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

2013 Report featuring the 2011 Scholars



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

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## 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. Though "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, 186 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.





## Letter from Edward H. Koo, MD Program Advisory Committee Chair

Speak to any Beeson Scholar about the significance of the award and, naturally, you will hear an expression of gratitude for the generous monetary value of the grants. But get beyond the money and you will hear even greater appreciation expressed for the career-changing mentoring and networking aspects of the program. Indeed, it is all the intangibles that are integral to the Beeson program beyond the training funds that make this program unique and uniquely successful.

When I was a Beeson Scholar, my mentor provided invaluable guidance and insight with regard to my research, introduced me to experts whom I might otherwise never have met, and identified skills I needed to develop so that my work would have the broadest possible impact. I am now a mentor and am experiencing the significant responsibility the program places on us to help maintain its high standards not only for quality research, but also for the development of the careers of this talented community of Scholars. In all these young investigators, it is the leadership qualities that most distinguish them among their peers.

The award's career development focus acknowledges that the field of aging research will advance much more rapidly and have more immediate impact on the lives of older adults if we share our findings across our various specialties and subspecialties. Scholars will tell you the networking opportunities provided by the Beeson annual meetings lead to precisely the type of cross-pollination and collaboration needed to spark new thinking and new approaches to intractable problems.

The Scholars featured in this report investigate a broad range of issues. However, there is a noteworthy common theme among their varied projects: quality of life. These researchers are including methods of gathering patient preferences regarding the care they receive. This is the sort of leadership that has become a hallmark of the Beeson Program and why I proudly introduce our 2011 Beeson Scholars.

**Edward H. Koo, MD**

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### Program Advisory Committee\*

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## Program Overview

Over the last 19 years, 186 investigators from institutions across the US and Ireland have been chosen as Beeson Scholars. Their research includes a representation of basic science, clinical, behavioral/social, epidemiology and health services.

In 2004, the funders addressed the evolving challenges of biomedical research in the 21st century. A strategic public-private partnership to fund and administer the Paul B. Beeson Career Development Awards in Aging Research Program was established between the National Institute on Aging (NIA), The John A. Hartford Foundation, The Atlantic Philanthropies, The Starr Foundation, and AFAR. This partnership enhanced and strengthened the original Beeson Program in several ways.

The NIA brought to bear the National Institutes of Health's (NIH) rigorous peer-review process. Inclusion of the Program in the NIH system raised awareness and now attracts a more diverse pool of applicants. The combined public-private support enabled larger awards, which attract top talent, while the flexibility of the private support ensured that the unique networking and mentoring aspects of the Program would be sustained.

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

## Program Success

In 2012, AFAR surveyed Beeson Scholars from the 2004-11 cohorts. Results affirm how the Beeson Award has significantly helped advance the careers of the scholars and their commitment to the field.

- ***Seventy-six percent (76%) of respondents report receiving a promotion since receiving their award.***
- ***Fifty percent (50%) hold leadership positions such as Center Director, Division Chief, Director of Fellowship Programs, or serve on advisory committees.***

Many respondents reported applying to the NIH for a coveted R01 research award. Receipt of the award indicates the researcher has earned prestigious independent investigator status. Forty-four percent (44%) of all survey respondents received R01 support, and that overall number of respondents includes Scholars who are in the early years of their Beeson projects and are not yet ready to apply.

Those respondents who provided general comments on the Program unanimously reported that the Program was critical to their career development and to getting established in the field of aging research.

The results of the survey clearly demonstrate that the Beeson Program continues to be an unqualified success, providing vital financial support to physician-scientists at a decisive juncture in their careers.



## Conversation with Marie Bernard, MD, Deputy Director of the National Institute on Aging

### *Why is the Beeson Program needed?*

Every single day, more than 10,000 Baby Boomers turn 65, and we have a demographic imperative to attract and train more doctors to improve health and health care for older Americans. The Beeson Program is particularly important given the pressure on these clinically-trained investigators to obtain their own research funding. As clinicians they are required to bring in the revenue necessary to support their salaries. Were it not for programs like this, many would need to do clinical work and forsake important research and teaching.

