Alzheimer’s disease research is evolving rapidly. In the last couple of years, we have seen major advances in techniques for detecting early signs of Alzheimer’s disease in the brains of living individuals. Unlike ever before, we are gaining a better understanding of how to identify and measure the disease process as it develops in the brain. This ability to measure early disease is a major key to prevention, because we believe medicines or lifestyle changes will be most effective before symptoms start.

Early detection methods are not available in a doctor’s office, but we are using them in research. In 2018, we introduced biomarker studies to WRAP, specifically positron emission tomography (PET) scans, lumbar punctures for cerebrospinal fluid (CSF) collection, and magnetic resonance imaging (MRI). These tests measure changes in amyloid plaques and tau tangles in the brain over time, as well as physical changes in the brain. (To learn more, see Page 3 of this newsletter.)

By using plaques and tangles as our reference point, we can learn much more about the genetic, health, and lifestyle factors that might drive the age at which Alzheimer’s disease-related brain changes appear, their rate of progression, and whether and when they may result in clinical symptoms such as memory loss. This information will help us determine the best time to test treatments and preventive measures in the search for a cure for Alzheimer’s disease.

The University of Wisconsin-Madison is one of the few places in the world capable of conducting this cutting-edge research. This is due in large part to the WRAP study, one of a small number of Alzheimer’s disease studies in the nation following participants from midlife. All of the years and ways in which you participate in the WRAP study makes this mission possible, and the National Institute on Aging (NIA) has recognized the incredible value of your contributions. I am pleased to tell you that the NIA recently awarded the WRAP study more than $19 million to allow our scientists to perfect and validate biomarker measures of Alzheimer’s disease. Biomarkers are the cutting edge of AD research, and the WRAP study now has the funding and infrastructure to collect these measures in as many participants as are willing to undergo these procedures.

Your contributions to science are advancing the field of Alzheimer’s disease research worldwide. Thank you. Onward, WRAP, and On, Wisconsin! ☀
**Staff updates**

Mary E. Murphy, MS Ed, MLIS, joined WRAP as a data specialist. Murphy comes to WRAP with experience from multiple research labs and libraries across UW-Madison. She has a passion for public health and is driven to address health disparities though the lens of biostatistics. When not immersed in data, Murphy can be found coaching (and skating in) the Madison Speed Skating Club, biking, and gardening.

After a 30-year career with the Department of Corrections and 10 years of retirement, Sharon Williams, BS, joined the GROW Study as a senior research specialist. In her new role, Williams will recruit biological family members of WRAP participants into research. Williams is active in community service and enjoys traveling, meeting people from diverse backgrounds, and jazz.

Isabel Cupino, MD, is a recent medical school graduate and the new WRAP research support specialist, focused on scheduling and research operations support. Prior to medical school, Cupino attended UW-Madison and graduated with a degree in Zoology and a certificate in Gender & Women’s Studies. She has previous clinical research experience from her work at the UW Center for Tobacco Research & Intervention.

The WRAP team offers a fond farewell to staff who recently moved into new phases of their careers. Departing staff include Lisa Bluder, research specialist; Susan Schroeder, senior research specialist; and Nygil Matthews, research nurse practitioner.

**Archive of WRAP participant data contributes to scientific findings**

Today, nearly 18 years after its inception, the Wisconsin Registry for Alzheimer’s Prevention (WRAP) includes more than 1,500 research participants, many of whom return every other year to contribute their data to the WRAP study. Researchers at UW-Madison publish dozens of research studies annually utilizing WRAP participant data. Below are three such studies.

**Exercisers have fewer Alzheimer’s disease-associated brain changes than people who are sedentary**

In this study conducted in Dr. Ozioma Okonkwo’s lab, 85 WRAP participants wore an accelerometer (an exercise tracker, like a FitBit) for one week. These participants also donated spinal fluid, which shows levels of amyloid plaques and tau tangles in the brain. The researchers found that participants who engaged in moderate physical activity had lower levels of amyloid and tau in their brains than participants who were sedentary. This study contributes to a growing body of research that shows a physically active lifestyle plays a protective role against Alzheimer’s disease.

Title: “Moderate intensity physical activity associates with CSF biomarkers in a cohort at risk for Alzheimer’s disease”

Journal: *Alzheimer’s & Dementia: Diagnosis, Assessment & Disease Monitoring*

**Obesity and high blood pressure escalate memory loss in people with evidence of Alzheimer’s disease**

A study led by Dr. Lindsay Clark showed people with evidence of amyloid in the brain who had hypertension or obesity experienced declines in memory and thinking skills at double the rate compared to those with healthy blood pressure and weight. Clark and her team studied 207 WRAP participants’ health, memory, and amyloid PET scans or spinal fluid collected during at least three visits over eight years. The next step in Clark’s research will be to determine if treating hypertension or obesity in midlife slows the rate of memory loss in those with amyloid buildup and delays the onset of dementia symptoms in later life.

