NIA – ADC Planning Panel

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Interim report – ADC Directors Meeting

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Objective

- Develop recommendations to determine how the investment in the ADC program can be maximized by increasing flexibility to contribute as effectively as possible to the NAPA objective of delivering a therapy by 2025.
- "Blue sky" considerations building on the existing strengths of the ADCs, e.g.:
  - Balance of required core structures vs. development of Center-specific strengths and innovation
  - Rational networking of Center capabilities for creating opportunities to build synergies among ADCs
  - Identification of knowledge gaps in disease mechanisms/risks that the ADCs are uniquely capable of addressing
  - Creation of synergies across the spectrum of translational research in AD, ADRDs and mixed dementias against the back-drop of healthy cognitive aging and resilience
  - Incentivization for collaborations/interactions among ADCs and related non-ADC research and initiatives
  - Consideration/development of worthwhile interactions with other relevant NIH- and VA-supported Center programs
  - Identification and development of infrastructural supports required to enable these interactions
  - Recognition that 2025 is not the "end-game". Outcomes of this exercise will support basic and clinical research beyond 2025.

Planning Panel Members

Name	Institution/Organization	Domains relevant to panel	Email
Barry Greenberg (chair)	Toronto Dementia Research Alliance	Big picture	bgreenbe@uhnresearch.ca
Kelly Bales	Pfizer	Drug Discovery/Development	Kelly.Bales@Pfizer.com
Maria Carrillo	Alzheimer's Association	Imaging, Biomarkers, Recruitment	maria.carrillo@alz.org
Phil De Jager	Broad Institute of MIT and Harvard	Systems Biology	pdejager@rics.bwh.harvard.edu
Rachelle Doody	Baylor College of Medicine	Clinical trials, patient care, recruitment, ADCS	rdoody@bcm.edu
Norman Foster	University of Utah	Neurology, Imaging, Care Coordination, FTD	norman.foster@hsc.utah.edu
Jim Galvin	Florida Atlantic University	Clin Core, Ed Core, NACC requirements, LBD module	galvinj@health.fau.edu
Ben Gelman	UTMB	National NeuroAIDS Tissue Consortium	bgelman@utmb.edu
Bill Jagust	UC Berkeley	Neuroimaging, ADNI	jagust@berkeley.edu
Jennie Larkin	NIH BD2K	Big Data	Larkinj2@od.nih.gov
Lenore Launer	NIA intramural program	Epidemiology, cardiovascular risk, international collaboration	Lenore.launer@nih.gov
Simon Lovestone	University of Oxford	Translation Neuroscience	simon.lovestone@psych.ox.ac.uk
Spero Manson	University of Colorado, Denver	Diversity/Recruitment, Cognitive Assessment, RCMAR	spero.manson@ucdenver.edu
Ian McKenzie	University of British Columbia	Neuropathology, FTD	ian.mackenzie@vch.ca
Anne Newman	University of Pittsburgh	Pepper Centers, Epidemiology	newmana@edc.pitt.edu
Wendy Nilsen	NSF	Technology	WNILSEN@nsf.gov
Chirag Patel	Harvard Medical School	Translation, Bioinformatics, Big Data	Chirag_Patel@hms.harvard.edu
Maureen Schmitter-Edgecombe	Washington State University	Neuropsychology, technology	schmitter-e@wsu.edu
Todd Sherer	MJ Fox	Therapeutics, biomarkers	tsherer@michaeljfox.org
Diana Shineman	ADDF	Drug Development	dshineman@alzdiscovery.org
Alan Tomkinson	University of New Mexico	Cancer Center	atomkinson@salud.unm.edu

Committee Structure

ADC Planning Committee

B. Greenberg, Chair
N. Silverberg, C. Elliott, NIA

Sub-committees

Interactions

S. Manson, A. Newman, Co-chairs
P. DeJager, N. Foster, B. Gelman, J. Larkin, S. Lovestone,
C. Patel, T. Sherer, D. Shineman, A. Tomkinson

Clinical

N. Foster, M. Schmitter-Edgecombe, Co-chairs
J. Galvin, B. Jagust, J. Larkin,
L. Launer, S. Manson, W. Nilsen

Disease Mechanisms & Risk

J. Galvin, B. Jagust, Co-chairs
K. Bales, M. Carillo, L. Launer, S. Lovestone,
I. Mackenzie, A. Newman, T. Sherer

Translational

K. Bales, D. Shineman, Co-chairs
M. Carillo, P. DeJager,
C. Patel, A. Tomkinson

Task force: Data Analytics *(under discussion)*

Process

- Full committee meets monthly by teleconference
  - Discussions of ideas, issues, sub-committee reports, moving towards crafting recommendations
  - "External" interactions to date:
    - ATRI: Paul Aisen, and ADCS: Howard Feldman
    - NIA Translational Program team: Suzana Petanceska, Laurie Ryan, Larry Refolo
- Sub-committees meet approximately monthly
  - More in-depth discussions for integration into full committee deliberations
- In-person full committee retreat, Nov. 7 in Bethesda
  - Presentations/discussions with Bud Kukull, NACC and Tatiana Faroud, NCRAD
  - Meeting with FDA and CMS representatives
  - Interactions with six invited ADC Directors, additional communications with Directors will follow
  - Initial draft recommendations to be produced for further discussion/development
- Committee recommendations to be finalized March 2017
  - Presentation to ADC Directors meeting in April 2017

