BU ADC Bulletin

Boston University Alzheimer's Disease Center

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In This Issue:

Skip Curtis: A Man Dedicated to Fighting Alzheimer's Disease

Charles W. "Skip" Curtis was only 59 years old when he received a diagnosis of early-onset Alzheimer's disease (AD). At the time of his diagnosis, he was extremely active in his New Hampshire community – serving on the Hillsboro Planning Board and as president of the Hillsboro Lions Club. When not spending time with his three children and three grandchildren, Skip was also busy helping his wife with their newly established dream bed and breakfast, Stonewall Farm. For Skip, living with AD would not mean an end to his active routine. Rather, faced with the diagnosis, he decided to participate in research opportunities at the Boston University Alzheimer's Disease Center (BU ADC), determined to give the next generation a future without the disease.

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Skip Curtis was a devoted research participant at the BU ADC and will continue to contribute to AD research through The Skip Curtis Fund for Clinical Research in Alzheimer's Disease.

What is Mild Cognitive Impairment (MCI)?

Several years ago, clinicians treating older adults began to diagnose "mild cognitive impairment" or "MCI;" however, there is much confusion among older adults about what this diagnosis means and how it differs from normal cognitive aging or dementia, such as Alzheimer's disease (AD). This article aims to describe symptoms of MCI and prognosis for individuals diagnosed with MCI.

MCI is a clinical diagnosis used to describe problems with thinking abilities that occur in older adults that are not typical for one's age. People with MCI experience difficulty with one or more areas of thinking, including memory, verbal communication, problem-solving, decision-making, or spatial abilities. The symptoms of MCI are sometimes noticeable to the person with MCI and people close to them, but the symptoms are not severe. People with MCI can complete basic activities of daily living, such as getting dressed or bathing, but they may have subtle difficulties with more advanced activities, such as driving or handling finances. Compared to other adults of the same age, people with MCI may experience more frequent lapses in memory. While it is normal for older adults to experience slight changes in memory and thinking abilities over time, individuals with MCI experience a more noticeable change that is not a part of normal aging.

MCI is not a form of dementia, such as AD or Dementia with Lewy Bodies. Many symptoms

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HOPE Participants Are All Aboard for Alzheimer's Research!

HOPE Study Participant Gladys Facey (left) and ADC Study Coordinator Patricia Johnson (right).

On June 22, 2010, the Boston University Alzheimer's Disease Center (BU ADC) celebrated the ongoing commitment of participants and study partners to the Health Outreach Program for the Elderly (HOPE) study at the HOPE Appreciation Brunch held at the Hilton Hotel in Dedham. The HOPE study follows individuals over 65 years of age throughout their lives and is the main research registry of the BU ADC. Participants contribute to research on normal and abnormal cognitive aging by attending a yearly HOPE evaluation and agreeing to participate in other Center-sponsored studies. Over 200 guests attended the event, themed *"All Aboard for Alzheimer's Research!"*

The day began with a warm welcome from HOPE study Program Manager, Eric Steinberg, who was also recognized for 10 years of dedicated service to the HOPE study. Michael Kincade of the Alzheimer's Association shared his passion as a longtime advocate for individuals and families affected by Alzheimer's disease (AD). Community partner, Juanda Drumgold, energized attendees and led group exercises, including hearty laughter that brought out smiles throughout the room.

The day's educational program began with a keynote presentation by BU ADC Clinical Core Director, Dr. Robert Stern, who reviewed the Center's journey in AD research and highlighted next steps and new initiatives for the BU ADC. The message of "hope and humor" as key ingredients in the fight against AD resonated with many audience members. Meg Curtis shared inspiring stories from "A Rider's Perspective," as a spouse and caregiver of a loved one living with AD (see cover article on her husband's recent passing). She illustrated by personal example the everyday courage it takes to proactively fight AD by participating in research activities that give hope to future generations. After Silvia Serrano, Outreach and Recruitment Coordinator, introduced the actively recruiting research opportunities at the BU ADC, HOPE participants were able to meet in person with study coordinators who answered questions and signed participants up for research projects. As per tradition, Dr. Stern closed the educational program by fielding many interesting and insightful questions posed by audience members.

