Study Finds Association between Youth Football and Later-life Cognitive Impairment

A NEW study of retired National Football League (NFL) players found an association between youth football and later-life cognitive impairment. Led by senior author Dr. Robert Stern, Boston University Alzheimer’s Disease Center Clinical Core Director, the study took a different approach in examining the potential risks of football participation by focusing on age of first exposure to tackle football and whether or not it was associated with cognitive difficulties later in life.

The study, published in the journal Neurology shortly before Super Bowl XLIX, used data from 42 former NFL players from the DETECT (Diagnosing and Evaluating Traumatic Encephalopathy Using Clinical Tests) study. These players, all of whom had reported memory and thinking problems over the last 6 months, were separated into two groups: those who began playing tackle football before age 12, and those who began to play at age 12 or older.

Players were given a neuropsychological testing battery and went through an extensive medical and athletic history, including history of concussions. The results showed that players who began tackle football before 12 years old had greater problems in memory, intelligence, and executive function. “We were surprised by how striking the results were,” said first author Julie Stamm, a PhD candidate at Boston University. “Every single test was significantly different, by a lot.”

The study team chose age 12 as the cutoff point because it appears to be a key age in brain development for boys, which may provide a window of vulnerability during which the brain is especially sensitive to repeated hits to the head.

The study is not without its limitations, however. The sample size is small and it focuses on professional football players. Thus, the results may not be applicable to those individuals who did not play professionally or to those who played other sports such as soccer and ice hockey. Future studies will be able to focus on larger and more diverse samples and on longitudinal designs. Nevertheless, this study is the first to suggest a link between age of first exposure to tackle football and later-life cognitive problems. It opens our eyes to the possible consequences of repetitive head trauma in youth athletes.
HOPE for the Present and A Cure for the Future

Providing HOPE is one of many goals of the Boston University Alzheimer's Disease Center (BU ADC). We hope to find a cure for Alzheimer’s disease and inspire others to believe that there is hope in finding a cure. Without research participation, the BU ADC could not perform its cutting-edge research that is so desperately needed to cure Alzheimer’s and help those with the disease.

HOPE is also an acronym for the main registry for participants in the BU ADC. HOPE stands for Health Outreach Program for the Elderly. People who join HOPE attend a yearly visit in which their memory and thinking abilities are evaluated. They also participate in other BU ADC-affiliated studies. Interested volunteers may join this important registry if they can attend a yearly visit with a study partner and are age 65 or older with or without memory concerns, or are age 50 or older with memory concerns.

Charlene Francis is a participant in our HOPE study and also serves on our Community Action Council. Ms. Francis has been enrolled in the HOPE study for 11 years. She was motivated to participate in research because her mother had passed away from Alzheimer’s disease in 2005. “By participating in HOPE, I learned that as you age things happen to you, and the HOPE team explains why there are changes and clarifies what is normal aging and what is not. Fear is still in the back of my mind, but by participating I gain knowledge about the signs and symptoms. I am then able to educate my friends and family,” said Ms. Francis.

Ms. Francis wants to help increase understanding of Alzheimer’s disease for the African American community. Ms. Francis states, “Community members have seen their loved ones age and may think it is ‘normal’ aging or think their loved one is just ‘senile’ if they don’t understand the disease.” The Alzheimer’s disease label can be very frightening, particularly if it is not well understood the first reaction is to not believe it or understand it. A person wants to know answers to questions such as, is it inherited, and does it happen to all old people? “ By participating in research, individuals will not only play an important role in helping find a cure and prevent for Alzheimer’s Disease in the future, but they will also gain a better understanding of the disease. “Research participation fulfills that most important need for everyone touched by the disease: a sense of hope,” said Dr. Robert Stern, BU ADC Clinical Core Director.

About Us

The Boston University Alzheimer’s Disease Center (BU ADC) aims to reduce the human and economic costs of Alzheimer’s disease through the advancement of knowledge. We conduct cutting-edge Alzheimer’s research and provide education about aging and dementia to professionals and communities in Boston and beyond. The BU ADC Outreach, Recruitment, and Education core publishes the BU ADC Bulletin twice per year. It includes stories about research findings, participants, new studies, and more.