### *Are there aspects of the program that are particularly effective in attracting talented new investigators to the field of aging research?*

First of all, the Beeson is a tough award to get. You have to be good and put together an excellent proposal just to be considered. Once you get the award, the mentoring and networking aspects of the program bring these people together to learn from one another

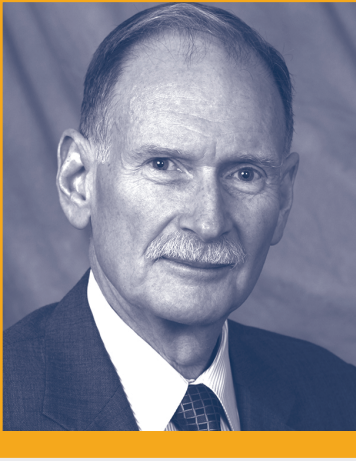
and collaborate. That's when marvelous things happen. Also, it is an enhanced training award, meaning the value of the award is higher than the standard amount for such awards. So an investigator with a higher salary can still have 75% or more of his or her time protected for research. This is very important for attracting top talent. The field of aging research would not have the same good outcomes without this whole package.

### *From your perspective, how well is the program working?*

Even before the NIA partnership, the Beeson Program had proven to be very effective in developing physician-researchers. By all recent measures, the program continues to work very well. For example, a high percentage of the Beeson Scholars go on to get follow up awards necessary to do larger, national studies, the results of which can lead to fundamental changes in how doctors care for older patients. This is a clear indication that these scholars are doing important work. The Beeson Program is a wonderful public-private collaboration. We really couldn't ask for more.



***“A high percentage of Beeson Scholars go on to get follow up awards necessary to do larger, national studies, the results of which can lead to fundamental changes in how doctors care for older patients. This is a clear indication that these scholars are doing important work.”***



## Letter from Richard Besdine, MD AFAR Medical Officer

This report celebrates the 19th year of the Paul B. Beeson Career Development Awards in Aging Research Program and introduces the 2011 Scholars. Their important work is helping to address the critical need for the study of the basic biology of aging and age-related diseases, and ways to improve clinical and supportive care for older Americans.

The 2011 Scholars are conducting research on topics that have major health, public health, economic, and health policy implications, such as the role of Vitamin D in improving immune function in older adults, the development of a decision aid to help both doctors and patients make choices about cardiac health, and methods for minimizing the negative effects of chemotherapy on older patients.

The Beeson program has been part of the growing interest in aging research and geriatric medicine, and is contributing to advances in nearly every area of age-related science. This award is recognized as one of the most prestigious and competitive in the field.

We take enormous pride in the accomplishments of the Beeson Scholars, and are grateful to our public and private partners for helping produce leaders in academic medicine, research, and clinical practice. They are advancing knowledge that is enhancing the health of millions of older adults.

A handwritten signature in black ink, appearing to read "Richard W. Besdine".

**Richard W. Besdine, MD**

***“The Beeson program has been part of the growing interest in aging research and geriatric medicine, and is contributing to advances in nearly every area of age-related science.”***



# William J. Ehlenbach, MD, MSc

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

Mentors: Sanjay Asthana, MD; J. Randall Curtis, MD, MPH; Eric Larson, MD, MPH



## *Cognitive outcomes and neuropathology in older adults following critical illness*

Critical illnesses that require treatment in an intensive care unit, such as respiratory failure and life-threatening infections, are very common in the United States, and individuals over 65 years are at the highest risk of suffering such illnesses. While mortality has decreased in recent decades, many survivors suffer significant health problems. Numerous studies have demonstrated that cognitive impairment following critical illness is common and often permanent.

Dr. Ehlenbach aims to improve our understanding of the ways that critical illness can affect brain function in older individuals. “My project,” he explains, “developed from experiences at the bedsides of patients. The therapies we provide in the intensive care unit (ICU) can extend and at times improve the lives of older adults. But they can also be a burden on individuals near the end of life. Patient-centered outcomes research has the potential to improve the quality of preference-sensitive care for older adults in the ICU.”

In 2010, Dr. Ehlenbach and collaborators at the Group Health Research Institute published in JAMA the first research that also accounted for a patient’s level of cognitive function prior to critical illness.

“The important question was always how much cognitive impairment was already there before hospitalization? This initial study was small and used administrative data to ascertain the patient’s treatment. It did not determine why cognitive dysfunction followed hospitalization.”

Dr. Ehlenbach’s Beeson project advances this earlier work by further characterizing associations between critical illness and cognitive outcomes in older patients. “This study will allow us to classify people more carefully but less strictly in order to bring a greater number of people into the study.”

The project closely examines patient medical records to glean aspects of critical illness that may have a connection to cognitive decline. His team is reviewing records to find periods of low oxygen, blood pressure issues, and other indications of how sick the patient was and comparing the findings with the patient’s level of cognitive damage.

