

# Alzheimer's Disease Information Network ADIN Monthly E-News

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**CTAD 2013**

6th Conference

Clinical Trials in  
Alzheimer's Disease

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## Undiagnosed Pre-Diabetes Highly Prevalent In Early Alzheimer's Disease



*"This result [of the resveratrol study] suggests that perhaps we should test all our patients with early Alzheimer's for glucose intolerance," says R. Scott Turner, director of Georgetown's Memory Disorders Program.*

A study by a Georgetown neurologist has found that undiagnosed pre-diabetes is much more common than previously thought in people with mild to moderate Alzheimer's disease.

Dr. R. Scott Turner of Georgetown University Medical Center (GUMC) began enrolling people with mild to moderate Alzheimer's disease into a nationwide study last year on resveratrol, a compound found in red grapes and red wine.

Resveratrol is thought to act on proteins in the brain in a way that mimics effects of a low-calorie diet, and Turner's study researches the potential for the compound to change glucose levels in patients with early Alzheimer's disease (AD).

### Shocking Results

Turner says he was "shocked" by how many study participants were found to have pre-diabetes.

*Continued on next page...*

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This newsletter is prepared monthly by the Alzheimer's Disease Cooperative Study at the University of California, San Diego. Content is intended to educate the public about AD research endeavors and other AD issues.

*Questions or  
comments?*

*Please email:  
[brainlink@ucsd.edu](mailto:brainlink@ucsd.edu)*

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## Undiagnosed Pre-Diabetes Highly Prevalent In Early Alzheimer's Disease continued...

“We know from animal studies that caloric restriction prevents diseases of aging such as diabetes and Alzheimer’s,” explains Turner, director of the GUMC’s Memory Disorders Program. “On the flip side of the coin, having diabetes increases one’s risk of developing AD. So perhaps by improving glucose tolerance, we will prevent or delay both diabetes and Alzheimer’s.”

To join the resveratrol study, participants were first given a fasting glucose tolerance test to obtain a baseline level, then retested two hours after eating. A high sugar level after two hours reveals glucose intolerance (pre-diabetes) or diabetes if the level is very high.

“The number of people with glucose intolerance (pre-diabetes) was much higher than expected,” says Turner. “I was surprised by how many people didn’t know they were pre-diabetic, and these are individuals who already get the best medical care.”

### Alzheimer’s Association Presentation

Of the 125 study participants who completed the two-hour test, 43 percent had pre-diabetes (38 people or 30 percent) while 16 individuals or 13 percent had results consistent with diabetes.

Turner presented his findings at the Alzheimer’s Association International Congress in Boston on July 14.

The Georgetown doctor is now researching whether glucose intolerance or diabetes leads to Alzheimer’s disease, if the inflammation associated with AD triggers glucose intolerance and if a “vicious cycle” of Alzheimer’s and glucose intolerance exists.

### A Simple Test

While Turner’s study isn’t designed to answer these questions, his research might provide important clues.

“This result suggests that perhaps we should test all our patients with early Alzheimer’s for glucose intolerance,” he says. “It’s a simple, inexpensive study that reveals critical health information.”

The resveratrol study is sponsored by the Alzheimer’s Disease Cooperative Study through a grant from the National Institute on Aging.



## Brain's 'Garbage Truck' May Hold Key To Treating Alzheimer's And Other Disorders



**By Mark Michaud**  
**University of Rochester Medical Center**

In a perspective piece appearing in the journal *Science*, researchers at University of Rochester Medical Center (URMC) point to a newly discovered system by which the brain removes waste as a potentially powerful new tool to treat neurological disorders like Alzheimer's disease. In fact, scientists believe that some of these conditions may arise when the system is not doing its job properly.

"Essentially all neurodegenerative diseases are associated with the accumulation of cellular waste products," said Maiken Nedergaard, M.D., D.M.Sc., co-director of the URMC Center for Translational Neuromedicine and author of the article. "Understanding and ultimately discovering how to modulate the brain's system for removing toxic waste could point to new ways to treat these diseases."

