Paul B. Beeson Career Development Awards in Aging Research Program

2012 Report

Featuring the 2010 Scholars

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

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.

It is a tribute to him that, to date, 178 physician-scientists supported by the Beeson Program have emerged as leaders in the field throughout the United States and the Island of Ireland, changing the landscape of geriatric medicine and aging research. Dr. Beeson's enduring legacy is that these leaders will not only provide the best possible care for older adults but will also go on to train the next generation of leaders.

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Letter from Edward H. Koo, MD

Chair of the Program Advisory Committee

I have had the privilege of leading the Beeson Program committee for four years and being among the first group of grant recipients. Receiving the Beeson Award was a career-transforming experience, as it has been for many Beeson Scholars, and it continues to be.

The Beeson Award helps physician-scientists thrive because it protects their precious time and resources to establish independent research programs. Obtaining grant funding has become much more competitive, perhaps more than ever before, and providing opportunities for scientists in their formative stages is critical to the continuing success of biomedical research. With the combined demands of clinical and administrative responsibilities, compounded by the need to prepare grant applications, the remaining time for research becomes ever more valuable.

The Beeson Program is novel because it offers unique mentoring activities. Further, the networking opportunities connect recipients from many medical specialties and subspecialties to an aging population, grounding their respective research specialties within the broader field of aging to help address the many and diverse health problems facing older adults, from basic biology of aging to causes of cognitive impairment to psychosocial factors that affect the body and brain.

The program also offers Scholars opportunities to make contributions beyond their individual research projects. At the Beeson annual meetings Scholars have the chance to network and learn about shared interests. Many have embarked on collaborative research endeavors as a result. For example, Dr. E. Wesley Ely (2001), a critical care specialist from Vanderbilt University Medical Center, and Dr. Helen Hoenig (1997), a geriatrician focusing primarily on rehabilitation at the Duke University Medical Center, recognized the growing population of older adults who would undergo cognitive and physical rehabilitation in their own homes after hospitalizations in the intensive care unit. A pilot study of the program they designed, which utilized teletechnology and in-home health care worker visits, found that it improved cognitive and functional status in ICU survivors undergoing in-home rehabilitation.

We hope to continue this tradition of collaboration and are proud to introduce the 2010 Beeson Scholars.

Edward H. Koo, MD

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Supporting the Beeson Program

A Conversation with Norman Volk, Chair of the John A. Hartford Foundation Board of Trustees

Why did the John A. Hartford Foundation become one of the founding sponsors of the Paul B. Beeson Career Development Awards in Aging Research Program?

The belief of the three foundations (the John A. Hartford Foundation, the Commonwealth Fund, and Atlantic Philanthropies) that established the Beeson Program in 1994 was that there were too few medical and health services experts in the field of aging and a critical shortage of physician-scientists devoted to aging research and geriatric medicine. Attracting outstanding junior medical faculty to leadership careers in this area was viewed by the foundations as a critical and necessary step toward expanding America's ability to serve its rapidly aging population.

Why has the John A. Hartford Foundation invested in the program for nearly two decades?

The Foundation seeks to make changes that can be sustained and has remained invested in the program because the shortage of outstanding scholars in the aging field is not one that can be immediately turned around in a few years or even a decade.

What do you see as the challenges facing geriatric medicine and aging research? How is the Beeson Program addressing these challenges?

The most fundamental challenge is that the number of older Americans is growing dramatically. The first Baby Boomers turned 65 on January 1, 2011, and every single day for the next 19 years, 10,000 Boomers will reach 65. People are living longer. The prevalence of chronic diseases (e.g. cancer, heart disease, and hypertension) increases with age.

How has the Beeson Program contributed to improving health care for older adults?

The Beeson Program is forging a unique intellectual network among physician-scientists dedicated to geriatric medicine, the care of older adults, and the basic science of aging. Beeson Scholars have already exceeded expectations—contributing to the frontiers of science in osteoporosis, age-related macular degeneration, heart disease, better understanding of longevity and cell senescence, and many other areas of aging research.

The Paul B. Beeson Career Development Awards in Aging Research

The Paul B. Beeson Career Development Awards in Aging Research Program is one of the largest and most successful public-private partnerships dedicated to developing leaders in the field of aging research and geriatric medicine. Since the program's inception in 1994, 178 early-career physician-scientists have received funding, creating a formidable brain trust committed to academic careers in aging-related research, training, and practice.

The Beeson Program was designed to address the growing need for well-trained doctors to address the myriad needs of an aging population. Equally important is the need to add outstanding scientists able to conduct research relevant to aging and clinical care. Although important progress has been made, further significant commitment is needed to train future leaders in aging and geriatrics.

The Beeson Program identifies and supports those physician-researchers most capable and passionate in spearheading this effort. With both the clinical and laboratory perspective, Beeson Scholars are revolutionizing geriatric care. Each year, approximately eight clinically trained researchers receive $600,000 to $800,000 over a three- to five-year period. The award is often life- and career-changing. Through the award, Beeson Scholars are assured of:

- flexible funding with ample resources to pursue an innovative research program.
- 75% of their time protected for research.
- an outstanding support system. Senior faculty members serve as mentors, and Scholars are matched with members of the Beeson Program Advisory Committee, some of the most talented leaders in geriatrics and aging research.
- extensive networking opportunities with current and alumni Scholars through the Beeson annual meeting, an interdisciplinary conference for Scholars, mentors, and leaders in the field.