He also aims to determine whether cognitive decline resulted from the illness and/or its treatment or if a neurologic disease was already in progress. This research draws on earlier study participants who agreed both to biennial visits and to autopsies. Dr. Ehlenbach expects to find, for example, specific markers of vascular blood vessel injury in the brain that might result from periods of low blood pressure or systemic inflammation in response to an acute illness.

The third component of Dr. Ehlenbach’s study relies upon individuals who survived a critical illness that included care in the ICU at the University of Wisconsin Hospital. With these subjects he will test hypotheses regarding associations among specific conditions, critical care therapies, and cognitive outcomes. This study will generate finer clinical data on its subjects and include an in-person interview a year after discharge. “Cognitive impairment at discharge is so common,” Dr. Ehlenbach explains, “that taking a benchmark at that point is difficult. So a one year benchmark is more meaningful for setting expectations with regard to long-term cognitive function.”

He hopes the hospital can improve outcomes in the ICU and learn if there are specific indicators that a patient should be discharged with some sort of outpatient rehabilitation strategy in an attempt to mitigate anticipated cognitive decline.

Dr. Ehlenbach is grateful for the community of scholars in the Beeson Program. “It is an incredibly creative community and I’m privileged to be a part of it.”

*“Patient-centered outcomes research has the potential to improve the quality of preference-sensitive care for older adults in the ICU.”*



## Adit Ginde, MD, MPH

Associate Professor of Emergency Medicine  
University of Colorado Anschutz Medical Campus

Mentor: Robert Schwartz, MD

### ***Vitamin D and Immunosenescence in Older Long-Term Care Residents***

What does emergency medicine have to do with the aging of our immune system? For Dr. Ginde, a physician-scientist in emergency medicine, the connection is the difference between merely saving a life and preserving quality of life. “An acute infection can take an independent older patient down to a much lower functional status,” he explains, “significantly diminishing her quality of life, even causing long-term disability. If an older patient’s immune responses to infections and vaccines can be improved, long-term outcomes can be improved.”

As life expectancy increases, the increased incidence and severity of infection associated with aging is becoming a critical public health issue. Infection impacts the function, independence, and survival of older adults, and is a major contributor to healthcare costs. Dr. Ginde’s Beeson project seeks to learn more about the role vitamin D plays in improving immune system response to infection and to vaccines, which ultimately will reduce the incidence and severity of infection in older adults. He is taking an uncommon and demanding approach by researching patients who are in long-term care facilities.

Infection in older patients presents many challenges. First, there are diagnostic challenges because infection doesn’t present in the elderly the same way it does in younger patients. There might not be a fever or other classic signs of inflammation. Diagnosis requires the doctor to throw a wider net, since the only observable symptoms of infection may be non-specific presentations such as delirium. The elderly are also more prone to complications like sepsis, so there are therapeutic challenges as well.

The greatest challenges are in long-term care facilities. Dr. Ginde reasons that if he can intervene to prevent infection and improve immune system responses in this population, treatments should prove of even greater benefit to community-dwelling older patients who are in better physical and cognitive condition.

“Our preliminary studies demonstrate that vitamin D deficiency is common in older patients, particularly in long-term care residents, and is associated with a higher risk for infection, sepsis, and mortality. This is the first clinical trial to evaluate the role of high dose vitamin D supplementation in improving the age-related decline in immune function.”

Dr. Ginde’s Beeson research builds on his preliminary research suggesting that vitamin D supplementation can prevent or reduce the severity of respiratory infection. He will explore the effects of increased vitamin D on the ability of his subjects to avoid respiratory infection. He is also looking at increasing the immune responses of the influenza vaccine in the elderly. Since a better immune response translates into better protection, Dr. Ginde is looking at serum antibody response in his high dose vitamin D patients versus those receiving lower doses. Dr. Ginde is also studying the shingles vaccine, which becomes less effective as we age, and how well the immune cells from his high dose vitamin D group respond.

The Beeson Program has been invaluable in facilitating Dr. Ginde’s ability to conduct research within the long-term care population. “Research in long-term care facilities is a tremendous challenge,” notes Dr. Ginde. “For good reasons, these facilities are very protective of their residents. I have to work closely with the administration, providers, families, and residents to ensure that we minimize any risk.” The program has allowed him to network with people who work with these patients and has provided access to leaders in the field of geriatrics research.

