

National Academies of Science

Workshop on Research Priorities for Alzheimer's Disease and Related Dementias

Jeffrey Cummings, MD, ScD_(HC)

Chambers-Grundy Center for Transformative Neuroscience

Department of Brain Health, School of Integrated Health Sciences

University of Nevada Las Vegas (UNLV)



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Research Priorities for Alzheimer Research

- Treatment for my patients with symptoms of Alzheimer's or another neurodegenerative disease
- Preventative treatments for individuals at risk for Alzheimer's or other neurodegenerative diseases
- Drugs and other interventions (lifestyle, devices, stem cells, biologics)

Today

171 trials for Alzheimer drugs

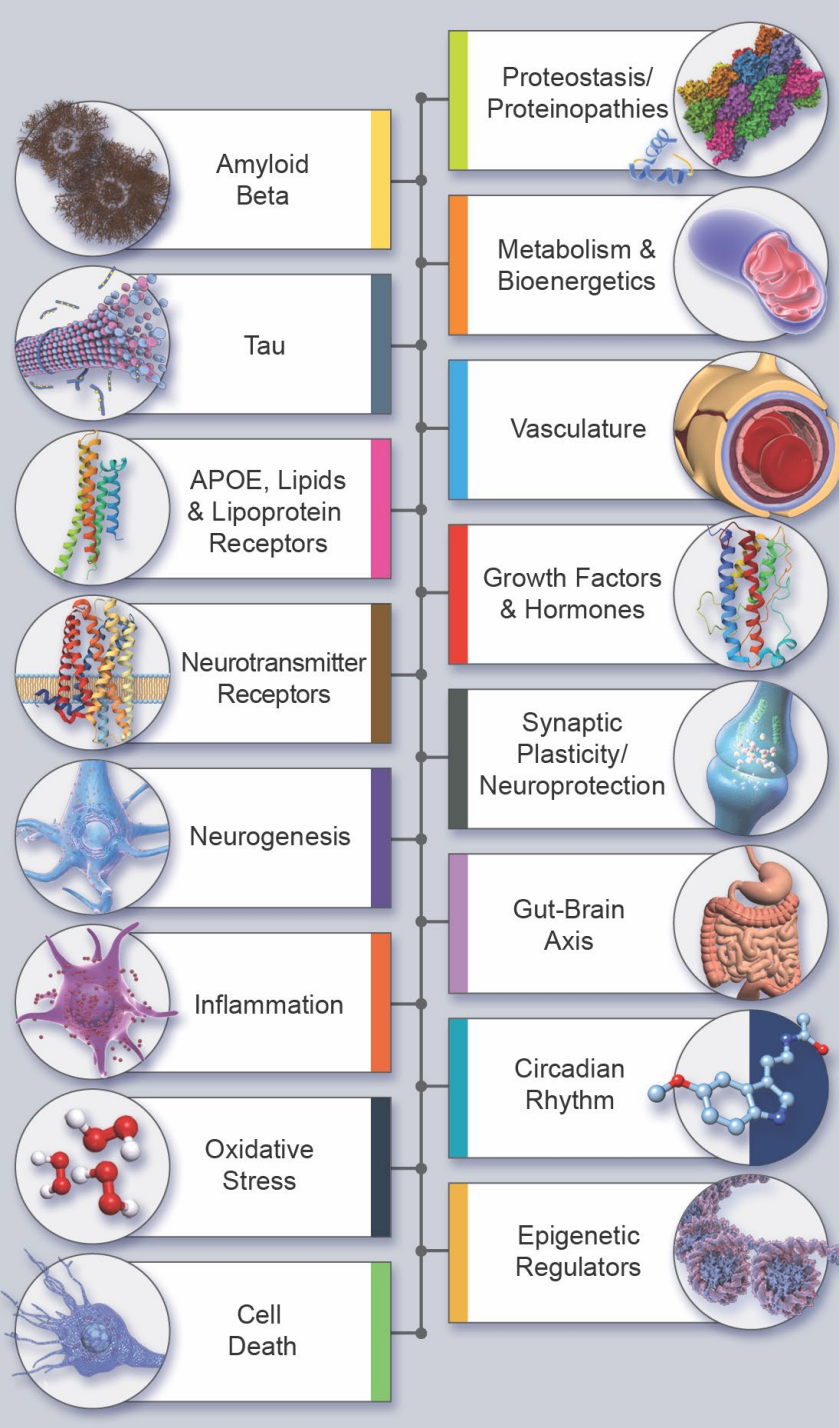
134 drugs being assessed

52,835 participants needed

Drug development takes 13 y (from laboratory to FDA)