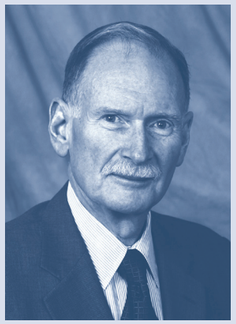
Beeson Scholars are improving clinical care and advancing research progress. Jürgen Unützer (2002) developed an evidence-based, patient-centered model of care that treats depression in older adults twice as effectively as conventional treatments. A care transitions program developed by Eric Coleman (2001) substantially reduces hospital readmissions and has been adopted throughout the country. Arti Hurria (2005) continues to develop better recommendations for physicians treating cancer in older adults, who have historically been underrepresented in clinical trials of cancer drugs. Like their fellow Scholars, they have already begun to bring about the revolution in care the aging population requires.

In addition to their own research, Scholars are also having a positive impact on medical schools, according a recent analysis by researchers at the University of Cincinnati (see "The Beeson Effect" on page 4).

Recipients of the Beeson Award are frequently asked to serve on editorial boards for prestigious journals, join national task forces on aging-related topics, and present their findings and opinions at national and international scientific meetings. Their work is regularly published in leading medical and scientific journals, including the *Journal of the American Medical Association, New England Journal of Medicine,* the *Lancet, Science,* and *Nature Medicine,* and consistently receives worldwide media coverage.

Letter from the AFAR Medical Officer

Richard W. Besdine, MD



This report celebrates the 17th year of the Paul B. Beeson Career Development Awards in Aging Research Program and introduces the 2010 Scholars. Their 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.

The 2010 Scholars are studying topics with major health, public health, economic, and health policy implications, such as the management of infectious disease in long-term care facilities, analysis of systems affecting heart failure hospital readmissions in older adults, and how low levels of L-tryptophan may increase the incidence of postoperative delirium.

The Beeson Program has been part of a growing interest in aging research and geriatric medicine, and is contributing to advances in nearly every area of age-related science. The Beeson Award is recognized as one of the most prestigious and competitive in the field. Since 1995, 178 physician-scientists have been named Beeson Scholars.

We take enormous pride in the accomplishments of the Beeson Scholars, and thank 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.

Richard W. Besdine, MD

The Beeson Effect

The Beeson Program doesn't just benefit individual award recipients. Beeson Scholars have made positive contributions to the development of academic geriatrics programs at U.S. medical schools, according to a University of Cincinnati study, "Paul B. Beeson Career Development Awards in Aging Research and U.S. Medical Schools Aging/Geriatric Medicine Programs," published in the August 2011 issue of the *Journal of the American Geriatrics Society*. Led by Elizabeth J. Bragg, PhD, RN, research associate professor in the Department of Family and Community Medicine, the researchers evaluated the influence of 134 Beeson Scholars on their medical schools' aging and geriatric medicine programs and on the field of geriatrics and aging research from 1995 to 2007. They compared 36 medical schools with Beeson Scholars with 34 similar medical schools without Beeson Scholars.

Nearly 95% of Scholars stayed at the institution where they trained during their Beeson Award and 89% were still practicing or conducting research in the field of geriatrics and aging. Nearly 20% had led institutional research mentoring awards, and 39% had held leadership roles in institutional program project grants. Beeson Scholars were more likely than the non-Beeson Scholars surveyed to study important geriatric syndromes such as falls, cognitive impairment, adverse drug events, osteoporosis, and functional recovery from illness and the interconnections among them.

"We saw a direct correlation between the total number of years all Beeson Scholars trained or worked at each school and more geriatric research faculty, suggesting that the experience of the Scholars helped promote the status of the school in geriatrics education, training, and career development," said Dr. Bragg. "In addition, research grants made up a higher percentage of the budget for geriatric medicine programs at Beeson schools than non-Beeson schools and Beeson schools had more annual research funding."

The study, funded by the Atlantic Philanthropies, confirmed that the presence of Beeson Scholars at medical schools enhanced geriatric medicine research programs and geriatrics education experiences for medical students, residents, and geriatric medicine fellows. Beeson Scholars also had a positive influence on the field of aging research and the development of geriatric medicine as a medical subspecialty.

Jeffrey Caterino, MD, MPH

Assistant Professor of Emergency Medicine
and Internal Medicine
Ohio State University College of Medicine

Mentor: Kurt B. Stevenson, MD, MPH

Expanding Antimicrobial Stewardship for Long Term Care Facility Patients

About 1.5 million people reside in nursing homes across the United States, according to the Centers for Disease Control and Prevention. Of those residents, nearly 90% are at least 65 years old, and infections are a leading cause of death and disease.

