### Summer 2017 | THIS ISSUE: The Aging Veteran

#### From the Chief Research and Development Officer

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Any health information in this newsletter is strictly for informational purposes and is not intended as medical advice. It should not be used to diagnose or treat any condition.
Honoring our aging heroes

Six months ago, I packed my bags and moved from New York City to Washington, D.C. One of the many good things about living in this city is that it is dotted with reminders about the importance of honoring our Veterans and the sacrifices they have made.

For those of you who have not seen it, the Vietnam Veterans Memorial is a stark wall of polished black granite cut in the shape of a “V.”

The names of the 58,318 U.S. service members who are missing in action or lost their lives for our country are carved into the surface. Millions of people visit the memorial each year, running their fingers over the names of these lost service members who were also daughters, sons, and vital members of their communities.

This year marks the 35th anniversary of the Wall. To honor the soldiers, sailors, Marines, and airmen who gave their lives so valiantly, the Vietnam Veteran’s Memorial Fund is hosting a ceremony in November that will include reading each and every name on the wall out loud, taking an estimated 65 hours over a four-day period.

As VA researchers, we strive to honor Veterans as part of our mission. In this issue of VA Research Quarterly Update, we highlight research that focuses on our aging Veterans. In the fall of 2017, the National Center for Veterans Analysis and Statistics projects that there will be 1.9 million Veterans between the ages of 60–64, 2.3 million between the ages of 65–69, 2.6 million between the ages of 70–74, 1.6 million between the ages of 75–79, 1.3 million between the ages of 80–84, and 1.6 million above the age of 85.

Certain illnesses, like cirrhosis or scarring of the liver, are much...
more prevalent in Veterans who seek care through the VA health system than in the general population. Cirrhosis can have serious neurological complications, and VA researchers are taking what might at first seem a surprising approach to combating these complications. In this issue, VARQU speaks with Dr. Jasmohan Bajaj, a liver transplant specialist and researcher at Hunter Holmes McGuire VA Medical Center in Richmond, Virginia. Dr. Bajaj is pioneering the use of fecal transplants to improve the health of Veterans who suffer brain damage due to a failing liver. It is truly revolutionary research: an early study showed that people who received the transplants had better cognitive function and fewer hospitalizations.

While Dr. Bajaj’s study might seem surprising, other VA research builds upon and quantifies common sense. Neurologist Dr. James Morley, a Career Development awardee at the Corporal Michael J. Crescenz VA Medical Center in Philadelphia, is studying the effects of a structured exercise program on Parkinson’s disease (PD). At present there is no cure for Parkinson’s disease, only drugs to treat motor symptoms. However, aside from the more recognized symptoms like tremor and poor balance, many Veterans with PD also suffer from impaired thinking and mood disorders. Dr. Morley says research is beginning to demonstrate that exercise can have positive effect not just on heart disease, but also on neurological disorders like PD. “We really push physical activity in the clinic,” he says. “We tell patients to think of it like another very powerful medicine.”

VA researchers are very often leaders, both in their respective fields and in their communities. For this issue of VARQU, we review not just academic awards, but also editorials written by VA researchers that were published in major medical journals.

I am excited to share the work that we are doing, so I could go on and on about the contents of this issue of VARQU. They range from a new initiative to grade the quality of care at VA-contracted nursing homes to studies that show the protective benefits of “young blood” given to aging mice who display Alzheimer’s-like symptoms. We do this work to honor the lives of Veterans by finding ways to improve their health and well-being. I hope you find this information useful, relevant, and worthy of sharing with your colleagues and fellow Veterans.

Rachel B. Ramoni, D.M.D., Sc.D.
Chief Research and Development Officer
Quality dashboard for VA-contracted community nursing homes

Nursing home care for Veterans can potentially be monitored using a new quality dashboard in development by QUERI researchers. (Photo for illustrative purposes only, ©iStock/Squaredpixels)

VA’s Quality Enhancement Research Initiative (QUERI) aims to support “the needs of a changing VA healthcare system, notably by supporting providers in the more rapid implementation of effective clinical practices into routine care.” To do that, the program funds research into implementation science and quality-care initiatives to help bring cutting-edge science into the exam room, so that Veterans have access to the latest and most innovative treatments available. “In essence, QUERI ensures that effective treatments get off the academic shelf and into the hands of Veterans and their providers quickly,” said Dr. Amy Kilbourne, director of QUERI.