HOPE Psychometrician Meenakshi Chivukula (left) presenting HOPE Study Participant Eileen Sussman (right) with a raffle prize.

Numerous recognition certificates and awards were presented to participants who have volunteered for other BU ADC-sponsored research studies and who have contributed to the HOPE study for eight or more years. Mrs. June Robertson, a longtime friend to the HOPE study, was recognized for her 12 amazing years of participation and, at 93 years of age, for being the oldest attending participant. Boston University Academy student and enterprising AD advocate, Max Wallack, presented special raffle prizes from his organization, *Puzzles to Remember*.

The BU ADC and HOPE study team would like to thank all participants, study partners and friends of the HOPE study who attended the event. We appreciate your commitment and collaboration in our efforts to advance AD research by "laying down tracks of HOPE" for generations to come!

The event was sponsored by the generous support of Carleton-Willard Village and Senior Living Residences.

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At the onset of his disease, Skip made a commitment to "do whatever it takes…to not just help himself but his children and his grandchildren," his wife Meg Curtis said. He became involved with multiple research programs at the BU ADC over the years, taking part in the Health Outreach Program for the Elderly (HOPE) Study, two clinical drug trials, and the PAIRS Program, through which he mentored a Boston University School of Medicine student. "Skip did not seem frustrated by his Alzheimer's [diagnosis]. I was surprised by his upbeat demeanor and general enthusiasm," recalled Skip's PAIRS Program student mentee, Max Rubenstein. "His sense of humor and willingness to participate in almost any activity made him a great buddy." Even when one of the clinical trials was discontinued due to the drug's ineffectiveness, Skip remained hopeful and enrolled in another clinical trial at the BU ADC.

Skip spent over four years battling AD, until his recent passing in August at the age of 64. In an effort to continue Skip's fight against the disease, his wife Meg has created The Skip Curtis Fund for Clinical Research in Alzheimer's Disease. "We decided to establish this fund because I had to believe that his life and battle with this disease was not totally in vain," Meg explained. "The only way I could do that was to set up a fund for research. In that way, we continue the battle in his name." The fund supports ongoing research at the BU ADC in an effort to prevent, treat, and better understand AD.

Having watched Skip's proactive nature in his fight with AD, each member of the Curtis family has become an advocate for increased research funding and participation so that other families do not have to lose a beloved husband, father, grandfather, or friend. "The long love affair that we had and his children's unbelievable love and respect for their father – it was all of us together that made that decision to keep the fight going," Meg said. "Skip always wanted to see it through. The fund is the only way we could imagine to see it through." The fund allows other families to donate in memory of Skip as a way to memorialize or honor their loved ones affected by the disease.

If you are interested in making a donation to The Skip Curtis Fund for Clinical Research in Alzheimer's Disease or learning about other ways you can support AD research, please visit our website (www.bu.edu/alzresearch/about/help/donate) or call Harriet Kornfeld at 617-638-5676.

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of dementia and MCI overlap, such as memory loss and difficulty performing advanced activities of daily living. However, symptoms of dementia are significant enough to disrupt normal daily living, while symptoms of MCI characteristically do not disrupt basic social and occupational activities.

MCI is surprisingly common, affecting five million adults over age 70. That means that approximately 1 out of 5 adults over age 70 has MCI. Individuals with MCI often ask what they can expect over time for their memory and thinking abilities. There are three possible outcomes for an adult with MCI. First, some people with MCI may experience an improvement in their memory loss and cognitive difficulties over time. Second, an individual may remain stable with MCI. Third, an individual with MCI may experience a worsening of symptoms and develop dementia. In fact, adults with MCI are more likely to develop AD than adults with normal cognitive aging. Therefore, MCI is often considered a stage in between normal cognitive aging and AD.