“I hope to use this research to learn how we can fundamentally change the trajectory of immune system decline and reduce the burden of infection in older adults.”

*“If an older patient’s immune responses to infections and vaccines can be improved, long-term outcomes can be improved.”*

# Alison Huang, MD, MAS

Assistant Professor of Medicine  
University of California, San Francisco School of Medicine



Mentors: Louise Walter, MD; Deborah Grady, MD; Jeanette Brown, MD

## A Multidimensional Approach to Urogenital Aging in Older Women

For Dr. Huang, when it comes to research and ultimately treatment of older patients, “If we don’t address the quality of life issues, we’re missing the point.”

Urogenital aging in women is among those health issues that have not received significant attention from the clinician-scientist community. Research has focused almost exclusively on the role of postmenopausal estrogen deficiency in the development of tissue-specific markers of urogenital atrophy. “But variations in serum estrogen levels or tissue markers of estrogen depletion do not adequately explain differences in the severity of women’s urogenital symptoms,” explains Dr. Huang, “nor does it get at the impact of these symptoms on quality of life or on patients’ responsiveness to treatment.”

Dr. Huang developed her desire to advance scientific knowledge about urogenital health and functioning in older women during her internal medicine residency. “While caring for a panel of primarily older Asian women, I saw many women who initially denied any complaints, only to request prescriptions for pads or diapers for urinary incontinence at the end of their visit. Some of these women confessed to having incontinence several times a week, often for years, as well as other urogenital symptoms such as soreness, dryness, or pain, without ever having discussed these problems with a clinician.”

This experience motivated Dr. Huang to conduct an epidemiologic study to determine if this was an issue unique to Asian women. While she discovered significant differences in the self-reported severity and type of urinary incontinence and other urogenital problems in older Asian versus Caucasian women, she learned that a substantial proportion of older women from all backgrounds suffer from these symptoms without seeking treatment from a clinician.

Dr. Huang realized she had come upon an understudied health issue that was incredibly common and burdensome to women in older age, despite not being a life-or-death concern. “Though this is a big deal for a lot of older women, it’s not something they are likely to discuss with their family or their doctor spontaneously. It’s as if there is a taboo against talking about what’s going on ‘down there.’”

She further found that current guidelines for evaluating incontinence in older women, which emphasize assessment of frequency and clinical type of incontinence, may neglect those factors that most strongly determine the impact on women’s lives or their desire for treatment. “It became clear to me that there is a need for a multidimensional model of urogenital aging that can be used to guide evaluation and management of urogenital aging symptoms in women.”

Her Beeson project seeks to determine how older age, greater comorbidity, functional decline, and frailty influence: 1) the development and severity of symptoms of urogenital aging in women after menopause, and 2) the quality-of-life impact and utilization of treatments for urogenital aging symptoms in women after menopause. “My hope is that this research will inform a much larger study that will lead to actionable measures and assessment tools that will be used to provide better patient-specific treatments and to evaluate the efficacy of those treatments,” Dr. Huang explains.

Dr. Huang considers the Beeson Program an ideal sponsor for her research. Not only does it provide generous funding for a project that would otherwise have been difficult to secure, it also expands her network of accomplished colleagues beyond women’s health into geriatrics. “There are specific issues that come up when talking about elderly patients that require access to information and to the insights of people with deep knowledge of existing research and clinical outcomes. My Beeson mentors and fellow scholars provide me access to that expertise.”

*“Though this is a big deal for a lot of older women, it’s not something they are likely to discuss with their family or their doctor spontaneously. It’s as if there is a taboo against talking about what’s going on ‘down there.’”*



## Richard King, MD, PhD

Assistant Professor of Neurology  
University of Utah School of Medicine

Mentors: Norman Foster, MD; Sarang Joshi, DSc

### **Cortical Complexity Changes in Normal Aging and Alzheimer's Disease**

What does a normal brain look like? A comprehensive answer to this question, says Dr. King, would go a long way toward being able to use brain imaging technology to detect and predict the progression of neurological diseases before they become symptomatic. Dr. King is getting closer to an answer.

Brain imaging technologies and the analyses they produce essentially look at two dimensional "slices" of the brain. To compare slices, the images are warped to fit a mapping grid, similar to creating a Mercator projection of the Earth. Such projections don't take into account measures such as cortical thickness when defining what "normal" looks like.

