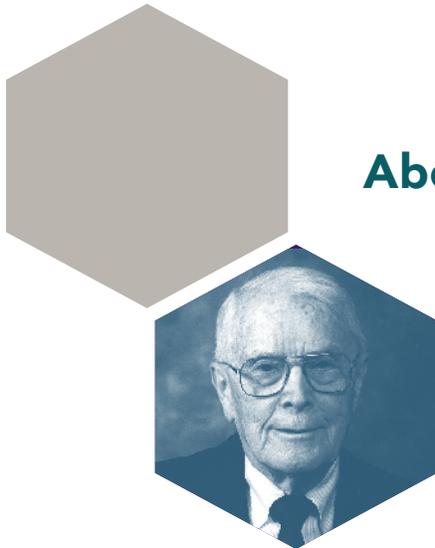




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**Paul B. Beeson**  
Career Development Awards  
in Aging Research Program

2015 Report featuring the 2013 Scholars



## About Paul B. Beeson, MD (1908-2006)

Dr. Paul B. Beeson, a renowned physician, researcher, and teacher, was the inspiration behind the creation of the Paul B. Beeson Career Development Awards in Aging Research Program. It was his vision to increase the number of physicians with a combined clinical, academic, and scientific expertise to care for a growing older population.

At the time of his death, Dr. Beeson was professor emeritus of medicine at the University of Washington. Although “retired,” he remained active in the field of aging research, attending meetings and advising many Beeson Scholars. In his long and distinguished career, he profoundly influenced the career paths of many physician-scientists and was stalwart in his concern for the care and dignity of patients.

To date, 210 scholars supported by the Beeson Program have become leaders in geriatric medicine and aging research throughout the United States and the Island of Ireland. The careers of these remarkable Scholars serve as a lasting testament to Dr. Beeson’s enduring legacy as they seek to provide the best possible care for older adults and train the next generation of leaders in aging research and geriatrics.

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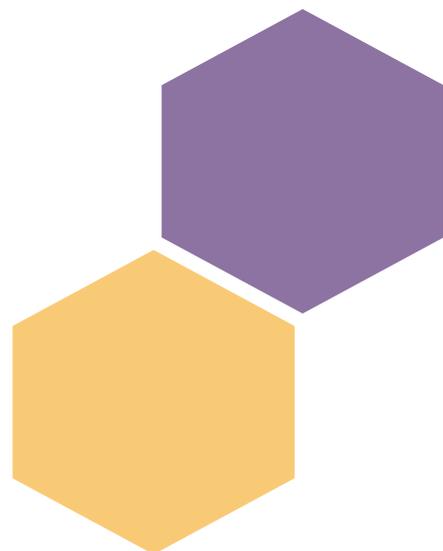
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## Letter from Thomas Gill, MD

Chair of the Program Advisory Committee

When the Beeson Program was launched in 1994, this new training vehicle focused exclusively on physician investigators. With the added support from the National Institute on Aging in 2004, the program dramatically expanded in both size and scope and began to include additional disciplines. That expansion was a key development—one that greatly strengthened the program by embedding it within multiple fields beyond medicine and by enabling years of fruitful, multidisciplinary collaborations.

Across the Atlantic, the 2007 expansion of the Beeson Program into the Republic of Ireland and Northern Ireland gave rise to another remarkable group of leaders in aging research. More recently, many of our scholars have taken advantage of the Beeson Scholars/Change AGENTS Action Fund, generously supported by the John A. Hartford Foundation. Some scholars are moving into policy realms that they may not have otherwise considered, while others are translating their research into efforts aimed at transforming patient care on a local and national level.

Many new ideas and partnerships have blossomed at our annual Beeson meetings, where we showcase the unique and important contributions of scholars from many disciplines in advancing the care and management of older patients.

We're delighted to introduce the 2013 Beeson Scholars, whose impressive accomplishments add significantly to this rich body of research talent. Remarkably, with an emergency medicine physician, geriatrician, neurologist, cardiologist, neuropsychologist, neuroradiologist, and nurse, no discipline is represented more than once. That extraordinary diversity not only reflects our increasingly broad pool of applicants but also provides a durable platform from which to expand our reach even further in broadening and deepening the knowledge base in aging research. In the Beeson Program, success builds success.

We're entering an era in which the opportunities for scientific discovery have never been greater. But we're also working in an environment where the resources needed to support that research are often in short supply. We're proud of the success of our Beeson scholars and graduates in competing for these precious resources, in acquiring new skills and in identifying the best opportunities to advance their own diverse disciplines.

Through their continued growth, inspiration, and collaboration, we're all enriched.



