New Initiatives

A blood sample is placed in a centrifuge as part of the process of separating out the DNA. VA is collaborating with NIH on efforts to boost the use of patients’ genetic profiles and other individual factors to personalize medical care.

VA develops new relationships with NIH

In 1988, the National Institute of Aging (NIA), a component of the National Institutes of Health (NIH), initiated a long-term study to examine the ways in which older adults’ changing health interacts with social, economic, and psychological factors, and with retirement decisions. The study, called the Health and Retirement Study (HRS), is managed through a cooperative agreement between the NIA, which provides primary funding for the study, and the University of Michigan, which administers and conducts the study.

Prosthetics challenge launched

On May 15, 2015, VA challenged designers, engineers, and problem-solvers throughout the nation to submit ideas to help VA find new ways to provide innovative prosthetic and assistive technology solutions to challenges faced by ill and injured Veterans and other Americans.
VA develops new relationships with NIH
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VA researchers are now working with NIA to gather a Veteran cohort from the study. VA’s health data is being merged with information that has been provided to the study over the years to help researchers answer key questions about the health and well-being of Veterans, including those who do not use VA for their health care.

The data will include information about Veterans’ income, work, assets, pension plans, health insurance, disability, physical health and functioning, cognitive functioning, and health care expenditures. It will be made available to qualified researchers in 2016.

In addition, VA and NIH are working to build a close working relationship between VA’s Million Veteran Program (MVP) and the new presidential Precision Medicine Initiative (PMI) that will be conducted by NIH. MVP is a national, voluntary research program that uses genetic information to better understand how genes, lifestyle, and military exposures affect health. PMI is a nationwide effort to make precision medicine the norm rather than the exception in health care. Precision medicine is an emerging approach for disease treatment and prevention that takes individual variability in genes, environment, and lifestyle into account.

The synergism between the two programs will ideally result in improved specialized treatment for specific diseases.

Prosthetics challenge launched
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The Prosthetics and Assistive Technology Challenge asked inventors for help in five specific areas:
- developing novel upper-extremity prosthetic devices for everyday use;
- creating a medication pillbox that allows the flexibility to hold medications that need to be taken up to eight times a day, with a reminder system for each time medication needs to be taken;
- designing a device to remotely change the speed and grip of a prosthetic device for Veterans with upper-extremity injuries;
- finding a way to reassign motion and buttons on gaming controllers to provide alternative access for Veterans who are using them in therapy; and
- creating a device that can dampen tremors when Veterans are performing fine-motor tasks.

The series, sponsored by VA’s Center for Innovation, will culminate in a two-day make-a-thon event, to be held July 28 – 29, 2015, at the Hunter Holmes McGuire VA Medical Center in Richmond, Va. At this event, designs submitted online to address each of the five challenges will be built and tested to show how they meet Veterans’ needs.

“VA has long been at the forefront of research and technology, discovering new ways to give our Veterans the best care possible,” said Secretary of Veterans Affairs Robert A. McDonald. “We’re reaching out to technology leaders in the corporate world and the public to find creative new solutions to help transform care and quality of life not only for our Veterans, but for the public at large. The innovations that come out of this challenge will benefit the Veterans we care for and will be open-source to help advance American medicine.”

Service members compete in the 2010 Warrior Games in Colorado Springs, Colo.
While our guiding principles have not changed, our organization has continually transformed itself to better accomplish its mission. One recent important transformation has been the development of the CREATE (Collaborative Research to Enhance Transformation and Excellence) funding mechanism to promote research that has a meaningful impact on Veterans Health Administration (VHA) priorities.

The CREATE initiative encourages Health Services Research & Development investigators to collaborate with other VHA health care professionals to conduct research on issues that affect the health and health care of Veterans.

CREATE is defined by a group of coordinated research projects conducted in focused areas by independent collaborating investigators and their partners. CREATE projects target critical areas of interest to Veterans. These include PTSD, women’s health, pain management, mental health—and long-term care, a subject of special importance to older Veterans and their families.

