

2022 - 2023
**IMPACT
REPORT**



VANDERBILT MEMORY AND ALZHEIMER'S CENTER

ADVANCING DISCOVERIES IN ALZHEIMER'S RESEARCH

LETTER FROM THE DIRECTOR

This year has been marked by significant advancements and promising discoveries in Alzheimer's disease and dementia research that bring us closer to understanding and combating this devastating disease.

Both worldwide and here at the Vanderbilt Memory and Alzheimer's Center, we have witnessed breakthroughs in many areas of study, ranging from genetics and biomarkers to novel therapeutic approaches.

During the 2022-2023 academic year, we made major strides within our local research program from implementing amyloid and tau positron emission tomography (PET) research scans to launching our brain donation program.

In this 2023 Impact Report, you will read about notable Center updates, highlights in community outreach, novel discoveries, and continued success in training the next generation of clinicians and scientists.

We are grateful for your continued support of our research at the Vanderbilt Memory and Alzheimer's Center.



DR. ANGELA L. JEFFERSON

Herbert O. and Vineta Christopher Director in Alzheimer's Disease
Director, Vanderbilt Memory and Alzheimer's Center
Director, NIA Exploratory Vanderbilt Alzheimer's Disease Research Center
Vice Chair of Scientific Strategy and Innovation, Department of Neurology
Professor of Neurology

TABLE OF CONTENTS

CENTER UPDATES 3-4

Tennessee Alzheimer's Project Achieves Enrollment Goal

Amyloid and Tau PET Scans Further Alzheimer's Research

VMAC Launches Brain Donation Program

OUTREACH 5

VMAP Participant Encourages Diverse Participation

Finding God in Alzheimer's Disease

NEW DISCOVERIES 6-8

Novel Discoveries in Alzheimer's Research

TRAINING 9

VMAC Trainees Earn Doctoral Degrees

4th Annual Alzheimer's Disease Research Day Addresses Disparities

COVER STORY: COMMUNITY SCREENING PROGRAM

At the Vanderbilt Memory and Alzheimer's Center, we acknowledge factors like transportation, time, and cost can be barriers to accessing preventative health care services, especially among underserved communities. To empower our local community with knowledge about their health, we launched our community screening program in fall 2022.

Since its inception, we have provided over 200 free memory screenings and free blood pressure screenings to community members throughout the Greater Nashville area.



OUR MISSION

The Vanderbilt Memory and Alzheimer's Center is an interdisciplinary team of scientists and clinicians focused on characterizing the pathways through which vascular risk and disease intersect with Alzheimer's disease and related dementia pathogenesis, progression, and clinical manifestation at the societal, systems biological, and cellular levels.

Modification of vascular risk and disease has demonstrated efficacy in improving Alzheimer's outcomes and is a leading target for drug discovery, early intervention and disease prevention.

TENNESSEE ALZHEIMER'S PROJECT ACHIEVES ENROLLMENT GOAL

In August 2020, The Vanderbilt Memory and Alzheimer's Center achieved a major milestone when we were awarded a 3-year, \$3.8M grant from the National Institute on Aging (NIA) to establish an exploratory Alzheimer's Disease Research Center (ADRC) at Vanderbilt University Medical Center. Over the past three years, the exploratory ADRC has laid the groundwork and infrastructure for Vanderbilt's eventual designation as an NIA-funded "Center of Excellence."



One major component of the exploratory ADRC was establishing a cohort of 150 older adults, known locally as the Tennessee Alzheimer's Project. It was crucial for this cohort to be diverse in terms of race, ethnicity, and cognitive status, ranging from cognitively unimpaired to early dementia symptoms.

In June 2023, our Center proudly enrolled our 150th participant in the Tennessee Alzheimer's Project, meeting our goal. Among the participants, 31% belong to underrepresented racial and ethnic groups, with 27% identifying as Black or African American. We are committed to ensuring that people of color are well-represented in our studies, especially in light of their higher vulnerability to dementia.

The Tennessee Alzheimer's Project includes individuals across the entire Alzheimer's disease spectrum, ranging from cognitively unimpaired to early dementia, including both carriers and non-carriers of apolipoprotein E-e4 allele (*APOE-e4*), the largest genetic risk factor for Alzheimer's disease.

