The Adult Changes in Thought Research Program

A Living Laboratory for the Study of Brain Aging

ACT

ADULT CHANGES IN THOUGHT STUDY

Updated 04/20/2022

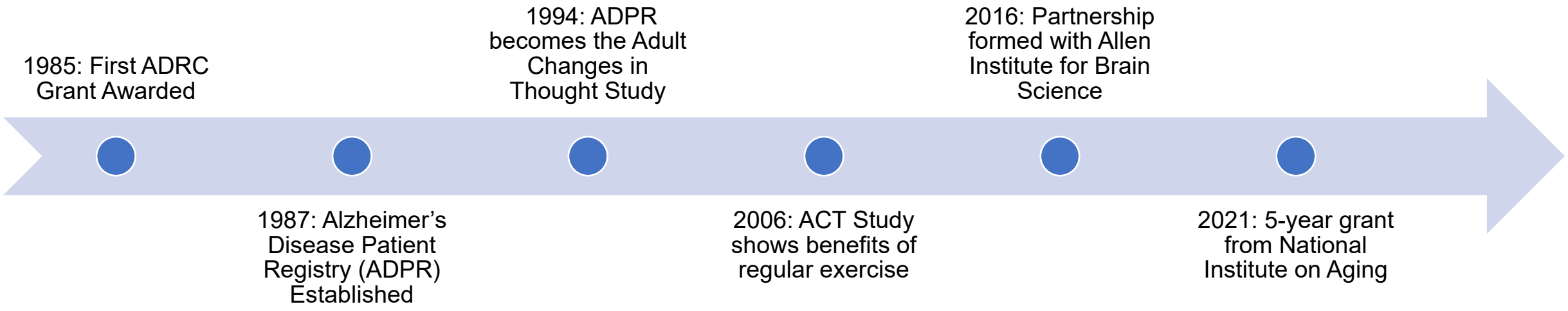
Overview

- History and Origin of the ACT Research Program
- Data Resources
- Culture of Collaboration
- Notable Findings and Contributions
- Shifting into the U19 – More than a Letter and Numbers

The Adult Changes in Thought (ACT) study is a landmark prospective investigation of older adults established in 1994 that uses a life course approach to determining risk factors that affect brain health and cognition, with a long-term goal of learning how to prevent cognitive loss and Alzheimer’s Disease/Related Dementias

Genesis of the ACT Study

- Many highlights and rich details underpin the ACT Study, which has been continuously funded and operational for ~30 years
- A vital element is the ongoing, productive partnership between Kaiser Permanente and the University of Washington



An evolving & growing resource thanks to a 2021 “U19” award from the NIA

U01 Attributes:

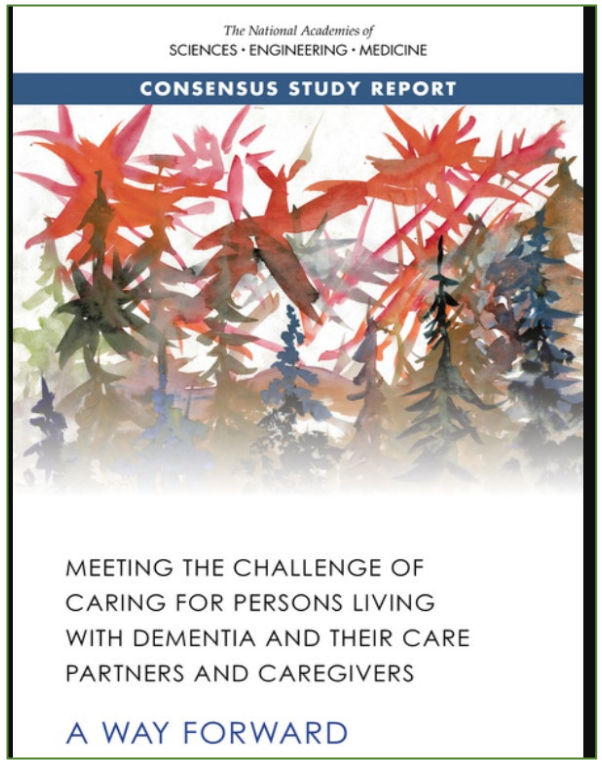
- $2 million budget/year
- UW and KPWHRI as primary partners
- A cohort of 2000 participants
- Data from biennial clinic visits and medical records

