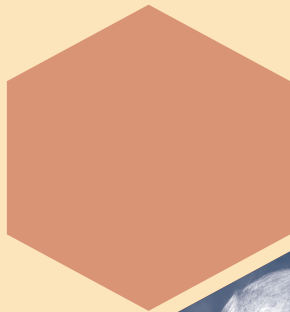




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**Paul B. Beeson  
Emerging Leaders  
Career Development  
Awards in Aging**

2017 Report featuring  
the 2015 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 Emerging Leaders Career Development Awards in Aging 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, 225 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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## Letter from Thomas M. Gill, MD

Chair of the Program Advisory Committee

The Beeson Program was launched more than 20 years ago with the intent of creating a new cadre of physician-scientists committed to teaching and mentoring as well as research. In recent years, and with the 2015 Beeson Scholars, we are seeing long-term rewards of this investment guiding careers: a second generation of Beeson Scholars is being mentored by Beeson alumni. It is great for the field that Beeson alumni are some of the strongest advocates of the Program, and are playing a major role in training the next generation of clinician investigators.

As in earlier years, the 2015 Beeson Scholars study aging from the vantage points of many different disciplines and subspecialties. However, the concept of vulnerability is a common theme among their research areas. What are the factors that make older persons vulnerable? Members of this Beeson class are trying to better understand the mechanisms by which older persons become frail, whether physically or cognitively, or in some cases, both.

Notably, this includes two Scholars from the field of anesthesiology—a discipline that, historically, has been underrepresented in the Beeson Program and in aging research more broadly. Two Scholars who join this Beeson class are supported in collaboration with the Center for Aging Research and Development in Ireland (CARDI)<sup>1</sup>, and they are also investigating aspects of predicting and preventing frailty in older adults.

Another remarkable feature of the 2015 Beeson Scholars is that, among the U.S. Scholars, 5 out of 7 are women. In the field of medicine generally, there is much concern that women have not achieved the same levels of advancement as men. Clearly, in aging, there are opportunities for both men and women—and it's also a field that has been very effective in attracting women investigators and then providing them with opportunities to become leaders within the field.

We are delighted to introduce here the 2015 Beeson Scholars. Their stellar accomplishments, and their continued growth, enrich both the knowledge and the pool of leadership to carry our field forward.



**Thomas M. Gill, MD**



<sup>1</sup> In September 2015 The Centre for Ageing Research and Development in Ireland (CARDI) became the Ageing Research and Development Division within the Institute of Public Health in Ireland (IPH).

# NIA Trains Future Leaders with the Beeson Award

One of the major goals of the Beeson Program is to encourage and assist the development of future leaders in the field of aging by supporting faculty members early in their careers to gain additional research training as needed and to establish independent programs in aging research. The Beeson Awards are included among the career development award programs from the National Institutes of Health (NIH) known as “K” awards. What distinguishes the Beeson Awards is the idea of leadership training. In the last year, the National Institute on Aging (NIA) has taken steps to strengthen this leadership focus.

The 2017 Request for Application (RFA) opens eligibility to applicants who:

- are early-stage investigator eligible, meaning that they are in their first 10 years of research following the end of their research training.
- have had prior career development awards or are currently on a career development award. In previous years, people with prior or concurrent K awards were excluded.

This follows on changes made in 2016, including the creation of a new K award number for the Beeson program, the K76. The program also was renamed as the Paul B. Beeson Emerging Leaders Career Development Awards in Aging.

“It’s a natural for somebody with a regular career development award to go on to a Beeson Award if they want to learn about leadership and then take a leadership position,” says Robin Barr, PhD, Director of NIA’s Division of Extramural Activities.

The review committee seeks candidates who are both building a track record in aging research and demonstrating leadership potential, for example, by having been chief resident or taking on organizational leadership.

“We want a mix of people pursuing research and advancing the science in aging,” says Dr. Barr. “We want PhD’s, and we also want physicians and other health professional scientists involved because they have an important perspective from working with patients. That perspective is vital to advancing our health sciences.”

Former Beeson Scholars are already taking high-level roles in healthcare. For example, one former Beeson Scholar is making a national impact by working with the U.S. Department of Justice to develop state-level guidelines on elder mistreatment. The Centers for Medicare and Medicaid Services have funded another former Beeson Scholar to establish a program for the clinical care of Alzheimer’s patients across the Midwest.

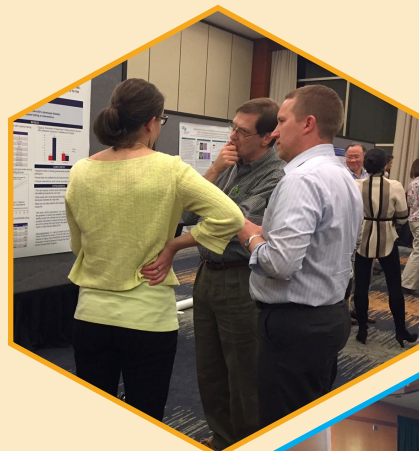
Says Dr. Barr, “They are R01 funded scientists who contribute to research in the field, but they are also going on to have considerable clinical leadership and to advance healthcare in the country.”

