

The National Cell Repository for Alzheimer's Disease

(NCRAD) is a data and specimen collection source for families with Alzheimer's disease (AD) or serious memory loss. Families having two or more living individuals with memory loss are encouraged to participate. We would like to thank the hundreds of families nationwide who are already participating in the National Cell Repository for AD. Many family members have provided blood samples, which researchers use to study AD and other related diseases. Our hope is that through the efforts of our participants, we will one day unravel the mystery of devastating diseases like AD. We are always eager to accept new families to help us move toward this goal.



INDIANA UNIVERSITY

SCHOOL OF MEDICINE

National Cell Repository for Alzheimer's Disease

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NCRAD Update

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The 90+ Study – Studies of The Oldest-Old



By **Maria M. Corrada**, ScM, ScD, Associate Adjunct Professor of Neurology School of Medicine and of Epidemiology School of Medicine, University of CA, Irvine and **Claudia Kawas**, MD, Professor of Neurology School of Medicine and of Neurobiology and Behavior School of Biological Sciences, University of CA, Irvine

The oldest-old are the fastest growing segment of the world's population, but little is known about factors affecting the health of this age group. With the profound increase in people living to age 90 and beyond, research identifying factors that promote quality as well as quantity of life is needed.

To bridge this knowledge gap, we began The 90+ Study in 2003. As one of the largest studies in the world of people 90 and older, our goals are to understand the clinical, pathological, radiological, and genetic correlates of successful aging and dementia in the oldest-old.

- What promotes people to live to age 90 and beyond?
- Do oldest-old people with dementia have the same brain abnormalities as younger people with dementia?
- What can people do to prevent memory loss and disability in their 90s?

This year marks the 12th year of The 90+ Study and the 34th year of its parent study, the *Leisure World Cohort Study*. These studies have delved into the mysteries of successful aging in older adults.

The *Leisure World Cohort Study* (LWCS) was initiated in 1981 when 13,978 residents (mean age 73 years) of Leisure World Laguna Hills, a southern California retirement community, completed a detailed health questionnaire. In 2003, The 90+ Study was founded with survivors of the LWCS who were 90 and older. More than 1,600 living participants in 36 states have joined The 90+ Study. Participants are examined every six months with neurological examinations,

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mental ability testing, blood assays, genetic samples, and brain autopsy after death. Last year, we added brain imaging to our procedures including magnetic resonance imaging (MRI) and amyloid positron emission tomography (PET).

The wealth of data collected has shown that:

- Wine, beer, hard liquor or coffee – all in moderation – are related to increased longevity.
- More exercise and participation in other activities may add years to your life.
- Be neither too fat nor too thin for longer life.
- Incidence of dementia continues to double with every five years of age in both men and women.
- Risk of dementia in centenarians is over 40% per year.
- People with hypertension are, surprisingly, less likely to suffer from dementia.
- Memory loss and dementia correlate poorly with brain findings on autopsy. About a quarter of those with dementia lack brain abnormalities, and half of those with brain abnormalities that cause dementia appear to be able to overcome these changes and are cognitively normal.
- Prevalence of disability continues to increase with rates tripling between ages 90 and 95 years.

This year our biggest initiative is to develop genetic research using DNA of these remarkable subjects. In collaboration with NCRAD we are working on making genetic material available to researchers around the world. ■

The 90+ Study is recruiting participants. Are you eligible to participate?

Researchers are looking for people who are:

- 90 years of age or older
- Live in the Southern California area
- Willing to undergo clinical assessments, memory testing, and other procedures every 6 months
- Willing and able to undergo one MRI and one amyloid PET scan
- Agree to brain donation upon death

More information about The 90+ Study can be found at www.90study.org or by calling the study coordinator at 949-768-3635.

NCRAD featured in Inside NIA: A Blog for Researchers



Creighton Phelps,
PhD, Deputy Director,
Division of
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NCRAD offers genetic samples and data vital to Alzheimer's research

Posted on December 17, 2014 by Dr. Creighton Phelps, Deputy Director, Division of Neuroscience.