The programs that QUERI has spearheaded are diverse and range from using team-based behavioral care, implementing care conversations with Veterans in long-term care, enhancing health care for women Vets, and optimizing appropriate medication use for Veterans, to name just a few.

QUERI also engages in partnered evaluation initiatives, where funding comes from a third party to analyze initiatives that could potentially have high impact on VA policy.

Disseminating a dashboard for VA purchased community nursing homes is one such initiative based out of Providence, Rhode Island. The initiative seeks to assess and improve the quality of care that Veterans receive in community nursing homes (CNH). The VA Geriatrics and Extended Care (GEC) Data and Analysis Center has created a dashboard that will allow facility leadership to assess care in VA-contracted community nursing homes using nationally published metrics.

The dashboard uses the Center for Medicare and Medicaid Services (CMS) Nursing Home Compare five-star quality rating system. The CMS website
— which is open to the public — collects and compiles data from onsite inspections, quality measures, and staffing levels at nursing homes across the U.S. The dashboard also allows comparisons between other nursing homes in the VA health care system.

Investigators will assess VA nursing home selection and monitoring by interviewing contracting officials and GEC leaders. In addition to evaluating the usefulness of the quality dashboard, they will create an educational module to improve the CNH selection process.

*Listen to Mitch Mirkin of VA Research Communications interview Dr. Amy Kilbourne, director of QUERI, about the program’s history and current work and how it is impacting Veterans’ care. Listen (23:01), Transcript*

Wilmington VA Medical Center and University of Delaware ink deal

On June 9, 2017, the Wilmington VA Medical Center and the University of Delaware in Newark signed an affiliation agreement to formalize collaboration between the two institutions. While UD has been involved in research efforts with the Department of Defense for many years, the Wilmington VAMC has not been active in biomedical research, until now.

UD and affiliate institutions like the Bader Consortium — which advances research in orthopedic rehabilitation for wounded warriors — conduct research in many areas that will dovetail with the needs of Veterans, such as traumatic brain injury, rehabilitative medicine, orthotics and prosthetics, and neuroscience.

The UD Science, Technology and Advanced Research (STAR) Campus is home to the Health Sciences Complex, which houses classrooms, research laboratories, and health care clinics. STAR Health offers primary care, physical therapy, speech therapy, mental health services, and wellness services to the citizens in surrounding Delaware and southern New Jersey.

Now that patient population could potentially include Veterans as well, through clinical training programs like physical therapy. “Veterans will get...”

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the rehabilitation they need while students get a foot in the door at the VA and ultimately help fill our growing need for health care practitioners in our region. That’s a win for everyone,” said U.S. Sen. Tom Carper, an alumnus of UD and a Navy Veteran, according to UDaily.

The Wilmington VA provides health care to more than 30,000 Veterans throughout Delaware and southern New Jersey.

**Surgery vs. radiotherapy to treat non-small cell lung cancer**

The tried and true treatment for patients with early stage non-small cell lung cancer has been surgical resection, or cutting out the diseased tissue from the lungs. Aside from longer hospital stays and greater costs, patients can expect a painful recuperation after an open surgical procedure.

For those lung cancer patients who cannot tolerate surgery, or have very small tumors, a special type of radiation treatment can be used, called
stereotactic body radiotherapy. This treatment modality targets therapeutic X-rays only in the area where the tumor is, sparing the rest of the body from the toxic effects of widely scattered radiation. That precision allows the medical team to increase the intensity of the X-rays and shorten treatment time — factors that are a boon for Veterans’ quality of life.

So which treatment is better? Over the last three years, Dr. Drew Moghanaki and his team have been trying to find out.