## Highlights from the 2016 Beeson Meeting

Over 100 current and former Beeson Scholars, mentors, NIA staff, and foundation supporters convened in Itasca, Illinois last year for the program’s annual meeting.

Organized by AFAR, the two-day meeting is designed to share research progress and enhance scholarship and leadership through poster sessions, panels, networking, and one-on-one-mentoring.

For updates on Beeson Scholars in the news, please visit [www.afar.org](http://www.afar.org) or follow AFARorg on Facebook and Twitter.



## Letter from Richard Besdine, MD

AFAR Medical Officer

It is more important than ever to support, promote, and disseminate the science that guides us in providing optimal care for our elders. Today's Beeson Scholars work in a daunting political climate that poses extraordinary challenges. Yet our current and future Beeson Scholars must succeed and flourish, and the work must go on.

Each year, with the Beeson Award, AFAR provides security and stability for a new cohort of talented investigators as they forge their careers in academic medicine. The program also has created a powerful leadership network. Nurturing leadership among the physicians with clinical, academic, and scientific expertise will help ensure that our growing older population will receive optimal care.

To date the Beeson Program has supported 225 Scholars and their mentors. This report highlights the exciting work of the Beeson Scholars who joined the program in 2015. The research of these outstanding professionals provides a robust grounding for improving health and healthcare, and for their future careers in gerontology and geriatrics.



**Richard W. Besdine, MD**



## Stacie Deiner, MD, MS

Associate Professor of Anesthesiology,  
Neurosurgery and Geriatric & Palliative Care,  
Icahn School of Medicine at Mount Sinai



Mentors: Mary Sano, PhD, and Kenneth Boockvar, MD

### *Optimizing Postoperative Cognition in the Elderly*

Feeling groggy in the hours after waking up from anesthesia often occurs for a variety of reasons including medications and the stress of surgery. But for about 15 percent of older adults, post-operative mental fog persists for days, weeks, and even months after surgery. Ultimately these changes can affect their ability to participate in rehabilitation, follow their doctor's instructions, take medications, and increase their risk of falls. With more than 40 million Americans already over the age of 65, who have increasing needs for surgery as they age, post-operative cognitive dysfunction, or POCD, is taking a significant toll on older adults.

"In line with the common concern that residual medications may be a 'smoking gun', I started off by comparing anesthesia drugs to see if one was advantageous over the other in terms of delirium and post-operative cognitive function," says Stacie Deiner, MD, MS. Delirium refers to severe confusion and other symptoms that can manifest—and that resolve—within several days after surgery.

"We found, squarely, no advantage to one medication over another" says Dr. Deiner. But during these studies she and her colleagues also recorded patients' brain activity while under anesthesia, using a technique called processed EEG. There, they discovered a hint that some characteristics of the brain waves might be associated with cognitive issues.

That observation led to Dr. Deiner's Beeson research. "Basically, we don't know whether more, or deeper, anesthesia is better or worse," she explains. As a Beeson scholar she is investigating what level of anesthesia protects people from POCD.

The study is enrolling 175 patients age 65 years and older who are scheduled for elective major surgery other than heart surgery. Before their procedure, patients take a battery of tests that evaluate two kinds of cognitive abilities—memory and executive function, which includes thinking speed, judgment, and language. Study participants take the tests again three months and one year after surgery.

During surgery, Dr. Deiner monitors her patients' brain activity with processed EEG. Depending on the "depth" of anesthesia, brain waves can vary from a pattern that looks like someone who is comatose, with almost no electrical activity, to nearly the activity of someone who is awake and thinking.

"People feel that general anesthesia is like sleep," notes Dr. Deiner, "but it actually is not like normal dreaming sleep at all. It's much more like coma. And you can make an argument that quieting down someone's brain waves could be helpful because there's less metabolic activity from the cells, and less is demanded from the cells that have to produce the brain waves. Or you could say that maybe it's harmful. Maybe there's something important about maintaining the process of electrical activity."

Dr. Deiner's study is beginning to point to some answers. "What we're looking to see is whether the brain wave pattern during anesthesia—the depth—influences whether people have later problems with their memory, or their judgment and processing speed." The study also evaluates how people with these different types of cognitive dysfunction recover their physical function—their ability to walk, take part in social activities, and cook for themselves, among other things.

So far, it appears that greater depth of anesthesia protects against cognitive changes; more patients with memory and executive function issues had the "lighter" anesthesia.