Title: “Hypertension and obesity moderate the relationship between β-amyloid and cognitive decline in midlife”

Journal: *Alzheimer’s & Dementia*

**Rare gene variants affect cognition differently**

Scientists have identified more than 25 genes that either elevate or lower a person’s risk for Alzheimer’s disease. Two recently discovered rare gene variants, TREM2 and PLD3, have shown associations with increased risk of Alzheimer’s disease, but little research has shown how these variants might be associated with cognition in late middle age. Dr. Corinne Engelman’s lab looked at cognitive tests of 1,449 WRAP participants who were evaluated for up to five visits. Participants with the PLD3 gene variant (13 out of 1,449) had significantly lower scores on story recall, visual learning and memory, and speed and flexibility tests. Those with TREM2 gene variant (15 out of 1,449) had only marginally lower speed and flexibility scores.

Title: “The effect of rare variants in TREM2 and PLD3 on longitudinal cognitive function in the Wisconsin Registry for Alzheimer’s Prevention”

Journal: *Neurobiology of Aging*

*Read more about these studies by searching their titles at www.pubmed.gov*
What are biomarker studies?

Biomarkers are indicators of a disease. They are clues that point to positive or negative health outcomes. For example, high blood pressure is a biomarker used to determine risk for stroke. In Alzheimer's disease, scientists have identified several biomarkers that indicate the disease has started. Below are descriptions of the tests WRAP uses to identify biomarkers.

**Magnetic resonance imaging, or MRI,** shows the brain’s structure. It points to physical changes in the brain, such as tissue shrinkage and vascular disease.

**Amyloid PET scans** show the amount of amyloid plaques in the brain.

**Tau PET scans** show the amount of tau tangles in the brain.

**Cerebrospinal fluid, or CSF,** is collected through a lumbar puncture. It indicates chemical makeup in the brain, including information about amyloid and tau proteins.

Initiative to End Alzheimer’s welcomes new development director

The Initiative to End Alzheimer’s (IEA) welcomes Steve Ramig as its new senior director of development. Ramig has nearly 20 years of fundraising experience in university and health care settings, including eight years with the University of Wisconsin Foundation Alumni Association (WFAA).

The Initiative to End Alzheimer’s supports the complementary goals of the Wisconsin Alzheimer’s Disease Research Center and the Wisconsin Alzheimer’s Institute.

Listen up!

*Dementia Matters* is a podcast about Alzheimer’s disease, produced by the Wisconsin Alzheimer’s Disease Research Center. Host Dr. Nathaniel Chin interviews experts on the latest Alzheimer’s disease headlines, research, and caregiver topics. Listen online at www.adrc.wisc.edu/dementia-matters, or subscribe on iTunes and other major podcasting platforms.
Selected open studies

**African-Americans Fighting Alzheimer's in Midlife (AA-FAiM)**

AA-FAiM is a sub-study of WRAP, looking to address modifiable risk factors for prevention of Alzheimer’s disease. AA-FAiM is enrolling African-Americans into WRAP who are age 40 to 65, have a parent diagnosed with Alzheimer’s disease, or who have a mother who lived to age 75 or older and a father age 70 or older, without memory problems. Participation includes enrollment in WRAP, medical and lifestyle assessments and questionnaires, blood draw, memory testing, answering questions about experiences of discrimination/life stressors and coping behaviors, optional lumbar puncture and/or MRI, optional post-study visit or call to discuss your study findings, and follow-up visits every two years. AA-FAiM offers payment for your time. If interested, please call (608) 263-8620.

**Wisconsin Brain Donor Program**

The Wisconsin Brain Donor Program is a repository of biologic specimens collected after death for the purpose of advancing Alzheimer’s disease and related dementias research. WRAP participants and their biologic parents can enroll in the Wisconsin Brain Donor Program. Healthy older individuals without memory difficulties are also encouraged to contact the program to be considered for enrollment. All donation costs are covered for those accepted into the donor registry. Participation is voluntary; enrollees are free to withdraw at any time. If interested, please call (608) 265-4000.

**Synapse Project**

Synapses are points in the brain where two brain cells connect and communicate. The Synapse Project uses positron emission tomography (PET) brain scans to visualize neuronal synapse density, amyloid plaques, and neurofibrillary tangles. The study will also obtain MRI data to investigate how these factors are affecting brain health. The study examines whether AD pathology affects the quantity of synapses, and whether loss of synapses over time is associated with cognitive decline. If you qualify for the study, we will ask you to complete three PET scans of your brain — one for amyloid, one for tangles, and one for synapse density. Completion of an MRI scan may also be required. If interested, please call (608) 262-9479.