“It has been begging the question,” Moghanaki told the Richmond Times-Dispatch, “if outpatient treatments that a patient could get potentially on their lunch break might be just as good as surgery, why are we still routinely recommending surgery?”

Moghanaki is a radiation oncologist and investigator at Hunter Holmes McGuire VA Medical Center in Richmond, Virginia. Along with Dr. Tomer Karas at the Miami VA Medical Center, he is co-chair of a new 10-year clinical trial that will compare the effectiveness of open surgery for non-small cell lung cancer to stereotactic radiation therapy: VA lung cancer surgery Or stereotactic radiotherapy trial (VALOR).

The clinical trial is now recruiting patients and hopes to enroll 670 Veterans at six VA medical centers, in Illinois, Indiana, Minnesota, North Carolina, Texas, and Virginia.

Researchers will assess overall patient survival, patient health-related quality of life, respiratory symptoms, lung cancer mortality, tumor patterns of failure, and respiratory function for each type of treatment.
Fixing a failing brain through the gut

Dr. Jasmohan Bajaj is an associate professor at Virginia Commonwealth University (VCU) and a liver transplant specialist at Hunter Holmes McGuire VA Medical Center in Richmond, Virginia, where he is instrumental in evaluating Veterans for potential liver transplantation. He also conducts clinical and translational research in fields pertaining to liver disease, its effect on the brain, and its effect on the microbiome (the community of microbes that live in the gut) in both Veterans and non-Veterans.

VARQU recently spoke with Bajaj about the research he is doing to develop revolutionary new treatments for hepatic encephalopathy, damage in the brain caused by a diseased liver.

KEY POINTS:

• Hepatic encephalopathy is damage in the brain caused by a liver that is not functioning properly. Toxins from the bowels that are normally cleared by the liver are able to reach the brain, which can cause confusion, and could result in a dementia-like state.

• Hepatic encephalopathy affects 30–45 percent of patients in the U.S. with cirrhosis, which is a common condition in the Veteran population. In 2013, a total of 60,553 Veterans were in treatment for cirrhosis, according to a study in Gastroenterology.

• While physicians are able to treat the symptoms of hepatic encephalopathy, patients tend to get sick with repeated episodes. They are much more prone to infections, which leads to repeated hospitalizations and even death.

• Dr. Bajaj and his team are studying the use of fecal transplants to treat patients with hepatic encephalopathy who are not candidates for liver transplant.
You have recently finished a clinical trial and are starting another one pertaining to hepatic encephalopathy. Can you explain what that is?

Hepatic encephalopathy is actually epidemic in patients with liver disease and cirrhosis and especially in the Veteran population. What it really means is what the word suggests: hepatic means liver and encephalopathy means disease in the brain. So we believe that it’s the liver disease that causes the brain to not function right. When the liver is not functioning properly, it cannot handle the toxins that reach it from the gut, which it normally handles. That causes a state of inflammation throughout the body and toxins also leach their way to the brain. In addition, patients with liver disease and cirrhosis at this stage also get problems with their muscles and their kidneys — which makes this really bad for the poor brain. So, the brain gets it from all sides.

The good thing about this is that if you treat the gut, people do get better, but not completely. Hepatic encephalopathy has two parts: a covert form and an overt form. The covert form is something that is very difficult to diagnose clinically, but if you give people who look completely alert and oriented some cognitive tests they’ll score really bad. That happens in about 40–50 percent of patients with cirrhosis. The covert stage makes it very difficult for affected patients to conduct activities of daily living. So their quality of life is very impaired, even if they look completely alert and oriented.

In the overt form of hepatic encephalopathy patients get disoriented, confused, they can get lethargic, and it can even lead to coma. The treatment for overt hepatic encephalopathy, once the patient is actually recovered, is to put people on such things as laxatives and non-absorbable antibiotics, which affect their gut to prevent future episodes of encephalopathy.

We have published research which shows that hepatic encephalopathy — the overt form — is the leading cause of readmissions in people with cirrhosis, across North America.

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You mention that hepatic encephalopathy and cirrhosis are very prevalent in the Veteran population. Could you explain?