Dr. Deiner's career illustrates the crucial role of the Beeson Program in launching independent scientists who take diverse paths to research on aging. Curiosity led her from private practice in anesthesia to a position in academia, and participation in a geriatrics study. Then a grant from the National Institute on Aging helped her transition to aging research. Now, the Beeson Award supports work that will provide a basis for future funding and becoming an independent investigator.

"The most remarkable thing is the ability to network at the annual meeting," says Dr. Deiner. "I've gotten lots of great feedback on the work I'm doing, and I keep in touch with other Beesons during the year."

# Raquel C. Gardner, MD

Assistant Professor, University of California San Francisco,  
Department of Neurology, Memory and Aging Center;  
Weill Institute for Neurosciences; San Francisco VA Medical Center

Mentors: Kristine Yaffe, MD, and Kenneth Covinsky, MD, MPH

## *Traumatic Brain Injury and The Aging Brain: Predictors of Clinical Trajectories*



Car accidents, playing football, military service, falling down—all can lead to a blow to the head that results in a person feeling dazed or confused, having a gap in memory, or even losing consciousness. Any one of these symptoms after a blow to the head may indicate that the person has suffered a traumatic brain injury (TBI), a condition that impacts nearly 2 million Americans every year.

Increasingly, doctors recognize that sustaining a TBI in young adulthood raises a person's risk for dementia, Parkinson's, and other neurodegenerative diseases later in life. Yet the causes of memory and movement symptoms, their course of development, and why some people are resilient and others decline over time, are largely unknown.

"As a dementia neurologist, I became interested in the long-term consequences of TBI through my clinical work at the San Francisco Veterans Affairs Medical Center," says Raquel Gardner, MD. She applied to the Beeson Program in order to study cognitive, movement, and mood symptoms in retired military veterans who had decades-old TBIs. "First we need to evaluate the clinical symptoms to better characterize what actually happens to older adults with TBI," she says. "Then we can dig deeper by examining genetic and lifestyle factors, biomarkers in blood, or changes on brain scans to understand mechanisms and to figure out why some people are resilient while others are not. Only then can we harness this information to develop treatments to optimize long-term brain health after exposure to TBI."

To understand the long-term effects of TBI in a broader population, Dr. Gardner has analyzed data from the US Health and Retirement Study, a national survey of aging. Her research is finding that in this group, as well as in military veterans, people with prior TBI tend to develop more problems with movement—climbing stairs or walking—than with memory. Furthermore, people with more severe injuries tended to develop worse problems later.

Dr. Gardner discovered an unanticipated benefit to joining the network of Beeson Scholars. "When you get an award, or you're planning for a grant, you meet all these people and then you discover new areas of

research, and knowledge gaps—really critical areas for research that you didn't know existed," she says. "While I was planning my Beeson proposal, I spent time with one of my mentors, neurosurgeon Geoffrey Manley, MD, PhD, at our local county hospital. I was just amazed by how many patients are admitted to the hospital for TBI who are over the age of 65." This led her to expand the project's scope to include older adults with recent TBI.

"It's a huge public health problem," she adds. "And even though it's such a common condition, and we have increasing numbers of older adults coming to the hospital for TBI, mostly from falls, we really have almost no guidelines about how to treat them." Some hospitals treat TBI aggressively, with surgery, while others will not even offer aggressive treatment to older adults.

With research using existing datasets and a pilot clinical study, Dr. Gardner is mapping the way to a better understanding of the consequences of TBI in older adults as well as how to predict their recovery over several years. Eventually, she says, "we'll be able to give an evidence-based answer, when a patient's family asks, 'Is mom going to recover?'"

The consequences of decades-old TBI in older adults and the difficulties of those with recent injuries "are two very different things," says Dr. Gardner. For both, her ultimate goals are to improve care and find strategies to prevent post-TBI neurodegenerative disease.

In the meantime, the Beeson Program supports her work in many ways. In addition to mentors who have helped her generate new ideas, as a Beeson Scholar Dr. Gardner also has had the opportunity to complete a certificate program in clinical research methods and biostatistics. This additional accreditation "has been extremely useful for my research," she says.

# Katherine A. Gifford, PsyD

Assistant Professor of Neurology,  
Vanderbilt University Medical Center

Mentor: Angela Jefferson, PhD

## *Cognitive Complaints in Aging Adults*



More than 5 million Americans live with Alzheimer's disease, and many more have dementia that goes undiagnosed. Mild cognitive impairment (MCI) can include difficulties with memory, language, thinking, and judgment that may not interfere with a person's daily life. Yet it, too, often goes undiagnosed, and up to 60 percent of people with MCI develop Alzheimer's within three years.

Primary care doctors are on the front lines of assessing cognitive changes in older adults. But when doctors are pressed for time, life-threatening—and treatable—issues like high blood pressure and cholesterol often tend to take priority.

