It’s difficult to summarize how exciting the past few months have been for our team. We have seen a seismic tide of new discoveries about Alzheimer’s disease and related disorders. With the announcement of positive clinical trials and new FDA approvals for disease modifying therapy for Alzheimer’s disease, we are entering a new era of treatments that slow and eventually prevent this disease are becoming a reality. As we look to the near future, clinicians will need better tools for early identification of Alzheimer’s disease, so those treatments can start early. This is precisely where WRAP comes in. We are testing whether the abnormal proteins in Alzheimer’s disease can be detected in a simple blood test. Our recently published early results strongly indicate this will be the case; and now we’re in the process of testing blood samples from WRAP dating back to approximately 2011. We are also embarking on a promising new pilot study to determine if a blood spot from a finger prick can successfully be used to detect abnormal AD protein levels. The development of a finger prick test is more affordable, scalable and accessible for more communities. We are excited to see where this leads!

For now, perhaps the area where you as a WRAP participant can make the strongest impact is to undergo one of our gold standard tests for amyloid and tau (which involves PET scan or spinal fluid donation) and provide a blood sample so that we can try new tests for blood and determine if the new tests agree with the gold standard tests.

As we wrote about in the last newsletter, more changes are coming to WRAP in order to assess other changes that may be happening in the brain, including vascular disease changes. To explore these links, we are now beginning to offer a carotid vascular ultrasound at some WRAP study visits. Through a partnership with UW School of Medicine and Public Health cardiovascular researchers, this non-invasive scan of the neck helps our team explore links between cardiovascular and brain health. Read more about how these scans work on page three.

The WRAP study continues to be a leading study in the field regarding the pre symptomatic phase of Alzheimer’s disease. As volunteers for WRAP, you are helping scientists tease apart normal aging from the very earliest signs of Alzheimer’s disease, perhaps as much as 20 years prior to symptoms. This is ground breaking work and only possible because of you. Thank you.
Each year, UW–Madison researchers publish dozens of research papers, often utilizing data contributed by WRAP participants. The following studies are a few recent examples of work published by our researchers.

**Characterizing onset and rate of Alzheimer’s biomarkers in people with Down Syndrome**

A study led by Bradley Christian, PhD, Matthew Zammit and Tobey Betthauser, PhD, investigated understanding of rates and onset of Alzheimer’s disease in people with Down Syndrome. A total of 177 adults with Down Syndrome from the Alzheimer’s Biomarker Consortium-Down Syndrome underwent imaging, and researchers compared levels of tau and amyloid in the individuals over a multi-year period. The findings highlighted a rapid accumulation of amyloid and early onset of tau and provide a strategy for characterizing Alzheimer’s disease progression specific to the Down Syndrome population and independent of age.

Title: “Characterizing the emergence of amyloid and tau burden in Down syndrome”

Journal: *Alzheimer’s & Dementia*

**Comparing word-list and story recall tests as diagnostic tools**

Word-list and story recall tests are used for dementia diagnosis. In this study, researchers aimed to establish how standard clinical metrics compared to process scores derived from word-list and story recall tests in predicting biomarker-determined Alzheimer’s disease. Data from 295 participants were drawn from the Wisconsin ADRC and Wisconsin Registry for Alzheimer’s Prevention (WRAP). Findings showed story recall tests may perform better than word-list tests for dementia detection.

Title: “A comparison of diagnostic performance of word-list and story recall tests for biomarker-determined Alzheimer’s disease”

Journal: *Journal of Clinical and Experimental Neuropsychology*

Read more about these studies by searching their titles at pubmed.gov.

**WRAP participant impact**

Thank you Dr. Loepfe

Dr. Thomas Loepfe retired December 1, 2023, from his career as a geriatrician and researcher at Mayo Clinic Health System in La Crosse, WI. Dr. Loepfe was the site leader of the WRAP research site in La Crosse, where he founded the study program. He is also a long-time physician, instructor and researcher. We are deeply grateful for his contributions to our study and his dedication to his patients and people impacted by dementia. He will be greatly missed. The WRAP research site in La Crosse will be supervised by Dr. Daniel Anderson, who we welcome to our program.

UW researchers in Amsterdam

More than 50 Alzheimer’s disease researchers from UW–Madison presented at the 2023 Alzheimer’s Association International Conference in Amsterdam, Netherlands. Our campus experts participated in a variety of ways, including as scientific reviewers, session moderators, oral presenters, and poster presenters. Data from WRAP was included in numerous studies presented at the event. Read a description of research at the event on our news web page: wrap.wisc.edu/news.
A research refresh in Milwaukee

The WAI Regional Milwaukee Office launched a research refresh in 2023. As one of WRAP’s research study sites, the busy team is launching this campaign to share the importance of participating in research.

The office is working to increase engagement and participation of under-represented populations, with specific attention to the African American community. They are reinstating blood draws, MRIs, and brief medical exams to research visits. To support this work, WAI Milwaukee is hiring a Nurse Practitioner, Phlebotomist, and Clinical Research Supervisor to the study team. As part of the relaunch, they also added three new study coordinators in 2023, creating more availability to coordinate and schedule study visits.