Thomas Gill, MD





## Program Overview

Over the past two decades, the Paul B. Beeson Career Development Awards in Aging Research Program has recognized 200 investigators as Beeson Scholars. Collectively, our awardees' research covers a wide range of aging-related topics in basic, clinical, behavioral, social, epidemiological, and health services sciences.

In 2004, the program's funders established a strategic public-private partnership to address the evolving challenges of biomedical research in the 21st century. An alliance forged by the National Institute on Aging (NIA), The John A. Hartford Foundation, Atlantic Philanthropies, The Starr Foundation, and AFAR began jointly funding and administering the Beeson Program. This dynamic partnership has greatly strengthened the Program in multiple ways.

For example, the Program benefits from the rigorous peer-review process of the National Institutes of Health (NIH), and the Program's inclusion in the NIH system has also raised awareness and attracted a more diverse pool of applicants. Combined public-private support, meanwhile, has enabled the Program to offer larger awards and draw top candidates. And thanks to the continued private support which has greater financial flexibility, the Program can sustain its unique networking and mentoring aspects.



The partnership supports other initiatives as well, such as an annual meeting for Beeson Scholars and alumni, field-building activities in aging policy and advocacy, and efforts to raise the profile of aging research in other areas of medicine.

This joint venture has paid off handsomely. More than half of the Scholars now hold leadership positions ranging from Center Director, Department Chair, Division Chief to Director of Fellowship Program. Many have received the coveted R01 research award, which bestows upon its recipients a considerable level of prestige as independent investigators. Those numbers will certainly rise as the Scholars in the most recent cohorts advance further along their career trajectories. The Beeson Program has proven critical to developing their careers and establishing them in the field of aging research. Together, these results have strengthened our conviction that the Beeson Program remains an unqualified success, providing vital financial, networking, and mentoring support to physician-scientists at a decisive juncture in their careers.

# The Multiplier Effect

In 2014, the Beeson Outreach Fund became the Beeson Scholars/Change AGENTS Action Fund, which supports projects by Beeson Scholars that align with the new Hartford Change AGENTS Initiative. The ambitious effort, with funding from the John A. Hartford Foundation, focuses on inter-professional collaboration and promoting change in how healthcare is delivered to older adults.

“Collaboration has been a hallmark of AFAR’s work and the Beeson Scholars program since its inception, and the recent partnership between the Beeson program and the Hartford Change AGENTS initiative has been especially meaningful to the Foundation as it perfectly embodies our strategies and vision for the future,” says Marcus R. Escobedo, Senior Program Officer at the John A. Hartford Foundation.

“While our legacy programs like the Beeson award have been developing experts in aging research and academia, our new initiatives such as the Change AGENTS seek to support and connect those experts so they can take their knowledge into health care delivery settings to create change in practice,” he says. “The Beeson/Change AGENTS Action Fund not only has supported innovative and collaborative practice change projects, but also it serves to encourage other Beeson Scholars to take their place in the Change AGENTS movement, and we couldn’t be more pleased.”

In other news, with funding from the Beeson Ireland Program, AFAR has partnered with the Center for Ageing Research and Development in Ireland (CARDI), to jointly support two research fellows in Ireland.

Finally, through grant extensions the annual meetings will be supported through 2018, ensuring that scholars and alumni will have continued access to this unique venue for mentorship and collaboration. The National Institute on Aging, has been a key co-sponsor and administrator of the program for more than a decade.

Chyren Hunter, PhD, Deputy Director and Training Officer in NIA’s Division of Extramural Activities, hails the Beeson award as an important vehicle for the shared vision of AFAR, the NIA, the Hartford Foundation and other sponsors in promoting the careers of researchers with a primary interest in questions about aging and growing older. “Since 2004, the NIA and AFAR have independently but jointly supported a stellar cadre of physicians and other clinically-trained individuals pursuing independent careers in basic, translational and clinical research in aging and geriatrics,” Dr. Hunter says. “We are delighted at the success that the Beeson Scholars enjoy and are proud that Beeson scholars are leaders in their respective fields. Their accomplishments do much to help address the growing challenges of our aging society.”

## Here are some highlights of recent Beeson Scholar-led projects supported by the fund:

**Daniel Matlock, MD, MPH (2011) and Daniel Kramer, MD, MPH (2013)**, joined forces to cohost a symposium on using implantable cardioverter-defibrillators in older adults. The event brought together experts in heart failure, geriatric palliative care, ethics and electrophysiology and generated multiple research ideas that could form the basis for new collaborations. The multidisciplinary group recently published a paper summarizing the ICD Use in Older Adults symposium in the journal *Circulation—Cardiovascular Quality and Outcomes*, to help identify critical clinical and research problems and suggest a roadmap for improvement.