U19 Attributes:

- $11 million budget/year
- Collaborators throughout the U.S. and around the world
- A cohort of 3000 participants
- Expanded range of clinical & neurological data (to complement clinic & EMR data
- Enhanced diversity

Contributing Factors to the Growth of ACT

- Pivotal reports by the National Academies & Lancet Commission
- Insightful and relevant research agenda
- Population Demographics – “the age wave”



Notable Findings from ACT Research

Annals of Internal Medicine

ARTICLE

Exercise Is Associated with Reduced Risk for Incident Dementia among Persons 65 Years of Age and Older

Eric B. Larson, MD, MPH; Li Wang, MS; James D. Bowen, MD; Wayne C. McCormick, MD, MPH; Linda Teri, PhD; Paul Crane, MD, MPH; and Walter Kukull, PhD

Background: Alzheimer disease and other dementing disorders are major sources of morbidity and mortality in aging societies. Proven strategies to delay onset or reduce risk for dementing disorders would be greatly beneficial.

Objective: To determine whether regular exercise is associated with a reduced risk for dementia and Alzheimer disease.

Design: Prospective cohort study.

Setting: Group Health Cooperative, Seattle, Washington.

Results: During a mean follow-up of 6.2 years (SD, 2.0), 158 participants developed dementia (107 developed Alzheimer disease). The incidence rate of dementia was 13.0 per 1000 person-years for participants who exercised 3 or more times per week compared with 19.7 per 1000 person-years for those who exercised fewer than 3 times per week. The age- and sex-adjusted hazard ratio of dementia was 0.62 (95% CI, 0.44 to 0.86; $P = 0.004$). The interaction between exercise and performance-based physical function was statistically significant ($P = 0.013$). The risk reduction associated with exercise was greater in those with lower performance levels. Similar results were observed in analyses restricted to participants with incident Alzheimer disease.

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Research

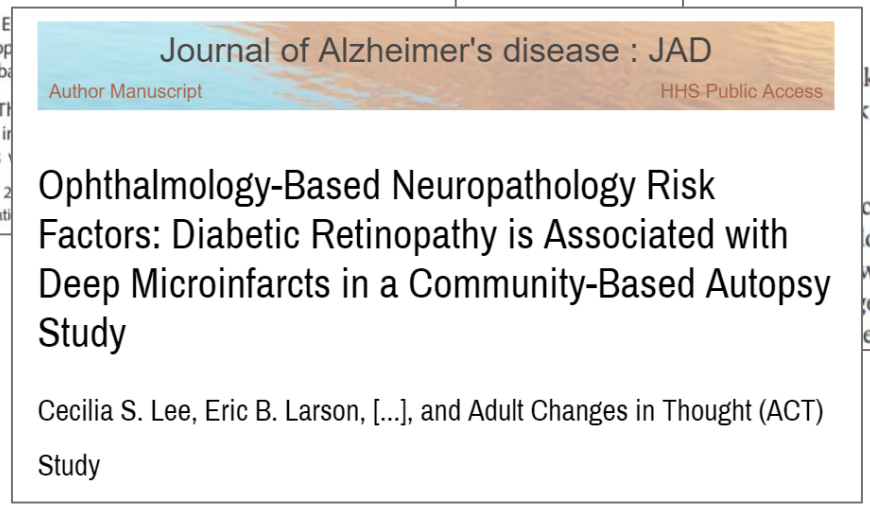
Original Investigation

Cumulative Use of Strong Anticholinergics and Incident Dementia

A Prospective Cohort Study

Shelly L. Gray, PharmD, MS; Melissa L. Anderson, MS; Sascha Dublin, MD, PhD; Joseph T. Hanlon, PharmD, MS; Rebecca Hubbard, PhD; Rod Walker, MS; Onchee Yu, MS; Paul K. Crane, MD, MPH; Eric B. Larson, MD, MPH

IMPORTANCE Many medications have anticholinergic effects. In general, anticholinergic-induced cognitive impairment is considered reversible on discontinuation of anticholinergic therapy. However, a few studies suggest that anticholinergics may be associated with an increased risk for dementia.