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Carmela Abraham, MD, Pilot Program Manager
Robert Cantu, MD, CTE-BU ADC Clinical Diagnostics and Therapeutics Leader

ADC University for Community Members
The Boston University Alzheimer’s Disease Center (BU ADC) kicked off ADC University in the summer of 2014 with a course titled AGewise. AGewise is a free classroom-learning environment that focuses on providing community members of all ages with engaging and up-to-date information on brain aging. The 6 weekly sessions are held once a year. Participants in the 6-week session gain a better understanding of how the brain ages normally and how this normal aging is different from Alzheimer’s disease. It also teaches about lifestyle practices that can improve successful brain aging as well as techniques for reducing some common problems that result from normal aging. “The biggest thing I took away from this class is learning how beneficial physical exercise can be for my brain. I recommend this course to all my friends and encourage everyone to attend,” said Carol Ann Yancey, who is a graduate of our AGewise class.

Charlene Francis, HOPE Participant

“The HOPE Team is the best group of people; they are friendly and they are like family! The atmosphere is perfect, and any questions you have, they listen and they are very open.”

Dr. Maureen O’Connor, Associate Director of the Outreach, Recruitment, and Education Core & ADC University Director, speaks on Local Cable TV Show titled Agewise.
Chronic Traumatic Encephalopathy Consensus

On February 26th and 27th, 2015, the first consensus workshop for Dr. McKee's UO1 grant—supported by the Foundation for NIH's Sports Health Research Program with funding from the National Football League—was held in Boston with the goal of defining the neuropathological criteria for the diagnosis of Chronic Traumatic Encephalopathy (CTE). Eight expert neuropathologists attended the meeting, representing seven different academic institutions.

The consensus process began with the participants independently reviewing and making diagnoses based on slides from 25 cases of different tauopathies completely blinded to all clinical information, including age, sex, clinical symptoms, and athletic exposure, using provisional diagnostic criteria for CTE developed by McKee et al. (Brain 2013). There was excellent agreement among the neuropathologists regarding the diagnosis of CTE, validating the provisional criteria. The group then came together in Boston to review the diagnoses, discuss the pathological features, and further refine the criteria.

The feature considered the pathognomonic lesion for CTE was the abnormal perivascular accumulation of tau in neurons, astrocytes, and cell processes in an irregular pattern at the depths of the cortical sulci. This lesion was not characteristic of any of the other disorders, including Alzheimer’s disease, age-related tauopathy, frontotemporal lobar degeneration, or progressive supranuclear palsy, and has only been found in individuals who were exposed to brain trauma, typically multiple episodes. This validation of the pioneering work of Dr. McKee’s research team is an enormous milestone in CTE research and lays the foundation for future studies defining the clinical symptoms, genetic risk factors, and therapeutic strategies for CTE.

Continuing Medical Education Course

The BU ADC provided a full-day Continuing Medical Education course for 60 medical professionals on October 27th, 2014. This multidisciplinary course covered the fundamentals of mild cognitive impairment and early Alzheimer’s disease, including diagnosis and clinical course, neuropathological underpinnings, risk factors and prevention, and pharmacological treatments.

Presentations included how to use feasible and effective office-based screening tools to distinguish normal aging from mild cognitive impairment and early Alzheimer’s disease, along with key clinical, research, and community-based resources for patients and their families.

Community Educational Events

Researchers from the BU ADC share their cutting-edge expertise at a variety of community events. Please check the BU ADC calendar for an event in your area.

Go to www.bu.edu/alzresearch/calendar

Questions about our education events? Would like the BU ADC to speak at your community event?

Contact the Education Programs Manager: JoinADC@bu.edu
### Actively Recruiting Studies