A radiologist looking at this type of scan is looking for fundamental structural abnormality, such as those caused by a stroke or cancer. Trying to determine how much the basic structure of the brain has changed is hard. The terms used to describe what they see are limited to descriptions such as "mild" or "age-appropriate." They have no quantitative standards for comparison. "Simply using age as a biomarker for comparison and for setting expectations of normal brain structure is not ideal," Dr. King observes. "There are too many variables related to a person's physical age versus their chronological age."

To address this limitation he is developing a tool that literally brings a greater depth of quantitative measurement to brain mapping. He has come up with a technique of independently warping each three-dimensional pixel of an image. He uses the technique to do 3-D geometric warping of the scans so that in addition to being able to observe structural abnormalities, analysts can compare brain structure in a more robust way.

"While this technique is very promising, it also presents significant challenges, especially when brains start changing due to various neurologic conditions." His work combines advances in imaging technology with detailed analysis of large existing patient databases in an attempt to establish standard measures of a normal brain. Once established, these standards can be compared to brains at various stages of age-related decline and/or disease, providing physicians with quantitative diagnostic and predictive data.

Tool development is progressing well. Dr. King has published his previous work and provided a proof of concept. Using his preliminary work, he was able to distinguish the brain structure of people who have Alzheimer's disease from those who don't.

The next step in his Beeson-supported research is testing to see if his tool can be used to predict who will develop the disease in a less homogenous population. Older patients often have several coexisting conditions ranging from cardiovascular decline to depression. The challenge is to be able to take all relevant information into consideration to come up with a meaningful measurement of how far a given brain is from normal and, therefore, how likely it is to develop various conditions over time.

"We have to figure out how to extrapolate the findings from studying a clinically homogenous sample to a broader patient population. This is challenging as we consider the potential influences of environment, nutrition, educational differences...all of these and more could potentially affect the predictive model. Inevitably, we will learn there is a lot of noise in the system. We need to devise a tool that picks up meaningful information through the noise."

Currently there is no intervention that prevents or cures Alzheimer's disease. Dr. King's model will provide a primary measure of an intervention's efficacy by tracking how the disease is progressing. It will augment visual interpretation with numerical references.

"Other funding would have been more technology driven as opposed to being focused on people," King notes. "The Beeson appropriately focuses my work on patient outcomes as opposed to technology."

*"Simply using age as a biomarker for comparison and for setting expectations of normal brain structure is not ideal. There are too many variables related to a person's physical age versus their chronological age."*

# Heidi D. Klepin, MD

Associate Professor, Hematology and Oncology  
Wake Forest University School of Medicine



Mentors: Stephen Kritchevsky, PhD; Bayard Powell, MD; Jack Rejeski, MD

## Minimizing Physical Function Decline in Older Adults Receiving Chemotherapy

Was it worth it? Would you do it again? Ask a doctor questions like these about the treatment she has provided and you will most likely get a response based on treatment-based outcomes. Did the intervention do what it was supposed to do? Does the post-treatment data tell us the medical procedure was successful?

But ask a patient these questions and the answer is based on a completely different set of criteria. How do I feel? How is my life different? What have I gained? What have I lost? Declining or accepting follow-up treatment is a good indicator of the patient's sense that the treatment was worth the trouble, pain and/or discomfort.

"Historically in oncology," says Dr. Klepin, "we've talked about surgical or drug-based outcomes. Did we get or shrink the tumor? We're just beginning to shift the paradigm to consider functional and quality of life assessments from the patient perspective at the same time that we're assessing the medical outcome."

Functional and quality of life issues are particularly important when dealing with older patients because post-treatment recovery in the elderly can be compromised by so many factors. Dr. Klepin's Beeson project focuses on improving pre-treatment assessment tools for geriatric cancer patients and on the impact cancer therapies have on functional and cognitive status in older adults. She is using epidemiological research methods to perform secondary data analysis as well as developing elderly-specific studies to investigate the association between disability and cancer in people receiving chemotherapy for acute myeloid leukemia (AML).

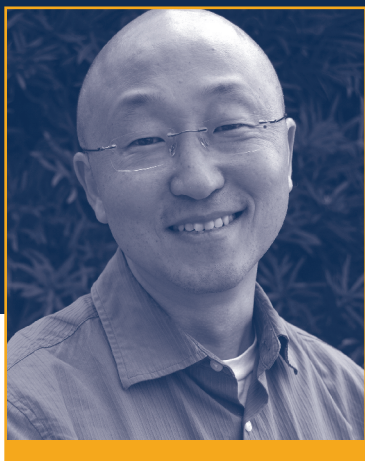
"Treatment-associated physical disability impairs quality of life, limits therapeutic options, and contributes to the social and economic burden of cancer care in the elderly," Dr. Klepin explains. "Despite this, few clinical trials capture disability as an outcome and no clinical trials have focused on whether it can be ameliorated." In oncology, older patients are less likely to be enrolled in clinical trials so there is almost no data for that age group. As an oncologist trained in geriatrics, her goal is to address this gap in knowledge.