Dr. Jeffrey Caterino says that urgent care providers in emergency departments often have trouble determining whether an older nursing home patient is really battling an acute infection. "That's because aging comes with a lot of changes to the body's response to infection. So you may not have a cough if you have pneumonia, you may not have a fever if you have an infection, you may not have a stiff neck if you have meningitis." A patient's weaker immune system, in other words, may not respond as strongly to external threats, leading to more subtle signs of illness.

Given the high infection rate and regular exposure to antibiotics, nursing home patients also are more likely to be infected with drug-resistant bacteria. "This whole diagnosis and antibiotic use conundrum has two sides," Dr. Caterino says. Doctors want to correctly identify an infection and prescribe the most appropriate antibiotics. On the other hand, they want to avoid overusing antibiotics in the absence of an infection, which could contribute to the growing problem of drug resistance.

To help emergency room physicians through that decision-making process, Dr. Caterino established two major goals for his Beeson project. "First we want to improve the knowledge base to allow emergency physicians to be more accurate when they're deciding if an infection is present or not," he says. "Secondly, we want to help them choose the correct antibiotics."

Beyond allowing him to take on a more comprehensive project than he otherwise could, Dr. Caterino says the Beeson Award has permitted him to develop his career through advanced coursework. As a result, he better understands how to run larger clinical trials and is acquiring expertise in how to integrate health information technology. "It's laying the foundation for a wider variety of future research endeavors," he says. And thanks to his interactions with several other Beeson Scholars, he hopes to further enlarge the scope of his research through a joint grant proposal. "The network has allowed me to establish collaborations with people that I otherwise wouldn't have been able to."

In the first phase of his Beeson project, Dr. Caterino and his colleagues are comparing the diagnoses of nursing home residents made by emergency department physicians with those made by a panel of infectious disease experts reviewing the same charts. The results will help guide the development of clearer diagnostic criteria for acute infections in older patients.

Another part of the project incorporates what is known as an antimicrobial stewardship program, in which teams of physicians and pharmacists independently review everything from a prescribed drug's dosage to potential alternatives. Many hospitals have adopted the strategy to optimize how antibiotics are prescribed and to prevent their overuse. This same assistance is much less common in emergency departments, an oversight Dr. Caterino hopes his research will help remedy. Through an independent review of antibiotic use, he hopes to highlight the unique challenges that an emergency department-specific program should address.

In a second phase, the accumulated information will be plugged into a computer-based tool to provide real-time support to help doctors make the right calls. "The optimal stewardship program would integrate as much patient-specific information as we have," Dr. Caterino says, "and then also bring in any other general principles to help with the decision, particularly in cases where we don't have specific information."

Dr. Caterino's research in aging and his clinical duties have both driven home the difficulty of diagnosing older patients. "As a practicing emergency physician, I'm faced with these dilemmas every day." For any assistance to be effective, however, he knows the time element will be critical. "Because the emergency departments are overwhelmed, you really need to have focused interventions." With his research, that invaluable assistance may soon be within reach.

Anna Csiszár, MD, PhD

Associate Professor
University of Oklahoma Health Sciences Center

Mentor: William E. Sonntag, PhD

Resveratrol Confers Endothelial Protection via Induction of NF-E2–Related Factor-2-driven Antioxidant Genes: Implications for Microvascular Aging

After receiving her medical degree in Hungary, Dr. Anna Csiszár was conducting research in cardiovascular physiology when her then-mentor sent her to a six-week physiology course at the Marine Biology Laboratory in Woods Hole, MA. "While I was there, I noticed that there was a molecular biology of aging course, so I just borrowed some course materials and I read it. It was actually love at first sight," she says. She's returned every summer since then, studying the mechanisms of aging in primates, bats, naked mole rats, and a species of clam that can live for 500 years. Upon her arrival at the University of Oklahoma in 2009, she applied her new expertise to a multidisciplinary effort to understand aging-related cognitive impairment in humans. The eventual goal, she says, is to identify molecular targets for therapy that might halt or even reverse mental decline.

A condition known as vascular cognitive impairment is one of the chief contributors to aging-related deficits in brain function. "This is clinically similar to Alzheimer's disease, in terms of memory loss, but it's far less well-studied and happens much more often than Alzheimer's disease," says Dr. Csiszár.

She hypothesizes that as part of the aging process, chronic inflammation of microvessels in the brain's hippocampus — the area responsible for learning and memory — leads to the gradual loss of these tiny vessels. The subsequent decline in blood flow to the hippocampus may then lead to cognitive impairment. One unanswered question is what causes the initial chronic inflammation, and Dr. Csiszár's multifaceted Beeson project is exploring the phenomenon in both mice and humans.

For one part of her research, the award allowed her to set up behavioral assays to test learning and memory in mice with vascular cognitive impairment. After giving the animals anti-inflammatory treatments, she and her collaborators were able to reverse the inflammation, induce new vessel formation in the hippocampus, and improve cognition, learning, and memory function. That demonstration, Dr. Csiszár says, bolsters the idea that the loss of blood vessels in the brain leads to cognitive impairment.