In addition, says Katherine Gifford, PsyD, "there's a lack of tools for quickly assessing cognition, and no gold standard. Physicians also may feel uncomfortable asking a patient questions when there is no treatment for Alzheimer's dementia."

These observations led Dr. Gifford to her Beeson project: creating a questionnaire to help primary care providers readily identify patients at risk for cognitive impairment or with early signs of it. The key, according to her research, is to ask patients to evaluate themselves.

It turns out that when people complain that their memory is slipping, it's not just talk.

"I found that people who are cognitively healthy at the time of asking about their memory, those who said they had a problem with their memory were two times more likely to go on to have cognitive problems three years later," she says. "And if their spouse or their loved one also reported a change, then that risk doubled."

But not everyone who complains about memory issues develops MCI or dementia. In a pilot study with more than 200 participants, Dr. Gifford began testing a questionnaire to see what questions about such "subjective cognitive decline" were meaningful.

"The crux of my Beeson research is to make sure that the questions are valid," says Dr. Gifford. "Are they actually assessing changes in the brain that are related to Alzheimer's disease, or the earliest signs of Alzheimer's?"

The more than 300 study participants, aged 60 to 92, are enrolled in a broader longitudinal study, the Vanderbilt Memory & Aging Project. Half had normal cognition and half had MCI at the start of the study. They complete a questionnaire directed at self-perceptions of memory, take a battery of cognitive tests, have a brain MRI, and have blood drawn at baseline, and after 18 and 36 months. Because heart health and brain health are closely related, they also undergo vascular testing such as an echocardiogram.

The current study began with 52 questions, with the goal of whittling down this number to the 10 that relate most closely to pathological or abnormal changes in the brain. In part, Dr. Gifford does this through statistical ranking of questions as easy (Have you noticed any changes to your memory?) or difficult (Have you ever gotten lost in a familiar area?).

In addition, questions are tied to biomarkers. For example, if a person answers yes to a particular question, are they more likely to have amyloid in the brain or cerebrospinal fluid, or smaller hippocampal volume on a brain MRI—all signs relating to Alzheimer's? In an iterative process, the researchers also test different versions of the questionnaire to find the questions that give the most valuable responses.

Ultimately, the tool should be "an easy set of questions to ask, about somebody's perceptions about memory—a nurse or office assistant could ask them," says Dr. Gifford, and provide a basis for making referrals for further testing.

"I feel very fortunate to have this opportunity," she adds. "The Beeson Award pushes you to the next level, with the guidance of a mentor, to be able to obtain funding—and also to be able to pay that forward by having your own trainees later in your career."

# May Hua, MD

Assistant Professor of Clinical Anesthesiology,  
Columbia University Medical Center

Mentor: Guohua Li, MD, DrPH

## *Determinants of Critical Care Intensity for Hospitalized Older Adults: The Effect of Hospital-Based Palliative Care Services*



When critically ill patients are rushed into an intensive care unit (ICU) at a hospital, medical personnel spring into action to save lives. “We have all this technology,” says May Hua, MD, “more machines than you could ever imagine—machines to replace your heart, your lungs, your kidneys.”

“I became an anesthesiologist because I wanted to practice critical care,” she continues. “As a fellow, I realized I was getting great training to use all this technology to keep people alive. But when it came to low-tech aspects of care—communication and asking people if they really wanted this level of care—it seemed that there was a lot of room for improvement.”

Yet asking such questions is important. In a typical ICU, half the patients are over the age of 65, and being there changes the trajectory of their lives, says Hua. People who survive often have general disability that hinders their ability to be independent. They can’t walk as far, don’t have as much strength, and can develop cognitive difficulties. And in fact, high-intensity treatment in the ICU may not align with the desires of older adults who have a poor prognosis.

As a result, many hospitals have made palliative care available to patients in the ICU—care that helps make treatment goals clear and often prioritizes managing symptoms and pain. “We know that when people understand they have a poor prognosis, they often don’t want very aggressive care,” says Dr. Hua. Studies of individual hospitals have found that treatment intensity in the ICU decreases when palliative care is available. The idea has broad appeal: patients get the care they want, physicians are not providing care that is potentially futile, and costs are reduced for hospitals and insurers.

But whether the successes of single institutions can be expanded to other settings remains an open question. Even at her home institution, which has several ICUs, Dr. Hua found wide variation in the use of palliative care—2 percent of patients in the cardiothoracic ICU received a palliative care consultation, whereas nearly 10 percent did in the medical ICU. So what happens when more hospitals put palliative care in place?