Additional research is needed to better understand a person's risk of developing MCI and factors that may determine different outcomes for people with MCI. The BU ADC has a number of research opportunities for individuals with MCI. One new opportunity is the Risk Evaluation and Education for Alzheimer's Disease (REVEAL) Study, led by Dr. Robert Green. This study offers individuals with MCI the opportunity to learn more about their risk of developing AD based on the diagnosis of MCI and the results of a genetic test. There are several additional research studies at the BU ADC currently recruiting individuals with MCI. For more information about research opportunities at the BU ADC, please contact Silvia Serrano at 617-414-1078 or sserrano@bu.edu.

This contribution was adapted from materials associated with the Education About Mild Cognitive Impairment Study, funded by the Alzheimer's Association and led by Dr. J. Scott Roberts at the University of Michigan.

Actively Recruiting Studies

Study Type	Study Title	Study Description
BU ADC Research Registry	Health Outreach Program for the Elderly (HOPE)	This longitudinal study examines age-related changes in memory and thinking. It serves as the Boston University Alzheimer's Disease Center (BU ADC) research registry, where participants agree to be contacted about other BU ADC-approved studies. HOPE participants are encouraged to participate in the actively recruiting studies summarized below.
Caregiving Support	Health Pathways	This study looks at how caring for a person with dementia affects one's physical and emotional health. Participants attend four yearly face-to-face interviews where they will be asked questions about their health and about the person they care for, along with some lab work.
Early Detection	RETINA Study	This study uses routine ophthalmological tests to detect biomarkers that predict the onset of Alzheimer's disease (AD). The study includes one visit to the Massachusetts Eye and Ear Infirmary. Participants must be 50 years of age or older and enrolled in the HOPE Study. Participants will need a study partner who can accompany them to study visits.
Education	PAIRS Program	This program pairs first-year Boston University medical students with patients who have early-stage AD. The program educates medical students about the care and support related issues faced by patients with AD, and provides patients with the opportunity to informally mentor students. Student-patient pairs meet monthly to participate in social activities throughout the academic year.
	REVEAL IV *new study	This study aims to provide adults with mild cognitive impairment (MCI) information about MCI and their chance of developing AD based on several factors, including genetics. This study requires a 12-month commitment involving phone calls and five center visits. Participants must be 55 years of age or older with mild memory problems or a diagnosis of MCI. Participants will need a study partner who can accompany them to study visits.
Evaluation of Daily Living	Activities of Daily Living (ADL) Assessment	This study investigates the relationship between office-based cognitive tests and independent functioning in the home. Adults age 60 or older with mild to severe dementia, living in the community or independently in a continuing care retirement center, are eligible to participate. Participants will need a study partner to provide information about the participant's day-to-day functioning.
	SAFE Drivers	This study aims to develop a brief, office-based evaluation of driving safety for older drivers that accurately predicts on-road driving performance. Two study visits involve office-based cognitive tests and an on-the-road driving evaluation conducted by a certified driving instructor. Study participation is open to adults 55-95 years of age who drive at least one time per week.
Memory & Cognition	False Memory in AD	This study seeks to understand why patients with AD and other dementias frequently remember things that never happened. The goal of this study is to provide ways to reduce false memories in patients with dementia. Study participation is open to cognitively normal adults age 50 years or older and adults with AD age 65-85.
	Vision & Cognition	This study examines the relationship between vision and thinking abilities in normal aging and AD. Participants perform tests of vision, cognition, and daily functions, and a free eye exam is included. Study participation is for adults age 55 or older.
Neuro-imaging	Alzheimer's Disease Neuroimaging Initiative (ADNI) *new study	This study uses different kinds of imaging to determine whether imaging of the brain can help predict the onset of cognitive changes and monitor such changes. Researchers are looking for persons 55-90 years of age and who are in good general health but have memory problems or concerns.
	Heart & Brain Aging	This study uses heart and brain imaging and memory tests to better understand relations between heart and brain health among aging adults with mild memory loss, particularly those individuals who have been diagnosed with MCI. Participants receive feedback about heart and brain health, and results are shared with the participant's physicians.