Her project includes a pilot study of high risk older adults using physical activity intervention to prevent or slow the rate of decline in physical function during chemotherapy. Patients with AML in some ways represent a worst-case scenario due to the intensity of the chemotherapy, the high short-term risk for side effects, and uncertainty about optimal management of older adults due to historically poor treatment outcomes. "In many cases," Dr. Klepin notes, "the functional decline associated with treatment prevents older patients from completing curative therapies. Our goal is to develop active strategies to prevent functional decline during treatment in order to maximize treatment benefits and quality of life."

Dr. Klepin is as passionate about the human aspect of her research as she is about the science. "Doctors are trained to cure disease. Patients are coached to fight for life. But in many cases, particularly when dealing with cancer, such attitudes amount to condemning patients to many years of post-treatment chronic disease and decline. We need to think about when and how we can extend life while maintaining quality of life as defined by the patient."

Dr. Klepin notes that the Beeson Program has been absolutely critical to her ability to pursue her goal of a much larger clinical trial. "Coming out of this study we will be able to say – 'Here's how we will design a study to answer real questions that have real value to doctors and patients making life and death decisions.' The Beeson award provides both the experience and a mentored educational component that will inform the writing and defense of a bigger grant application."

*"We need to think about when and how we can extend life while maintaining quality of life as defined by the patient."*



**Sei J. Lee, MD, MAS**  
Assistant Professor of Medicine  
University of California, San Francisco School of Medicine

Mentors: Kenneth Covinsky, MD; Louise Walter, MD; Sara Knight, MD

**Individualizing Treatment for Nursing Home Residents with Diabetes Mellitus**

How much blood sugar control in an older, frail adult is enough? The answer is, Dr. Lee suspects, it depends. Factors including desired physiological outcomes and patient preferences may determine the best level of blood sugar control. "With older patients, moderate control rather than tight control may be better, because the risks of tight control are higher in frail older adults."

While diabetes mellitus (DM) is increasingly common among nursing home residents, there is significant uncertainty regarding the optimal level of blood sugar control for these patients. This stems from the fact that most of the research on DM to date has focused on middle-aged patients and excluded frail elders. Today, 70-80 year olds are the largest group of new DM patients. This trend will likely continue as the Baby Boom Generation ages.

"The issue is that with younger patients," Dr. Lee notes, "DM might be the only, or at least primary, health issue. With nursing home patients you are often dealing with multiple conditions and medications. Virtually nothing is known about whether glycemic control is associated with desirable geriatric outcomes in the nursing home." Controlling blood sugar tightly as one would with a healthy younger patient can lead to undesirable consequences in frail patients, such as hypoglycemia and falls due to dizziness.

Dr. Lee's projects combine analysis of a national Veterans Affairs nursing home electronic medical record database with qualitative data from interviews with patients to elicit their goals and preferences. Dr. Lee's work builds on his earlier research on the question of

how tightly to control sugars in frail adults who are trying to avoid entering a nursing home. He interviewed patients and doctors and thought patients would be thrilled to learn that not managing blood sugar so tightly would mean fewer skin pricks and insulin shots. "What we found was that many patients said they feel cared for when they are being monitored. Fewer skin pricks and shots were seen as receiving less care, not better care. These patients perceived their diabetes care as tangible evidence that someone is looking out for them."

For Dr. Lee, findings such as these reinforce the importance of combining both quantitative and qualitative measures, particularly when discussing the care of older patients. The overall focus should be on quality care and quality of life. "When it comes to treating DM in this population, we can't be slaves to the numbers," he says. "Falls, incontinence and even the feeling of being cared for can have profound effects on quality of life. By determining the current practices and the relationship between the level of blood sugar control and geriatric outcomes, we will help patients and clinicians make individualized decisions about diabetes care."

Dr. Lee is particularly grateful for two benefits of the Beeson Program: The opportunity to network with other emerging leaders and the assistance he receives in learning how to better communicate to various audiences.