In addition to developing and participating in community engagement events throughout the year, the team hosts a signature event, Breaking the Silence: Addressing Dementia in Communities of Color, each April in recognition of minority health month.

The Amazing Grace Chorus® hosts live-streamed performances on Saturdays every fall and spring, providing vital connection, respite and resources for people living with memory changes and caregivers. All are welcome to join and sing along from home. Find details at wai.wisc.edu/chorus.

Open Study

WRAP participants are invited to enroll in PREDICT3, a study open to people ages 45 or older, with or without memory concerns. The study is examining biomarkers, such as PET and MRI scans, to determine when symptoms of Alzheimer’s disease begin, how changes happen over time, and how they relate to memory, thinking, genetics, health, and lifestyle factors. This study is longitudinal with two visits over an approximate 2-3 year interval. The goal is to improve the ability to diagnose Alzheimer’s disease.

Contact: Teresa Hellenbrand
Email thellen@medicine.wisc.edu or phone (608) 262-3724

Meet our WRAP Milwaukee study coordinators

Pictured (left to right): Study coordinators Rainy Von Gunten, Julie Leach and Heidi Bucci joined Ian Canovi and Celena Ramsey in 2023.

Understanding vascular carotid ultrasounds

A vascular carotid ultrasound is a non-invasive procedure used to measure thickness of the walls of arteries in the neck, called carotid arteries. Participants lie on their back for 25-30 minutes with electrocardiogram leads attached to their wrists and chest. Then, a sonographer uses an ultrasound wand to take pictures of the carotid arteries. Images from this scan can show thickness of the carotid, plaques, and measure the artery stiffness. Generally, when the walls of the carotid artery become thicker, this could be a sign of cholesterol buildup and indicate increased risk of heart attack or stroke.

At WRAP, we are now studying if this buildup is related to dementia development. Using advanced techniques developed at UW School of Medicine and Public Health, we are studying if brightness and contrast of carotid artery walls are related to dementia. These images also allow us to see stiffness of the arteries and if they expand and contract properly as the heart beats. Images from a study visit are read by sonographers and reviewed by a cardiologist. Infrequently, there may be something found that is medically important for a participant to know. Some examples include major artery blockages, nodules or cysts in the thyroid gland, enlarged thyroid gland, or blood pressure changes. These findings will be reported to you through the study team staff. Please note the carotid ultrasounds are not a formal medical imaging test and, like other biomarker visits, the findings are not automatically placed in a medical record or accessible by your health care team.

Pictured: A photo depicting a person undergoing a vascular carotid ultrasound. The sonographer places an ultrasound probe on the side of the neck to take images of the arteries in the neck.
Researcher Spotlight

Rachael Wilson, PhD

Dr. Wilson is a Fluid-Based Biomarker Scientist for the Wisconsin Alzheimer’s Disease Research Center, where she leads the brain biomarker lab’s work analyzing fluid samples from tests like blood tests or lumbar puncture.

Q: Can you tell me about an interesting study you’ve recently contributed to?

I’m working on one now looking at the biomarker SNAP-25 in cerebrospinal fluid (CSF) and how it relates to Alzheimer’s disease biomarkers such as amyloid and tau PET and fluid biomarkers. Right now, we have good biomarkers for measuring amyloid and tau, but we don’t have established markers for tracking neurodegeneration that occurs as the disease progresses. Neurodegeneration is the process of neurons breaking down, so they don’t function properly anymore, which leads to the cognitive symptoms of Alzheimer’s disease. SNAP-25 is a protein involved in transmitting messages between neurons, and other studies have seen in increase in SNAP-25 levels in the CSF with neurodegeneration. Our study found that the levels of SNAP-25 increase in a very similar way to how phosphorylated tau (pTau, an Alzheimer’s disease biomarker) levels increase in CSF, which suggests that SNAP-25 may be a useful biomarker for tracking neurodegeneration in early stages of Alzheimer’s disease.

Q: After years of working in Alzheimer’s disease services, have you changed any of your personal behaviors?

I am a newcomer to Alzheimer’s disease research, but after working here for almost a year, I am definitely more aware of how overall wellness can impact aging in general. It makes me more mindful of prioritizing diet and exercise for the long-term effects.

Q: Did anything surprise you about these findings?

Other groups have reported similar trends between Alzheimer’s biomarkers and SNAP-25, but we were surprised with how close the relationship was between SNAP-25 and phosphorylated tau. It’s especially important considering the majority of our samples were from cognitively unimpaired participants, so we may be detecting early neuronal dysfunction.

Q: What comes next?

My primary goal at the moment is to establish our plasma biomarker program so we can test blood for Alzheimer’s disease biomarkers here at UW-Madison. We have already begun running some of the blood samples that we have stored using new blood-based assays. Because blood tests are less invasive than lumbar punctures and less expensive than PET scans, we are trying to understand how these tests perform over time, so that we can eventually use blood biomarkers for detecting Alzheimer’s disease. We are also interested in exploring CSF and blood tests for other proteins that can occur along with amyloid and tau.

Q: Anything else you’d like to share with WRAP participants?

I can’t say thank you enough to all the participants and study partners. The findings from this study have contributed so much to Alzheimer’s disease research, and we could not have done it without you all!