<table>
<thead>
<tr>
<th>STUDY TITLE</th>
<th>CURRENTLY RECRUITING</th>
<th>STUDY DESCRIPTION</th>
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<tbody>
<tr>
<td><strong>Health Outreach Program for the Elderly (HOPE)</strong></td>
<td>Healthy adults, MCI, AD</td>
<td>HOPE is the main registry of participants. People who join HOPE attend a yearly visit in which their memory and thinking abilities are evaluated. They also participate in other BU ADC-affiliated studies. Interested volunteers may join this important registry if they can attend a yearly visit with a study partner and are 65 or older with or without memory concerns or 50 or older with memory concerns.</td>
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<tr>
<td><strong>Anti-Amyloid in Asymptomatic Alzheimer’s Disease Study (A4)</strong></td>
<td>Healthy Adults</td>
<td>This clinical trial is examining the effects of Solanezumab in patients who have not been diagnosed with AD, but have concerns about their memory. Patients are asked to come to the BU ADC once a month for 3 years. Interested volunteers may be eligible if they are between 65-85 years old and are able to attend monthly visits with a study partner.</td>
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<td><strong>BAN2401 Clinical Trial for MCI and early AD</strong></td>
<td>MCI</td>
<td>This clinical trial is examining the effects of BAN2401 in patients with MCI. Patients are asked to come once every 2 weeks for 18 months. Interested volunteers age 50-80 with a diagnosis of MCI, and who can attend bi-monthly visits with a study partner, may be eligible.</td>
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<tr>
<td><strong>NOBLE Study</strong></td>
<td>Mild to Mod. AD</td>
<td>This clinical trial aims to evaluate the safety and efficacy of an oral medication (T817MA) compared to placebo in subjects with mild to moderate AD. Subjects between 55 and 85 years old who are currently receiving treatment with Aricept (donepezil) or the Exelon patch may be eligible.</td>
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<tr>
<td><strong>Amylin, Amyloid-beta Peptide, and Alzheimer’s Disease</strong></td>
<td>Healthy adults, MCI, AD</td>
<td>This study aims to develop a blood test for Alzheimer’s disease by repurposing an FDA-approved diabetes medication called Pramlintide, which also has the potential to diagnose and treat AD. Participation involves one visit, which will include one injection of the medication, followed by several blood draws. Volunteers age 50-50 may be eligible if they do not have diabetes.</td>
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<tr>
<td><strong>Challenge Diagnostic Test for Alzheimer’s Disease</strong></td>
<td>Healthy adults, AD</td>
<td>This proof-of-concept trial is a follow-up study of the Amylin, Amyloid-beta Peptide, and Alzheimer’s Disease study. It aims to further develop a blood test for Alzheimer’s disease by evaluating different dose levels of a repurposed FDA-approved diabetes medication called Pramlintide. This study takes place over three visits. Volunteers age 50-90 may be eligible if they do not have diabetes.</td>
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<tr>
<td><strong>Emotional Perception, Neuropsychiatric Symptoms and Caregiver Experience in AD</strong></td>
<td>Healthy adults, AD</td>
<td>Researchers are examining how changes in emotional perception in people with dementia due to Alzheimer’s disease impact the experience of their caregivers. The goal is for the results of this study to be used to improve services for people with Alzheimer’s disease and their caregivers. The researchers are looking both for couples affected by Alzheimer’s disease and couples in which both spouses are not experiencing memory loss.</td>
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<tr>
<td><strong>Alzheimer’s Association Dementia Care Coordination Project</strong></td>
<td>All forms of dementia, MCI</td>
<td>This study’s goal is to evaluate approaches to care coordination and patient/caregiver education for those with AD or other dementias. Caregivers are recruited to complete questionnaires both pre- and post-testing, after which they will be assigned to one of two groups. The treatment group will receive dementia care coordination from the Alzheimer’s Association immediately. The control group will be referred to the Alzheimer’s Association after a 2-year delay. Volunteer participants may be eligible if they are age 50-110 and are caring for someone with AD or another kind of dementia.</td>
</tr>
<tr>
<td><strong>AMARANTH Study</strong></td>
<td>MCI, Mild AD</td>
<td>The purpose of this study is to assess the efficacy and safety of AZD3293 compared with placebo in subjects with MCI due to AD and early stage (mild) dementia of the Alzheimer’s type. Subjects between 55 and 85 years old may be eligible to participate.</td>
</tr>
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<td><strong>FORUM Study</strong></td>
<td>Mild to Mod. AD</td>
<td>This clinical trial aims to evaluate the safety and efficacy of an oral medication compared to placebo in subjects with mild to moderate AD. Subjects 55-85 who are currently receiving treatment with Aricept (donepezil) or the Exelon patch may be eligible.</td>
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<tr>
<td><strong>Memory in Alzheimer’s Disease and Mild Cognitive Impairment</strong></td>
<td>Healthy adults, MCI, AD</td>
<td>This study seeks to better understand why patients with AD and MCI frequently remember things that never happened and to find ways to reduce false memories in patients with dementia. Subjects between 65 and 90 years old may be eligible to participate.</td>
</tr>
<tr>
<td><strong>Aerobic Exercise, Neurotrophins, and fMRI</strong></td>
<td>Healthy adults</td>
<td>This study is investigating the effects of exercise and cardiovascular fitness on cognitive processes, brain function, and levels of certain proteins in the blood. Eligible participants will be randomized to either an aerobic or non-aerobic exercise program for 12 weeks. You may be eligible if you are a healthy, sedentary adult aged 18-35 or 55-85.</td>
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<tr>
<td><strong>Memory Benefits of Sleep in Healthy Young, Elderly and Mild AD Patients</strong></td>
<td>Healthy adults</td>
<td>The goal of this study is to examine the effects of sleep on memory processing for healthy young adults and healthy elderly individuals. Volunteers participate in a daytime nap study or an overnight study. Participants may be eligible if they are between the ages of 65 and 80, are in good physical and mental health and do not have any sleep complaints.</td>
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<tr>
<td><strong>Health Pathways</strong></td>
<td>Healthy adults, Caregivers</td>
<td>The Health Pathways study looks at how caring for a person with dementia affects physical and emotional health. Participants attend four annual face-to-face interviews in which they are asked questions about their health and about the person they care for. They also complete lab work. Participants may be eligible if they have no memory concerns and are age 60 or older.</td>
</tr>
<tr>
<td><strong>Impact of Physical Fitness on Cognition and Brain Function</strong></td>
<td>Healthy adults</td>
<td>The focus of the study is to determine whether physical fitness and activity levels have a positive impact on cognitive abilities and function in older adults. Volunteers between ages of 55 and 85 may be eligible.</td>
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Interested? Contact the BU ADC recruitment coordinator at 617-414-1078 or joinADC@bu.edu.
Research Updates