**Alexander Smith, MD, MPH (2012)**, received funding to support the creation of a series of teaching videos for the *ePrognosis* website and the *ePrognosis: Cancer Screening* smartphone app. *ePrognosis* provides a repository of published geriatric prognostic indices for clinicians to obtain evidence-based information on their patients’ prognosis, while the app can guide conversations with older patients on whether to start, stop, or continue breast cancer and/or colorectal cancer screening.

**Liana Apostolova (2005) and Jason Karlawish (2000)** are working closely to assemble a multidisciplinary group of experts in order to 1) create recommendations for how to communicate a diagnosis of mild cognitive impairment, or MCI, and 2) assess whether and how the recommendations should change when clinicians use an imaging method called amyloid PET to detect evidence of MCI. The group hopes to spur additional discussion and research in the field to improve upon the clinical care of persons with MCI.

**May Reed, MD, FACP (1996)** and an interdisciplinary team will use established electronic medical record systems to improve the drug prescription process in emergency departments. The project will help providers improve their drug selection and be more judicious in the use of selected medications such as analgesics, anti-emetics, sedatives, hypnotics, and anti-psychotics for older patients in emergency departments.

## Letter from Richard Besdine, MD

AFAR Medical Officer

The Beeson program came into existence after a series of Institute of Medicine reports that, beginning in 1978, highlighted a growing need for physicians trained in geriatrics and aging research. After the 1993 report called for more support of geriatrics research and training, a group of foundations and nonprofit organizations came together to create the Paul B. Beeson Physician Faculty Scholars in Aging Research Program, now known as the Paul B. Beeson Career Development Awards in Aging Research Program. These funders sought to play a catalytic role by making strategic investments in individuals and organizations positioned to advance research and training that ultimately would result in better care for older Americans. And they succeeded in doing all that and more.

Now, 21 years later, more than 200 clinically-trained investigators proudly can call themselves Beeson Scholars, contributing to advances in nearly every area of aging-related science, and making a real difference in the lives of older adults.

The Beeson Scholar designation is career changing, and solidly establishes Scholars in their area of aging research in their home institutions. Key features that make the Beeson brand so precious include flexible and generous funding, an outstanding support system of Beeson mentors and alumni, and extensive networking opportunities. Scholars are selected from leading medical schools and research institutions across the country.

I proudly introduce the 2013 Scholars, and am confident that they too will be maturing into the leadership role so critically needed for advancing the knowledge, treatment and care of millions of older adults.



Richard W. Besdine, MD



# Marian “Emmy” Betz, MD, MPH

Assistant Professor of Emergency Medicine,  
University of Colorado School of Medicine

Mentor: Robert Schwartz, MD

## *Physician Screening of Older Drivers: Decision Rules for Geriatric Injury Prevention*



The ability to drive has long been associated with freedom. “We know from a lot of studies that driving is important to older adults because it helps them stay mobile and independent,” says Marian “Emmy” Betz, MD, MPH. “People who stop driving too soon can become depressed and even die early.” On the other hand, many common conditions and medications can reduce the ability of seniors to drive safely.

“The problem is that there is no single diagnosis or no single age when suddenly someone is unfit to drive,” she says. Also, older adults are unlikely to bring up the topic unless they are already having significant difficulties.

Dr. Betz hopes to make such conversations easier and more useful by developing a screening tool that would let doctors briefly and routinely evaluate the driving capacity of older individuals. Those identified in need of a driving evaluation could be referred to a specialist and receive additional counseling and other resources.

“We need to recognize there comes a time when most people need to stop driving and we need to support older adults so that they can stay active, independent and healthy,” Dr. Betz says. “There is life after you hang up the keys.”

For her Beeson project, she is validating a screening tool dubbed CRASH, an acronym based on five questions:

- **C** is for confusion:  
*Do you ever feel confused when you’re driving?*
- **R** is about driving regularly:  
*Are you driving regularly and drive long distances?*
- **A** refers to avoidance:  
*Are you avoiding driving alone?*
- **S** stands for seeing:  
*Do you have any difficulty seeing while driving?*
- **H** references handing over:  
*Has anyone asked you to hand over the car keys?*

Although the questionnaire won’t identify everyone in need of more testing, Dr. Betz hopes it will provide the basis for a practical, rapid, and regular screening process. She and her colleagues also are soliciting feedback from older drivers, healthcare providers, and driving specialists. The goal is to combine the screening tool and additional input “to build a program that makes sense and might be feasible instead of just saying to doctors, ‘Here’s one more thing you should do.’ That’s not very useful,” she says. If her system works as expected, it also may offer a template for other feasible, acceptable, and effective injury prevention plans.