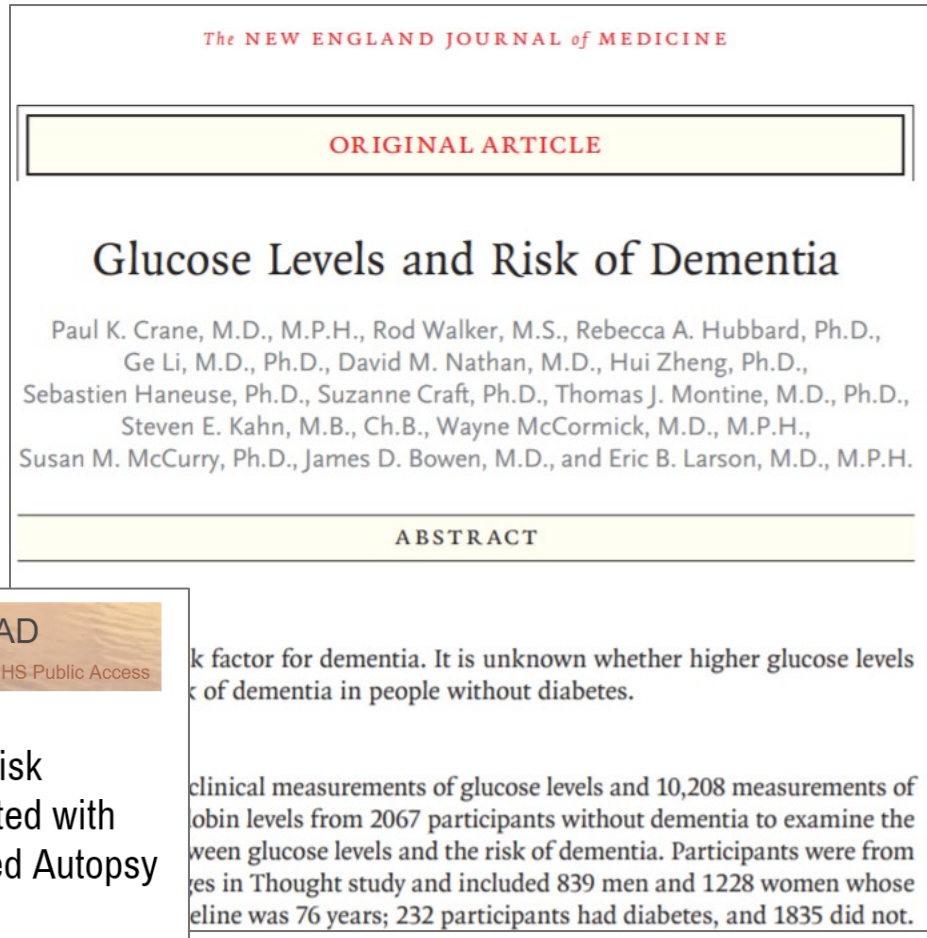


Journal of Alzheimer's disease : JAD

Author Manuscript HHS Public Access

Ophthalmology-Based Neuropathology Risk Factors: Diabetic Retinopathy is Associated with Deep Microinfarcts in a Community-Based Autopsy Study

Cecilia S. Lee, Eric B. Larson, [...], and Adult Changes in Thought (ACT) Study



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Glucose Levels and Risk of Dementia

Paul K. Crane, M.D., M.P.H., Rod Walker, M.S., Rebecca A. Hubbard, Ph.D., Ge Li, M.D., Ph.D., David M. Nathan, M.D., Hui Zheng, Ph.D., Sebastien Haneuse, Ph.D., Suzanne Craft, Ph.D., Thomas J. Montine, M.D., Ph.D., Steven E. Kahn, M.B., Ch.B., Wayne McCormick, M.D., M.P.H., Susan M. McCurry, Ph.D., James D. Bowen, M.D., and Eric B. Larson, M.D., M.P.H.