In 2014, a cooperative grant from the National Institutes of Health (NIH) — bolstered by major funding from the National Football League (NFL) — was awarded to Dr. Ann McKee and her research team. Started in January of 2014, the NIH and NFL-funded UNITE (Understanding Neurologic Injury and Traumatic Encephalopathy) study is a retrospective analysis of former athletes, military veterans, and others who have been exposed to repetitive traumatic brain injuries prior to death. Participant brains are donated to the VA-BU-SLI Brain Bank in Bedford, MA, where they are pathologically examined. Loved ones of participants provide medical information to correspond with the pathological analysis. The primary goals of UNITE are to:

- Establish pathological criteria to distinguish CTE from other neurodegenerative diseases
- Examine the relationship between cumulative brain trauma and CTE
- Examine neuroimaging biomarkers for CTE pathology

Dr. Wendy Wei Qiao Qiu, a physician scientist and part of the Boston University Alzheimer’s Disease Center team with funding from the National Institute on Aging and the Alzheimer’s Association, has been conducting research studies to repurpose existing, approved drugs for other diseases and examine them in Alzheimer’s. Many of her Alzheimer’s patients seek care because they are frustrated with their deteriorating cognitive function, and their behavior or mood symptoms are causing tremendous burdens for their caregivers. Motivated by her desire to help patients with the devastating disease, Dr. Qiu, together with Dr. Haihao Zhu and others on her team, feels the urgency to develop an effective treatment for it. Recently they have found that a diabetic drug, pramlintide, potently reduces the Alzheimer’s pathology and improves learning and memory in Alzheimer’s mouse models. Pramlintide, an analog of a naturally occurring peptide (amylin) produced by pancreas, can get into the brain easily and also has a favorable safety profile. Their study also found that Alzheimer’s patients have a lower level of amylin in blood compared to those without this disease. Their research work reveals that both amylin and pramlintide can remove the amyloid-beta peptides that cause plaques from the brain. Independently, a research group from Case Western University found that pramlintide can increase some key molecules for learning and memory in the brain. Taken together, these studies suggest that amylin and similar drugs may provide a new avenue for both the treatment and diagnosis of Alzheimer’s disease. A clinical trial for pramlintide for patients with Alzheimer’s disease is under way, and if it proves beneficial, this drug can be FDA approved for Alzheimer’s patients in only 3-5 years. The work of Drs. Qiu and Zhu was recently published in Molecular Psychiatry.