Unfortunately Veterans have an over-representation of hepatitis C and alcohol use disorder, for multiple reasons. They are therefore much more prone to get the consequences such as cirrhosis, which in turn makes them much more prone to get encephalopathy. Cirrhosis is relatively common in Veterans; it is one of the leading causes of illness and death in this population. So therefore, if you have more cirrhosis you are also going to have more hepatic encephalopathy.

Can you tell us about the research you are doing, investigating the use of fecal transplants to treat hepatic encephalopathy?

The fecal transplant seems very radical. However, a lot of our focus in treating hepatic encephalopathy is dependent on the gut. The medicines that are currently used to treat the disease may not be enough to help the patient get better — because ultimately they are not fixing the liver, which is diseased. When that happens, the preferred treatment is a liver transplant. However there are not enough donated livers to make this a viable option for most liver disease patients.

Patients who are waiting for a liver transplant are ranked according to an impartial system that takes into account many different factors. Sicker patients are generally given more points to help put them higher up on the transplant list. However, since 2002, hepatic encephalopathy has been removed as a priority criterion for liver transplantation. If a Veteran has hepatic encephalopathy, he doesn’t get any extra priority points for that.

The current treatments for people with recurrent overt hepatic encephalopathy can still result in a lack of response, so that is why we chose this population in this study. We didn’t want to take a population that was earlier in the disease process, because we have FDA-approved treatments for them. So we only took people into the
study for whom the current FDA-approved treatments have been used and they still have problems with their brain function.

We randomized these people into two groups. One group we treated with the standard of care. The other group got the standard of care, and in addition to that, after five days of broad-spectrum antibiotics to clear their naturally occurring bacteria in their gut, we gave them one enema from one stool donor. Everybody who was randomized to the fecal transplant group got the enema from a single donor.

**What happens during a fecal transplant? Do you actually take a little bit of stool from a healthy individual and transfer that via an enema to someone who is sick?**

That is correct. The donor came from [OpenBiome](http://openbiome.org), who is our collaborator in this study. It is a nonprofit stool bank. We collaborated in the study with Massachusetts Institute of Technology, George Mason University, OpenBiome, and the Imperial College London.

Ultimately we ended up choosing just one donor, based on the bugs that were missing in our patients. So this one donor’s stool was instilled by enema into the 10 people who were randomized into the fecal transplant arm. And then we followed everyone for the next five to six months, per FDA guidelines.

Ultimately we found that this treatment was safe. But what we were not expecting to find was that it was not only safe, it was also effective. It actually reduced patients’ hepatic encephalopathy readmissions. In the patients who were randomized to the fecal transplant arm, there were no readmissions for encephalopathy. There were five patients in the standard-of-care arm who were admitted six times over five months; this is what you would expect in the natural course of hepatic encephalopathy. What we did find is that the infections were found only in people who were randomized to the standard-of-care arm. This is very encouraging to us, because these are patients who are very prone to infections, and the treatment seemed to be safe. And the other thing we found is that when we did some specialized cognitive tests, brain tests, patients improved, in the short term.

This study is very interesting in the sense that we did not expect to see these changes. That is why we need to take the results with a little bit of caution because it is a very small sample size, and it is the first salvo. It does need to be repeated and of course we asked the patients afterward, “If you had a choice between a pill and an enema, which would you choose?” And...
they all chose a pill. That’s why our next study that is already undergoing recruitment at VCU and McGuire VA hospital is based on the oral capsules — again, supplied by OpenBiome. Both the enema and capsule are currently approved only for the treatment of C. difficile in the U.S. You cannot get it from OpenBiome or anywhere else outside of a research study for hepatic encephalopathy.

This treatment is pretty revolutionary, yes? Essentially it is not a drug. It is a transplant; it is considered tissue. It’s kind of at a crossroads, because it is not really a drug. With a drug, the FDA requires that the composition of each and every “capsule” is the same. That is not possible in feces; it depends a whole lot on who you are, what you eat, how old you are, what medicines you are on, etc. And it is not really an “organ” so to speak. But it’s at a very interesting crossroads, and the FDA has come a long way — speaking with leading patient advocates and groups, especially those with C. difficile, stool banks, and people who want to do this to help their patients. So unlike regular drugs, if it is approved for one condition or disease, you can use it only in those patients. With fecal transplants, you have to talk to the FDA for each and every indication, which is good because their primary goal is to ensure the safety of patients.