In a separate arm of her research, she and her colleagues are focusing on a protein called Nrf2, which is responsible for an "orchestrated and synchronized" defense mechanism that protects the body from a type of aging-related cellular damage known as oxidative stress. From previous research, scientists believe the protein may mimic the beneficial effects of calorie restriction on longevity, a mechanism that Dr. Csiszár calls the "Holy Grail" of aging research.

The underlying pathway may help reduce the chronic inflammation of small blood vessels in the brain, thereby preventing their gradual loss and maintaining proper blood flow. Through their research on Nrf2 in mice, Dr. Csiszár says she and her colleagues hope to find out whether they can trigger that mechanism through a pharmaceutical intervention instead of through an extreme reduction in daily caloric intake.

With assistance from the Beeson Award, Dr. Csiszár is launching a third arm of her research focused on older patients with a common condition called peripheral artery disease. Due to narrowed arteries, reduced blood flow to patients' legs can cause pain and muscle loss. "My goal will be to test this population for cognitive function, and see how different blood serum factors potentially influence the inflammation of the vessels, and eventually cognition, and whether home-based exercise can improve their situation," she says.

The Beeson Award gave her the resources needed to "jump-start" her research, Dr. Csiszár says. "The award provided protected time and resources to make this big leap, to produce enough preliminary data to be able to secure other funding sources." Her first annual Beeson Meeting, she adds, was a special highlight that helped her realize the particular benefits of her dual background in clinical medicine and basic research. "The Beeson Meeting made me aware of the fact that I can be the translator or the bridge between these two areas," she says. "And ever since then, I've been building on that."

Leora Horwitz, MD

Assistant Professor of Internal Medicine
Yale School of Medicine

Mentors: Harlan M. Krumholz, MD
Mary Tinetti, MD

Heart Failure Readmissions in Older Adults: A Systems Perspective

One in four older patients hospitalized with heart failure will be readmitted within 30 days of their initial discharge. However, Dr. Leora Horwitz says those sobering numbers tell only part of the story. Beyond the clear risks to patient well-being, Dr. Horwitz says unnecessary rehospitalizations waste billions in Medicare costs and highlight troubling failures in communication and care transitions from hospitals to outpatient settings.

"For a long time, people accepted readmissions as the price you pay for being in the hospital. The thinking was, 'If you're sick enough to be in the hospital, it's hardly surprising that you'd be sick enough to come back,'" she says. "We really didn't think of ourselves as responsible for that, and we didn't think of readmissions as particularly avoidable."

Times have changed, and health experts now widely agree that many rehospitalizations are dangerous, costly, and avoidable. Flawed communication between health care providers in and outside of the hospital may contribute to these unnecessary rehospitalizations. As both a researcher and a primary care provider, Dr. Horwitz says the issue resonates strongly with her. "I'm the one on the receiving end of patients showing up in my clinic who were just discharged from the hospital, and I didn't even know they were there."

Dr. Horwitz decided to take a closer look at the disconnect between inpatient and outpatient care after directing a large study at Yale that examined the fate of 400 older patients hospitalized with heart failure, pneumonia, or a heart attack. "We were staggered by the degree of error and the lack of attention to transitional care that we found when we looked at their charts and when we interviewed the patients," she says. "It's like out of sight, out of mind."

Among the eye-opening results, the researchers discovered that 30 percent of the hospital discharge summaries were never sent to the doctors who would be providing outpatient care, while nearly two in three patients had no follow-up appointments scheduled before leaving the hospital. More than one-fourth of the patients had errors on their discharge medication lists. And even intentional changes made by the inpatient doctors weren't well communicated; during the follow-up interviews, patients couldn't remember 80 percent of those revisions.

"So we did a terrible job of educating our patients about what to do after they went home," Dr. Horwitz says. Yale's 966-bed medical center, one of the nation's largest, has performed well on a range of inpatient quality measures. But given the lack of attention to patients after their discharge, she wondered, what was going on in other hospitals around the country?

Her Beeson project is an effort to address largely overlooked hospital and community factors that might contribute to high readmission rates among geriatric heart failure patients. "Whether people survive in the hospital after a heart attack is pretty strongly determined by hospital care," she says. "Readmissions are a whole different kettle of fish in that they relate to the kind of care a patient gets in the hospital, the transitional care the hospital provides to ease the patient back home, and then what happens at home."

To identify the potential factors at play, Dr. Horwitz and her collaborators are examining everything from hospital quality and bed capacity to competition between health care facilities and the ratio of primary care doctors to specialists. The goal is to "really develop a comprehensive, statistical view of the community in which the patient lives and the hospital that they go to, so we can use these different factors to tease out what accounts for differences between hospitals."

The Beeson Award, Dr. Horwitz says, has been "amazing" for her career development, giving her the time and opportunity to expand her skills and the flexibility to work on multiple related projects. At the annual meetings, she values the unique focus on networking with other scientists who are interested in the same kinds of research. Already, her talks with fellow Beeson Scholar Dr. Amy Kind have led to a sharing of research tools. And based on her success so far, Dr. Horwitz is expanding her focus to develop a comprehensive measure of patients' readmission risk that will include nearly all hospitalized adults.