Recruitment is the major bottleneck to testing drugs more rapidly

Small changes are not enough; transformation is required to achieve our goals

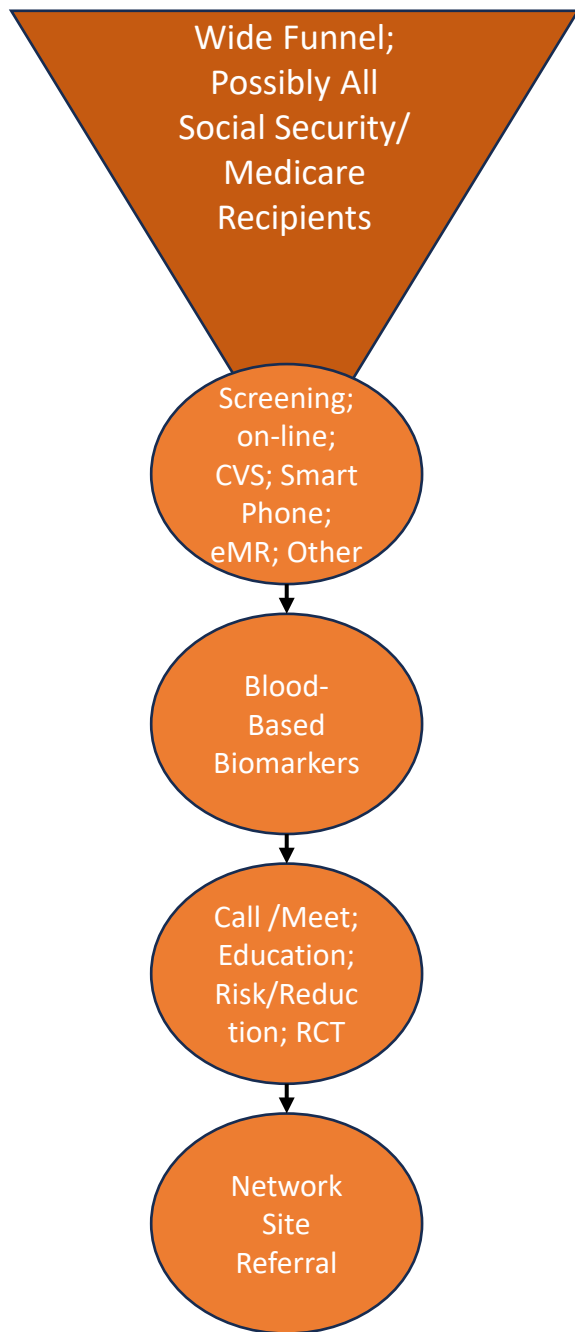


Common Alzheimer's Disease Research Ontology (CADRO)

CADRO

- Recognizes 16 disease processes
- CADRO processes are targets for drug development
- CADRO categories are applicable across neurodegenerative disorders
 - All CADRO processes are objects of AD drug development
 - 20% of the pipeline addresses neuroinflammatory targets
 - 10% of the pipeline addresses synaptic plasticity targets
- Learnings from AD pipeline will generalize
 - Parkinson's disease
 - Dementia with Lewy bodies
 - Frontotemporal dementia
 - Other rare neurodegenerative disorders

Refolo LM, et al. Common Alzheimer's Disease Research Ontology: National Institute on Aging and Alzheimer's Association collaborative project. *Alzheimers Dement.* 2012 Jul;8(4):372-5. doi: 10.1016/j.jalz.2012.05.2115