The body defends the brain like a fortress and rings it with a complex system of gateways that control which molecules can enter and exit. While this "blood-brain barrier" was first described in the late 1800s, scientists are only now just beginning to understand the dynamics of how these mechanisms function. In fact, the complex network of waste removal, which researchers have dubbed the glymphatic system, was only first disclosed by URMC scientists last August in the journal *Science Translational Medicine*.

The removal of waste is an essential biological function and the lymphatic system – a circulatory network of organs and vessels – performs this task in most of the body. However, the lymphatic system does not extend to the brain and, consequently, researchers have never fully understood what the brain does with its own waste. Some scientists have even speculated that these byproducts of cellular function were somehow being "recycled" by the brain's cells.

One of the reasons why the glymphatic system had long eluded comprehension is that it cannot be detected in samples of brain tissue. The key to discovering and understanding the system was the advent of a new imaging technology called two-photon microscopy which enables scientists to peer deep within the living brain. Using this technology on mice, whose brains are remarkably similar to humans, Nedergaard and her colleagues were able to observe and document what amounts to an extensive, and heretofore unknown, plumbing system responsible for flushing waste from throughout the brain.

The brain is surrounded by a membrane called the arachnoid and bathed in cerebral spinal fluid (CSF). CSF flows into the interior of the brain through the same pathways as the arteries that carry blood. This parallel system is akin to a donut shaped pipe within a pipe, with the inner ring carrying blood and the outer ring carrying CSF. The CSF is drawn into brain tissue via a system of conduits that are controlled by a type support cells in the brain known as glia, in this case astrocytes. The term glymphatic was coined by combining the words glia and lymphatic.

## Brain's 'Garbage Truck' May Hold Key To Treating Alzheimer's And Other Disorders continued...

The CSF is flushed through the brain tissue at a high speed sweeping excess proteins and other waste along with it. The fluid and waste are exchanged with a similar system that parallels veins which carries the waste out of the brain and down the spine where it is eventually transferred to the lymphatic system and from there to the liver, where it is ultimately broken down.

While the discovery of the glymphatic system solved a mystery that had long baffled the scientific community, understanding how the brain removes waste – both effectively and what happens when this system breaks down – has significant implications for the treatment of neurological disorders.

One of the hallmarks of Alzheimer's disease is the accumulation in the brain of the protein beta amyloid. In fact, over time these proteins amass with such density that they can be observed as plaques on scans of the brain. Understanding what role the glymphatic system plays in the brain's inability to break down and remove beta amyloid could point the way to new treatments. Specifically, whether certain key 'players' in the glymphatic system, such as astrocytes, can be manipulated to ramp up the removal of waste.

“The idea that ‘dirty brain’ diseases like Alzheimer's may result from a slowing down of the glymphatic system as we age is a completely new way to think about neurological disorders,” said Nedergaard. “It also presents us with a new set of targets to potentially increase the efficiency of glymphatic clearance and, ultimately, change the course of these conditions.”



## Gene Discovery Offers New Path For Alzheimer's Research

**By Dr. Gregory Jicha**  
**University of Kentucky Public Relations**

A new gene variant has been linked to Alzheimer's disease, and this association is strongest among elderly blacks.

Though not the first gene to be linked to the condition, the identification of this gene variant is a breakthrough, as it reveals another way Alzheimer's may be triggered in the brain.

We in the medical profession have known for a long time that blacks over the age of 65 have a greater chance of developing Alzheimer's disease than do Caucasian adults the same age. Researchers have identified a gene (ABCA7) that helps explain this increased risk in African Americans, according to a recent report in the Journal of the American Medical Association. The report, based on a large government-funded study, not only sheds new light on why African Americans are at increased risk for the disease, but also offers a possible new focus of future research in the battle against Alzheimer's.

ABCA7 is linked to production and metabolism of cholesterol and lipids. We have known for years that vascular problems stemming from high cholesterol and atherosclerosis seem to increase the risk of Alzheimer's disease. This discovery supports previous evidence that vascular health may be a particular contributor to the development of Alzheimer's among blacks. But we have also seen evidence that Alzheimer's is influenced by other genes, as well as by environmental factors and lifelong health habits. Taking this new evidence into consideration, it appears that there may be multiple mechanisms that control the onset and progression of this devastating disease.