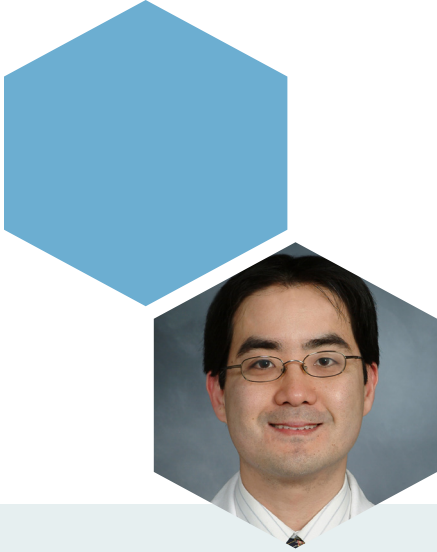
Dr. Hua’s Beeson research addresses this question: knowing that hospitals have different cultures, and that palliative care is complicated—involving a team that may include social workers, physical therapists, counselors, and others—can palliative care be successfully scaled up?

To get a birds-eye view of the problem, Dr. Hua spent her first year as a Beeson Scholar assembling and merging administrative data for all discharges from the nearly 200 hospitals in New York State. Included are details on patients and clinical care, as well as hospital size, number of surgeries performed, and other characteristics giving an indication of treatment intensity at each institution.

Her goal is to see whether patients cared for in a hospital with a palliative care program have a different intensity of treatment—in terms of length of stay, invasive procedures, dialysis, and other measures—compared to hospitals that don’t have a palliative care program.

To balance this data-driven perspective, Dr. Hua is also interviewing two to three dozen palliative care and ICU providers—attending physicians, nurses, and others—to ask what factors they feel impact the use of palliative care services in the ICU setting. In other words: what makes people “on the ground” either use the services or shy away from them?

Beyond supporting her research, the Beeson Program provides “great opportunities for networking,” says Dr. Hua. “One of the most fun things about research is that you get to be part of an amazing community, and you feed off of one another, and collaborate with each other. After the annual meeting, you feel invigorated and ready to go back out there and do your work!”



## Makoto Ishii, MD, PhD

Assistant Professor in Neuroscience and Neurology,  
Weill Cornell Medical College

Mentors: Costantino Iadecola, MD, Jeffrey Friedman, MD, and  
Richard Mayeux, MD, MSc

### *Pathobiology of Hypothalamic and Metabolic Dysfunction in Normal Aging and Alzheimer's Disease*

Forgetfulness may be the first outward sign of Alzheimer's disease, but scientists now know that the brain changes underlying the disease can begin decades before a person notices difficulty with memory. And by that time, the memory centers in a person's brain are already filled with toxic deposits of amyloid beta protein, and twisted fibers of another protein called tau.

In addition, doctors have long been aware of another early sign of Alzheimer's: unintentional weight loss. Seeing patients brought this home to Makoto Ishii, MD, PhD, who is both a laboratory neuroscientist and a practicing neurologist. In particular, he says, "While I was a resident, my grandmother was diagnosed with Alzheimer's. I saw clearly first hand that before the cognitive decline, she was losing weight."

"No one really knew what to make of it," he says. "Many people just assumed that as patients' cognitive and memory skills declined, they were just not eating. But the fact that it can occur 5 or 10 years prior to any memory symptoms, suggested to me it wasn't just because of memory problems."

As a PhD student, Dr. Ishii had studied how the brain regulates body weight, and the role of the hormone leptin in this process. Most Alzheimer's research had focused—logically—on changes to the brain's memory center, or hippocampus. But the hypothalamus controls body weight. So Dr. Ishii began laboratory studies to investigate whether Alzheimer's also affected this brain area.

Dr. Ishii found that mice engineered to develop key features of Alzheimer's had significantly low body weight even before amyloid beta plaques began to build up in their brains. The mice also had low levels of leptin compared to normal animals. In addition, Dr. Ishii discovered that a key subtype of neuron in the hypothalamus was malfunctioning—it was not responding to leptin and other metabolic signals.

Dr. Ishii's Beeson research delves deeper into these molecular studies of weight loss in mouse models of Alzheimer's. At the same time, he is working to translate

these findings to the clinic. To that end, he is studying a group of about 160 cognitively normal people including many, based on biomarkers in their cerebrospinal fluid, who are at high risk to develop Alzheimer's. Over time, he will analyze their blood plasma and cerebrospinal fluid for markers linked to changes in body weight regulation.

"Whatever is triggering Alzheimer's disease, is, we think, affecting the hypothalamus early," says Dr. Ishii. "It's been woefully understudied on a clinical level and much less on a molecular level. We want to better understand this manifestation on a molecular level. By doing so, we believe we can find a way to intervene that will benefit our patients."

Ultimately the research could lead to a new biomarker for detecting Alzheimer's disease early. Such a biomarker would help identify appropriate study participants for clinical trials of potential therapies. And when new therapies become available, it would help doctors determine which patients will benefit from them.