To Achieve Success: *America's Brain Health Initiative*

America's Brain Health Initiative; preserving America's greatest resource

- Cast broad net to ensure research equity and reduce research disparity
- There is insufficient site capacity for direct referral from funnel to site
- Blood-based biomarkers have made remarkable progress
- Human touch will be key
- Education about brain health and brain disease risk reduction
- Clinical trial education and possible referral is one aspect of the education
- Can be linked with other programs – CDC, NIH Alzheimer Clinical Trial Consortium and related, CTSA, NeuroNext

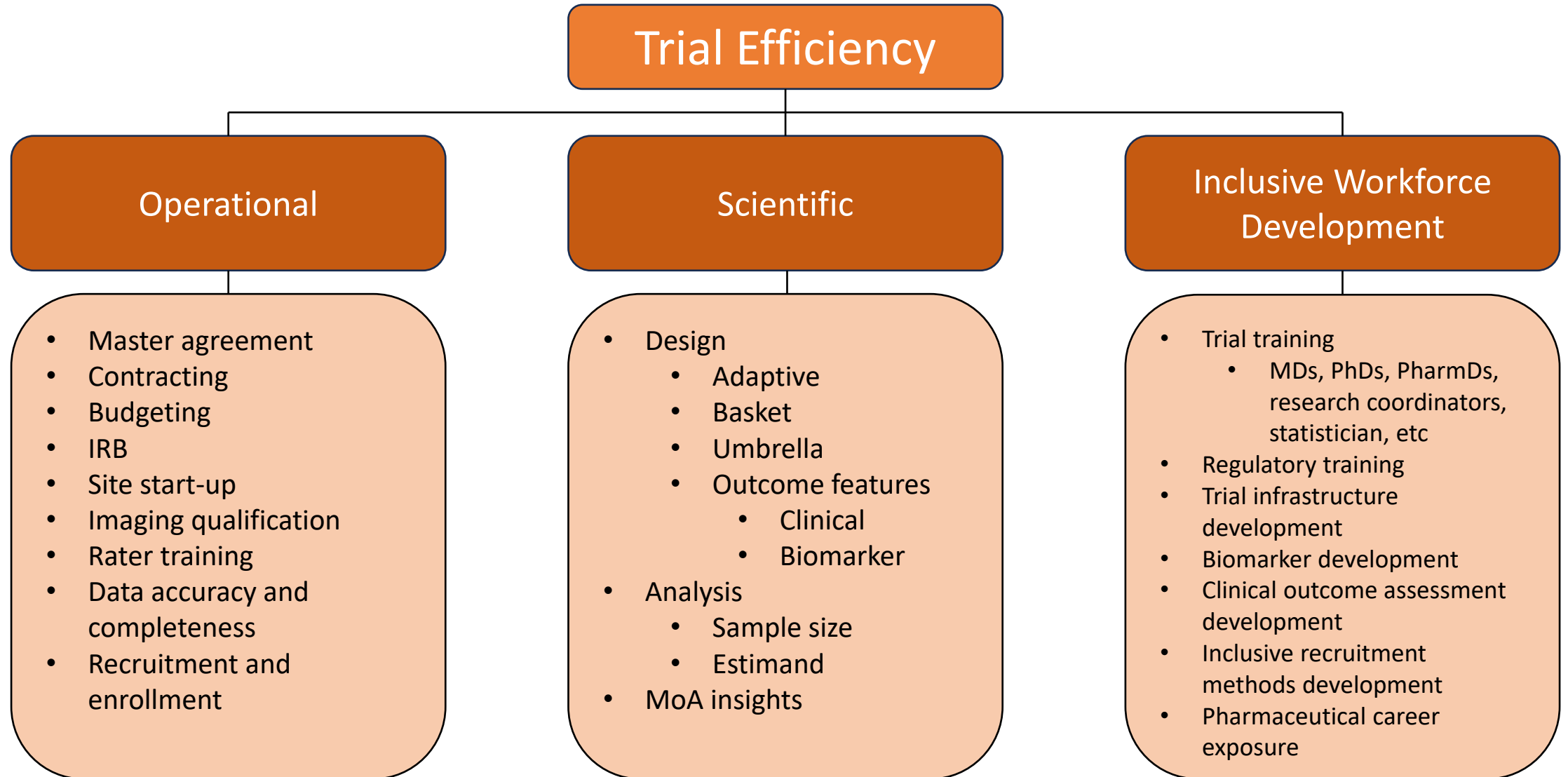
eMR - electronic medical record; RCT – randomized clinical trial