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Actively Recruiting Studies < *continued from page 4*

Study Type	Study Title	Study Description
Treatment	CONCERT (Dimebon)	This multi-center Phase III drug trial will evaluate a new oral medication, Dimebon. Dimebon may stabilize unhealthy changes in brain cells in individuals with mild or moderate AD. Participants must be 50 years of age or older and have been taking Aricept (Donepezil) for at least six months. Participants will need a study partner to accompany them to study visits.
	ICARA (Bapineuzumab)	This multi-center treatment trial will evaluate whether a new medication, Bapineuzumab, increases the clearance of Abeta from the brain. Abeta is believed to be the initial cause of AD. This treatment study is for adults 50-89 years of age with an AD diagnosis. Participants will need a study partner to accompany them to study visits.
	Nutritional Supplements Combination Therapy *new study	This study will determine whether nutritional supplements are well tolerated and safe for cognitively normal older adults and whether the supplements have an effect on brain health. The study requires three visits over nine months. Participants must be 60-90 years of age, be willing to take nutritional supplement pills, and agree to lab work.
	Vitamin E and Memantine in AD	This multi-center clinical trial will evaluate the combination of memantine and Vitamin E in the treatment of mild to moderate AD. Memantine has been shown to improve function and cognition in late stages of AD, while Vitamin E has been found to delay the progression of AD. The study is only open to veterans with a diagnosis of mild to moderate AD. Participants need a caregiver to accompany them to all visits.

For more information or to get involved in these studies, please contact the BU ADC Outreach & Recruitment Coordinator, Silvia Serrano, at 617-414-1078 or sserrano@bu.edu.

BU ADC Happenings

Welcome

The Boston University Alzheimer's Disease Center (BU ADC) extends a warm welcome to new staff members: **Christine Baugh**, research coordinator for the Center for the Study of Traumatic Encephalopathy (CSTE); **David Riley**, research assistant for the CSTE; and **Sunali Shah**, psychometrician for the Health Outreach Program for the Elderly (HOPE) Study.

The BU ADC would also like to welcome new research postdoctoral fellows: **Dr. Katherine Gifford**, a neuropsychology fellow working with Dr. Angela Jefferson; and **Dr. Erika Oleson**, a geriatrics fellow completing her Master's in Science of Health Services Research with Dr. Angela Jefferson.

Congratulations

The CSTE, co-directed by BU ADC faculty members **Drs. Robert Stern** and **Ann McKee**, received a one-million-dollar unrestricted gift from the National Football League to support research on chronic traumatic encephalopathy, a neurodegenerative disease found in athletes with a history of repetitive concussions.

Dr. Robert Green was recently awarded funding from the National Institutes of Health to conduct a study entitled *Impact of Direct to Consumer (DTC) Genetic Testing*. The goal of this project is to use online surveys to assess the impact of DTC genetic testing on consumers who utilize the services of 23andMe and Navigenics.

Dr. Angela Jefferson recently received funding from the National Alzheimer's Coordinating Center (NACC) as part of a multi-center collaborative project investigating ethnic and racial differences among research subjects in their willingness to assent to brain donation. The collaborative project is being led by Dr. Linda Boise at the Layton Aging and Alzheimer's Disease Center.

The BU ADC would like to congratulate **Dr. Alpaslan Dedeoglu** on his recent promotion to Associate Professor of Neurology.

Goodbyes

Thank you and best of luck to former BU ADC faculty member **Dr. Brandon Ally**, who accepted a position in the Department of Psychology at Vanderbilt University in August 2010. Dr. Ally has also received appointments in the Departments of Neurology and Psychiatry at Vanderbilt Medical Center.

Many thanks and best wishes to ADC staff members: **Elana Cook**, former psychometrician for the HOPE Study, who left to complete a post-baccalaureate premedical program at Hunter College before applying to medical school; and **Megan Wulff**, former research coordinator, who left to attend Yale Law School.