Identifying the genes involved in Alzheimer's disease and related dementias is of course no easy task. From among the thousands of gene candidates in the human genome, we need to determine which are involved in onset and progression, and which increase risk or offer protection.

Where can researchers find the biological specimens needed to unlock these mysteries?

I have the answer to that important question: The NIA-funded National Cell Repository for Alzheimer's Disease, or NCRAD, a veritable treasure trove of biological material located at the Indiana University School of Medicine in Indianapolis.

Storehouse to the stars (of genetic research)

For nearly 25 years, the repository has been the go-to resource among researchers investigating the genetic underpinnings of dementia. Its original mission: to collect and store data

and samples from a small number of Alzheimer's disease families.

Today, NCRAD houses samples and data from over 900 families with Alzheimer's disease, and has expanded its scope to include many thousands of samples from people with sporadic Alzheimer's disease, frontotemporal, and other Alzheimer's related dementias, as well as from older, cognitively healthy volunteers.

Having sent some 160,000 biological samples to over 120 investigators and labs across the world, NCRAD

has fine-tuned the art of working closely with researchers to identify samples that meet specific research needs. In addition, they offer a platform for investigators interested in sharing samples with the wider research community.

NCRAD specimens are further enriched by clinical data collected on each volunteer. Depending on the sample set, this could include information about health histories, education, lifestyle choices, as well as data collected during neurological and physical exams.

Casting a wide net for samples, data

Collaboration from NIA-supported research programs and initiatives—including the Alzheimer’s Disease Centers (ADC), the Alzheimer’s Disease Neuroimaging Initiative (ADNI), the Alzheimer’s Disease Genetics Consortium, and the Alzheimer’s Disease Sequencing Project—has been key to building NCRAD’s wealth of sample and data.

NCRAD also runs a robust outreach program aimed at finding families across the country with memory problems or a diagnosis of Alzheimer’s or a related dementia. The repository sends—at no charge to volunteer research participants—blood sampling kits to bring to their doctor’s offices. In addition to the DNA collected from the blood samples and sent back to the repository, NCRAD collects and periodically updates each volunteer’s family and personal health histories.

- The NCRAD study continues to look for families with two or more living members with Alzheimer’s disease or symptoms of serious memory loss. Approximately

700 participants have had an autopsy to confirm the presence or absence of AD. NCRAD offers participating families a brain-only autopsy to confirm, pathologically, the presence or absence of Alzheimer’s disease. Brain tissue will then be made available for research studies.

- The LOAD (Late Onset Alzheimer’s Disease) study is recruiting families with two or more living siblings diagnosed with Alzheimer’s disease after the age of 60 and a third family member who has been either diagnosed with memory loss or Alzheimer’s disease after the age of 50, or is older than age 60 and free of memory loss.

NCRAD also directs potential volunteers to an array of active studies on dementia, from international efforts involved in early-onset Alzheimer’s disease, to older people free of cognitive symptoms and those with frontotemporal dementia.

Modified from <http://nia.nih.gov/research/blog/2014/12/ncrad-offers-genetic-samples-and-data-vital-alzheimers-research> ■

National Alzheimer’s Project Act



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In January of 2011, President Obama signed the National Alzheimer’s Project Act (NAPA) into law. NAPA charged the Secretary of Health and Human Services (HHS), then Kathleen Sebelius, with the responsibility of developing the first United States Plan to Address Alzheimer’s Disease. As such, Secretary Sebelius convened an advisory committee to assist her and her staff in developing the Plan.

The Advisory Council for Research, Care and Services for NAPA was comprised of approximately 12 federal members representing various federal agencies that deal with Alzheimer’s disease and 12 nonfederal members representing advocacy groups, caregivers, care providers, state agencies, and researchers. The group also includes a member with diagnosed Alzheimer’s disease. The Advisory Council meets quarterly and provides recommendations

to the Secretary and directly to Congress suggesting how to address the primary goal of NAPA which is to “Prevent and Effectively Treat Alzheimer’s Disease by 2025.”