*Dr. Bajaj is beginning the second phase of his clinical trial, “Oral Fecal Transplant in Cirrhosis.” For more information see [ClinicalTrials.gov](https://clinicaltrials.gov).
A simple treatment for a complex neurological disease

Dr. James F. Morley is a board-certified neurologist with sub-specialty training in Parkinson’s disease and movement disorders. He is associate director for research at the Parkinson’s Disease Research, Education and Clinical Center (PADRECC) at the Corporal Michael J. Crescenz VA Medical Center in Philadelphia, and assistant professor of neurology at the Perelman School of Medicine, University of Pennsylvania.

VARQU spoke with Morley about his Career Development research award, in which he will investigate the effects of exercise on drug-induced Parkinsonism and Parkinson’s disease.

Dr. Morley, can you briefly describe Parkinson’s disease and how it affects the body?

Parkinson’s disease is a progressive, devastating, neurodegenerative disease that unfortunately does not have a cure. It’s been traditionally described as affecting movement, causing difficulty with tremors, as well as slowness and stiffness of movement, and loss of balance.

More recently, it’s been appreciated that there are a number of non-motor symptoms that are associated with Parkinson’s disease, including mood disorders, sleep problems, and cognitive dysfunction. Those symptoms can actually be more troublesome to patients because traditional treatments for PD are more effective for motor than non-motor symptoms.

KEY POINTS:

• Parkinson’s disease is a progressive neurodegenerative disease that affects close to 1 million adults in the U.S. At present, there is no cure.

• Early diagnosis of Parkinson’s disease is difficult, because brain damage can occur years before symptoms are evident.

• Dr. Morley’s research focuses on using an aerobic walking program to potentially alleviate or eliminate the symptoms of Parkinson’s disease.
How common is Parkinson’s disease in the U.S. and the Veteran population?

Parkinson’s disease affects about 1 million adults in the U.S. and about 80,000 U.S. Veterans. Additionally, the VA connected Parkinson’s disease to Agent Orange exposure for Veterans who served in Vietnam, and many of these Vietnam Vets are in the age range for developing Parkinson’s disease. That’s made PD an additional priority area for VA research.

Why it is difficult to identify Parkinson’s disease in its early stages?

One of the most common early symptoms of Parkinson’s disease can be tremor, which is usually obvious and sends people to the doctor. However, not everyone has tremor. Some patients just have slowness and stiffness. At the age range where this is happening, in the 60s and 70s, there’s some overlap with normal aging and people say, “Oh maybe I am just getting older and slowing down. It’s a little harder to walk.” We commonly have patients that have had symptoms for a number of years before they show up in our clinic. That’s one part of it.

Another factor that makes diagnosis of early Parkinson’s disease difficult is that once patients present in the clinic with a tremor and other signs of Parkinson’s disease, we know that there has already been extensive destruction in the brain areas that are responsible for Parkinson’s disease symptoms. That’s why one of the major strategies in contemporary Parkinson’s disease research is to make the diagnosis earlier, perhaps even before the motor symptoms begin.

There are a number of symptoms, including loss of sense of smell or sleep disturbances, that commonly happen in Parkinson’s disease patients before the motor symptoms. That provides an opportunity, potentially, to make the diagnosis early. That potential for early diagnosis is part of what we are trying to exploit in the research component of my Career Development award.

How effective are the current drug treatments for Parkinson’s disease?

All of the drug treatments that we have for Parkinson’s disease really just control symptoms. So they can improve tremor, they can improve walking speed, they can improve muscle stiffness. They can be very effective and improve the motor symptoms for years, but I think that most people would agree that the holy grail of Parkinson’s disease research is trying to find
treatments that we would call disease-modifying. And that is something that instead of just improving the symptoms in the short term, it can actually slow down, if not stop, the progression of the disease.