From this evidence, it appears that there are variations of Alzheimer's disease, with different causes - much like different types of cancer. If this is true, the treatment an individual receives may need to be tailored to the particular variant of the disease that they have. At this time, it is not recommended that individuals seek genetic testing for Alzheimer's because the relationship between the gene variants and the disease has not been firmly established. Many people have an associated gene variant, but do not go on to develop Alzheimer's.

Approximately five million people in the U.S. have Alzheimer's disease; this number is expected to more than triple by the year 2050, when the disease will cost \$1.1 trillion annually. According to the Alzheimer's Association, it is the only disease among the top ten killers that has no effective treatment.

The discovery of ABCA7 provides us with a clear strategy for trying to reduce the risk for Alzheimer's in all of us, but most importantly for blacks. It shows the need to control your cholesterol and vascular risk factors. At the UK Alzheimer Disease Center/Sanders-Brown Center on Aging, we have recently been awarded two National Institute of Health grants focused on doing exactly this. These two studies are looking for volunteers with or without memory problems that want to lower their risk for Alzheimer's disease.



*Dr. Jicha is the McCowan Endowed Chair in Alzheimer Research at the UK Sanders-Brown Center on Aging.*

## Americans Would Enroll In Clinical Trials But Doctors Don't Mention Them, Poll Finds

While nearly three out of four Americans said they would be willing to participate in a clinical trial upon recommendation from a doctor, fewer than a quarter said their health care provider had mentioned the idea, according to a poll released by Research America. Mary Woolley, president and chief executive officer of Research America, said in a statement that the poll reveals certain challenges for recruitment, but it also provides clues on how to overcome those challenges. “Most Americans believe in the promise of research and are willing to share their personal health data to advance research; yet for many years now the percentage of people who participate in clinical trials has remained incredibly low,” Woolley said.

Specifically, Research America's “National Poll: Clinical Research” found that 72 percent of Americans likely would participate in a clinical trial if recommended by their doctor, but only 22 percent said a doctor or other health care professional spoke to them about medical research. The findings are based on an online survey of 1,006 adults in the United States conducted in May by Zogby Analytics for Research America. This poll focused on opinions about clinical research in the United States. About 16 percent of those surveyed said they or someone in their family have participated in clinical trials.

### Reasons for Nonparticipation in Trials

Respondents identified a number of reasons for not participating, such as a lack of awareness (53 percent), a lack of trust (53 percent), concerns about risk (51 percent), adverse health outcomes (44 percent), little or no monetary compensation (35 percent), privacy concerns (27 percent), and worries that it takes too much time (27 percent).

Physician Robert Califf, vice chancellor of clinical and translational research at Duke University Medical Center, a co-sponsor of the poll, said in a statement that it is critical for providers and health systems in the United States to recognize the importance of generating knowledge about which treatments are best through participation in clinical trials. “Advances in common diseases like Alzheimer's and diabetes, as well as rare diseases, depend on physicians and other members of the health care team offering their patients a chance to participate in clinical trials,” Califf said.

### More Education on Clinical Trials Needed

John Lewis, vice president of public affairs at the Association of Clinical Research Organizations, another co-sponsor of the poll, said the findings clearly indicate the need for more education about the importance and benefits of clinical trials. “More participation in clinical trials means more treatments being made available to patients sooner. Industry, academia, government, physicians and patient advocates must all work together to encourage people to participate in this lifesaving research,” Lewis said.

In terms of important factors for determining whether or not to consent to enrolling in a clinical trial, those surveyed indicated their top priorities were the reputation of the people or institution conducting the research and the opportunity to possibly improve their own health (89 percent); followed by whether medical bills are covered if injury occurs as a result of the study (88 percent); the opportunity to improve the health of others (86 percent); their physician's recommendation (80 percent); privacy and confidentiality issues (79 percent); and whether they would be paid to participate (77 percent).

For more information and to read the poll:  
<http://www.researchamerica.org/uploads/June2013clinicaltrials.pdf>

*Medical Research Law and Policy Report, June 19, 2013*

## People With Early-Stage Alzheimer's Mentor Medical Students To Increase Knowledge and Reduce Stigma

While the global population is aging, and the personal and economic burdens due to Alzheimer's disease and related disorders are skyrocketing, the number of doctors trained to effectively diagnose and treat people with Alzheimer's is already woefully inadequate. Experts in health policy and practice have indicated the need for more comprehensive education for health care professionals in dementia and aging to meet the needs of the growing number of older adults in the United States.