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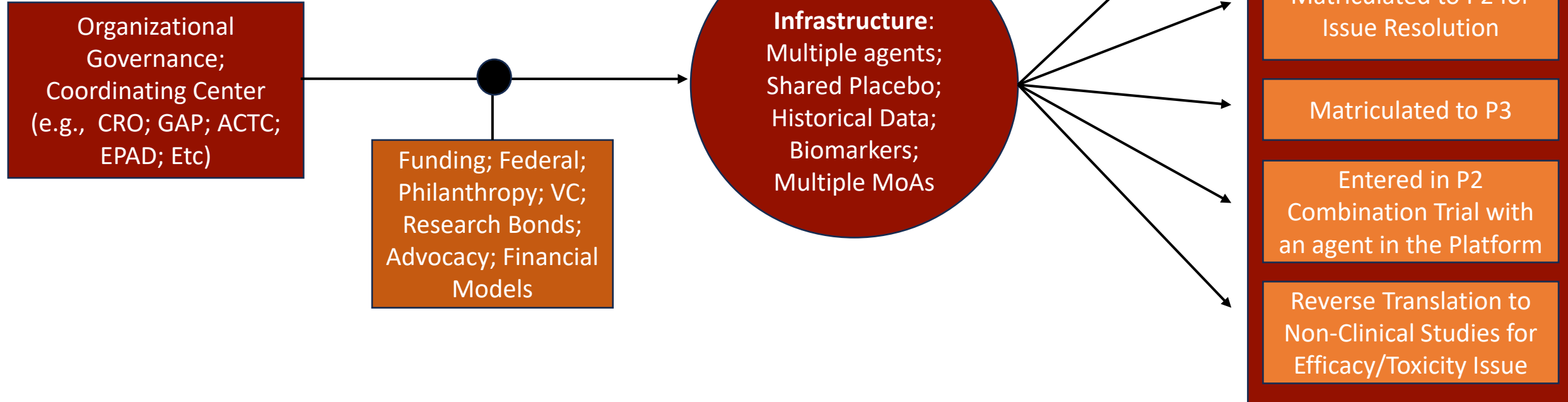
What is Needed to
Achieve Success with
Our Research
Priorities:
**Sustainable
Clinical Trial
Infrastructure**

- We currently rebuild the stadium for every match
 - Build infrastructure sites in neighborhoods of under-represented groups (race, ethnicity, gender, socioeconomic stress, rural locations)
 - Hub-and-spoke structure with surrounding areas
 - Public-private collaborative support (pharma/biotech/academic/NIH/ advocacy)
- 
- A series of yellow dashed lines in the bottom right corner, forming a curved shape.

