboration for Alzheimer's Prevention (CAP) established principles to guide data/sample sharing in preclinical AD trials (**Figures 3 and 5**).

Figure 3 **Collaboration for Alzheimer's Prevention (CAP)**



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Collaboration for Alzheimer's Prevention: Principles to guide data and sample sharing in preclinical Alzheimer's disease trials

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Methods

Historically, CPAD's mission has been focused on data sharing, understanding of data, disease modeling, and biomarkers - with many accomplishments, such as:

- Qualification of a Clinical Trial Simulation Tool (FDA and EMA)
- Development of AD CDISC standards (v1.0 and v2.0)
- FDA Letters of Support (for biomarkers)

Efforts of the Collaboration for Alzheimer's Prevention (CAP) (**Figure 3**; **Ref. 1**) are being facilitated by the Fidelity Biosciences Research Initiative (FBRI), the Alzheimer's Association, the National Institutes on Aging, and the U.S. Food and Drug Administration. Focus is on several academic-led prevention trials:

- A4 (Anti-Amyloid Treatment in Asymptomatic Alzheimer's Disease) Study (2/2014 through 12/2020), lead sponsor: Eli Lilly and Company
- DIAN-TU (Dominantly Inherited Alzheimer Network Trials Unit), Washington University
- API (Alzheimer's Prevention Initiative), Banner Alzheimer's Institute
- TOMMORROW, Takeda Pharmaceutical Company Ltd.

CAP has been a forum for academic trial investigators to discuss key issues as these groups plan and implement preclinical AD treatment trials. Discussions focus on (**Ref. 2**):

- Optimal trial designs
- Harmonization of fluid/imaging biomarkers and cognitive endpoints across trials
- Rapid and maximized access and sharing of data/biological samples from preclinical AD trials
- Ensuring that lessons learned are generalized as quickly as possible to inform the entire field

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Results

Partnerships that inform the scientific and regulatory communities to develop sound DDTs are of high importance and have the potential to accelerate the advancement of AD treatments (**Figure 4**). These efforts inform the understanding of the natural history of AD, inform the size and design of future trials, clarify the utility of biomarker and cognitive measurements, and accelerate the evaluation of prevention treatments. With trial sponsors agreeing to CAP's principles for data and sample sharing (**Figure 5**), a close dialogue with CPAD's industry members will widen the spectrum of trial sponsors that adhere to these data sharing principles. This proposed collaboration will allow for:

- The creation of a sustainable, curated data repository for CAP-sponsored AD trials that is linked to **GAAIN** (**Ref. 3**)
- Expansion of the CPAD database to include earlier stages of the disease, and to augment the existing regulatory-approved models with contemporary studies that include biomarkers to support the quantitative development of the *NIA-AA AD Research Framework* (**Ref. 4**)
- 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.

Figure 4 **Collaboration for Alzheimer's Prevention (CAP) and Critical Path for Alzheimer's Disease (CPAD) composition and vision**

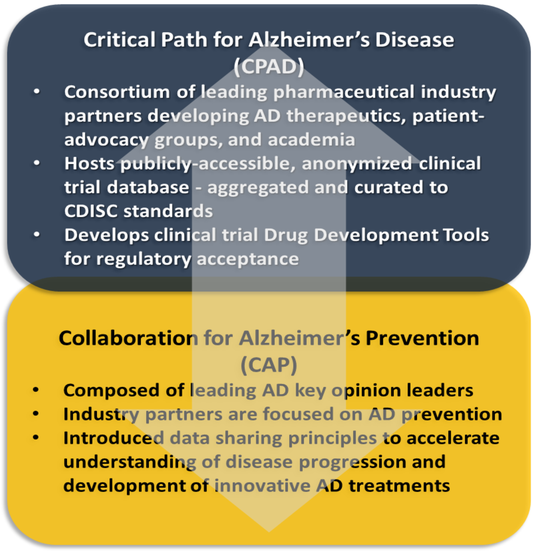

Figure 5 **Collaboration for Alzheimer's Prevention data sharing principles (Ref. 2)**

- **Where possible, standardized data acquisition techniques and assessments should be included to enhance the ability to compare data between trials.**
- **Measurement of multiple potential biomarkers should be included in trial designs to facilitate the identification of biomarkers of disease evolution and treatment response that could be used in future trials.**
- **Screening and pre-randomization baseline data should be made available to the scientific community within 12 months of enrollment completion.**
- **Emerging data from ongoing trials should be made available as soon as possible without compromising trial integrity, as progress in the field will be accelerated greatly by timely access to interim results such as well-characterized longitudinal fluid and imaging biomarker data.**
- **All study data should be made available to the scientific community after the earlier of either regulatory approval of the tested treatment or 18 months after the completion or early termination of the trial.**
- **The first priority for sample use is proper conduct of the study, which includes appropriate retention of samples in sufficient quantities for analyses during ongoing trials as well as for confirmatory testing after trial completion.**
- **Remaining study samples should be made available to the scientific community at the time that the associated data are released.**

Conclusion

Sharing of data and biological samples from preclinical AD trials as early as possible is important to expedite utility of knowledge gained through individual trials toward progressing the field as a whole. Data and samples from preclinical AD trials will help to inform our understanding of the natural history of AD, inform the size and design of future trials, clarify the utility of biomarker and cognitive measurements, and accelerate the evaluation of preclinical treatments for AD.

CAP's efforts are highly consistent with and complementary to CPAD's strength and deep experience in creating data repositories, disease progression models, and DDTs. Leveraging C-Path's existing infrastructure and competencies in data aggregation, CPAD, with a new focus on AD prevention (identifying patients early before the disease has clinically manifested) and early intervention, together with CAP's data sharing principles, will provide the means of efficiently sharing data and learnings with all stakeholders in the community as a driver of change and advancement.

1. Weninger *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.
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