According to the American Geriatrics Society:

- There are currently approximately 7,500 certified geriatricians and fewer than 1,600 certified geriatric psychiatrists in the United States. It is projected that approximately 30 percent of the 65-plus patient population will need to be cared for by a geriatrician and that each geriatrician can care for a patient panel of 700 older adults. Based on these numbers, approximately 17,000 geriatricians are needed now to care for about 12 million older Americans.
- Due to the projected increase in the number of older Americans, it is estimated that approximately 30,000 geriatricians will be needed by 2030. To meet this need, this would require training approximately 1,200 geriatricians per year over the next 20 years.
- Few graduates of medical schools in the United States are pursuing advanced training in geriatrics. In 2010, a mere 75 residents in internal medicine or family medicine entered geriatric medicine fellowship programs. This is down from 112 in 2005.

"This is a challenging situation for older individuals, families and our healthcare system," said Maria Carrillo, Ph.D., Alzheimer's Association vice president of medical and scientific relations.

At the same time, a program developed by the Northwestern University Alzheimer's Disease Center in Chicago — and replicated now in Massachusetts, Missouri and New Hampshire — provides opportunities for first-year medical students and persons diagnosed with early stage Alzheimer's to participate together in experiential learning programs. In the Buddy Program, medical students are paired with individuals with dementia, and the "buddies" plan a year of regular meetings around mutually satisfying activities.

These programs are improving medical student knowledge and familiarity with Alzheimer's while also heightening sensitivity and empathy toward people with the disease, according to new data reported today at the Alzheimer's Association International Conference® 2013 (AAIC® 2013) in Boston.

The goals of the Buddy Program are to:

- Educate medical students about Alzheimer's disease by increasing their knowledge base, heightening their awareness of skills and strengths that remain in persons with Alzheimer's and familiarizing them with care/support issues and effective communication skills.
- Introduce students to research and practice opportunities in fields related to aging and dementia.
- Provide persons living with dementia an opportunity to serve as a mentor to a future doctor.

"We want to expand future physicians' knowledge of, interest in and attitudes toward Alzheimer's and dementia in order to increase the number of physicians capable of caring effectively and compassionately for patients with these diseases and their families," said Darby Morhardt, MSW, LCSW, research associate professor in cognitive neurology at the Northwestern University Feinberg School of Medicine.

## People With Early-Stage Alzheimer's Mentor Medical Students To Increase Knowledge and Reduce Stigma continued...

To date, the Buddy Program has paired 167 medical students and persons with dementia over 16 years. Scores on a Dementia Knowledge Test, created by Morhardt and colleagues in 2000, reveal modest improvement in student knowledge. Analysis of student journal entries, a program requirement following each activity, yield themes that include heightened sensitivity and empathy toward persons with Alzheimer's, increased recognition of remaining strengths and a change in students' preconceptions of dementia.

According to Morhardt, "Many students remark on the comfort and enjoyment they experience with their mentor and for some an increased comfort over the course of the year."

For example, one student wrote, "I feel like my interactions with (my mentor) are becoming more fluid as I begin to ask fewer complex questions and incorporate his viewpoint into my own speech. I also feel more comfortable 'jumping in' when (my mentor) struggles for too long with a word or sentence without threatening his independence. I understand so much more about (my mentor's) experience than I could even imagine before we met."

First-year medical students are selected based on interest and willingness to commit to these program requirements: 1) attendance at two 90-minute orientation sessions and monthly process meetings; 2) four hours per month in activity with their buddy for one academic year; and 3) submission of a semi-structured journal report following each visit. A pre-/post-dementia knowledge test assesses student's objective learning, and student journal entries are qualitatively analyzed for themes.

### Three Successful Replication Programs

The program has been successfully replicated at Boston University (2006), Dartmouth College (2010) and Washington University (2012). Each replicating program has integrated unique modifications while keeping the primary elements in place.