Research Updates

Aβ Derivatives Form Center of Plaques

Dr. Richard Fine and his colleagues recently used mouse models of Alzheimer's disease (AD) to show that two derivatives of the protein amyloid-β (Aβ), namely $Aβ_{pE3}$ and $Aβ_{pE11}$, form spherical deposits at the center of senile plaques in the brains of both AD patients and healthy older adults. The deposits are not co-localized with full-length Aβ but are surrounded by full-length Aβ and additional aggregates. These data suggest that both $Aβ_{pE3}$ and $Aβ_{pE11}$ serve as generating sites for senile plaque formation and potentially for the formation of toxic oligomeric aggregates. Dr. Fine will present these findings at the upcoming 40th annual meeting of the Society for Neuroscience in San Diego, California.

AD Link in Eyes of Patients with Down Syndrome (DS)

Drs. Lee Goldstein and Juliet Moncaster and their team recently reported findings on the link between AD and DS pathology in the lens. Their study was published in the May 20th issue of *PLoS ONE* and shows that the same toxic protein that causes AD pathology in the brain, known as Aβ, also leads to distinctive cataracts in the eyes of people with DS. In DS, AD-type dementia is often observed by the age of 30, which is due to an extra copy of a key AD gene that leads to increased Aβ accumulation in the brain. The study showed that the Aβ protein starts to accumulate very early in the lens of the eye in DS and is detectable even in young children.

African American Elders and Brain Donation

In a recent article published in *The Gerontologist*, Dr. Angela Jefferson and colleagues, including Susan Lambe, Nicole Cantwell, Fareesa Islam, and Dr. Kathy Horvath, reported recommendations for minimizing racial disparities in brain donation program participation based on focus group findings with African American older adults in the Health Outreach Program for the Elderly (HOPE) Study. Results suggest cultural mistrust and family objections influence decisions not to donate. Providing information about rates of AD among African American elders and specific benefits of donation to African American communities could be useful tools in increasing donation enthusiasm. Participants recommended developing culturally relevant program materials and holding peer discussion groups as outreach tools to increase participation among the African American community.

Dementia Screening Measures

On behalf of several Boston University Alzheimer's Disease Center (BU ADC) researchers, including Drs. Neil Kowall, Wendy Qiu, Angela Jefferson, Robert Green, and Robert Stern, Dr. Brandon Gavett recently presented new research findings at the 30th annual conference of the National Academy of Neuropsychology in Vancouver, BC. Results suggest that there is a lack of equivalence between two commonly used screening tools to measure the severity of dementia, including the Mini-Mental State Examination and the Clinical Dementia Rating. These findings have implications for the criteria used to enroll participants into clinical trials and to determine whether an individual can be diagnosed with dementia or mild cognitive impairment.

Heart Function and Brain Aging

Dr. Angela Jefferson and her colleagues at the Framingham Heart Study recently published an article relating heart function to brain health in the journal *Circulation*. Findings suggest participants with the lowest level of cardiac index, a measure of how much blood is pumped from the heart to the body and brain, had smaller brain volumes than people with the highest level of cardiac index. The difference was equivalent to about two years of advanced brain aging. Participants in the middle cardiac index group, who had low but normal levels of blood pumping from the heart, had brain volumes similar to those individuals in the lowest cardiac index group. These results were present in older adults without any heart disease and suggest that heart function and brain health are closely related.

Ibuprofen Treatment in Mice Protects Against AD Pathology

In a new report that was published by Dr. Alpaslan Dedeoglu and his research team in the journal *Experimental Neurology*, the effects of the non-steroidal anti-inflammatory drugs ibuprofen and celecoxib on immunohistological and neurochemical markers were compared at two different ages in AD mice. Comparisons were made using measurements of amyloid plaque deposition, Aβ peptide levels, and neurochemical profiles measured by magnetic resonance spectroscopy. Ibuprofen treatment significantly decreased the Aβ42/40 ratio in the frontal cortex and also provided significant protection against N-acetylaspartate and glutamate loss. The studies were performed in collaboration with Dr. Bruce Jenkins from Massachusetts General Hospital.