Long-term care is an important part of the transformation process currently underway throughout VHA, and the projects the long-term-care CREATE is undertaking reflect that transformation. Currently, our researchers are partnering with VA’s office of Geriatrics and Extended Care to transform VA’s long-term-care system from one that is institutionally based to one that is more Veteran-centric and community-based.

The four projects our researchers are working on include:

- Improving the culture of care in VA’s community living centers (CLCs) by creating a toolkit that will help CLC leadership and staff to facilitate culture change;
- Reducing the number of hospitalizations among CLC residents by enhancing staff skills and improving care processes through staff training interventions;
- Documenting successes and variations among VA facilities in accelerating the discharge of CLC residents, so that they can return to a less restrictive setting more quickly; and
- Evaluating the safety and efficacy of the medical foster home concept, a community-based long-term-care program that is an alternative to nursing-home placement for Veterans who prefer care in private homes instead of institutional settings.

Each of these projects focuses on a transformation initiative the office of Geriatrics and Extended Care is undertaking: from improving care within CLCs, to realigning the discharge process, to examining the role of alternative community service programs. We are proud to share our expertise with our VHA partners.

Long-term care is just one area of significant importance to older Veterans and their families. VA researchers are pursuing new treatments, care models, and preventive strategies to improve the quality of life of “golden Veterans” and to support their caregivers. This issue of VA Research Quarterly Update includes information on many exciting advances our researchers have made recently to combat the conditions of aging. Since more than half of all Veterans are above the age of 60, meeting the challenges they face is of special importance to us.

The Office of Research and Development remains committed to optimizing the health and well-being of older Veterans, and all older Americans, just as we were 90 years ago. I hope you find the information in this issue interesting and useful.

**Timothy O’Leary, M.D., Ph.D.**  
Chief Research and Development Officer

Residential Care Residents of VA’s Little Rock (Ark.) community living center take part in a therapeutic “drum circle” with recreation therapists and volunteers.
A Chat with Our Experts

Reflections on the VA Normative Aging Study

Dr. Avron Spiro, with VA and Boston University, has been an investigator on VA’s Normative Aging Study since 1986, looking at the influences of health and disease on the aging mind, and conducting long-term examinations of personality, well-being, and mental health.

Dr. Avron (Ron) Spiro is a senior research career scientist with the Massachusetts Veterans Epidemiology Research and Information Center (MAVERIC), and a research professor in epidemiology and psychiatry at the Boston University schools of Public Health and Medicine. In 1986, he joined the VA Normative Aging Study (NAS) as a research psychologist and methodologist. Spiro, who collaborates with researchers at the Center for Healthcare Organization and Implementation Research at the Bedford and Boston VA medical centers, is also the principal investigator for a National Institutes of Health (NIH) grant on Lifespan Outcomes of Military Service, and is co-investigator on several projects funded by NIH and VA that study health, personality, cognition, and aging. He spoke with VARQU about his work with NAS and the Lifespan Outcomes study.

VARQU: The Normative Aging Study began in 1963. Can you tell us about the study and its aims?

Spiro: This study started at what used to be the Boston VA outpatient clinic, which was set up in the 1940s for returning World War II Veterans. Among other things, in the 1960s researchers at the clinic were studying a group of Spanish-American War Veterans who were all in their 80s and 90s. This was a group of about 100 men, and they were all extremely healthy.

And the researchers said: “Isn’t it interesting how these men got to be that way. Why don’t we look at World War II Veterans (at this time it was 15 or 16 years after the war) and start with a bunch of healthy guys and see what happens to them as they get old?” They wanted to know whether healthy men stay healthy, or whether they get different problems later. Basically, they wanted to know if aging inevitably leads to disease, or if some men could age relatively successfully without getting serious disease.

So the original objective of the NAS was to look at healthy men—since most Veterans were men at that time—and to take a look from the beginning and see what happened as they got older, so that you could see what made aging different from disease and issues like that. They took a group of mostly Veterans, recruited them through the community, and they were enrolled over a period of 10 years or so, aged 20 to 80. They were all healthy at the time of enrollment. The men aged 65 or older were almost as healthy as the 20-year-olds based on the selection criteria.
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We had a super-healthy group of older men, and a typical group of younger men. Over the next 25 years or so, the older group didn’t seem to die! The mortality rate was pretty low for the first 15 years of the study. When I joined the group in the mid-’80s we were trying to do some work looking at mortality, and only 5 to 10 percent of the study group had died, dropped out, or been lost, so we really couldn’t do much. At this point, 50 years later, I think we’ve lost about two-thirds of the cohort, but we also still have a healthy group. We’ve had a couple of 100-year-olds, and the average age of participants is now in the mid-70s and early 80s.