The Boston University program (PAIRS, Partners in Alzheimer's Instruction Research Study) produced several innovations, including the use of a textbook geared toward students and non-specialists; an additional comprehensive dementia knowledge test to better assess students' factual learning; scales to measure attitudes toward Alzheimer's and dementia; measures of physician empathy; and an end-of-the-year reflective essay encompassing students' PAIRS program experiences — including what they have learned throughout the program and how they envision that these experiences will affect their subsequent careers.

"Students in the PAIRS program have consistently demonstrated improvement in factual knowledge, as well as gaining valuable new experiences and perspectives related to caregiver and personal aspects of Alzheimer's disease, such as the frustrations of living with memory loss," said Andrew Budson, M.D., director of the education core at the Boston University Alzheimer's Disease Center. "Students' empathy for patients and caregivers has increased, and they report decreased stigma and negative attitudes toward people with Alzheimer's."

The Dartmouth TALEs (The Alzheimer's Learning Experience for Students) program has modified the structure of the Northwestern Buddy Program in the following ways: (1) In addition to first- and second-year medical students, Dartmouth College pre-medical students and master of public health students are permitted to enroll in the program; (2) two students are paired with each person with Alzheimer's and generally visit the person with Alzheimer's together; and (3) students in the program are given a survey of attitudes about Alzheimer's disease before beginning the program and after completing it. Nine medical students, 11 graduate students and 42 undergraduates have enrolled since the program began in 2010.



## People With Early-Stage Alzheimer's Mentor Medical Students To Increase Knowledge and Reduce Stigma continued...

"While our students typically enter the program with generally positive attitudes toward Alzheimer's disease and those who have it, the experience of being in the program further improves their attitudes on nearly every dimension that we assess," said Robert B. Santulli, M.D., associate professor of psychiatry at the Geisel School of Medicine at Dartmouth.

Modifications to the model by Washington University (DUO, Dementia Understanding Opportunity) include a reduced time requirement to two hours per month and a modified recruitment partnership focusing on students with general geriatric interest, in lieu of neurology students. The DUO Program is midway through its pilot year and has recruited 40 percent more student participants than anticipated with a wait list for interested persons with dementia. In addition to the quantitative measures implemented from the Buddy Program, participant feedback and monthly reflections continue to provide rich data for future qualitative analysis. Several themes for further analysis, such as whether DUO's fewer partner hours can provide the same benefit as the longer hourly requirements of the existing Buddy-inspired programs, have already been identified.

According to the Alzheimer's Association 2013 Alzheimer's Disease Facts and Figures report, more than 5 million Americans are living with Alzheimer's disease. By 2050, the number of people with Alzheimer's could be as much as three times that amount. Yet too many people with Alzheimer's disease are undiagnosed — by some estimates, as many as 50 percent. Alzheimer's disease is the sixth-leading cause of death in the United States and is the only leading cause of death without a way to prevent, cure or even slow its progression.

### **About AAIC**

The Alzheimer's Association International Conference (AAIC) is the world's largest conference of its kind, bringing together researchers from around the world to report and discuss groundbreaking research and information on the cause, diagnosis, treatment and prevention of Alzheimer's disease and related disorders. As a part of the Alzheimer's Association's research program, AAIC serves as a catalyst for generating new knowledge about dementia and fostering a vital, collegial research community.

### **About the Alzheimer's Association**

The Alzheimer's Association is the world's leading voluntary health organization in Alzheimer care, support and research. Our mission is to eliminate Alzheimer's disease through the advancement of research; to provide and enhance care and support for all affected; and to reduce the risk of dementia through the promotion of brain health. Our vision is a world without Alzheimer's. Visit [www.alz.org](http://www.alz.org) or call 800.272.3900.

## UK's First Dementia Dog Gives Couple 'Their Lives Back'



*Pilot scheme in Scotland sees specially-trained pet partners helping care for the elderly*

**By Adam Withnall**  
**UK News from The Independent**

Man's best friend has been lending a helping paw since time immemorial, and most people will be aware of the roles they play as guide dogs, sniffer dogs, even search and rescue dogs.

But have you ever heard of a dementia dog?

An elderly couple in Scotland said they have been given their lives back after they were partnered up with two-year-old golden Labrador Kasper – who is one of the first dogs in the UK to receive special training to assist dementia-sufferers.