Her study is recruiting 200 older drivers from primary care clinics; as part of the assessment, Dr. Betz and her team are asking additional questions to predict which of the drivers might score lower on a subsequent one-hour road evaluation. At the same time, the researchers have helped normalize such conversations by embedding questions about driving status into the routine clinical template used by primary care providers.

As an emergency physician, Dr. Betz has a strong interest in injury prevention. “Forteen drivers,” she says, “research-based policies such as graduated licensing have helped save lives.” She began to wonder whether similar research could be translated into improving safety at the other end of the age spectrum. That angle, in turn, helped expand her interest in geriatric emergency medicine into aiding other difficult but necessary discussions of injury prevention among older adults, such as suicide prevention.

The Beeson award “is phenomenal because it’s given me the space that I really need to develop, and my productivity has exploded over the past two years.” The award also has helped Dr. Betz become active in women’s leadership training programs and in mentoring junior women researchers in academic medicine. Unlike other career development awards, Dr. Betz notes, the Beeson Program promotes networking opportunities with both senior leaders and peers in the field. “Really seeing what someone else is doing, encourages you to think big.”

# Constance Fung, MD, MSHS

Assistant Professor of Medicine, David Geffen School of Medicine at the University of California, Los Angeles

Mentor: Cathy Alessi, MD

## *Improving Older Adults' Decision Making for Obstructive Sleep Apnea Treatment*



In severe cases of obstructive sleep apnea, the throat muscles of a sleeping patient may relax and block the airway 30 times an hour; in extreme cases, the frequency of these obstructions can soar to as many as 120 per hour.

The sleep disorder, if left untreated, can contribute to serious health problems ranging from car crashes caused by sleepy drivers to an increased risk for stroke and heart arrhythmias. Constance Fung, MD, MSHS, estimates that roughly one fifth of older adults have sleep apnea. Far fewer have had it properly treated, much less diagnosed.

Doctors have developed three main strategies to keep the airway open: a snug-fitting mask that delivers continuous positive airway pressure (commonly called CPAP), a mouthpiece or oral device that keeps the throat clear, and surgery that removes tissue from the back and top of the throat. For her Beeson research, Dr. Fung is focusing on the barriers that prevent older adults from accepting or sticking to a treatment plan that could significantly decrease their symptoms.

Eventually, the work could shape a new intervention that more fully engages each patient in the treatment decision. Crucially, the decision aid could help older patients—especially those dealing with other medical conditions—communicate their goals, values and concerns. She notes: “Are they looking more for optimizing quality of life versus extending how long they’re living?”

In Phase I, Dr. Fung is exploring the range of factors that influence the decision-making process in older adults. Beyond considerations such as whether a treatment seems unnecessary, unaffordable or uncomfortable, she is focusing on factors such as whether patients can learn and remember how to use the treatment and adjust the settings.

From focus groups, Dr. Fung and colleagues also found significant variability in how much providers were telling older sleep apnea patients about the disorder and its

treatment options. “Most of the patients want to know about their disease,” she says. “They want to know not just what’s first line or what the most obvious choice is but they want to know what the alternatives are.”

That information can be critical, as multiple patients have revealed that they had never known about alternatives to CPAP. When that initial therapy proved unworkable for some, Dr. Fung says, “they never came back to see a doctor because they sort of figured there was nothing else to do.”

For Phase II of the project, Dr. Fung and her team are using the collected data and additional input from both patients and providers to craft a decision aid specifically for older adults. “We’ll recruit patients and show them versions of the prototype and then we’ll make changes and try to make it better,” Dr. Fung says.

The Beeson award has been invaluable by giving her the protected time to pursue her research aims and career development activities, she says. Already, she has attended training courses and seminars to learn more about health coaching, decision-making, choice analysis, and constructing a good decision aid. Dr. Fung says the support from her multidisciplinary mentoring team and the networking opportunities at the annual Beeson meetings also have been critical to her success.

She has always been interested in how people make decisions. During successive fellowships in geriatrics and sleep medicine, Dr. Fung cared for many older patients who didn’t adhere to their prescribed therapy after being diagnosed with obstructive sleep apnea. She then wondered: How could she optimize their treatment plans? Her current research focus is now giving her the best of both worlds: “I’m marrying my interests in decision-making with my interests in improving sleep in older adults.”

# William Hu, MD, PhD

Assistant Professor of Neurology,  
Emory University School of Medicine

Mentor: Allan Levey, MD, PhD

## *Early Cerebrospinal Fluid Detection of Frontotemporal Lobar Degeneration*



A group of diseases, known as frontotemporal lobar degeneration, ranks second only to Alzheimer's disease as the most common types of dementia in people under the age of 65. Unlike Alzheimer's, these disorders usually spare memory early on but can fundamentally alter patients' behavior, personality, speech, and decision-making skills.