**Can you explain why exercise is protective for Parkinson’s disease?**

I talk about this to patients all the time in the clinic. We should really be thinking of exercise as a medicine.

When you look at exercise, the best-characterized benefit is probably for cardiovascular disease, but also there is emerging evidence of benefit for many different disorders, including neurologic disorders. And probably the reason that exercise can reach so many different disease states is that it affects a lot of different biochemical pathways and growth factors.

In experiments both in animals and humans, there are many different biochemical pathways that are changed by exercise, many of which protect neurons. A pill that you take is usually meant to affect just one biochemical pathway — for example, increasing dopamine levels in Parkinson’s disease. Exercise affects many different biochemical pathways, and that may be the power that allows it to affect so many disease states and to do more than just improve one symptom.

**Your Career Development research is focused on investigating the effects of exercise on Parkinson’s disease. What do you hope to find?**

There’s a very strong body of evidence that supports the idea that exercise improves motor symptoms in Parkinson’s disease. What is not clear is whether exercise could be a disease-modifying therapy. But there is intriguing evidence that suggests that it could be the case.

There are a number of large epidemiologic studies that have suggested that higher levels of exercise in mid-to-late adulthood are associated with lower risk of ultimately developing Parkinson’s disease, suggesting that exercise may delay the onset or protect against development of Parkinson’s disease.

As we talked about earlier, one of the perceived limits of disease-modifying drugs is that by the time someone presents with motor Parkinson’s disease,
there’s actually been quite a bit of destruction in the brain. So people are trying to make this diagnosis earlier.

One strategy that we’ve employed in Veterans is to look at folks who have Parkinson’s-like symptoms because of exposure to certain drugs that block dopamine. These are often antipsychotic drugs that are used to treat not just schizophrenia but a variety of psychiatric disorders. What we are learning is that just like running on a treadmill can bring out chest pain or changes on an electrocardiogram, these dopamine-blocking drugs can act as a stress test for the brain. They can bring out motor symptoms in patients with early-stage Parkinson’s disease that wouldn’t have developed on their own until years down the road.

With the help of VA pilot funding, we conducted a study that found 20 percent of Veterans with Parkinson’s-like symptoms caused by one of these drugs actually had findings on a brain scan that looked like Parkinson’s disease. Those are the kinds of subjects that we are trying to enroll in the exercise arm of the study.

The overall goal is to conduct a randomized control trial of exercise as a symptomatic and potentially disease-modifying therapy for Parkinson’s disease. The exercise subjects are asked to perform aerobic walking either in their homes if they have a treadmill, or in the community if they have access to a gym or track. We are monitoring their compliance using a weekly phone call and remote monitors that can track how much exercise they’ve been doing. We are measuring a number of different outcome variables, including physical fitness and motor symptoms, as well as blood markers of biochemical changes caused by exercise.

Really the primary goal of the study is to examine whether there are differences in the progression of the dopamine brain scan over one year in the exercise group versus the normal care group.

**What do you see as the next steps in your research?**

I think there are a lot of places we could go from here. The hope with this study is to test whether exercise has an effect on disease progression. And we are looking at a very specialized population: the patients with early Parkinson’s disease that has been uncovered by these antipsychotic drugs. So the next direct step would be to look at a broader population of patients with early to mid-stage Parkinson’s — to find if you could see a similar effect of exercise.
I think this concept of exercise as medicine is important and offers a variety of different opportunities. We really push physical activity in the clinic, and we tell patients to think of it like another very powerful medicine. Parkinson’s patients take their medicine at least three times a day, and so we ask them to “take their exercise” three to five times a week, which is what the American Heart Association recommends for all adults.

Unfortunately, and not unexpectedly, patients probably aren’t “taking” their exercise as much as we would like. Even if our current study suggests that exercise affects disease progression, much more work will be needed to help us understand how to motivate patients to exercise vigorously, but safely enough to derive the full benefits.

Find out about the latest in VA research by listening to the ‘Voices of VA Research’ podcasts. Visit our website or subscribe on iTunes.