As a result of this process, the Secretary of Health and Human Services (HHS) published the First U.S. Plan to Address Alzheimer’s Disease in May of 2012. The Plan involved five goals pertaining to research, clinical care, caregiver support, education and awareness, and metrics to assess the effectiveness of the Plan. The overall purpose of the Plan was to create and maintain an integrated national plan to overcome Alzheimer’s disease, coordinate Alzheimer’s disease research services across all federal agencies, accelerate the development of treatments that would prevent, halt or reserve the course of Alzheimer’s disease, improve early diagnosis and coordination of care and treatment of Alzheimer’s disease, improve outcomes for ethnic and racial minority populations that are at higher risk for Alzheimer’s disease, and coordinate with international bodies’ to fight Alzheimer’s globally.

The NAPA law requires that the Secretary revise the Plan on an annual basis for

15 years. As such, the Advisory Council constantly monitors progress toward the goal and revises its recommendations to the Secretary regarding these issues. The Council also sends its recommendations directly to Congress.

Since NAPA has become law, there have been several accomplishments thus far, but the Advisory Council believes that a great deal of work still needs to be done. There has been a modest increase in Alzheimer’s disease funding at the federal level in spite of overall general reductions in the federal budget. This increase in funding has led to new initiatives including clinical trials in Alzheimer’s disease, and the research community is hopeful that these efforts will be sustained. Nevertheless, one of the primary recommendations of the Advisory Council was to increase the federal budget for Alzheimer’s disease research to \$2 billion a year. The current federal budget is approximately \$600 million; so, much is left to be done. Nevertheless, most individuals in the Alzheimer’s community believe that NAPA is a major step forward toward ending this devastating disease. ■

Research Opportunities:

4 Repeat Tauopathy Neuroimaging Initiative (4RTNI)

- Purpose: To identify the best methods of analysis for tracking PSP and CBD over time. The results from this study may be used in the future to calculate power for clinical drug trials, as this study aims to identify the most reliable outcome measures.
- Eligibility: Men and women ages 45 to 90 years, diagnosis of Progressive Supranuclear Palsy or Corticobasal Degeneration (CBD)
- Locations: CA
- Contact: PH: 415-476-9578 or 4RTNI webpage: www.memory.ucsf.edu/research/studies/4rtni

Longitudinal Evaluation of Familial Advancing Research and Treatment for Frontotemporal Labor Degeneration (ARTFL)

- Purpose: "New therapies targeting some of the molecular causes of FTLT are rapidly becoming available for testing in human clinical trials. The ARTFL's goal is to prepare for clinical trials of these new therapies by evaluating people who might eventually be candidates for participation in clinical trials and by developing new diagnostic technologies to evaluate the effectiveness of new treatments for FTLT." (Citation: <https://www.rarediseasesnetwork.org/ARTFL/index.htm>)
- Locations: CA, FL, IL, MA, MD, MN, MO, NC, NY; Canada
- See this website for more information: <https://www.rarediseasesnetwork.org/ARTFL/index.htm>

Dominantly Inherited Alzheimer Network (DIAN)

- Purpose: To study brain changes in people who carry an Alzheimer's disease mutation in order to determine how the disease process develops before the onset of symptoms.
- Eligibility: Men and women ages 55 to 80 years, diagnosis of mild to moderate Alzheimer's disease, good general health and medically able to undergo neurosurgery.
- Locations: USA - CA, IN, MA, MO, NY, RI; United Kingdom; Australia
- Contact: PH: 314-286-2683 or DIAN webpage: <http://www.dian-info.org>

Frontotemporal Dementia Subjects (LEFIDS)