"From imaging studies, we think that different circuits in the brain are affected," says William Hu, MD, PhD. Researchers have further subdivided frontotemporal lobar degeneration into two main subgroups: one associated with an abnormal protein called TDP-43, and the other linked to an abnormal protein known as tau. Frustratingly, clinicians normally cannot distinguish between these subtypes until they visually inspect the brain after an autopsy, complicating efforts to diagnose patients or enroll them in clinical trials when there is still an opportunity to intervene.

"If we have a drug and we can't identify the right patients, then we can't really do an effective trial. Even if we do, we will have to grossly overpower it to account for people who don't have the right disease," Dr. Hu says. "If clinicians can't predict which patient has what subtype, how would they even figure out which drug to test?"

During his residency, Dr. Hu started looking for any behavioral features that might predict the underlying frontotemporal lobar degeneration subtype. "And really, there weren't any," he says. "It was a frustrating project, but it got me interested in this field." He has since focused on identifying molecular markers that could help clinicians confirm the diagnosis beyond subjective clinical phenomenology. "Because we're talking about behavior changes in the context of life-long behaviors, sometimes it can be tricky to know whether someone is developing abnormal behaviors or just becoming more eccentric as one ages."

So far, he has discovered that a reduction in the ratio between two specific proteins within the cerebrospinal fluid is highly predictive of the TDP-43 disease subtype; three other research groups have since replicated the

finding. "It's very exciting and encouraging that this may potentially become a clinically useful test," Dr. Hu says, noting that the same test might prove useful for amyotrophic lateral sclerosis, also known as Lou Gehrig's disease or ALS.

For a biomarker-based test to be useful, however, clinicians need to have further options when the test result isn't clearly positive or negative. "It's the indeterminate calls that frustrate clinicians, scientists, and patients," Dr. Hu says. "If there are many indeterminate calls, then we're back to the problem of not being able to accurately diagnose patients."

Although Dr. Hu was first drawn to mathematics, he decided that his passion lay more in using the discipline to solve biochemical and molecular problems. For his Beeson research, he is making good use of this background by classifying test results with a data analysis method called machine-based learning. The method uses multiple lines of data—such as age, gender, genetic profile and age of disease onset—to build a model which yields a probability that a patient has one disease subtype or the other. With a more reliable method for classifying patients, clinicians can more easily recruit them for the proper clinical trials and potentially optimize the applicability of candidate drugs.

"In the ever-changing environment of academic medicine, the Beeson award provides a robust mechanism to guarantee me the time and effort to not only pursue my research interests—including my Beeson project—but also additional training," Dr. Hu says. He has already completed courses on biomarkers and machine-based learning that he would not otherwise have had the opportunity to take.

He also values the leadership training, camaraderie, collaboration and mentorship at the Beeson meetings. "I'm really appreciative of the question and answer period during which some of the more senior Beeson awardees and faculty provide on-the-spot mentoring for common questions and concerns. The award provides the protection and the leadership training that are crucial for my success in these activities."

## Daniel Kramer, MD, MPH

Assistant Professor of Medicine, Harvard Medical School,  
Assistant Scientist, Hebrew SeniorLife Institute for Aging Research

Mentor: Susan Mitchell, MD, MPH

### *Patient-Centered Outcomes of Implantable Defibrillator Therapy in Older Patients*



Every year, doctors place more than 50,000 devices known as implantable cardioverter-defibrillators (ICDs) in patients aged 65 and older. These patients have experienced a life-threatening disturbance of the heart's rhythm—a condition known as arrhythmia—or are at risk of developing one due to a prior heart attack, heart failure, or reduced muscle function from another cause.

Daniel Kramer, MD, MPH, has long appreciated the device's "extraordinary" ability to monitor the heart's rhythm, detect the emergence and persistence of a dangerous arrhythmia, and then deliver a shock to reset the beat and save a patient's life. Less understood, however, is the quality of life of older patients with ICDs.

"Older people are particularly sensitive to questions around whether they will live not just longer, but will they be independent, or will they be functional," Dr. Kramer notes. In other words, will their quality of life be high enough to make its prolongation desirable given the device's side effects? "And then for older patients, even if the defibrillator does extend their lives, eventually they will have to confront some end-of-life care issues," such as wanting the device turned off as they near death.

Through his Beeson project, Dr. Kramer hopes to gain a clearer understanding of patients' experience living with ICDs, and then use that information to help improve their quality of life. He is delving into large databases of those who have received ICDs to examine how long they live afterward, where they live—such as a nursing home, hospice, or their own home—and how well they function.