Addressing homelessness in Veteran populations

Erica Sprey of VA Research Communications speaks with Dr. Jack Tsai, a clinical psychologist and researcher at the VA Connecticut Healthcare System and the New England Mental Illness Research, Education and Clinical Center (MIRECC) in West Haven. Tsai’s research focuses on addressing and improving outreach and services for homeless Veterans, so that they can successfully live in independent housing.

Read more: Improving services for homeless Veterans

Listen (7:56), Transcript
Provider challenges in delivering end-of-life cancer care—

To learn about provider perspectives on end-of-life cancer care, researchers at the VA Palo Alto Health Care System, Stanford University, and Washington University interviewed 75 oncology providers (physicians, nurses, and social workers) and patient advocates to solicit their views on EOL cancer care and ask for suggestions to improve practice design.

Studies show that both providers and cancer patients are interested in improving the effectiveness of EOL cancer care. However, little work has been done to measure provider support for care delivery improvements.

The study results were published online July 10, 2017, in the American Journal of Hospice and Palliative Medicine.

The researchers conducted semi-structured interviews that were transcribed, coded, and analyzed using a “constant comparative” method — based on thematic analysis — to identify recurring themes.

The provider interviews revealed six common themes that fell into two categories: roadblocks to providing the best patient care, and ways to improve practice design.

Providers said they experienced these challenges in delivering quality cancer care to their patients:

1. Lack of time for educating patients and caregivers.
2. Ambiguity in determining prognosis/timing of palliative care.
3. Lack of systems to support non-face-to-face patient communication.

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Providers said they felt these clinical practice improvements would help them manage their time better:

1. Use of a lay health worker to assist in care planning.
2. Use of non-face-to-face patient communication to address symptom management.
3. Use of in-home/community cancer care services.

Concerning in-home care, one nurse said: “We give chemotherapy to kids all the time at home. There are a lot of things we could do in the home for adult patients as well, but we don’t because the payment system is set up to reward doing this in the infusion center. Many of our chemotherapies can be safely given to patients at home ...”

Most of the suggested solutions were not unique and had been proposed in previous studies. The researchers concluded that physicians and other cancer care providers should have more input on barriers to EOL cancer care and should be asked for their suggestions on practice improvements.

Cancer care in the United States is complex and costly. It requires a multidisciplinary patient care team composed of physicians, nurses, technicians, social workers, and patient advocates. Care providers are often pressured to see large volumes of patients, and in the midst of administrative and financial pressures, end-of-life care can inadvertently be given short shrift.

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**Fish oil therapy improves eye damage in diabetic rats**—Dr. Mark Yorek, an investigator with the VA Iowa City Health Care System, is studying the effects of menhaden (fish) oil on diabetic neuropathy in rats. He and his team have shown that fish oil can improve and sometimes even reverse nerve damage in the eyes of diabetic rats. The effects were even more profound when fish oil was combined with alpha-lipoic acid, as seen in the image below.

New research shows that fish oil can improve and sometimes reverse nerve damage in the eyes of diabetic rats. (Photo ©iStock/JanIngesKogheim)

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an antioxidant found in the body, and enalapril, a blood pressure medication.

The study results were published in the June 2017 issue of *Cornea*.

The researchers fed 12-week-old rats a high-fat diet for eight weeks, and then gave them streptozotocin, a drug that is toxic to the insulin-producing beta cells in the pancreas. After the rats had experienced high blood sugar for 16 weeks, the team then gave them treatments that consisted of menhaden oil, α-lipoic acid, enalapril, or a combination of all three.

“Treatments were not initiated until after development of significant vascular and neural impairment, including a decrease in corneal sensation and loss of subepithelial corneal nerves,” wrote the study authors. This was done purposefully so that the investigators could test for reversibility of peripheral neuropathy and return of corneal nerve function in the rats.

The rats were put through a number of tests to measure blood sugar tolerance, thermal sensitivity, corneal sensation, and nerve conduction. At the end of the study, all treated rats had lost weight. Their non-fasting blood sugar measures had increased significantly, indicating impaired glucose clearance.