With the dedication of our team and the participation of our generous participant volunteers, we submitted a grant application in June 2023 to establish an NIA-designated Center of Excellence at Vanderbilt University Medical Center. We look forward to receiving notice from the NIA in early 2024 regarding our application's outcome.

YOUR SUPPORT OF THE VANDERBILT MEMORY AND ALZHEIMER'S CENTER ASSISTS WITH



Novel discoveries at the
intersection of Alzheimer's
risk and resilience



Community outreach
and commitment to
translational science



Training the next generation
of Alzheimer's disease
scientists and clinicians

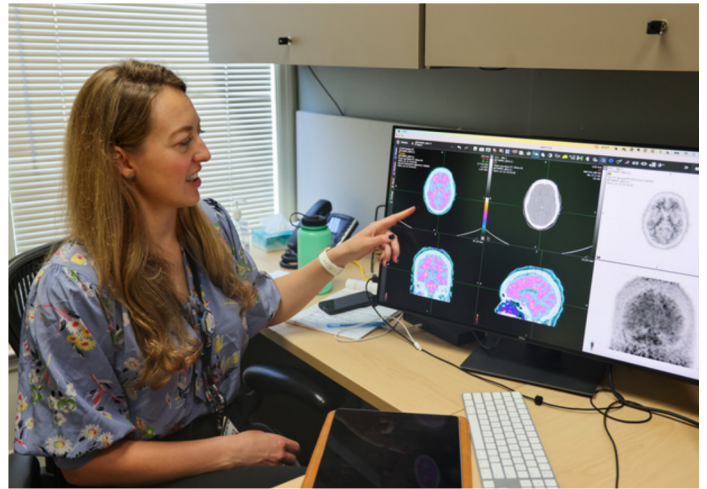
TO LEARN HOW TO DONATE TO THE VANDERBILT MEMORY AND ALZHEIMER'S
CENTER AND ADVANCE RESEARCH EFFORTS HERE IN TENNESSEE, VISIT

WWW.VUMC.ORG/VMAC/DONATE

AMYLOID AND TAU PET SCANS FURTHER ALZHEIMER'S RESEARCH

For a long time, researchers could only detect the abnormal proteins associated with Alzheimer's disease by examining the brain under a microscope after death. Now, with positron emission tomography (PET) scans, we have radioligand tracers that let researchers see the abnormal proteins in the brain that build up in Alzheimer's disease. These tracers produce colorful images that allow us to quantify the burden of these proteins in the brain and how much they change over time.

Alzheimer's researchers primarily focus on two proteins: amyloid and tau. In Alzheimer's disease, amyloid proteins clump together to form plaques that collect between nerve cells and disrupt function. Tau proteins collapse into twisted strands that form tangles inside of the nerve cell, disrupting communication between cells. We can image both of these abnormal proteins in the brain with tracers used in PET scans.



In 2021, Vanderbilt Memory and Alzheimer's Center received a \$860,000 supplement grant to establish amyloid and tau PET protocols for the Tennessee Alzheimer's Project cohort. These protocols were implemented in fall 2022. Recently, we have also begun to implement amyloid and tau PET scans within our Vanderbilt Memory and Aging Project cohort using funds from a generous donor.

The information obtained from these scans assists in improving diagnostic accuracy, tracking disease progression, and identifying the underlying mechanisms linking risk factors to Alzheimer's disease pathology.

VANDERBILT MEMORY AND ALZHEIMER'S CENTER LAUNCHES BRAIN DONATION PROGRAM

Brain donation is a necessary resource in our mission to prevent, treat, and ultimately cure Alzheimer's and related diseases. In fall 2022, the Vanderbilt Memory and Alzheimer's Center launched our brain donation program to better understand the causes of memory loss in aging and find ways to treat, cure, and prevent Alzheimer's disease and related conditions.

We are proud to share that over the last year, nearly 300 participants in the Vanderbilt Memory and Aging Project and Tennessee Alzheimer's Project have assented to brain donation.

INTERESTED IN JOINING A STUDY?