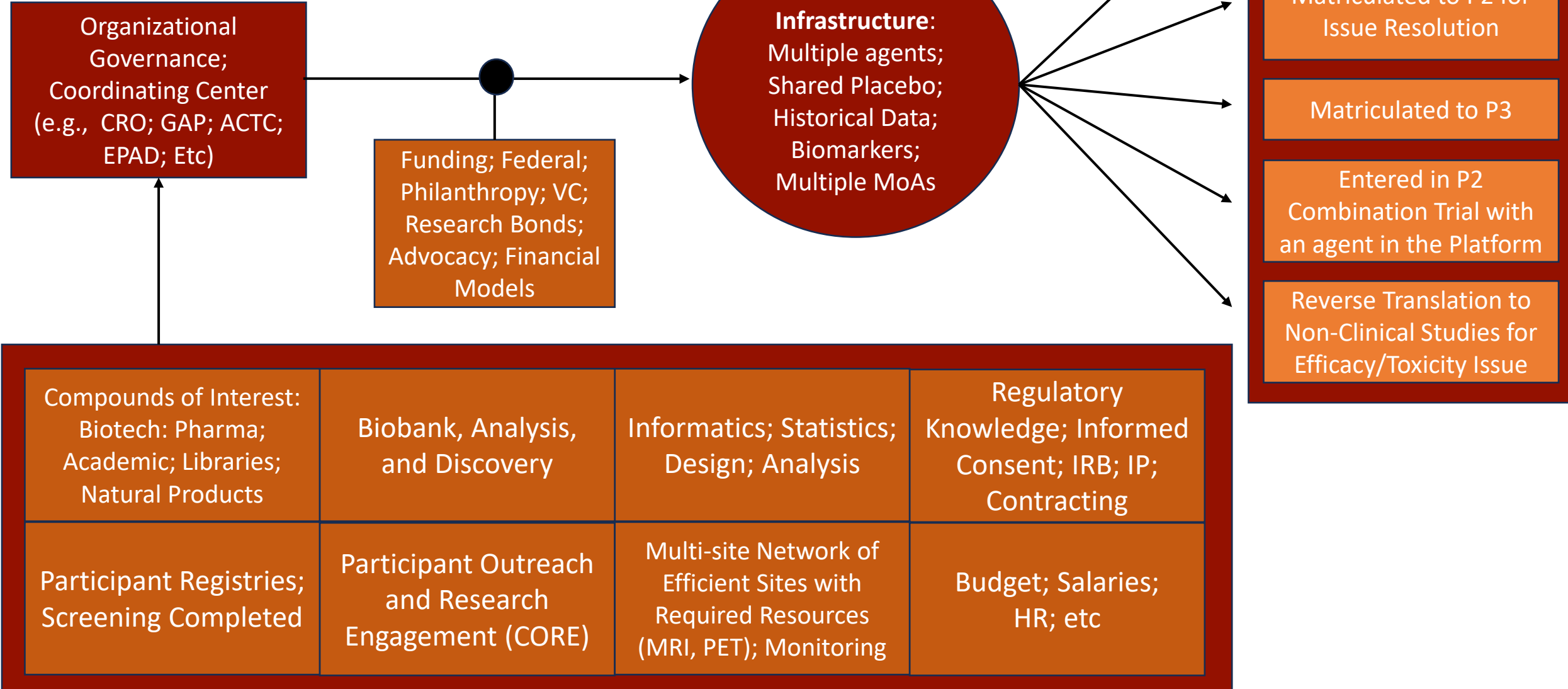
What is Needed to Achieve Success with Our Research: Trial Efficiency – Obtaining Rigorous Answers with the Fewest Participants and Resources