Amy Kind, MD, PhD

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

Mentors: Maureen A. Smith, MD, MPH, PhD
Sanjay Asthana, MD, FRCP

The Hospital Discharge Summary's Impact on Sub-Acute Care Patient Outcomes

When highly vulnerable older adults move from one care setting to another, such as from the hospital to home or to a nursing home, many of them fall through the cracks. "If they get sick or they have trouble accessing their medications, or they need a special kind of care that isn't communicated well by the hospital, they may not be able to advocate for themselves to get the care they need," says Dr. Amy Kind.

One potential consequence of a bumpy transition process is ending up back in the hospital or emergency room, sometimes known as a bounce-back. In fact, nearly one in five Medicare patients is readmitted to the hospital within 30 days of being discharged, accounting for $17.4 billion in the federal program's annual spending.

For her Beeson research, Dr. Kind is studying how to reduce the frequency of these bounce-backs, with a particular focus on patients with hip fractures or strokes who move from the hospital to a nursing home. These two patient groups are among the most common in rehabilitation settings.

Currently, communication between the hospital and the nursing home relies primarily on a document called the discharge summary. The hospital-based care team seldom follows a patient to the nursing home, and primary care doctors are increasingly unlikely to do so either, meaning that the nursing home team of providers must rely primarily on the discharge summary for guidance. Trained as a geriatrician, Dr. Kind has cared for vulnerable older adults in both the hospital and the nursing home. "Having been on both sides of the coin," she says, "I can understand the critical importance of high-quality communication between these two settings."

Her team has developed an assessment tool that examines the content of discharge summaries, permitting the researchers to analyze the quality of that communication and its impact on care. Using a Medicare dataset of hip fracture and stroke patients, the project first assesses the association between discharge communication quality and patient outcomes, including cost of care, rehospitalizations, and visits to the emergency room.

A second aspect of the project examines the impact of a patient's dementia on the quality of a discharge summary. "If someone has dementia, the importance of discharge communication becomes even more pronounced," Dr. Kind says. A cognitively impaired patient, for instance, may be less able to speak up if nursing home care providers fail to dispense the proper heart medication.

For the third aim, Dr. Kind and her colleagues are running focus groups of nurses from skilled nursing facilities to learn what they need from the hospital and what other systems should be in place to ensure smooth patient transitions. The team is also using an automated tool in the electronic medical record system that creates a discharge summary with input from every care provider. "Our premise is that if we actually have a team of people create these documents, they could be of higher quality."

The Beeson Award has been "truly instrumental" in her career development, Dr. Kind says. "It has allowed me to network with other professionals through the Beeson Meeting, which has been incredibly invaluable." With her time protected for research and education, she has been able to receive additional training in systems engineering and has increased her productivity with grants and publications. And thanks to the Beeson support, she completed her PhD in population health sciences and has expanded her research program. "It's been a wonderful, wonderful resource."

Through her work, she now views the discharge summary as "necessary but not sufficient" for properly supporting patients in transit. Also critical, she says, is ongoing communication among the providers in each care setting, with a give-and-take discussion before and after a hospital discharge. "If some of our work could help prevent at least a portion of rehospitalizations, and improve a patient's experience during those really challenging first days out of the hospital," Dr. Kind says, "I think we will have had a good impact."

J. Michael McWilliams, MD, PhD

Assistant Professor of Health Care Policy and Medicine
Harvard Medical School/Brigham and Women's Hospital

Mentors: John Z. Ayanian, MD, MPP
Tom McGuire, PhD

Reforming Medicare: Beneficiary Choice, Plan Payment, and Accountable Care

As a clinician who cares for many older and medically complex patients, Dr. J. Michael McWilliams has seen how the nation's health care system often fails those with chronic illnesses and encourages wasteful overuse of resources. "As a physician working in a dysfunctional health care system," he says, "I have been frustrated by the overutilization, fragmented care, disparities, and struggles my patients have in navigating the system and getting the care they need."

For his Beeson project, Dr. McWilliams has combined his clinical background with his training in health policy to critically examine how Medicare delivers health care to older Americans. "The overarching goal is to inform the development of policies to improve the value of the Medicare program for its beneficiaries and society." With significant reforms, the country's largest insurer could create "rippling effects across the whole health care system," he explains.

One arm of his project focuses on how Medicare beneficiaries choose traditional benefits or one of the managed care plans known as Medicare Advantage. "In many areas, people have to choose from 30 to 70 plans," he says, raising a critical question: "Is there such a thing as too much choice?" A high prevalence of cognitive impairment and dementia among seniors, Dr. McWilliams says, compounds the difficulty in making rational decisions. In some areas where "the number of options really went through the roof," he found correspondingly lower enrollment in Medicare Advantage, suggesting that overwhelmed seniors are defaulting into traditional Medicare.

Moreover, he found those with poorer cognitive functioning were less responsive to increasingly generous benefits in Medicare Advantage, such as lower premiums and better drug coverage. Because suboptimal enrollment decisions fail to reward high-value plans and stifle healthy competition, his findings raise a red flag for policies relying on market forces to improve care for the elderly. One solution, he says, would be to have an objective intermediary group, like an insurance exchange, standardize benefits and help seniors select the best plan from a more limited and accessible range of choices.