PLEASE CONTACT OUR TEAM AT 615-875-3175 OR VMAC.RESEARCH@VUMC.ORG

PARTICIPANTS NEEDED FOR VUMC STUDY
VUMC STUDYING EARLY DRIVERS OF ALZHEIMER'S DISEASE



VANDERBILT MEMORY AND AGING PROJECT PARTICIPANT ENCOURAGES DIVERSE PARTICIPATION

In February 2023, Tonya Brown, a participant in the Vanderbilt Memory and Aging Project, sat down for an interview with reporter Olivia Michael from Nashville's *NewsChannel5* to discuss her study experience and the importance of encouraging others to participate. Tonya emphasized the significance of diverse representation in Alzheimer's research, as Black and African American adults are nearly twice as likely to develop the disease compared to their White counterparts.

Tonya's family history of the disease inspired her to get involved in the study, and her faith and opportunity to make a difference for future generations continues to drive her.

"A lot of African Americans are afraid to get involved in research, but times have changed. Anything that I can provide to help find a cure — I feel that I am making a difference."

- Tonya Brown, VMAP Participant



FINDING GOD IN ALZHEIMER'S DISEASE

In partnership with the Meharry-Vanderbilt Alliance, the Vanderbilt Memory and Alzheimer's Center hosted our first annual Finding God in Alzheimer's event in October 2022. We brought together faith leaders, researchers, academic leaders, and community members to have an open and honest discussion. The group collaborated on how we can all address racial inequities surrounding Alzheimer's disease in the African American community, who experience an unequal burden of dementia.

We were fortunate to have so many attendees and speakers willing to share ideas to create better partnership between our Center and the communities we serve.

NEW DISCOVERIES IN ALZHEIMER'S AND DEMENTIA RESEARCH



RACIALLY AND ETHNICALLY DIVERSE PATIENTS LESS LIKELY TO HAVE AMYLOID PLAQUES NECESSARY FOR ALZHEIMER'S TREATMENT

A study led by Vanderbilt Alzheimer's Disease Research Center Associate Director Dr. Consuelo Wilkins found that fewer Black, Hispanic, and Asian patients meet qualifications for landmark clinical trials that may slow Alzheimer's disease progression by targeting amyloid plaques. Alzheimer's disease impacts Black and Hispanic people at a higher rate than White non-Hispanic people. However, both Black and Hispanic people are about 30% less likely than White non-Hispanic people to have amyloid in their brains.

"Our findings illustrate the urgency of understanding the underlying causes of memory loss in racially and ethnically diverse communities. These populations have higher rates of hypertension and diabetes, which are associated with vascular diseases of the brain," said Wilkins. "There are far-reaching implications on the patients and their families, if new treatments are less effective because they are less likely to have amyloid PET positivity."

NEW FINDINGS RELATED TO ALZHEIMER'S GENETIC RISK FACTOR

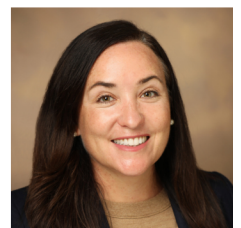
A genetic variant of apolipoprotein E (*APOE*), a protein involved in fat metabolism, is the strongest common genetic risk factor for Alzheimer's disease. However, many *APOE-e4* carriers remain cognitively normal throughout life, suggesting there may be *APOE* modifiers that protect the brain.



Using Vanderbilt Memory and Aging Project data, Vanderbilt Alzheimer's Disease Research Center Biomarker Core Leader Dr. Timothy Hohman led a study using whole blood RNA sequencing to identify genes that change the association between *APOE-e4* and cognitive performance. The team found that a higher expression of the *RNASE6* gene, which has roles in immunity, related to worse baseline memory among *APOE-e4* carriers.

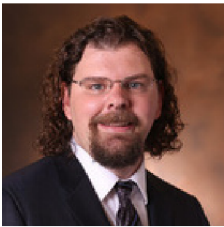
IRREGULAR SLEEP, HEART HEALTH, AND BRAIN HEALTH

A study led by Assistant Professor of Medicine Dr. Kelsie Full found sleep irregularity was associated with a higher risk of atherosclerosis, or hardened arteries. Sleep irregularity is defined as frequently disrupted sleep and varying sleep durations night after night.