Every few years, study participants would come back for a medical exam and fill out some questionnaires and other things. We’d send them questionnaires in the mail every so often to find out what else was going on in their lives. There are two parts to the study: the biomedical part, which looks at health and disease and other aspects of medical functioning; and the psychosocial part, which looks at how participants think they are doing, how do they feel about things, what makes them happy or sad, what kind of person are they, how many friends do they have, and issues like that. I’ve mostly been involved in the psychosocial work.

I’ve done a fair bit of work on the personalities of the men and how that relates to health, and also on cognition and how that relates to health.

**VARQU: What sort of things have you found?**

**Spiro:** Let me tell you about a couple of things I think are interesting, and that we’ve tried to make the case for. The typical view of personality 15 or 20 years ago, both within the field of psychology and outside of it, was that by adolescence or early adulthood your personality is largely stable. If you are a cranky old man, it’s probably because you were a cranky young man. If you are a bit of a free spirit as an older person, it’s probably because you have always been that way. We looked to see whether that was the case, and our belief going in was that it’s very likely that people change—and they can become more or less extroverted, neurotic, or conscientious as they get older.

Since the mid-80s, we’ve been collecting data on personality from these men. We’ve done a number of papers showing that personality does seem to change. People can become—and I think I’ve noticed this in my own behavior—a little more extroverted and a little less neurotic. It goes the other way for some people. People who became less neurotic in this study were somewhat less likely to die over time. So having what I’d call a healthier outlook on the world is probably a good thing. We’ve found changes in life satisfaction and well-being—how happy people are with the world and themselves.

Others have had similar findings. All of our subjects are men, almost all of them are Veterans, and all of them are, in some sense, reasonably healthy compared to a general sample of the population. We have a unique group of people in our sample, but it seems that other researchers, once they started looking and thinking that personality might change, started finding similar sorts of things. So that’s one of the contributions that we’ve made to the world of personality and aging.

The other area is cognition. My colleagues and I have been trying to promote a view of cognitive aging. Cognitive aging is the shorthand term we use for the decline in everything that happens when we get older. From your 50s, you probably start forgetting people’s names and where the car keys are and so forth—and
by the way, it’s not dementia until you forget what the car keys are for.

Most people in the field of psychology, in which I was trained, thought cognitive aging was due either to just getting older, or to some more basic mental processes, like memory, that tend to decline with age. The argument we’ve been making over the last 15 years or so, using the medical data we have as well as the cognitive data we’ve been collecting, is that you not only have memory problems when you get old, but you also start having respiratory problems, heart problems, often in midlife, all sorts of conditions that can affect the brain, which affects cognition.

So if you look at the prevalence of diseases of aging, something like half the older population has hypertension; somewhere between 20 and 30 percent have diabetes; and some of the imaging data that people have collected in studies of large groups suggests that there are all sorts of things going on in the brain with aging, and all of these are likely to affect thinking and memory and all sorts of cognitive processes.

What we’ve tried to demonstrate is the notion that it’s less aging that causes cognitive declines than it is the fact that people tend to get more illness or diseases as they get older—and that these diseases increase the risk of cognitive declines and account for why older people often have more memory or decision-making problems or other sorts of things.

If you really want to understand what cognitive aging is about, you need to consider the health of the people you’re studying, and not just assume health is irrelevant. That’s because these diseases reduce blood flow to the brain, or lead to greater inflammation, or all sorts of physiological processes that impair cognitive function. If we all were perfectly healthy, we might all be perfectly cognitively competent.

VARQU: What’s the future for the NAS study?