Dr. McWilliams is also studying whether different ways of paying physicians and insurers might impact the cost and quality of care. One unintended consequence of Medicare's traditional policy for paying Medicare Advantage plans, he says, is a strong incentive for plans to attract the healthiest — and potentially least costly — beneficiaries to maximize profits. Consequently, Medicare Advantage plans tend to have enrollees with lower risks than the traditional Medicare option, representing "an overpayment by the government to these plans to take care of healthier patients."

To correct that imbalance, Medicare has limited how often enrollees can switch between plans and boosted payment rates to insurers enrolling seniors with chronic conditions while lowering rates for healthier patients. So far, Dr. McWilliams's research suggests that these corrective efforts may be paying off, leading to a more even distribution of higher-risk patients and fairer payments. More broadly, his research suggests that this same strategy might help preserve a more level playing field among providers and plans in other emerging settings, such as insurance exchanges and accountable care organizations.

The project also examines whether better-integrated health care delivery systems offer more bang for the buck. Compared to independent smaller practices, larger health care systems are more likely to use interconnected electronic medical records, decision support systems, and advanced models of care. But if such systems dominate an area, they may actually reduce competition, command higher prices from commercial insurers, and increase overall health care use.

The upshot, Dr. McWilliams says, is that linking up the country's fragmented health care delivery system may require a big investment that may be harder to recoup unless accompanying payment reforms reward efficiency and discourages waste.

With the Beeson Award, Dr. McWilliams says he's been far more productive in his analysis of Medicare. "It has provided outstanding financial support to protect my time and do the research that I want to do." As one of the few awardees focused on health policy, he's also gained new perspectives from the basic science and clinical research of other experts in aging, particularly at the annual meeting. "It's a very close knit group," he says, "which facilitates more meaningful connections to other researchers and mentors than the typical annual research meeting."

Timothy Miller, MD, PhD

Assistant Professor of Neurology
Washington University School of Medicine in St. Louis

Mentors: David M. Holtzman, MD
Alison Goate, PhD

Changing Tau Protein Levels and Tau Protein Isoforms in Mouse Models of Dementia

According to the Alzheimer's Association, an estimated 5.4 million Americans are now living with Alzheimer's disease, with direct costs reaching $200 billion annually.

"There are treatments that temporarily improve function to some extent, but there are no treatments that halt the progress of the disease," says Dr. Timothy Miller, who sees a "burning need" for better options. Through his application of new genetic methods in mice, Dr. Miller is testing out a potential therapy that might finally slow progression of Alzheimer's.

"My group has developed techniques to shut down or turn off genes in the brain and the spinal cord, and we've also developed a technique to change the 'flavor' of a particular protein," Dr. Miller says. His team is applying those tactics to a protein named tau that is involved in both Alzheimer's disease and a related type of neurodegenerative disease known as frontotemporal dementia.

Scientists have identified two main hallmarks of Alzheimer's disease: plaques, which are accumulations of protein fragments among the nerve cells of patients' brains. "And tangles, heaps of proteins all gathering in one area within the cell, and there's a lot of tau in those tangles."

Tau also seems to be involved in frontotemporal dementia. Mutations in the tau gene can cause a familial form of frontotemporal dementia and abnormal tau staining is seen in some patients with the non-familial form of frontotemporal dementia. Whereas forgetfulness is usually one of the first symptoms among Alzheimer's patients, Dr. Miller says patients with frontotemporal dementia do not initially have memory problems, but instead may have difficulty with speaking and understanding, and in their interactions with people due to behavioral changes.

Within the past five years, studies in mice bred to develop Alzheimer's have found that deleting the gene for the tau protein from birth may dramatically reduce symptoms. "It was clear that tau was involved in Alzheimer's disease, but it wasn't clear up until then that a decrease in the levels of tau could be a fair therapeutic strategy," Dr. Miller says. Other research has suggested a wrinkle, however: a complete absence of the protein from birth or for long periods of time may yield unintended consequences such as a buildup of iron or behavioral abnormalities.

Dr. Miller's techniques are allowing him to tamp down production of the protein in adult mice instead. The method is based on chemicals known as antisense oligonucleotides, developed in collaboration with Isis Pharmaceuticals, Inc. These oligonucleotides bind tightly to RNA molecules that carry instructions from a specific gene, preventing that gene from directing the mass production of proteins. In this case, the result is lower levels of tau protein.

Researchers can then assess whether changing the amount of tau improves the neurological behavior and other symptoms in adult mice. "This is an important test, because it would identify the way we would treat people," he says.

With his broad interest in neurodegeneration, Dr. Miller is also investigating a separate antisense oligonucleotide as a potential therapy for Amyotrophic Lateral Sclerosis, also known as Lou Gehrig's disease, first in mice and now in human patients. Intriguingly, some of those patients also suffer from frontotemporal dementia. "With that kind of experience, I looked at tau as one of the next best targets for treating neurodegeneration."