Example Topics Under Discussion

- ADC structure considerations
- Clinical research and outcomes
- Collaborations across ADCs
- Data and analytics requirements
- Translational research
- Interactions with non-ADC Center and other programs

ADC Structure Considerations

- What cores should be required, and which should be optional and/or networked?
  - Rationale:
    - Regimentation = issue at cost to idiosyncratic value. Existing requirements do not fully capitalize on strengths
    - Alignment and networking of optional and required cores will create synergies among cross-Center strengths
  - Required: Administrative, Clinical, Data Management, Neuropath (brain autopsy), ORE
  - Networkable/optional: Neuropath (analysis), Imaging, DLB, FTD, VCI, Clinical Trials, Biomarkers, Translational Research
  - P30/P50 discussions
    - Potential future elimination or re-structuring/re-focusing of P50 projects?

Clinical Research and Outcomes

- What are the major scientific areas where ADCs are poised to contribute new knowledge, and what is needed to accomplish this?
- What are the barriers in the current system?
- What are the types of cohorts evaluated among Centers? How can this be structured across Centers to maximize coverage/value?
  - Importance of studying all disease stages
  - Validation of accepted diagnostic biomarkers across disease progression
  - Establishment of overall prospective longitudinal studies including underserved populations and impacts on care-givers, clinical care, outcomes
  - Integration of new technologies for disease monitoring and evaluation of outcomes
  - Imaging: core imaging sequences consistent with ADNI for data-sharing with flexibility for local innovation
  - Encourage formalized interactions between memory clinics and Centers where these do not exist

Collaborations Across ADCs

- Rationale: Crucial to address issues that transcend individual Center capabilities
- Consider establishing optional Collaboration Cores with incentives for research
- How to maximize sharing of data and biospecimens?
  - Catalog existing interactions and establish clearinghouse of information to facilitate cross-disciplinary collaboration
  - Develop central inventory of brain tissue/biospecimens, with "navigator" to assist access to samples identified through NACC and other sources
  - Streamline MTA, specimen sharing, IRB processes across Centers
  - Data created from centrally obtained sources to be put into central database
  - Consensus conferences on standardization and reporting where disciplines are appropriately mature to create value. Avoid premature standardization in developing disciplines but require standardization on reporting.
    - i.e. some psychometrics, some imaging modalities, some biomarker collection methods and measurements

Data and Analytics Requirements

- Rationale: Obviously necessary to support cross-ADC functions. Early discussions.
- Infrastructure development to enable sharing of protocols, promote data integration and enhance collaborative discovery
- Build on NACC and other data infrastructures, i.e. GAAIN, Synapse, etc.
  - Creation of data catalogues that describe and integrate each Center dataset, structure, source, particularly when not collected uniformly
    - To include non-UDS data, enable data integration/assimilation across Centers, create leveraged value
  - Aggregation of cloud-based data from each Center, downloadable by others for replication/extension/central sharing to add power and facilitate meta-analyses

Translational Research

- 2025 horizon limits focus to repurposing and validation studies, and leveraging interactions between Center research/patient assets with developing/existing initiatives
- Improved interactions with NIA-NINDS-NICHD translational programs on natural history studies, and drug discovery through late stage clinical trials
  - AMP-AD, M^2OVE-AD, AD Translational Center for Animal Model Resources (U54), Alzheimer's Biomarkers Consortium – Down Syndrome, ADNI
  - Mechanisms for conducting clinical trials, i.e. ADCS, ATRI, NeuroNEXT
  - Upcoming in FY2017-2018: AD Clinical Trials Consortium (ACTC), Resilience Initiative, Translational Bioinformatics Approaches to Advance Drug Repurposing and Combination Therapies, Quantitative Systems Pharmacology Centers for Predictive Drug Development
- Interactions with additional translational/clinical initiatives
  - e.g., GAP-AD, including but not limited to support for cohort enrollment
- Clinical trial infrastructure will also relate to research on biomarker validation through disease progression and treatment responsiveness

Interactions with non-ADC Center Programs

- Rationale: Promote leveraged opportunities among Center programs studying aging, ADRDs
  - e.g., Udall, Pepper, Shock, RCMARs, Roybal, Demography Centers, GRECCs, etc.
- Incentivize partnerships across Center programs
  - Identify approaches to optimize interactions
  - Establish steering committee with cross-representation to:
    - Promote alignment of assessments across Center programs and interactions of respective Cores that differ among programs
    - Identify thematic focus with mandate to develop specific research questions
    - Develop working groups, career development opportunities
    - Address barriers that exist across NIA Divisions and NIH Institutes

Summary

- Since May there have been 6 monthly Panel meetings and 17 sub-committee meetings
  - This presentation = high-level summary of far more granular ongoing discussions
- Panel mandate is to suggest recommendations to NIA that will be useful for consideration, NOT to establish requirements for individual Centers or the ADC program
- Feedback and input from ADC Directors is welcome and encouraged at any time, and will be formally sought before recommendations are finalized