Spiro: There is a high possibility the study will wind down in the next couple of years, at least in terms of doing the medical exams, because of the retirement of the people who have done that part of the study. What I am hoping is that over the next five or 10 years we can continue to do study activities by mail. The ultimate goal would be to get information on the last man, which sounds kind of morbid, but death is pretty much inevitable for all of us. We can’t use the electronic medical record for data, because most of the men are not VA patients, although we did the study in the VA. Only about 20 percent of the cohort use VA on a regular basis.

VARQU: You are also involved in an NIH-funded study on the lifespan outcomes of military service. Would you tell us about that study, and how it complements NAS?

Spiro: Maybe two-thirds of the men in our sample were World War II Veterans, and another third were Korean War-era Vets. What we have learned about in NAS is the aging of those Veteran cohorts. But every war is different, and so are the people who go to fight them. We tried, 15 years ago or so, to set up a comparable study of Vietnam War Vets, who would have been the same age as most of our guys were when they started the study, so that we could find out what happened to this group of Veterans as they aged, but we couldn’t get funding.

Now, Vietnam Veterans are the “old guys,” and we think they’re different from the World War II and Korean War Veterans who used to be the “old guys.” For one, they report a lot more mental health problems—maybe because they have them, or maybe just because they are more likely to admit to them. It’s not entirely clear. And we’ve had two wars since Vietnam; the first Gulf War didn’t have a particularly sizeable number of participants, and the second one has had a sizeable number with TBI and PTSD.
A Chat with Our Experts

Some other things have happened to the military as well. One of them is the all-volunteer force, and related to that is the fact that we now deploy many more National Guard and Reserve troops than we did before. So the kinds of things current generations of combat Vets are dealing with and will carry into their old age are different than what the Vietnam or the older guys had.

So the NIH grant funded us to start a research network. What we’re doing in this network is getting a group of investigators to study Veterans, using other people’s public use data, to find out how Veterans might age differently from the non-Veteran groups in those data. Then, we’ll make some suggestions on why we should study Veterans as they age, and how the different wars might affect Veterans’ aging differently over time. Without these kinds of data, we’re not going to be well-prepared for treating aging Veterans with brain injuries and missing limbs when they get into their 60s or 70s, and we’re not going to be able to project what their needs might be and what sorts of providers and health care we would need to provide them.

Everyone seems to be concerned more with the short-term consequences of the current wars, and what we need to do to help Veterans now, but we also need to be thinking about whether there is anything we know about the people who are aging now that might help us understand or begin to get prepared for the Vets who will be aging in 20 years—who they’ll be and what kind of services they might need most.

We might begin thinking about what we should do, and how we can work with medical schools to train people in the specialties we might need, and the kinds of service and configurations of care that might be better-suited to Iraq and Afghanistan Veterans as they age. I hope that we can raise some questions that will make people think maybe we ought to do that.

I’ve had some interactions with VHA’s national task group on dementia over the years, trying to project the number of dementia cases VA will see in the future. How will traumatic brain injury [TBI] and posttraumatic stress disorder [PTSD] affect that? They both seem to be risk factors for dementia. We’ve got a third of the last war’s two million plus Veterans coming home with TBIs. The whole notion of “accelerated aging,” in which illnesses seem to accelerate aging and cognitive declines—well, TBI may be one of those illnesses. Some of these guys may begin exhibiting dementia symptoms at 55 or 65, instead of 75. This means another 10 years or so of dependency, or respite care, or caregiving.

The projections we make now, such as VetPop [VA’s official Veteran population projection], are linear projections. There are things that can modify them and move them up or down—but these projections don’t include the disruptive changes that can happen.

What if everyone had a smart phone that woke them up and told them to start exercising? And if exercising results in a 10-percent reduction in cognitive decline and people could live on their own for an extra year and a half without going into nursing care? These small sorts of things can add up and result in large changes. So in some sense, it’s important to think about what we know and about what changes might take place in the next 30 years. What if we could find the genetic basis for different kinds of cancer and start curing a couple of them? And if we cut fatalities from lung cancer in half, what’s the implication of that? Some people will live longer, but maybe with more impaired health.

I read a lot of science fiction when I was growing up, and a lot of what interested me were disruptors and unintended consequences. When you do straight-line linear projections, everything looks fine—but when someone throws a curve ball, all of a sudden there’s a huge difference. If people aren’t dying from heart disease or cancer ... then they’re going to develop dementia [unless we have found cures].