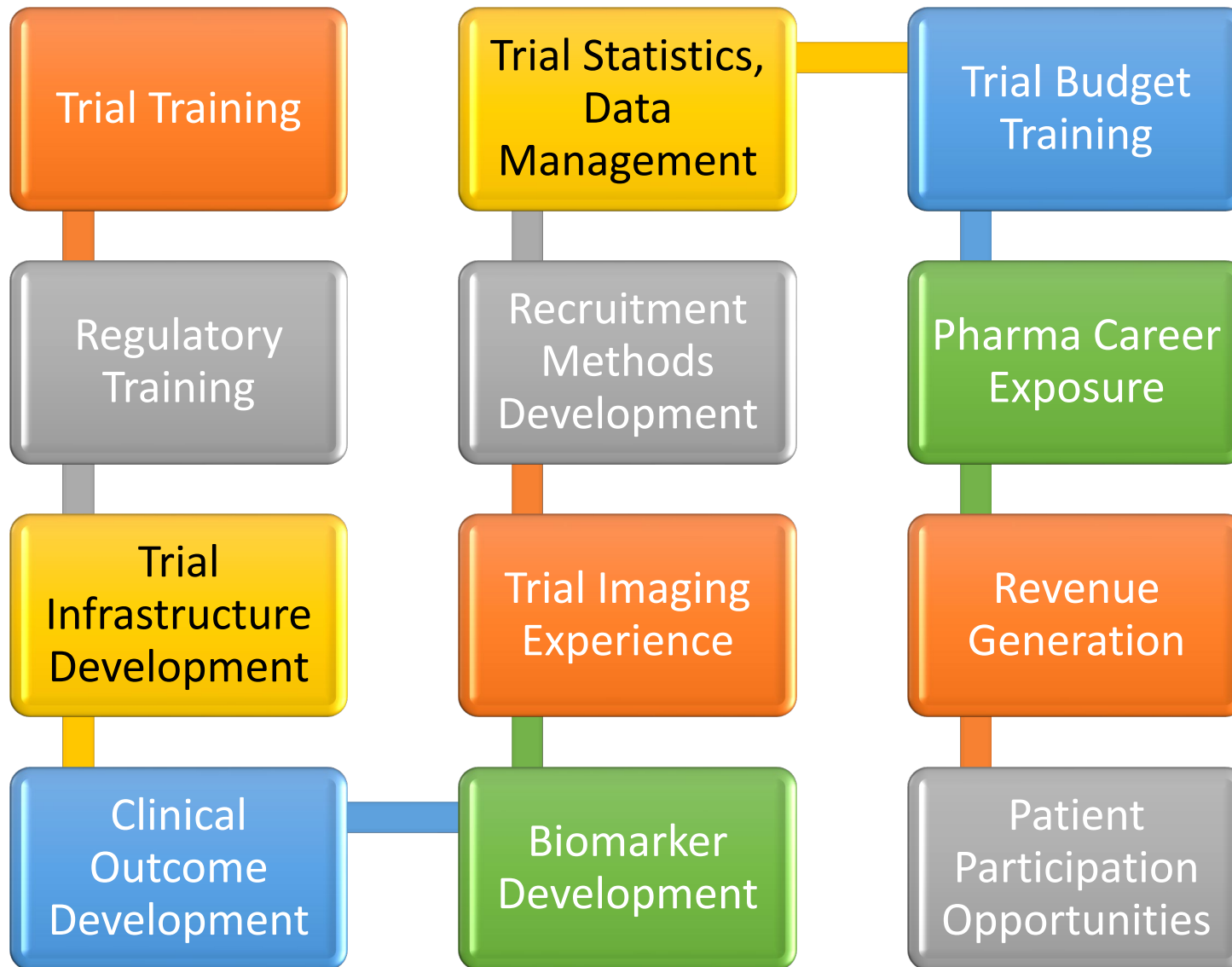
Platform Trial: Phase 2-Focused with Purpose of Eliminating or Advancing Candidate Agents



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Value of Clinical Trials in Academic Medical Centers



- Why do drug development in academic medical centers?
- Let's let pharma do the trials.

- Clinical trial participation by students and residents should be purposeful
- Understand the biography of every therapy
- Interpret new drug efficacy and safety

Mullen CG, et al. J Clin Transl Sci. 2023 May 18;7(1):e127. doi: 10.1017/cts.2023.550; Obeid JS, et al. J Clin Transl Sci. 2018 Oct;2(5):267-275. doi: 10.1017/cts.2018.332; Austin CP. Clin Transl Sci. 2021 Sep;14(5):1629-1647. doi: 10.1111/cts.13055



Data Sharing Should Be Mandatory

- Most trials show no drug-placebo difference
- Data from negative trials is very informative
- Biomarker data from all placebo groups would create a tremendous resource
- Data collection must be standardized with interoperability
- Data sharing must include industry trials (minimally from the placebo groups)

What is Needed to Succeed in Achieving AD Research Priorities

- Large organized education/recruitment initiative (America's Brain Health Initiative)
- Trial infrastructure
- Trial efficiency
 - Operational
 - Scientific
 - Educational
- Stakeholder collaboration
- Legislation to incentivize
 - Trial participation
 - Trial referral
 - Development of generic drugs
 - Data sharing





Thank You