Through a small pilot study of older and sicker patients implanted with defibrillators at Boston's Beth Israel Deaconess Medical Center, Dr. Kramer hopes to better understand their goals, decisions, discussions with providers, and end-of-life experiences. Eventually, his research could aid the decision-making process by expanding quality of life descriptions along with survival rates and potential complications. "Telling somebody that they'll be alive in a year is not the same as telling them that they'll be alive and independent," he says.

"We might be able to improve or add a little more depth to the kinds of discussions that we would like patients to have before they elect to get an ICD." In addition, the research might identify patients at higher risk of requiring nursing home or hospice care after receiving the devices, giving doctors a better chance to ward off preventable transfers or initiate end-of-life discussions.

Dr. Kramer first became interested in heart rhythm cardiology and ICDs as a medical student: "I was really struck very early on in my training about the power of these particular devices," he says, noting that he also has a personal connection to his research specialty. "I have had a few family members die suddenly from cardiovascular disease. It's not uncommon for me to think about that when I'm taking care of these patients or putting in these devices myself."

The Beeson award has provided critical support for his research: "It's a career development award like no other. It comes with the funding and the networking and the resources that I think otherwise would make this kind of science very difficult." As a sub-specialist, he also has benefited enormously from networking with other researchers at the annual meetings and receiving career development advice. "I'm trained as a cardiac electrophysiologist; I'm not a geriatrician," he says. "so I have learned a lot from working with and hearing from other people in the program who have exclusively focused on the needs of older patients."

From his ongoing research and discussions, Dr. Kramer has broadened his focus to glean even more information from ICDs. "I think there are a lot of opportunities just using some of the data sources that I'm pulling from to more clearly characterize the experience of living with these devices as the underlying disease progresses," he says. The devices themselves capture critical data that could more clearly illuminate each patient's functional status and disease trajectory. Together, the information could play a major role in shaping interventions that improve outcomes, enhance quality of life and inform critical end-of-life decisions

# Ozioma Okonkwo, PhD

Assistant Professor of Medicine,  
University of Wisconsin School of Medicine and Public Health

Mentor: Sterling Johnson, PhD

## *Early detection of asymptomatic middle-age adults at risk for Alzheimer's disease*



By 2025, an estimated 7.1 million Americans aged 65 and over will have Alzheimer's disease—a remarkable increase of 40 percent from current levels. Warding off a public health crisis may well depend on detecting the disease while it is still asymptomatic and potentially treatable with experimental therapies.

"The field is beginning to appreciate that therapeutic agents are more likely to be effective if they are administered at the earliest stages of the disease, before the individual has experienced irreversible neuronal loss and related brain lesions," says Ozioma Okonkwo, PhD. "But in order to administer or implement the interventions at such an early stage, you have to be able to identify the individuals who are at that stage."

A recent revision of the diagnostic criteria for Alzheimer's formally recognizes pre-clinical Alzheimer's as the earliest stage of disease progression. At this point, individuals are still cognitively normal but beginning to accumulate the pathological signs of disease that will eventually lead to dementia. To identify this early stage, doctors must do an invasive lumbar puncture to look for changes in the cerebrospinal fluid or conduct an expensive PET imaging scan to identify specific biomarkers of disease in the brain.

One goal of Dr. Okonkwo's Beeson project is to identify a diagnostic method that is less expensive, less invasive, and more widely available while still accurately reflecting this preclinical stage. He is tapping the Wisconsin Registry for Alzheimer's Prevention, a group of more than 1,500 middle-aged adults who are asymptomatic but at increased risk of Alzheimer's because they have one or two parents with the disease. The study participants have undergone cognitive and clinical assessments over time, including MRI-based imaging. Some also have had PET scans and lumbar punctures.

By combining the available PET, CSF, and cognitive data, Dr. Okonkwo aims to identify those individuals in Stage 3 preclinical Alzheimer's, the last stop before they shift into a more clinically apparent stage marked by mild cognitive impairment. For a control group, he hopes to identify patients at Stage 0, who lack any signs of neuronal dysfunction or cognitive impairment. For both sets

of patients, he will then use cheaper and non-invasive MRI-based scans to image the brain over time: one type of MRI measures brain structure and a second assesses its perfusion. Dr. Okonkwo can then apply a sophisticated statistical tool to model the pattern of structure-perfusion changes in the brain that typify Stage 3 preclinical Alzheimer's. This can then be summarized into a risk score that will be tested against core Alzheimer biomarkers such as  $\beta$ -amyloid.