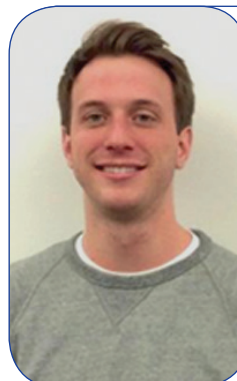
- Purpose: To model the rates of decline in clinical function of those suffering from Frontotemporal Labor Degeneration (FTLD) and identify genetic and biofluid factors that modify these rates.
- Eligibility: Must be a member of a family with a known mutation, have a reliable informant who personally speaks with or sees that subject weekly, the subject and informant must be fluent in English, the subject must be willing to undergo yearly evaluations for a period of three years, and the subject must be willing to undergo neuropsychological testing and MRI imaging.
- Locations: CA, FL, MA, MO, NY, PA; Canada
- Contact: Mayo Clinic Rochester
Alzheimer's Disease Research Center
507-284-1324

Mayo Clinic Florida
Memory Disorder Clinic
904-953-6523

NCRAD Welcomes Your Ideas and Suggestions

We hope that you and your family find the NCRAD Newsletter informative. We would welcome suggestions on future topics for articles, questions you would like to ask the NCRAD doctors or anything you would like shared with our readers about your family's experience with Alzheimer disease. Please send us your ideas by email or by phone.

- Phone: 1-800-526-2839
- Email: alzstudy@iupui.edu
- Website: www.ncrad.org



Meet the newest member of our NCRAD staff, Drew Mitchell

Drew Mitchell joined NCRAD in November 2014 after graduating from Indiana University-Purdue University Indianapolis in May 2014. Drew serves as a research coordinator and performs data validation, sample tracking and family follow up mailings. He also assists with annual chart reviews.

Sources for Information and Support

*Alzheimer's Association

<http://www.alz.org>

Tel: 312-335-8700 or 800-272-3900

*Alzheimer's Disease Education and Referral Center (ADEAR)

<http://www.nia.nih.gov/Alzheimers>

Tel: 301-495-3311 or 800-438-4380

** ADEAR lists all 29 Alzheimer Disease Centers (ADCs) and their contact information.

Assisted Living Directory, Assisted Living Facilities Information & Senior Care

<http://www.assisted-living-directory.com/>

The Association for Frontotemporal Dementias (AFTD)

<http://www.theaftd.org>

Tel: 267-514-7221 or 866-507-7222

Family Caregiver Alliance

<http://www.caregiver.org>

Tel: 415-434-3388 or 800-445-8106

National Parkinson Foundation

<http://www.parkinson.org/>

Tel: 305-547-6666 or 800-327-4545

Parkinson's Disease Foundation (PDF)

www.pdf.org

Tel: 212-923-4700 or 800-457-6676

Society for Progressive Supranuclear Palsy

<http://www.psp.org>

Tel: 410-486-3330 or 800-457-4777

National Organization for Rare Disorders (NORD)

<http://www.rarediseases.org>

Tel: 203-746-6518 or 800-999-NORD (6673)

Center for Disease Control and Prevention (CDCP)

<http://www.cdc.gov>

Tel: 800-311-3435

Creutzfeldt- Jakob Foundation Inc. (CJD)

<http://cjd.foundation.org>

Tel: 954-704-0519 or 305-891-7579

***ClinicalTrials.gov** is a registry of federally and privately supported clinical trials conducted in the United States and around the world. ClinicalTrials.gov gives you information about a trial's purpose, who may participate, locations, and phone numbers for more details. This information should be used in conjunction with advice from health care professionals.

<http://www.clinicaltrials.gov/>

***Research Match** is a free service that pairs volunteers interested in participating in research opportunities from surveys to clinical trials with researchers. Open to all, including healthy volunteers.

<http://www.researchmatch.org>

National Society of Genetic Counselors

<http://www.nsgc.org/>

Tel: 312-321-6834

*These are good sources for research opportunities in your area.

10 Signs of AD

1. Memory loss
2. Difficulty performing familiar tasks
3. Problems with language
4. Disorientation to time and place
5. Poor or decreased judgment
6. Problems with abstract thinking
7. Misplacing things
8. Changes in personality
9. Changes in mood or behavior
10. Loss of initiative

For more information, call the Alzheimer's Association at (800) 272-3900

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