We need to think about what aging Veterans are going to be faced with, and how to better prepare for what they might ask of our system.
Noteworthy Publications

Mild TBI may cause early brain aging—

Mild traumatic brain injury (TBI) is associated with a number of changes to the brain, including to its white matter structure. White matter is a component of the central nervous system that affects how the brain learns and functions.

Researchers with VA’s Translational Research Center for TBI and Stress Disorders (TRACTS), located at the Boston VA Medical Center, asked 249 Iraq and Afghanistan Veterans detailed questions about their combat history, and screened them for a variety of mental and physical health issues. They found that 195 of the Veterans had been exposed to bomb blasts within 100 feet, and 56 had not.

Each of the Veterans in the study underwent a brain-imaging procedure called functional MRI. The procedure showed how the parts of their brain communicated when they were not involved in any particular task. The research team found that Veterans exposed to bomb blasts showed fraying in their white matter structure—the same type of fraying that happens in the normal aging process, only at a much faster rate. Those exposed to a higher number of blasts tended to exhibit that fraying even more quickly.

“These are exposures to blasts, not necessarily blasts that lead to concussion, but feelings of fuzziness or getting knocked out,” TRACTS director Dr. Regina McGlinchey told CBS News, “These are events where the Veterans themselves thought they were just fine.” Her TRACTS colleague Dr. William Milberg told USA Today that “the most important message...is that they show that exposure to explosions in combat affects the brain whether or not the soldier showed symptoms of a concussion at the time of the explosion.”

According to CBS News, the consequences of this potentially premature brain aging could be increased rehabilitation time and earlier need for health care for aging issues like dementia. (Brain, June 1, 2015)

Heart benefits to intensive type 2 diabetes management—

In January 2009, VA researchers published the initial results from the VA Diabetes Trial in the New England Journal of Medicine. The study confirmed that tight glucose control can be achieved safely in most patients with diabetes. However, patients with long-standing diabetes and at high risk for cardiovascular disease (CVD) received only modest benefits in reducing their CVD over a five-to six-year period.

The spring 2015 issue of this newsletter included an interview with Dr. Peter Reaven, a Phoenix VA Medical Center researcher who is one of three lead...
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www.research.va.gov/pubs/varqu

Gestures make memories, but what kind? Patients with impaired procedural memory display disruptions in gesture production and comprehension. NB Klooster et al. Frontiers of Human Neuroscience, Jan. 13, 2015

Treating age-related macular degeneration: comparing the use of two drugs among Medicare and Veterans Affairs populations. S Pershing et al. Health Affairs, Feb. 2015

Comparative effectiveness of high-dose versus standard-dose influenza vaccination in community-dwelling Veterans. DM Richardson, et al. Clinical Infectious Disease, March 31, 2015 (epub ahead of print)

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Heart failure risk falls to normal 15 years after most smokers quit—Reuters News Service and other outlets reported on a VA study of former smokers that found that for most former smokers who quit at least 15 years ago, the risk of heart failure and death are the same as those of someone who never smoked.

However, researchers from the Washington, D.C., VA Medical Center reported that heavy smokers—those who smoked at least a pack a day for 32 years or more—still have an elevated risk of developing heart disease and dying.

The study, published on June 2, 2015, in the journal Circulation: Heart Failure, looked at adults over age 65, including 2556 people who had never smoked, 629 current smokers, and 1,297 former smokers who had quit at least 15 years earlier. Of those who had quit, 312 had been heavy smokers.

After 13 years of follow-up, about 21 percent of those who had never smoked and 21 percent of former smokers experienced heart failure. However, about 30 percent of those who were heavy smokers suffered heart failure. Current smokers, after researchers adjusted for factors like age, sex, education, and other health conditions, were about 50 percent more likely than those who had never smoked or former smokers to have heart failure.

“While all individuals who quit smoking will benefit from a decreased chance of death, to achieve the full complements of health benefits of smoking cessation of one who has never smoked, smokers need to smoke less and quit early, and for those who are not smokers—never start smoking,” Dr. Ali Ahmed, lead researcher for the study, told Reuters.