Dr. Ishii's research also offers new approaches to therapy. It may be that reversing weight loss can slow Alzheimer's progression. "Obviously it won't be a cure, but even coming up with a good symptomatic treatment, or something that might help delay the progression, might be very beneficial in the clinic," he says.

Networking with other Beeson Scholars and alumni has broadened Dr. Ishii's "disease specific and neurological perspective" on aging, he says. "At the Beeson meeting I can talk to people in different fields, from the geriatricians, to epidemiologists, to basic scientists like me. It's a small meeting too, where you get to know everyone. Afterward you can just call up anyone, and say 'Hey, I have this idea, what do you think?' and exchange ideas and collaborate."

# Dae Hyun Kim, MD, MPH, ScD

Assistant Professor of Medicine,  
Harvard Medical School

Mentors: Jerome Avorn, MD, and Lewis Lipsitz, MD

## *Development and Validation of a Frailty Index Using Claims Data for Pharmacoepidemiologic Studies in Older Adults*



Every year the US Food and Drug Administration (FDA) approves new drugs based on the results of clinical trials that establish safety and effectiveness. But certain groups of people aren't included in clinical trials because the risk of harm is too great—older adults are one of these groups, and especially frail older adults.

Although many new drugs could potentially help older people, those who are frail could require different dosing, or experience more severe side effects than healthier individuals. As a consequence, "physicians who are treating frail older people are reluctant to put somebody on a brand new drug whose safety and effectiveness have not been confirmed in this vulnerable subgroup," says Dae Hyun Kim, MD, MPH, ScD.

So how can clinicians and others predict whether new medications will be safe for older adults? That's where the field of pharmacoepidemiology comes in—a field that studies populations to understand how new drugs and other therapies are being used, and their safety, effectiveness, and adverse events after FDA approval.

Dr. Kim is a pharmacoepidemiologist with first-hand experience as a geriatrician in assessing frailty in older adults. A few years ago he started a prospective study to better understand how older adults fare after heart surgery. In this ongoing study, he has found that frailty status may predict mortality and functional decline, and could inform how physicians assess surgical risk and prognosis.

"That was really a motivating example," he says. "If I can predict outcomes after cardiac surgery after frailty assessment, can I do similar things for drug safety?"

Dr. Kim looked to administrative claims data, mainly from Medicare, for answers. He quickly discovered a challenge: "Medicare administrative claims don't have detailed clinical information. And there is no diagnosis code for frailty. So we don't know if a patient requires help with their activities of daily living, or how frail they are. This is important information a physician considers when prescribing a medication to older patients. But it's missing in the claims data set."

However, the datasets do reveal useful information such as prescriptions filled for a particular drug over time, diagnoses, doctor visits, and other ways that people use health care that provide insight into their overall health. For his Beeson research, Dr. Kim is creating a frailty score that can be calculated from this data. Then the score can be used to classify subgroups of older individuals based on their frailty level.

"With this score we will be able to do more safety studies of drug use in older populations," says Dr. Kim. "Physicians are making an educated guess about whether a new treatment will be safe in frail older adults. I want to be able to confirm that is the case."

Dr. Kim is now testing how well his frailty score works by comparing data on warfarin and a new anticoagulant, as well as a traditional diabetes drug and a new one that physicians tend to prescribe to frail patients. Ultimately, the frailty score is intended to improve research that uses large administrative databases to compare the use of new therapies in populations, and to ensure that differences are not due to differences in the frailty of the populations.

To take the next step in his research, and help launch his career as an independent investigator, Dr. Kim has collaborated with a senior investigator in the Beeson network to submit an R01 grant to the National Institutes of Health. "Among all the meetings I go to, the Beeson meetings are the most helpful," he says. "The peer networking and the informal mentoring are really valuable."

# Claire T. McEvoy, PhD, RD

Research Fellow,  
Queen's University Belfast



Mentors: Kristine Yaffe, MD, Bernadette McGuinness, MD, and Jayne Woodside, PhD

## Mediterranean Diet and Cognitive Decline: Strengthening the Evidence Base and Encouraging Behavior Change

Dementia is the most feared, and the most costly, disease of aging, affecting more than 5 million Americans and as many as 50 million people worldwide. Recent research suggests that about a third of dementia cases could be prevented by changes in lifestyle—for example, increasing exercise, quitting smoking, and controlling high blood pressure and diabetes.

Could changes in diet also prevent cognitive decline? Claire McEvoy, PhD, RD, is tackling this question with her Beeson research. “We know that changes in diet quality can have profound effects on vascular health,” she says, “and we know that vascular and cognitive health are closely linked.”

“I’m using a range of research methods to figure out which type of diet—combination of foods or nutrients—could help to preserve cognition as we get older,” says Dr. McEvoy. “My ultimate goal is to develop effective public health dietary recommendations to offer protection against cognitive decline during aging.”