Dr. Miller credits his "outstanding" Beeson mentors, David Holtzman and Alison Goate, for sharing their wealth of experience in Alzheimer's disease and dementia. Their mentorship and other connections established through the Beeson Award "really allowed me to forge new territory for our therapeutic approach to neurodegeneration." With the technology developed for his Beeson-supported projects, he has also widened his effort to understand the effects of decreasing tau protein levels in adult mice — knowledge that will be critical for any human clinical trials. Although Dr. Miller's research is still very much a work in progress, he says, "it's been a very hopeful and successful entrée for me into that world."

Thomas Robinson, MD

Associate Professor of Surgery
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Mentors: Robert Schwartz, MD
Marc Moss, MD

A Placebo Controlled Trial of L-Tryptophan in Postoperative Delirium

During his tenure as head of the general surgery service at the Denver VA Medical Center, Dr. Thomas Robinson stumbled upon a maddeningly common but poorly understood complication that has since helped to define his research career. From his daily rounds with surgical residents, he learned that postoperative delirium was one of the most widely encountered problems among the medical center's older patients following major surgery. "So I started studying delirium," he says. "It's very clear that not only is postoperative delirium common, but it's also related to complications and is costly to the health care system."

Surgeons often struggle in their risk assessments of how older patients are likely to fare after an operation. Dr. Robinson says surprisingly few tools are available to help them, even though more than one-third of all inpatient surgeries in the United States now occur in patients 65 or older. The most frequent complication after any operation in that age group, he says, is delirium.

"Delirium is an acute onset of mental status changes that results following a stress, and the stress that we as surgeons give patients is an operation," he says. The relative risk of the brain dysfunction, as he and other researchers have learned, depends upon a patient's age, preexisting mental state, and other complicating conditions such as chronic disease and malnutrition. Some patients may have a single, brief episode of delirium, while others can have periodic bouts for a month or more.

"When patients have postoperative delirium, what it represents is underlying physiological vulnerability, which is another way of saying that a patient is compromised in their ability to tolerate the stress of an operation," Dr. Robinson says. Given their reduced ability to withstand the stress, such patients may be more likely to develop life-threatening complications like pneumonia or heart problems. Those with delirium, he says, are also much more likely to be admitted to a nursing home or another institutional care facility instead of sent home.

Half of Dr. Robinson's current research focuses on frailty as a pre-operative risk, while the other half looks at how that vulnerability manifests itself as post-surgical delirium. "I tackled the two topics that I most commonly encountered as a clinical surgeon," he says. Pre-operative assessments are often tailored toward specific surgical specialties, he notes. But the physiological stressors that can trigger delirium can occur with any surgery, meaning doctors must take a more holistic view of their patients' vulnerabilities.

Through an initial study of operating room patients that examined potential biological markers, Dr. Robinson and his colleagues found that patients at higher risk for delirium had lower levels of the amino acid tryptophan. That discovery led to an immediate question: "If you supplemented tryptophan, could you potentially decrease the occurrence of delirium?" The compound, often thought of for the sleep-inducing effects of turkey, serves as the precursor for the brain chemicals serotonin and melatonin. When present in lower-than-normal levels, both chemicals have been implicated in delirium, although researchers haven't yet figured out the complex molecular pathway.

Two other studies have similarly shown lower tryptophan levels in patients with delirium, but Dr. Robinson's Beeson-funded clinical trial is the first to ask whether a therapeutic dose of the amino acid may help lower the risk. In the randomized trial, he and his colleagues are giving patients either a placebo or tryptophan after surgery, and then they follow the molecular fate of the amino acid and its potential effect on the patients' clinical status and on the levels of multiple biomarkers.

"My investigation into the effect of tryptophan on postoperative delirium has been critical for my career," he says of his Beeson-supported research. As a specialist in minimally invasive surgery, he believes the award has helped to introduce him to a "Who's Who of Aging Research" and provided a valuable link to a new area of scientific study. Geriatricians, he says, may readily grasp the potential repercussions of post-surgical delirium in older patients, but the topic is still relatively new in surgical circles. "We are definitely bridging two different worlds by talking about delirium," he says.

Stephen M. Thielke, MD, MSPH

Assistant Professor of Psychiatry and Behavioral Sciences
University of Washington School of Medicine

Mentor: Jürgen Unützer, MD, MPH

Development and Evaluation of a Depression Risk Calculator

Depression has cast a long shadow over older adults in the United States, with significant symptoms affecting more than one in ten seniors, according to Dr. Stephen Thielke. Despite the availability of effective treatments, he says, clinicians haven't done nearly enough to make those options available to patients in need.

"If you look across a community, less than half of the older adults who are identified as having depression receive an evidence-based treatment for it, and that's only among people who are identified." With patients often feeling like they're "swimming in concrete," they may be unable to take proactive steps to get help on their own.

One initial barrier to care is the difficulty in assessing the presence and severity of depression. "It's not like having a cut toe or something where you can see the injury or have a specific bodily symptom," Dr. Thielke says. To help doctors and patients overcome that obstacle, he is developing a "depression risk calculator" to estimate an older individual's future risk for depression and assess the likelihood of the disease continuing. The tool will also provide estimates of what might happen with effective treatment interventions.