Dr. Maureen O’Connor (BU ADC Outreach, Recruitment, and Education Core Associate Director), Dr. Renee Beard, and Mr. Ryan Daley are seeking to understand the lived experience of spousal couples impacted by Alzheimer’s disease. Data is being collected about relationship satisfaction, caregiver burden, depression, and anxiety associated with Alzheimer’s disease. Structured interviews are also being conducted to better understand couples’ joint approach to the impacts of Alzheimer’s disease. Preliminary findings from 12 interviews (24 participants) suggest that couples express either a “We/Us” approach, where the symptoms of Alzheimer’s disease are experienced by the couple as a unit or team, or an “I/Me” approach where the symptoms of Alzheimer’s disease are experienced as impacting the caregiver and diagnosed participant individually. All of these couples have taken a decidedly positive approach to coping with the impacts of the disease, through acceptance, optimism and humor, despite a “We/Us” or “I/Me” approach. Further analysis will be conducted to understand the interaction between these approaches and coping styles, with anxiety, depression, and caregiver burden presentations.
Get to know our new faculty:  
Mr. Christopher Nowinski &
Dr. Robert Cantu

Christopher Nowinski is the founding and Executive Director of the Sports Legacy Institute, and serves as the Public Policy Leader and an Outreach, Recruitment, & Education Core Member at the Boston University Chronic Traumatic Encephalopathy (CTE) Center. Mr. Nowinski completed his undergraduate degree from Harvard University, where he received his BA in Sociology. He currently attends Boston University, where he is working toward his PhD in behavioral neuroscience. Mr. Nowinski participated in collegiate football during his years at Harvard University and also was involved with the World Wrestling Entertainment until he had to retire due to post-concussion syndrome caused by repetitive brain trauma over five years. During this time, he met Dr. Robert Cantu, and together they partnered to bring awareness and research about concussions through the Sports Legacy Institute. Currently, Mr. Nowinski conducts research with former professional athletes, and works to translate these findings and others from the center to current athletes to reduce the risk of concussions. Mr. Nowinski also performs outreach for the CTE Center and Sports Legacy Institute. “The part of my job that I enjoy the most is working with families of our legacy donors by helping them and bringing positive comfort from a tragic loss,” said Mr. Nowinski. When not at work you can find Mr. Nowinski studying or out on the basketball court.

Dr. Robert Cantu was one of the original founders of the Boston University Chronic Traumatic Encephalopathy Center (CTE Center) and currently serves as the Clinical Diagnostics and Therapeutics Leader for the CTE Center and a member of the CTE-BU ADC executive committee. Dr. Cantu performs clinical research and attends the CTE clinical consensus meetings. Dr. Cantu also serves as a mentor for a number of PhD students, serving on their dissertation committees. Dr. Cantu attended medical school and at the same time pursued his master’s degree in endocrinology at the University of California Medical School in San Francisco. Following a surgical internship at Columbia-Presbyterian Hospital in New York City, he began his neurosurgery residency at Massachusetts General Hospital in Boston, in addition to acting as a research fellow in physiology at Harvard Medical School. As an athlete himself, Dr. Cantu enjoys playing competitive tennis and long-distance running. “As a neurosurgeon, it was natural to help athletes and focus my research on brain injuries and prevention,” said Dr. Cantu. Dr. Cantu’s research has focused strongly on protecting athletes from injury, specifically among youth athletes. As an expert on concussions, Dr. Cantu has spoken in nationally televised sports programs on a variety of related issues, and he is also an author of numerous books as well as articles on sports medicine topics.

BU ADC Happenings

Welcome
The Boston University Alzheimer’s Disease Center (BU ADC) and its affiliate, the Chronic Traumatic Encephalopathy Center (CTE Center), would like to extend a warm welcome to new interns and employees:

Diane Essis, BU ADC Recruitment Coordinator. Formerly a Psychometrician for the Health Outreach Program for the Elderly (HOPE) Study, Diane graduated from Connecticut College with a BA degree in Biological Sciences and is completing her MA of Science in Management with a concentration in Eldercare Administration from Lasell College. Katie Babcock, CTE Center Research Assistant. Katie graduated from Indiana University, where she studied Psychology and Neuroscience. Kaitlyn Perry, Study Coordinator. Kaitlyn graduated from the University of Kansas in 2013 with a BA of Science in Biology, concentrating in Neurobiology. She is currently pursuing her MA of Public Health at Boston University School of Public Health with a concentration in Health Law, Bioethics and Human Rights.