"These results suggest that sleeping close to the same total amount of time each night, between 7-9 hours, may play an important role in preventing cardiovascular disease," said Dr. Full.

Past research has found that atherosclerosis is associated with an increased risk of dementia, meaning your sleep habits not only affect your heart health but your brain health too.



HEALTH CONDITIONS ASSOCIATED WITH ALZHEIMER'S DISEASE AND VASCULAR DEMENTIA

A study completed by Dr. Bennett Landman, the Biomarker Core Co-Leader for the Vanderbilt Alzheimer's Disease Research Center, suggests several health conditions are associated with future dementia. Some conditions were found to begin at least five years before dementia diagnosis.

The team found that the earliest and most consistent associations with Alzheimer's disease were depression, erectile dysfunction, gait abnormalities, hearing loss, and nervous and musculoskeletal symptoms. An enlarged heart, overactive bladder, non-melanoma skin cancer, and pneumonia did not show significant association with dementia until one year before dementia diagnosis.



LARGE SPACES AROUND BRAIN BLOOD VESSELS LINKED TO COGNITIVE DECLINE

Perivascular spaces are compartments filled with fluid adjacent to blood vessels. These spaces are thought to help fluid move in and out of the brain, carrying waste away to keep the brain healthy. Perivascular spaces are considered a form of vessel disease when they become large enough to see on a magnetic resonance imaging (MRI) brain scan.

Utilizing Vanderbilt Memory and Aging Project data, Vanderbilt Memory and Alzheimer's Center researchers found higher enlarged perivascular spaces (ePVS) volume was associated with worse cognitive outcomes. Greater arterial stiffness related to worse ePVS burden, suggesting cardiovascular aging as a potential cause.

These findings suggest that vascular risk factors, such as aging and high blood pressure, may lead to cognitive decline.

SEX DIFFERENCES IN THE COGNITIVE RESILIENCE TO ALZHEIMER'S DISEASE

Approximately 30% of older adults are cognitively unimpaired at time of death despite the presence of Alzheimer's pathology in the brain at autopsy, a phenomenon known as cognitive resilience. A recent study led by Vanderbilt researchers, including Drs. Timothy Hohman and Logan Dumitrescu, revealed that while cognitive resilience is highly heritable among both men and women, several sex differences exist.

The team found differences in the role cognitive resilience plays in autoimmune disease risk, cardiovascular traits, and RNA processing between men and women. These differences could be due to a variety of factors, including the influence of sex hormones, differences in hormonal changes, and differences in how men and women process nutrients and energy.

Better understanding the differences between men and women as it relates to cognitive resilience will be crucial to developing targeted treatments and interventions for Alzheimer's disease.





EARLY BRAIN CHANGES PREDICT FUNCTIONAL DECLINE

Using Vanderbilt Memory and Aging Project data, a study led by Assistant Professor of Medicine, Dr. Corey Bolton, found smaller grey matter volume and greater white matter hyperintensities at study entry predicted faster decline in the ability to complete complex everyday tasks. Grey matter throughout the nervous system enables individuals to control movement, memory, and emotions. White matter hyperintensities are white matter lesions in the brain, which have been associated with cognitive decline. These neuroimaging markers can be present in the brain years before cognitive decline begins.

Importantly, associations between grey matter volume and the decline in the ability to complete complex tasks were consistently stronger in individuals at increased risk of Alzheimer's disease. This finding includes individuals with mild cognitive impairment and *APOE-e4* carriers, the largest genetic risk factor Alzheimer's disease.

WHITE MATTER CHANGES IN ALZHEIMER'S PROGRESSION

In a recent study led by Assistant Professor of Neurology, Dr. Derek Archer, researchers used an imaging method called diffusion magnetic resonance imaging (dMRI) to measure white matter changes in the brain. Researchers also used a novel technique called "free-water elimination," which helps us more easily visualize changes inside versus outside brain cells.



Using data from multiple cohorts, including the Vanderbilt Memory and Aging Project, researchers found changes in the brain's white matter, especially in areas linked to memory, are associated with Alzheimer's progression.

In addition, these findings show that different methods can provide complementary information about brain changes, which is crucial for developing a better understanding of the disease and finding new ways to diagnose or treat Alzheimer's disease.