IDENTITY Study Stopped Early

Earlier this summer, the IDENTITY study, one of the double-blind, placebo-controlled phase III clinical trials being conducted at the BU ADC, was stopped earlier than expected by the study sponsor Eli Lilly. This study was researching the use of the drug semagacestat, a gamma secretase inhibitor, as a potential treatment for AD. On August 17th, a press release issued by the sponsor shared that the preliminary data from two ongoing studies showed that the drug did not slow disease progression and was associated with worsening of clinical measures of cognition and the ability to perform activities of daily living. Participants were all notified and provided with this information immediately. The current plan is to follow active study participants to collect safety data, including cognitive scores, for at least six months after stopping the study drug and placebo.

Protein TDP-43 Linked with Stress Granules in the Brain

Dr. Benjamin Wolozin and his research group recently published a manuscript in the journal *PLoS ONE*. The team showed that the protein TDP-43 is linked with a newly discovered inclusion, termed the stress granule. Stress granules control which proteins are produced by injured neurons. TDP-43 accumulates in some brains of patients with AD, some subjects with chronic traumatic encephalopathy and in all subjects with frontotemporal dementia and amyotrophic lateral sclerosis (a.k.a. Lou Gehrig's disease). This work opens up new avenues for drug discovery in neurodegenerative disease.

Greater Boston Memory Walk

The Memory Walk is the Alzheimer's Association's largest fundraising event. Walks take place annually in more than 600 communities nationwide. On Sunday, September 26th, the faculty, staff, participants and friends of the Boston University Alzheimer's Disease Center (BU ADC) and one of our continuing care retirement community affiliates, Senior Living Residences, participated in the Greater Boston Memory Walk in Cambridge, Massachusetts. This year's team raised over $5,000 for the Alzheimer's Association!

The BU ADC team supported the Massachusetts Alzheimer's Association at its annual Memory Walk fundraiser.

Honorary and Memorial Contributions

The Boston University Alzheimer's Disease Center (BU ADC) is involved in a variety of clinical, research, and educational activities. These activities are funded by grants awarded from the National Institutes of Health and non-profit organizations. Often, research study participants, families, or community leaders wish to contribute to the fight against Alzheimer's disease (AD), and these private donations are equally important to advancing the BU ADC's mission. The BU ADC welcomes honorary and memorial donations, as these gifts are an excellent way to pay tribute to a family member or friend while making a contribution to the advancement of research in the field of AD. Please call Harriet Kornfeld at 617-638-5676 or visit us online at www.bu/edu/alzresearch/about/help/how-to-donate if you would like to make a donation. The BU ADC would like to recognize the following private donors for their greatly appreciated contributions:

In memory of Charles W. "Skip" Curtis

Michele Ackerman
Nils Bergstrom
Sally Bowden
Matt and Amy Chambers
Wayne and Katie Crokus
Abigail Krist
Joe Monforton
Jeanne Strining
Brooke Sugaski
Tara Zucker
Steve's Wine Beer Spirits

In memory of Henry Martin

Mr. and Mrs. Robert Sampson

In memory of Caesar John Palotta

Stefan Salomon

In honor of Rae Stone

Peter Cury

Alzheimer's Disease Center Leadership

The Boston University Alzheimer's Disease Center (BU ADC) is primarily supported through a grant from the National Institute on Aging. The BU ADC supports cutting-edge research and provides education and clinical care to individuals and families affected by Alzheimer's disease. Its leadership is listed below, alphabetically by Center Core.

Neil Kowall, MD, *Center Director and Administrative Core Director*

Andrew Budson, MD, *Center Associate Director*

Richard Fine, PhD, *Pilot Grant Program Director*

Robert Green, MD, MPH, *Center Associate Director and Clinical Core Associate Director*

Robert Stern, PhD, *Clinical Core Director*

Christine Chaisson, MPH, *Data Management & Statistics Core Director*

Angela Jefferson, PhD, *Education & Information Transfer Core Director*

Ann McKee, MD, *Neuropathology Core Director*

Alpaslan Dedeoglu, MD, PhD, *Translational and Transgenic Core Associate Director*

Lee Goldstein, MD, PhD, *Translational and Transgenic Core Director*

The *BU ADC Bulletin* is published twice annually (**Dr. Angela Jefferson,** *Editor*; **Dr. Kathy Horvath,** *Co-Editor*; **Nicole Cantwell,** *Editorial Assistant*).

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