Dr. McEvoy worked for a decade in clinical nutrition, helping people make changes to their diet to optimize healthy aging. Her patients inspired her interest in cognition, she says. “Patients were really interested in what dietary changes could improve brain health, but there wasn’t much research evidence available.”

For her Beeson research, Dr. McEvoy is making use of data from several large population studies that have collected information on both diet—in particular, adherence to a Mediterranean diet—and cognition. The Mediterranean diet—rich in fruits, vegetables, whole grains, nuts, olive oil, and fish—already has been proven to have benefits for vascular and metabolic health.

These studies include data on populations of different ages who’ve been followed for up to 30 years. The pathological changes underlying dementia are known to begin decades before any symptoms of cognitive change are evident. “Looking at risk relations between diet and cognition across different populations with a wide age-span, will help us to understand the most salient time to intervene with preventive dietary strategies.”

Dr. McEvoy is analyzing these data in order to discern dietary patterns, and to look at whether adherence to a high quality dietary pattern such as the Mediterranean diet has an impact on cognitive function, risk of cognitive impairment, and incidence of dementia. In some cases this includes neuroimaging data showing changes in brain structures. Her findings based on the nationally representative US Health and Retirement Study have already shown strong links between adherence to the Greek Mediterranean diet and better cognitive function.

However, clinical trials are needed to find out whether changes in diet can ward off cognitive decline. Dr. McEvoy has begun recruiting study participants for such a trial, to be carried out in Northern Ireland. She also has developed educational materials to guide people in easy, low-cost ways to change their eating habits toward a Mediterranean diet.

The study participants have been newly diagnosed with mild cognitive impairment and half will receive the Mediterranean diet intervention. Dr. McEvoy will follow them for one year to see if they can achieve the dietary changes toward a Mediterranean diet and whether these changes impact their cardiovascular and cognitive health. The results will inform the design of larger dietary intervention trials.

Dr. McEvoy notes that her research has evolved during her time as a Beeson Scholar from focusing solely on the Mediterranean diet to looking at different types of dietary patterns in populations. Despite the attention it has received, “the Mediterranean diet may not be the most optimal dietary pattern for brain health,” she says. “We do need to examine other dietary patterns as well.”

Through the Beeson Program, Dr. McEvoy has valued the opportunity to network and engage with clinicians and researchers in other fields. “I’m the only dietician who is part of the program,” she says. “The Beeson meeting is a great opportunity to engage and learn from the diverse range of scholars dedicated to optimizing healthy aging and care for older people.”

# Sofiya Milman, MD

Assistant Professor of Medicine (Endocrinology and Geriatrics),  
Albert Einstein College of Medicine

Mentor: Nir Barzilai, MD

## *Effect of Longevity Genomes on the GH/IGF-1 Phenotype and Disease-Free Survival*



Why do some people live to be 100 or older, remaining active and mentally sharp, while most of us do not? The short answer, according to both conventional wisdom and recent research: good genes.

Discovering those genes, and understanding how they work and interact to promote a long and healthy lifespan is the aim of research started nearly 20 years ago by scientists at Albert Einstein College of Medicine. Ultimately, what they learn could lead to drugs that mimic the effects of so-called longevity genes.

The initial studies focused on 500 people between the ages of 95 and 112 and their children. A new group of study participants has since been added who are aged 65 and over, and whose parents lived, or are living, past 95. Sofiya Milman, MD, is leveraging this research infrastructure to validate the findings of the first studies, and to ask more detailed questions about specific genes.

“We believe that people who are offspring of centenarians carry genes that protect them from age-related diseases,” says Dr. Milman. Such genes make them less likely to develop, for example, Alzheimer’s, type 2 diabetes, and heart disease—or to develop them at a later-than-average age.

But genes are not simple on-off switches. Rather, they regulate proteins and molecular pathways, with many genes interacting. Researchers have long known that genes that control growth hormones, called GH and IGF1, play a role in regulating aging. Laboratory animals lacking the genes live longer, for example, as do animals with low levels of GH/IGF1 signaling.

“I’m trying to understand what genes in particular regulate this GH/IGF1 pathway,” says Dr. Milman. To this end, her Beeson research focuses on genetic studies of the new cohort of children of centenarians and an age-matched control group. Study participants come in for annual tests of physical and cognitive health, so the researchers can follow their trajectories as they age.

Dr. Milman’s study is characterizing genes one at a time within the GH/IGF1 pathway to see what effect they have on markers measured in blood samples, and is also looking at the interactions of multiple genes. With a technique called whole exome sequencing it’s possible to analyze variability in each individual participant.

Growth hormone levels change throughout a person’s lifespan—rising from birth through the teenage years, and tapering off with increasing age after that. Beyond giving children their growth spurt, the hormone also helps muscles grow and is associated with tissue repair.