"It's difficult to work in this field without thinking in terms of care coordination," he points out. Diabetes treatment involves diet, exercise and medications. Effective care needs to coordinate nutritionists, nurses, other doctors, caregivers and the patient. This requires effective communication at a number of levels, making diabetes a great model disease to think about how doctors can effectively communicate to various audiences. The Beeson meetings have helped reinforce the importance of communication.

"We are all in this to have a larger impact and to change the world. Part of that is communicating what we are learning to as broad an audience as possible to help spread good information and assist in the education of the general population."

*"What we found was that many patients said they feel cared for when they are being monitored... These patients perceived their diabetes care as tangible evidence that someone is looking out for them."*

# Daniel D. Matlock, MD, MPH

Assistant Professor of Medicine  
University of Colorado Anschutz Medical Campus



Mentors: Jean Kutner, MD, MPH; Frederick Masoudi, MD, MSPH

## *Implanted Defibrillators and Older Adults: A Model of Decisions and Technologies*

"I believe there is a need," Dr. Matlock says, "to challenge the paternalism that persists in medical decision making in general and decision making for older adults in particular. I am doing research that, I hope, will fundamentally improve how older adults make decisions around invasive technologies." Dr. Matlock aims to facilitate decision making that puts as much emphasis on patient preferences as it does on medical evidence.

His research uses Implantable Cardioverter-Defibrillators (ICDs) as a model. Dr. Matlock has surveyed 1200 physicians about the criteria they consider when recommending an ICD. They rated various factors from high to low. "Medical evidence rated very high. Patient preferences rated low. The culture in which doctors are sole decision-makers needs to be challenged. Patient preferences currently matter too little."

Dr. Matlock's Beeson project takes a three-pronged approach to developing the resources necessary to facilitate productive conversations between doctors and their patients. He'll perform observational data analysis, do qualitative research, and use those findings to develop shared decision making tools.

His data analysis will provide real world estimates of the risks and survival rates for ICD therapy, which are essential for informed decision making. Working with data on the benefits of ICD, Dr. Matlock will try to refine patient characteristics in order to provide more individualized decision making support. While this data offers general guidelines on the benefits of ICD, each patient's situation carries unique risks or benefits. "At the very least," notes Dr. Matlock, "we hope to be able to say to a patient, 'This is the best data on possible outcomes for you.'"

The qualitative research will build upon Dr. Matlock's prior research to answer additional questions about important aspects of ICD decision making for older adults and their family members. A particularly challenging question around ICDs, for example, is how to discuss the trade-off between sudden cardiac death versus potentially living longer with progressive heart failure. The challenge with qualitative questions is how does the doctor present this trade-off? This study will provide a clearer understanding of ICD decision making as it applies to older adults.

The final component of the project will use an established framework for decision support and decision aid development guidelines to create and pilot test a web-based ICD decision aid. The goal will be to produce four tools: short and long paper versions, a video, and the online version.

The challenges in developing the decision aid include making it accurate, unbiased, easy to use, as unemotional as possible, and readable at a 5th grade English reading level. "The urge," Dr. Matlock says, "is to create a tool that tries to capture various nuances in the decision making process. We have to trust that the patient and clinician will provide the necessary nuances for each situation."

This project is particularly innovative because it is being done in collaboration with patients and cardiologists, allowing for a full understanding of the decision making context and maximizing future implementation. "There are a number of decision aids available to doctors that sit on shelves because they were developed with a focus solely on the patient." Dr. Matlock hopes that by involving cardiologists, he will be able to create a decision aid that is beneficial and useful to both doctors and their patients.

Dr. Matlock's appreciation of the Beeson Program goes beyond the funds supporting his research. "This is such a prestigious award. The work that is done by these scholars pushes thinking forward. And I get to meet and collaborate with these people. The annual meetings have already led to two new projects."

*"The culture in which doctors are sole decision-makers needs to be challenged. Patient preferences currently matter too little."*



## Keith Vossel, MD, MSc

Assistant Professor of Neurology  
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Staff Scientist, Gladstone Institute of Neurological Disease

Mentors: Lennart Mucke, MD; Bruce Miller, MD

### **Mechanisms and Treatment of Network Dysfunction in Alzheimer's Disease**

Alzheimer's disease (AD) is well known for its sinister pathology that leads to the death of brain cells and cognitive decline. But it is another component of the disease—increased incidence of seizures—that intrigues Dr. Vossel. These seizures, as well as over-excitation of the neurons not severe enough to create noticeable symptoms (a.k.a. silent seizures), may contribute to the cognitive deficits experienced by victims of AD.