Can people in comas hear their loved ones’ voices?—CBS News and other news outlets reported on a study by researchers at the Hines, Ill., VA hospital and Northwestern University that answered a question many family members ask when their loved ones with traumatic brain injuries are in a coma: Can they hear me? According to the study, the answer is yes.

The researchers found comatose patients became normal in the way they responded to visual and auditory stimuli, including their loved ones’ voices.
more responsive after hearing recordings of a loved one telling a familiar story several times a day for weeks. While none of the eight patients who got the treatment emerged to full consciousness during the study, they appeared to be more aroused and aware than a comparison group when assessed according to a standard coma scale.

The study included 15 patients in comas and vegetative and minimally-conscious states, around 70 days, on average, after each one’s traumatic brain injury. Eight of the patients listened to recordings of stories from their past told by people they know well. The recordings were played for 10 minutes, four times, per day, for six weeks. The others lay in silence for the same periods.

When patients heard the voice of a family member calling their names out and reciting stories while they were undergoing MRI scans, their brains showed increased neural activity. Dr. Theresa Louise-Bender Pape, lead researcher for the study, told CBS News that the researchers saw changes in the blood oxygen level in brain regions associated with retrieving long-term memory and understanding language. “That means,” she said, “they were using those regions of their brains.”

CBS News also interviewed Godfrey Catanus, the only person in the study to have eventually recovered full consciousness from his coma after the study was completed. He recalled hearing his wife and his brothers’ voices while he was in a state of disordered consciousness. “It was comforting to think that they were there with me,” he wrote in an email. “It helped me by giving my brain something to connect with.”

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study the brain wave patterns of people walking on a treadmill, and use the Anklebot to gradually retrain the brain and muscles of stroke victims, helping them to recapture, to some extent, they way they walked before they had their stroke. As stroke victims move incrementally toward a more normal gait, robotic assistance diminishes, and patients can increasingly perform movements on their own.

More than 200 venture capitalists, biotech entrepreneurs, and business development executives helped to choose the Anklebot for the award, by evaluating a range of presentations from startup and university-affiliated recipients.

**Berlowitz receives health services research award**—Dr. Dan R. Berlowitz has received VA’s 2015 Under Secretary’s Award for Outstanding Achievement in Health Services Research. The award is the highest honor given to a VA health services researcher.

A former VA HSR&D Career Development awardee, Berlowitz is recognized for his expertise in quality assessment, risk adjustment, and the use of large databases. His work focuses on assessing and improving the quality of Veterans’ health care, with a particular emphasis on ambulatory and long-term-care settings.

His studies on Veterans with hypertension have led to a reevaluation of how clinicians think about the problem of uncontrolled hypertension. Hypertension control rates are now over 70 percent in VA, in large part due to reductions in what Berlowitz termed “clinical inertia.”

Since 2012, Berlowitz has served as acting chief of staff for the Edith Nourse Rogers Memorial VA Hospital in Bedford, Mass. He is the former co-director of HSR&D’s Center for Healthcare Organization and Implementation Research, and also served as director of HSR&D’s Center for Health Quality, Outcomes, and Economic Research from 2004 through 2013.

**Kowluru honored by Wayne State University**—Dr. Anjaneyulu (Anjan) Kowluru, senior research career scientist and chief of the Beta-Cell Biochemistry Research Laboratory at the John D. Dingell VA Medical Center in Detroit, received the 2015 Distinguished Graduate Faculty Award for outstanding scholarly achievements in research and teaching at Wayne State University, and for other contributions to the university.

Kowluru is a professor of internal medicine in the division of endocrinology and metabolism at Wayne State University’s School of Medicine. He is also the associate dean for external scientific affairs in Wayne State’s Eugene Applebaum College of Pharmacy and Health Sciences.

In addition to being honored by Wayne State, Kowluru recently received an adjunct professor appointment in interdisciplinary science and technology research at the University of Pune, in India, and will be chairing a scientific session on beta cell biology and insulin resistance at the 4th Annual World Congress of Diabetes, to be held in Taiwan in November.

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