In earlier research, Dr. Milman and colleagues showed that lower levels of growth hormone in older adults were associated with longer lifespan. Her Beeson study is finding that low IGF-1 also increases healthspan. “Female centenarians who have lower levels manifest better cognitive function,” she says.

“We also did not find any detriment to muscle function,” says Dr. Milman, contrary to what might be expected from low levels of a muscle-maintaining hormone. The finding helps address a concern that low growth-hormone levels could exacerbate the loss of muscle tissue that typically comes with aging. It also calls into question the practice of some physicians of prescribing growth hormone to increase vigor in older adults.

A benefit of the Beeson Program is how it brings together Scholars with diverse skills and backgrounds, says Dr. Milman. “I think as our science advances, and as the technology advances, it becomes very difficult for a single individual to really keep up with all of it. You’ll find very few investigators who can really do cutting edge science alone. We just don’t possess all of the skills that are needed to move the science. That speaks to our need to work together to tackle problems that are of mutual interest.”

## Matthew O'Connell, PhD

Fellow, Department of Medical Gerontology,  
School of Medicine, Trinity College Dublin

Mentor: Rose Anne Kenny, MD

### *Novel Physiological Determinants of Functional Decline Across Ireland*



Long before an older person has a fall or develops cognitive difficulties, subtle changes may be taking place in their blood pressure, kidney function, blood glucose levels, or other measures of how well the body keeps its systems in balance.

Individually, these physiological changes don't indicate a disease, and they might not seem serious. But taken together, could they predict which healthy older adults are at higher risk of frailty and even death? If so, identifying and monitoring such subclinical signs could open opportunities to intervene.

"Frailty measures, like grip strength and speed of walking, often tend to be focused on changes in function," says Matthew O'Connell, PhD. But behind signs of frailty that affect daily life are less obvious physiological changes. With his Beeson research, Dr. O'Connell is using data to put these less-understood changes on a scientific footing, in order to "predict changes in function, and validate some different markers of physiological aging."

Orthostatic hypotension—loosely defined as low blood pressure on standing that lasts more than a minute—has provided Dr. O'Connell with an opening wedge into studying these physiological changes. This condition is common in older adults, and has long been known to increase a person's risk of falling. In addition, repeated swings in blood flow—as blood-pressure dips on standing and is then brought back to normal—could damage organs, including the kidneys, heart, and brain.

In research that laid the groundwork for what would become his Beeson project, Dr. O'Connell and his colleagues established reference data on blood pressure stabilization in older adults. By analyzing precisely measured blood pressure data from some 5,000 participants in The Irish Longitudinal Study on Ageing (TILDA), they found that impaired ability to stabilize blood pressure increases with age and affects more than 40 percent of people over the age of 80.

Carrying this research further, as a Beeson Scholar, Dr. O'Connell and colleagues analyzed data relating chronic

kidney disease to blood pressure, finding that poor kidney function doubles the likelihood that a person will have sustained orthostatic hypotension.

As part of his Beeson Award, Dr. O'Connell also spent six months at the Center for Aging and Population Health at the University of Pittsburgh. During his time there, he used data from the US Health Aging and Body Composition Study to investigate a broad range of physiological measures—changes in blood pressure, glucose levels, lung function, cognitive function and kidney function—and how they change over the course of 10 years, and predict mortality among adults in their 70s.

Cognition is the next area that Dr. O'Connell will analyze through data from TILDA to relate blood pressure to brain Magnetic Resonance Imaging (MRI) scans and measures of brain blood flow. The goal is "to link these peripheral markers, which we believe reflect what's going on in the brain, more closely to what might actually be happening in the brain," he says.

During his Beeson fellowship, Dr. O'Connell also will compare data on the health of older adults in Northern Ireland with those in the Republic of Ireland. "The work to date suggests there's a big difference in health, north and south, but it's all self reported," he says. "One of the things to do would be comparing more objective health measures. When we can more closely match the datasets and actually start to adjust for things like levels of disease and availability of care, we might start to explain what the differences are and what's causing them."

Ultimately, better measures of a range of physiological changes that take place with aging could make a difference in healthcare for older adults. Says Dr. O'Connell: "In the longer term there may be possibilities of using these biomarkers to screen people for markers of functional decline, with the potential for interventions."

# Beeson Scholars

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is a national, nonprofit organization whose mission is to support and advance healthy aging through biomedical research. AFAR is devoted to creating the knowledge that all of us need to live healthy, productive, and independent lives as we grow older. Since 1981, AFAR's grant programs have contributed over \$175 million to the field of aging research, supporting more than 4,400 investigators and students. AFAR'S work has led to significant advances in our understanding of the processes of aging, age-related diseases, and healthy aging practices. Learn more at [www.afar.org](http://www.afar.org).

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## Credits

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