ABSTRACT

k factor for dementia. It is unknown whether higher glucose levels
k of dementia in people without diabetes.

clinical measurements of glucose levels and 10,208 measurements of
obin levels from 2067 participants without dementia to examine the
ween glucose levels and the risk of dementia. Participants were from
es in Thought study and included 839 men and 1228 women whose
eline was 76 years; 232 participants had diabetes, and 1835 did not.

With the U19, we are uniquely positioned to study brain outcomes leveraging rich data

Specific Aims:

- Expand ACT cohort enrollment and modernize and improve follow-up with emphasis on increasing racial/ethnic diversity
- Support key Projects studying the spectrum of healthy functioning to ADRD in older adults
- Expand and improve ACT's dissemination of exceptional resources to the research community

Our Mission, Vision, and Values

MISSION

The mission of the ACT U19 Program is to utilize our scientific expertise, collaborative ethos, data resources, and contributions from study participants to conduct and facilitate exemplary research on brain aging.

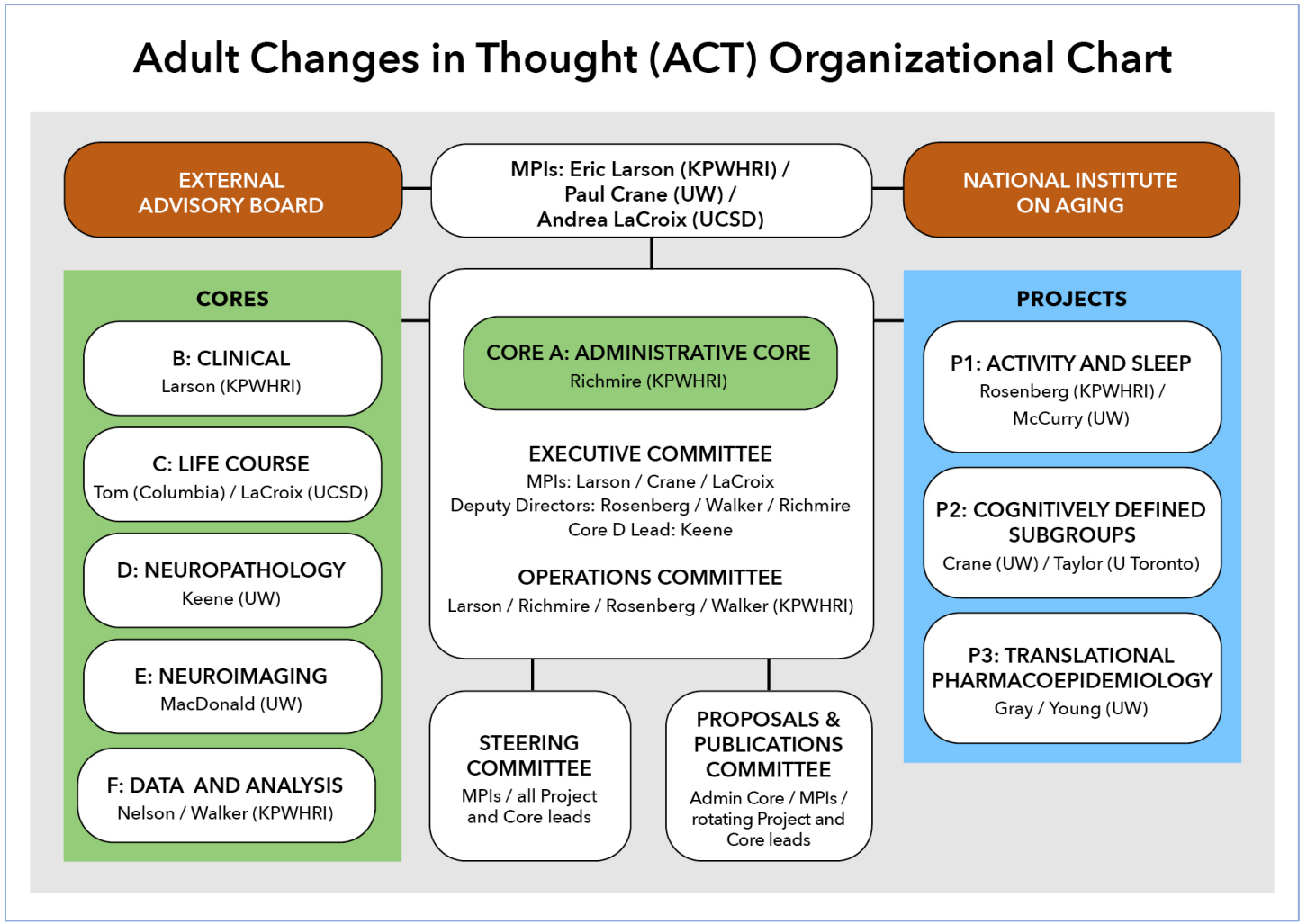
VISION

The ACT U19 will serve as a rich, innovative, and enduring resource that contributes pathbreaking scientific knowledge about late-life cognition, well-being, and healthy aging.

ACT U19: Organizational Structure

The organizational structure of the ACT U19 is designed to maximize integration, interaction, productivity and efficiency across Projects, Cores, and Governance Committees

And coming soon: A Community Advisory Board



Specialized cores support research

U19 structure intentionally includes 6 cores with topic-specific expertise that are organized to support the needs of current and future projects