Dr. Vossel is using his wealth of experience and his collaborations with investigators studying epilepsy and others working with sophisticated imaging technologies to investigate strategies to counter seizures in AD. Based on his research to date, he is convinced that, "By fighting seizures we're fighting the pathology of the disease. Over-activation of circuits is an early manifestation of the disease. As the disease progresses, activity decreases."

Two components of the harmful brain deposits characteristic of Alzheimer's disease, amyloid-beta (Abeta) and tau protein, disrupt the function of cellular components that would normally regulate brain cell activity. Dr. Vossel's research is focused on achieving a better understanding of how Abeta and tau impair the transport of critical cell parts and molecules from one part of the cell to another.

Earlier studies have shown that reducing tau protects against seizures in mouse models of AD. His Beeson project seeks to determine the mechanisms by which reducing tau protects against seizures. "Until 2007," Dr. Vossel notes, "the relationship between tau and seizures was not known. Early studies showed that

tau reduction both improved memory and prevented seizures." In these studies, knocked down tau did not cause other problems in brain cells.

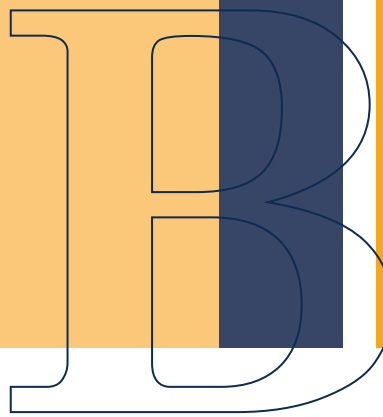
"We have never knocked tau down completely in adult mice, so we don't yet know if removing tau is safe." But Dr. Vossel says it could be tau performs non-vital tasks that can be handled by redundancies in our cellular biology and that restricting it completely may be no more harmful than removing one's appendix. His team is currently looking at a growing list of binding partners for tau to better understand its role.

Another aspect of Dr. Vossel's project is a clinical investigation to identify people in the early stages of AD who could benefit from tau-targeted strategies or the use of existing antiepileptic drugs. Preliminary studies have shown that over-activation of the circuits between brain cells, particularly in the form of silent seizures, occurs most noticeably in the early stages of the disease. Dr. Vossel's team will compare the frequency of this activity in subjects with either mild cognitive impairment (MCI) or AD to age-matched normal subjects and subjects with other diseases. The goal of the study is to identify people with cognitive dysfunction and seizure activity who are most likely to benefit from seizure-stabilizing drugs in future clinical trials.

Having come to neurology from an engineering background, Dr. Vossel is particularly impressed by the collaborative nature of the Beeson program. Dr. Edward Koo and other investigators he has met through Beeson meetings have helped immeasurably with his project, including providing practical advice on day to day activities and helping with recruiting of subjects for his clinical study.

"The research we are doing on axonal transport and seizures is relevant to many issues of the aging brain. Being connected to so many outstanding investigators who are also practicing doctors talking to patients every day is incredibly valuable to me, as I hope my findings will be to them."

*"The research we are doing on axonal transport and seizures is relevant to many issues of the aging brain. Being connected to so many outstanding investigators who are also practicing doctors...is incredibly valuable to me, as I hope my findings will be to them."*



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AFAR is a nonprofit organization whose mission is to support biomedical research on aging. It is devoted to creating the knowledge that all of us need to live healthy, productive, and independent lives. Since 1981, AFAR has awarded approximately \$150 million to more than 3,000 talented scientists as part of its broad-based series of grant programs. Its work has led to significant advances in our understanding of aging processes, age-related diseases, and healthy aging practices. Learn more about AFAR's innovations at [www.afar.org](http://www.afar.org).

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### **The National Institute on Aging (NIA)**

The NIA, one of the 27 institutes and centers of the National Institutes of Health, leads a broad scientific effort to understand the nature of aging and to extend the healthy, active years of life. In 1974, Congress granted authority to form the National Institute on Aging to provide leadership in aging research, training, health information dissemination, and other programs relevant to aging and older people. The NIA's mission is to support and conduct genetic, biological, clinical, behavioral, social, and economic research related to the aging process, diseases and conditions associated with aging, and other special problems and needs of older Americans, foster the development of scientists in aging and communicate information about aging and advances in research on aging to the scientific community, health care providers, and the public. [www.nia.nih.gov](http://www.nia.nih.gov)



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We would like to thank the Beeson Scholars for reviewing this report for scientific accuracy.



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