In addition, the Beeson-funded project uses customized decision aids to elicit patients' values and preferences, provide feedback, and encourage discussions with primary care providers about goals and therapeutic options. "There hasn't been much work done in use of decision aids for depression and definitely not these tailored or customized decision aids, so there's a lot to learn about how the process might work and if it will make a difference."

During his residency in psychiatry, he says, "I became interested in the complex interplay of factors that are involved in the lives and experiences of older adults." Depression, he realized, is often a central part of that interplay. "Research has shown again and again how depression is strongly associated with problems like chronic pain and chronic diseases like diabetes, heart failure and lung disease, as well as with geriatric syndromes." Seniors with depression are also at higher risk for suicide.

Depression is "more than just having a bad day," Dr. Thielke emphasizes. "This is a significant constellation of symptoms that persists for weeks to months. It not only causes internal psychological suffering for the people who are experiencing it, but it's also associated with negative consequences such as disability and low quality of life."

Health care providers, he says, must first recognize the problem, and then explain to patients how depression can impact their lives and encourage them to try treatments that they may initially resist. A "doctor knows best" approach that may come across as patronizing, however, is likely the very worst option. "So the question is, 'What are other models?' and the one that I think really has a lot of utility and that I'm pursuing in this research is a more person-centered medicine approach."

Dr. Thielke's strategy considers the unique circumstances, challenges, and strengths of each patient and then works collaboratively to identify their goals and how best to achieve them. "Instead of just handing somebody a pamphlet or a DVD about depression, the goal is to gather information about what their symptoms are and what their experience has been and then to give them tailored feedback about how depression is influencing their lives."

The inspiration and expertise Dr. Thielke has received from his mentors have been key to his success so far. "There are three mentors who really were instrumental in helping me to develop my interest and also to develop research around it," he says. "All three of them are Beeson Scholars, so it nicely points out what a fantastic community it is." Likewise, his Beeson-mediated connection to a collaborative group of aging researchers has been "fantastic. The award has really been an opportunity for me to explore more innovative approaches than I would have been able to do otherwise."

Beeson Scholars in the News

Radiation Therapy: Few Benefits But Still Given to Older Women

According to research by 2004 Beeson Scholar **Cary P. Gross, MD**, Yale School of Medicine, too many older women with early stage breast cancer are given radiation therapy in addition to breast-conserving surgery when there are few health benefits, high costs, and possible side effects. His research, published in the March 5, 2012 online edition of the *Journal of Clinical Oncology,* found that 75% of women 70 and older with stage 1 breast cancer were given radiation therapy to prevent a recurrence in addition to the standard surgical treatment even though it does not improve survival and current clinical treatment guidelines do not recommend it.

A Link between Statins and Lower Depression Risk

The use of statins, drugs that lower cholesterol levels, is also associated with a lower risk of depression, according to a study from 2001 Beeson Scholar **Mary Whooley, MD**, and colleagues at the San Francisco VA Medical Center. The study, which was published online February 21, 2012, in the *Journal of Clinical Psychology,* followed over nine hundred patients with coronary artery disease and found that statin users were both less likely to have depression symptoms when the study began and less likely to develop them over the six years of the study. Although this correlation does not necessarily mean that statin use directly lowers the risk of depression, Dr. Whooley suggested in a *HealthDay* report on the study that statins' effect on blood vessels may play a role in the decreased rates of depression.

Tracking Transmission of Tau

2000 Beeson Scholar **Scott Small, MD**, and colleagues at Columbia University Medical Center received worldwide media attention for research showing that the abnormal tau protein — responsible for the fibrous tangles that accumulate in the brain cells causing Alzheimer's disease — spread like an infection, by jumping from neuron to neuron rather than developing independently in vulnerable parts of the brain. This new understanding of cell-to-cell transmission could drive development of treatments such as those that block tau, allowing clinicians to intervene early and halt its progression. This research, published in the February 1, 2012, online journal *PloS One* may also prove useful in understanding how other neurodegenerative diseases such as Parkinson's disease spread.

Interactive Ways to Determine Lifespan

The January 10, 2012, *New York Times* featured an article about the interactive assessment tool developed by 2011 Beeson Scholar **Sei Lee, MD**, and colleagues at the University of California, San Francisco, which determines the likelihood of death in older adults. The tool, ePrognosis.org, was reviewed in the January 11, 2012 issue of the *Journal of the American Medical Association*. Its use can help prevent under-treatment in healthier patients or over and unnecessary treatment in those who are very ill.

Directing End-of-Life Care

In the October 5, 2011, issue of the *Journal of the American Medical Association,* 2003 Beeson Scholar **Kenneth Langa, MD, PhD**, along with University of Michigan colleagues, published an analysis of the impact of advance directives, which include living wills, on end-of-life care and associated Medicare spending. Their study found that having an advance directive lowered Medicare spending. They also found that in most regions of the country, patients with advance directives were less likely to die in the hospital and were likely to receive hospice care.

Beeson Scholars

The list below reflects only academic affiliations.

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