If validated, this risk score could be used to discern whether other asymptomatic patients, who have only undergone MRI imaging but not PET scanning or lumbar puncture, are at increased risk for Alzheimer's as a result of harboring the same pathological changes seen in Stage 3 preclinical Alzheimer's. After identifying this telltale pattern and at-risk individuals, Dr. Okonkwo says other differences are likely to emerge: some patients may progress quickly to clinically apparent Alzheimer's, while others barely change. "What is it that some individuals remain resilient to the otherwise expected effects of the brain disease?" he asks.

That question lies at the heart of his research and its unifying theme of how to promote successful aging. For example, he says, "Two people could arrive at the same clinical diagnosis via slightly different pathways." Understanding that distinction could be crucial when trying to determine which therapy to use.

Dr. Okonkwo has long been curious about the brain and cognition. "I started to think that I would like to study these things not just in theory but in human beings."

The Beeson award and the annual meeting "have helped me get in touch with my peers in the field who are doing very exciting work that complements and even help expand my work," he says. From talking with another Beeson Scholar during the annual meeting in 2014, for example, "we found out that we were both interested in this notion of resilience to aging and disease." The two scholars have since submitted an NIH grant proposal to explore the genetic basis of resilience. "It is this type of connection that the Beeson program helps to establish and sustain."

# Janey C. Peterson, EdD, MS, RN

Associate Professor of Clinical Epidemiology in Medicine,  
Weill Cornell Medicine

Mentor: Mark Lachs, MD



## INSPIRE: Intervention to Support Participation in Regular Exercise in the Elderly

As the United States population ages, more people are living longer with chronic illnesses which also means that they are at higher risk of becoming disabled. Physical activity can stave off disability and even improve the functional status of older adults who have already begun to face illness-related complications.

“There’s a window of opportunity where we can help people to maintain or improve their function through increasing physical activity, but health providers prescribe exercise to only about a third of older adults,” says Janey Peterson, EdD, MS, RN. The U.S. Surgeon General, by contrast, has recommended that adults should get at least 150 minutes of moderate-intensity exercise every week. Those guidelines, however, can be overwhelming to older individuals with multiple serious chronic diseases such as a history of congestive heart failure, diabetes or myocardial infarction.

Dr. Peterson hopes to find the right balance with recommendations that are both effective and reasonable for older, high-risk patients living with combinations of high-risk chronic conditions. Her early data suggest that even low levels of physical activity for this largely sedentary group can have a very meaningful impact on extending life and decreasing the risk of major morbidity and mortality. To help motivate her patients, Dr. Peterson has developed an intervention that induces Positive Affect—a feeling of happiness or wellbeing. Positive Affect, she explains, can lead to greater confidence and motivation and promote more flexible thinking and healthier behaviors. “That’s really the secret sauce to long-term behavior change,” she says.

Her research team adapted the intervention, initially developed and tested on healthy young adults on college campuses, and translated it to older clinical populations with chronic disease. “We ask people, ‘What are some small things in your life that make you smile, that make you feel good?’” Then, we send them surprise gifts, like a picture frame for a photo of loved ones, to help strengthen the induction of positive affect. The researchers also ask the patients to identify core values and life priorities that are important to them, a second construct which is

called Self-Affirmation. “Combining Positive Affect and Self-Affirmation is an important motivator for people, because it enables them to connect behavior change to things that are important in their life.”

In a previous, randomized controlled trial of patients recovering from coronary angioplasty, she says, “we had phenomenal results.” Compared to patients who were given only educational materials, people who received the Positive Affect intervention were 1.7 times more likely to achieve their one-year exercise goal: engaging in physical activity the equivalent of walking just over 4 miles/week. The Positive Affect group had nearly double the improvement in activity expenditure by one year: they were expending kilocalories at a rate equivalent to walking nearly 7.5 miles/week, compared to the control group who were expending kilocalories at a rate of about 4.1 miles/week.

Dr. Peterson cautions that a longer-term study would be needed to determine the impact of induction of Positive Affect on life expectancy, major complications and disability in older adults. Nevertheless, the effects on physical activity were so compelling that she and colleagues have further adapted the intervention to motivate other patient populations, including her group of older patients with a high burden of chronic disease. Every study participant will receive a FitBit®, a wireless device used to track daily exercise, and will be followed closely for a year. After developing a tailored exercise plan together, the patients and Dr. Peterson will track their progress and recalibrate the regimen if necessary. Her next step will be a larger randomized controlled trial to validate the intervention’s usefulness as a new tool for healthcare providers to employ in older adults with high burdens of chronic disease.

“My own parents have chronic illness and I’ve worked in clinical research for many years,” Dr. Peterson says, so she wanted to apply her experience, skills, and passion to help older adults navigate the trials she encountered with her family. “That’s what the Beeson mission is all about—working together with other leaders in aging, leveraging our knowledge and collaborating, to improve the health of older adults.”