Kasper's skills include fetching medicines when a reminder alarm goes off, waking up his owners at the right time and carrying items between them.

Mr Will, 79, was diagnosed with vascular dementia three years ago, and his wife Mrs Will, 66, took on the role of carer.

And she explained how challenging her husband's condition became, saying: "We've been married 48 years but often I've sat and looked at him and thought, 'I don't know who this person is'."

That all changed with the arrival of Kasper. As well as helping out around the house with his practical training, the family pet has relieved a great deal of stress for the couple and encouraged them to get out and about.

## UK's First Dementia Dog Gives Couple 'Their Lives Back' continued...

Mrs Will said: "Kaspa has totally given us our lives back. Ken is much happier because he's got the dog and we can go out now. We can go shopping together, we can even go on holidays.

"We are a lot more relaxed since the dog came because if Ken gets in a mood and angry, the dog comes and nudges him and he forgets his problems. I've got a good bit of him back again."

The team behind the project said that carers find they spend less time giving reassurance to their partner because the dog provides a "calming" new focus.

Speaking about the first time the couple went shopping with Kaspa, Mr Will said: "I was tensed up and after two or three steps he just brushed against me and looked up as if to say, 'am I doing OK?' and the stress just went."

Kaspa was joined in his training by Oscar, a two-year-old golden retriever who now helps another Arbroath couple, Frank and Maureen Benham.

Mrs Benham, 69, has been diagnosed with Alzheimer's, and her husband said: "Maureen and I can't imagine going back to what it was like before we got Oscar."

The Dementia Dog project was originally a brainwave from a group of product design students at the Glasgow School of Art. The programme's director Gordon Hush said they had exhibited "the ability to re-design experiences", above and beyond "the traditional domain of material manufacture".

The project got started with the help of Alzheimer Scotland, Dogs for the Disabled and Guide Dogs Scotland, as well as with funding from the Scottish Government and UK Design Council. It is expected to be rolled out further, and another two dogs have already begun their training.

Helen McCain, training director at Dogs for the Disabled, said: "Oscar and Kaspa have settled in well to their new homes and are already making an impact on the lives of their new partners.

"This new project has provided us with an opportunity to bring together our skills and experience to help with a different kind of challenge. We really believe that the dementia assistance dog could make a significant contribution to the Government's national dementia strategy."

Alzheimer Scotland called it a "ground-breaking project", and Logan Anderson from Guide Dogs Scotland said: "The Dementia Dog pilot has shown, not just how the dogs have provided practical benefits to those living with Alzheimer's, but also the mood-enhancing and emotional benefits as well."

**<http://www.independent.co.uk/life-style/health-and-families/health-news/uks-first-dementia-dog-gives-couple-their-lives-back-8709179.html?origin=internalSearch>**



# ADCS Trials Enrolling...

## Studies That Will Be Open for Enrollment Soon

For Information: <http://www.adcs.org/Studies/clinalResearchStudy.aspx>

### **A4 – Anti Amyloid in Aysymptomatic Alzheimer’s Disease**

# A4

### **SNIFF – the Study of Nasal Insulin to Fight Forgetfulness**



The Dominantly Inherited Alzheimer Network (DIAN). DIAN is an international research partnership of leading scientists determined to understand a rare form of Alzheimer’s disease that is caused by a gene mutation. Understanding of this form of Alzheimer’s disease may provide clues to decoding other dementias and developing dementia treatments.

Funded by a multiple-year research grant from the National Institute on Aging, DIAN currently involves thirteen outstanding research institutions in the United States, United Kingdom, Germany and Australia. John C. Morris, M.D., Friedman Distinguished Professor of Neurology at Washington University School of Medicine in St. Louis, is the project’s principal investigator.

DIAN is currently enrolling study participants who are biological adult children of a parent with a mutated gene known to cause dominantly inherited Alzheimer’s disease. Such individuals may or may not carry the gene themselves and may or may not have disease symptoms ([click here for information about genetic testing](#)).

To register for DIAN drug trials or DIAN, visit [www.DIANExpandedRegistry.org](http://www.DIANExpandedRegistry.org).



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