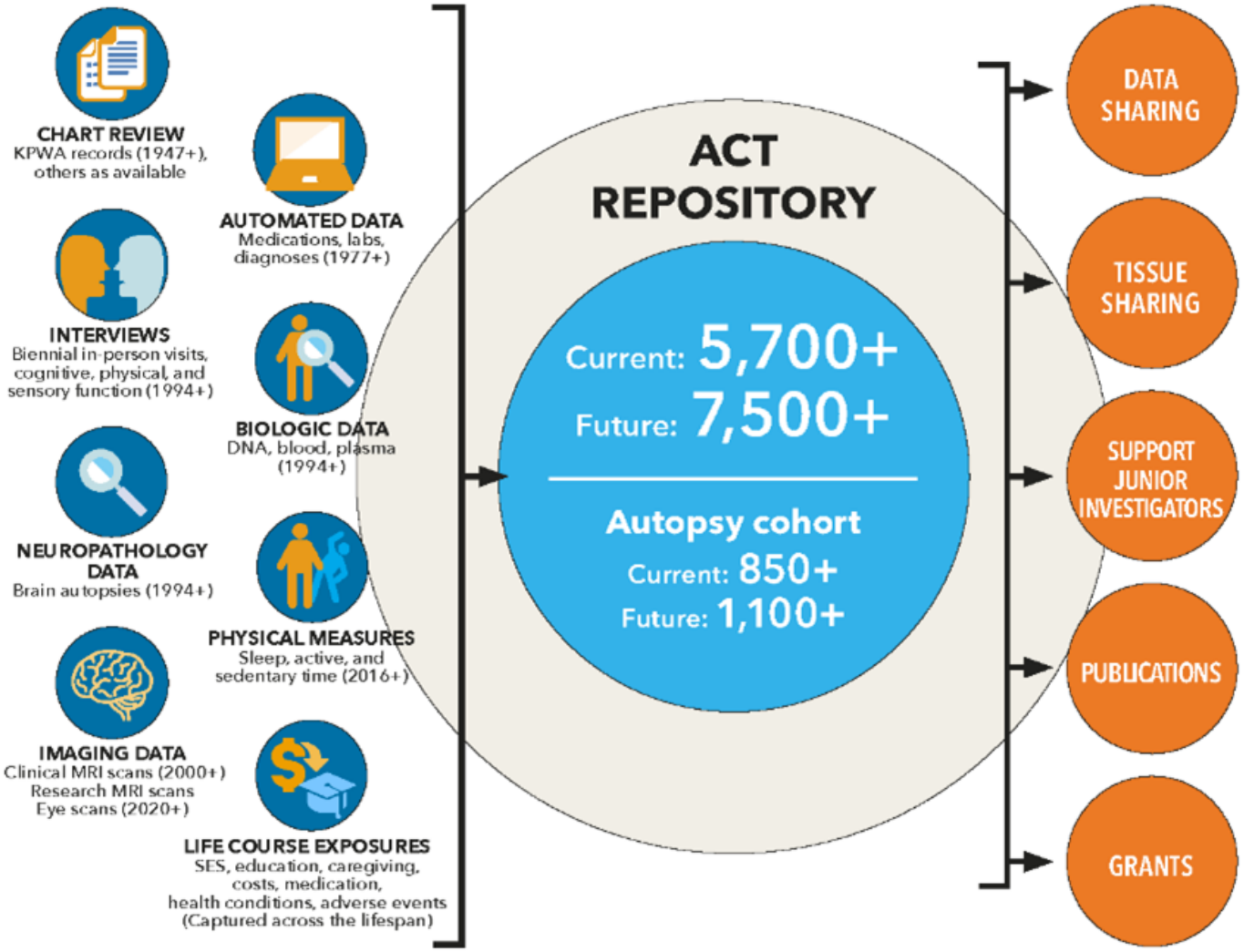
- Administrative Core
- Clinical Core
- Life Course Core
- Neuroimaging Core
- Neuropathology Core
- Data & Analysis Core

U19 Projects

- **Project 1** will test novel hypotheses regarding associations between **physical activity, sedentary behavior, and sleep** across the 24-hour activity cycle and cognitive and functional health, using wearable devices to capture data from every day lives of our cohort members
- **Project 2** asks pioneering questions about **whether "Alzheimer's disease" should be considered a single entity** and will use innovative data from the Neuropathology and Neuroimaging Cores to elucidate brain structural differences underlying different subgroups
- **Project 3** is a unique marriage of pharmacoepidemiology and stem cell science that will address questions on **commonly used drugs in older adults – anticholinergic and antihypertensive medications** – which could lead to evidence-based recommendations for treatment for older adults

Along with these new projects, the ACT research program is comprised of dozens of other affiliated studies and related analyses, including studies of vision health, traumatic brain injury, and even air quality, all as they relate to brain health as we age

ACT Repository Data is the Cornerstone



We will enroll an additional 1,000 volunteers to contribute data to the Repository, with an emphasis on increasing the diversity of participant data

Summary

- ACT has made timely and enduring research contributions that leverage our ability to enroll and follow a large cohort of participants recruited from a community-based health system
- The new ACT U19 is specifically equipped to tackle important scientific questions that can best be answered with large population-based studies and longitudinal data from electronic health records
- Over the next five years, we will enhance the ACT Research Program by
  - Recruiting a more diverse patient population
  - Modernizing data collection approaches
  - Augmenting our repository of data resources
  - Creating efficient approaches to sharing the ACT Repository to maximize its potential
- We have a world-class (and worldwide) scientific team committed to success
- ACT is an important living laboratory for research on older adults and on dementia and Alzheimer’s and we look forward to the opportunity to continue and enhance that position

Thank you!

Contact us: kpwa.actproposals@kp.org

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https://www.kpwashingtonresearch.org/our-research/research-areas/aging-geriatrics

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