# Vivek Prabhakaran, MD, PhD

Assistant Professor of Neuroradiology,  
University of Wisconsin School of Medicine and Public Health

Mentor: Patrick Turski, MD, FACR

## Stroke Plasticity



Stroke, characterized by a sharp reduction or interruption of the brain's blood supply, is one of the leading causes of death and disability in the United States. With about 800,000 strokes occurring annually, the population of survivors has swelled to an estimated 4 million. "That basically means that there are more people that need adequate rehabilitation so that they can be functionally better in being able to participate in real-world activities," says Vivek Prabhakaran, MD, PhD.

To help patients achieve the best post-stroke rehabilitation, however, researchers need a better understanding of how brain networks change and adapt to the injury, a phenomenon known as stroke plasticity. "The initial stroke can lead to network dysfunction," Dr. Prabhakaran says, "and then the question is what happens later on and how does the network reorganize and recover? And how can we shape the recovery process in a way that's adaptive towards function as well as suppress some of the maladaptive plasticity changes that may occur, which may actually be impairing functional recovery?"

Beyond conducting research into how doctors might encourage adaptive rewiring in the brain and discourage maladaptive changes, Dr. Prabhakaran's Beeson project is also aimed at understanding the critical time window for intervening and shaping the plasticity in a way that's helpful. Finally, he is developing methods to help predict which patients will recover more fully than others. For those likely to struggle with their recovery, for example, doctors might want to pursue more aggressive rehabilitation strategies.

Dr. Prabhakaran and colleagues are collecting data from up to 75 stroke patients and also collecting extensive neuropsychological datasets as well as utilizing advanced neuroimaging techniques to collect data of functional and structural assessments of each patient's brain. "We think these additional imaging measures have very important information that can be helpful in understanding their recovery, prognostics and the critical time window for intervention," he says.

The researchers start their assessments within a week of each patient's stroke and follow up at specific time intervals until a year after the initial brain injury. The

extensive time frame can help them relate changes in the neuroimaging measures to changes in a patient's neuropsychological measures. From the emerging relationships, Dr. Prabhakaran may be able to determine the hallmarks of a good or bad recovery and use these patterns to better inform stroke rehabilitation strategies.

Immediately after a stroke, the "stunned brain" largely shuts down in the acute phase, before dramatically ramping up its activation of various networks in the sub-acute phase and then pruning some of the connections to remodel its networks during the chronic phase. "This is occurring over weeks to months, really, in terms of the whole shaping of brain plasticity and corresponding behavioral changes," he says.

Dr. Prabhakaran has long been interested in normal aging, cognition and the mechanisms that underlie changes in the brain's networks. "As I moved to my clinical years, I became more and more exposed to clinical patient populations who suffered a stroke. Stroke is very devastating and has an incredible morbidity and mortality associated with it," he says. He began asking some of the same questions about altered brain networks and cognition in stroke patients. Because of the definitive onset of a stroke injury with the sudden interruption of blood flow, he realized that he would be able to track the entire recovery process.

The Beeson award, he says, has been a "tremendous" asset in letting him pursue such an ambitious research agenda. The award has been an important stepping-stone to additional grants and awards that have allowed him to branch out by focusing on his own stroke rehabilitation technique.

The innovative method, called a brain-computer interface technique, gives patients immediate biofeedback of their own brain in action while they conduct a specific task, such as moving a hand. The technique, which Dr. Prabhakaran is refining in patient populations, links the brain's central activity with peripheral movement. "They're able to modulate the brain activity to improve their outcomes," he says. "So it basically harnesses brain plasticity for recovery."



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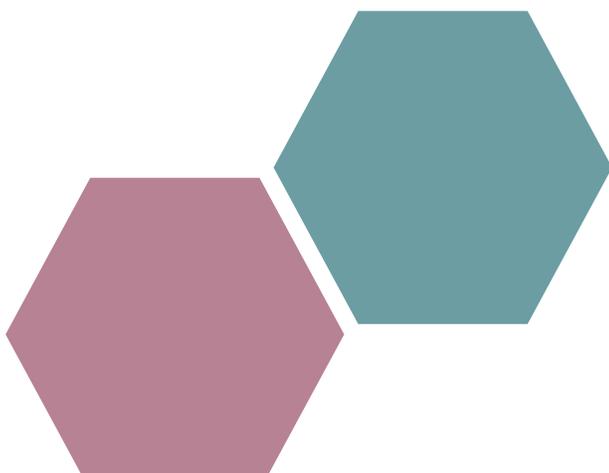
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