Goodbyes
Many thanks and best wishes to departing BU ADC and CTE Center staff:

Alexandra Bourlas, BU ADC Recruitment Coordinator. Formerly a CTE Center research intern, she left to pursue her medical school degree at Ohio University Heritage College of Osteopathic Medicine. Julie Stamm, BU ADC Graduate Researcher, recently completed her degree at Boston University, where she received her PhD in Anatomy and Neurobiology. Nathan Fritts, BU ADC Research Coordinator, left to pursue his medical school degree. Todd Solomon, BU ADC Post-Doctoral Fellow and CTE Center Co-Investigator, will be relocating to Philadelphia, working as a Clinical Scientist at Bracket Global.

Farewell, Dr. Fine
Dr. Richard Fine retires after working with the Boston University Alzheimer’s Disease Center for nearly 20 years. Dr. Fine had an extremely successful career full of many accomplishments in the field of basic neuroscience at Boston University and the Department of Veterans Affairs in Bedford. He played an important role in the founding and success of the BU ADC.

Congratulations, Max Wallack
Congratulations to Max Wallack on the successful defense of his baccalaureate thesis at Boston University and his acceptance to Harvard Medical School. Max is continuing his quest to become a geriatric psychiatrist/researcher. This quest was inspired by his interaction with his great-grandmother, Gertrude Finkelstein, who took care of Max until Alzheimer’s changed their relationship and Max became one of her caregivers. Realizing that puzzles are a good activity for those with Alzheimer’s disease, Max came up with a simple but ingenious idea to get puzzles into the hands of those with dementia. He started a non-profit organization called Puzzles To Remember that collects new and used puzzles and distributes them to facilities that care for patients suffering from Alzheimer’s and dementia. He also worked with Springbok to create puzzles with fewer pieces for those with Alzheimer’s.

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Honorary and Memorial Contributions

The Boston University Alzheimer’s Disease Center is involved in a variety of clinical, research, and educational activities. Research study participants, families, and community leaders often wish to contribute to the fight against Alzheimer’s disease. We welcome honorary and memorial donations. These gifts are an excellent way to honor a family member or friend while contributing to the advancement of Alzheimer’s research. To make a donation, please call Kate DeForest in the BU Development Office at 617-638-4969 or visit us online: www.bu.edu/alzresearch.

The BU ADC would like to recognize the following private donors for their greatly appreciated contributions made between January 2014 and December 2014. Please note that anonymous donors are not listed.

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In Memory of Valerie Mullaney
Stella Antipas
Edward Daniels
Susan L. Flannagan
Philip P. Jameson
Janet T. Troy
Peter Veglas
THE NEWSREEL:

Partnering in Alzheimer’s Instruction Research Study (PAIRS) Documentary

COMING SOON — A documentary highlighting our Partnering in Alzheimer’s Instruction Research Study (PAIRS) will be featured in June of 2016. PAIRS is an educational program for medical students and patients with early-stage Alzheimer’s disease and other cognitive impairment. The documentary will feature interactions between a current PAIRS student (Oscar; a medical student), his buddy (Mr. Johanson), and his buddy’s caregiver (Mrs. Johanson). Oscar will discuss how his experience in the PAIRS program is teaching him lessons that he can use in his own practice, and that he could teach—either through his own clinic, or as a colleague—to others. We are currently recruiting PAIRS Participants for Fall 2016.

Interested? Contact: Christina DiTerlizzi at 856-364-2140 or cditerli@bu.edu

HOPE study to host thank-you event for volunteers

The Boston University Alzheimer’s Disease Center’s main research registry — HOPE, or Health Outreach Program for the Elderly — is planning a special event for the study’s 400 volunteers. The HOPE APPRECIATION BRUNCH, scheduled for Monday, August 17th, will give BU ADC leadership an opportunity to thank HOPE participants for the contributions they make to a variety of studies and to a future without Alzheimer’s.

HOPE participants will receive more details in the mail soon. Please contact Angela Dwyer at 617-414-1189 with any questions.