HIGH BLOOD PRESSURE IS LINKED TO ALZHEIMER'S DISEASE

Hypertension, or high blood pressure, affects nearly 60% of aging adults and is an important risk factor for vascular cognitive impairment and late-life dementia. Assistant Professor of Medicine, Dr. Monica Santisteban led a scientific review focused on the mechanisms underlying these harmful effects.

Her review found that chronic high blood pressure can harm the blood vessels and brain tissue over time, putting individuals with hypertension at higher risk for developing dementia. Findings showed that hypertension was associated with several pathways of injury, including the buildup of amyloid plaques, inflammation, and breakdown of the blood-brain barrier.

A personalized precision medicine approach is likely to hold the key to prevent cognitive decline in individuals with hypertension, utilizing a combined assessment of early markers of disease, inflammatory status, other vascular and metabolic conditions, and demographic and genetic factors.

TRAINING AND PROFESSIONAL DEVELOPMENT

Fostering a rich training environment for the next generation of scientists and clinicians is core to our mission at the Vanderbilt Memory and Alzheimer's Center. Over the past year, we were fortunate to celebrate achievements of both faculty and trainees as they further their career in Alzheimer's research.



14 EARLY CAREER RESEARCHERS RECEIVED INDEPENDENT FUNDING



21 EARLY CAREER FACULTY AND TRAINEES PRESENTED RESEARCH AT THE 2023 ALZHEIMER'S ASSOCIATION INTERNATIONAL CONFERENCE



20 "WORKS-IN-PROGRESS MEETINGS WERE HELD TO SUPPORT FACULTY AND TRAINEES WITH GRANT SUBMISSIONS

VMAC TRAINEES EARN DOCTORAL DEGREES

This past year, we also celebrated multiple trainees who completed their doctoral degrees including Francis Cambroner, PhD, Jaclyn Eissman, PhD, and Ketaki Katdare, PhD.



4TH ANNUAL ALZHEIMER'S DISEASE RESEARCH DAY ADDRESSES DISPARITIES IN ALZHEIMER'S RESEARCH

In March 2023, we held our 4th Annual Vanderbilt Alzheimer's Disease Research Day. The event showcased Alzheimer's disease and related dementia research across campus, including Vanderbilt University Medical Center, Vanderbilt University, and Meharry Medical College.

This year's theme focused on disparities in Alzheimer's and related dementia research. We were fortunate to have a day full of compelling faculty lectures along with an inspiring keynote presentation by Dr. Jonathan Jackson, Executive Director of the Community Access, Recruitment, and Engagement (CARE) Research Center at Massachusetts General Hospital and Harvard Medical School.

This annual event is a great opportunity for researchers across our institutions to collaborate and share the latest findings in Alzheimer's and related dementia research.



OUR VISION

We envision a world without Alzheimer's disease. We work to ensure that future generations can age without the fear of developing Alzheimer's disease or related dementias.



The most courageous people I have ever met are caregivers and individuals with Alzheimer's disease. I can confidently say I've learned more from listening to the experiences of families living with Alzheimer's disease than I have from reading any book or article. They inspire me each day to continue working toward a world without Alzheimer's and dementia.

Leslie Gaynor, PhD
Assistant Professor of Medicine

My grandmother was diagnosed with Alzheimer's disease when I was a teenager. I saw the impact the disease had on my grandmother and my whole family as my mother and her siblings took on the role of caregiver. I remember wishing for better treatment options or research opportunities - anything that could give us answers or even a few more years of joyful memories with her.

Marina Velez, PhD
Participant Recruitment Manager

Growing up, I heard many stories about Alzheimer's disease as it impacted multiple family members of mine. What stood out to me was the profound effect it had not only on the patients but also on their loved ones. During my MD/PhD training, I have had the privilege of hearing inspiring stories from patients, research participants, and their families. Witnessing the strength displayed by individuals affected by Alzheimer's and their loved ones has been a continuous motivation for me to study this devastating disease.

Hailey Kresge
MD/PhD Student



THANK YOU FOR YOUR SUPPORT

From participation in research studies to financial donations, we want to thank you for the continued support of our Center. Our advancements in Alzheimer's research would not be possible without your contributions.

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