However, rats who had received monotherapy with fish oil, α-lipoic acid, or enalapril showed lower serum lipid (cholesterol and triglycerides) levels, and those who were treated with a combination of all three returned to normal lipid levels. In a similar fashion, rats who received the combination treatment also experienced a reverse in vascular dysfunction and a return of corneal sensation.

The results of this study are especially useful, noted the study authors, since corneal sensitivity is being promoted as a test for early diagnosis of diabetic peripheral neuropathy.

Diabetes is a profound disease that can affect many areas of the body. The body’s inability to process and absorb sugar into the cells for fuel can damage tiny blood vessels and nerves. One painful side effect of diabetes is neuropathy: literally nerve disease or damage.

Continued on next page
Peripheral neuropathy can cause burning or tingling sensations in the lower legs and feet. However, nerve damage can also occur in organs like the eye, bladder, or intestines, causing vision problems, urinary incontinence, or diarrhea.

Using ‘young blood’ to treat Alzheimer’s disease—Alzheimer’s disease — a neurodegenerative disorder of the brain which leads to dementia — has no cure. At present, there are no drugs or treatments that can delay disease progression, and very few that can help with symptom control.

Hopefully that won’t be the case forever.

Dr. Tony Wyss-Coray is a VA investigator with the Center for Tissue Regeneration, Repair and Restoration at Palo Alto, California. He and his team have demonstrated the rejuvenating effects of blood taken from young mice and given to older mice with Alzheimer’s-like disease.

The study results were published November 2016 in *JAMA Neurology*. 

Young mouse blood improves thinking and memory in older mice with induced Alzheimer’s-like disease, suggesting new avenues of research in drug development. (Photo ©iStock/JacobStudio)
The team, which included researchers from Stanford University and the University of California, San Francisco, was interested in discovering if “young blood” could improve deficits in thinking and memory in genetically modified old mice. To find out, they used transgenic mice that harbored a mutated version of the human amyloid precursor protein (APP) gene, which causes accumulation of beta-amyloid plaques in humans and cognitive defects in mice that are similar to those in Alzheimer’s disease.

Wyss-Coray’s team gave young blood harvested from two- to three-month-old mice to aged transgenic mice via plasma injection or through a surgical process called parabiosis — in which two mice are joined together surgically so that they share a single blood circulation. Following surgery, the researchers tested for overall health and recovery by monitoring weight, nesting behavior, grooming, and stress response in the mice.

The mice that had received young blood plasma injections were given several cognitive tests. The APP mice that had received young blood experienced a significant improvement in both working memory and associative memory.

The results of the study also showed that old APP mice that were paired to healthy young mice experienced an increase in synaptic and calcium-binding proteins after five weeks of shared circulation — proteins that are significantly reduced in humans who have Alzheimer’s disease. At the end of the study, the mice were restored to normal calcium-binding protein levels in the hippocampus, compared to the control group.

The researchers said the mice in this study showed improvement in memory without reducing the presence of beta-amyloid plaques. That could suggest a new avenue of drug research for Alzheimer’s patients. Several clinical trials of drugs that target beta-amyloid plaques have failed to show improvements in memory loss in humans.
‘Where’s My Choice?’ — Dr. Jack Tsai, an investigator with the VA New England Mental Illness Research, Education and Clinical Center (MIRECC) in West Haven, Connecticut, and his team interviewed a group of VA providers and Veterans about their experiences in providing or receiving care for hepatitis C through the Veteran’s Choice Program.

The study was published in the July 2017 issue of the journal Medical Care.

The Choice Program was created to give Veterans access to community-based care if they live more than 40 miles from a VA health care facility, or are unable to see a VA provider within 30 days. Specialty care for Veterans is also part of the program.

The program employs a system of third-party administrators to help manage the referral process so that Veterans can be treated for hepatitis C in the community. They also serve as the intermediary between VA providers, community physicians, and Veterans — helping with eligibility determination, scheduling visits, records exchange, claims submissions, and payment.
The investigators interviewed in-person or by phone 38 Veterans with hepatitis C and 10 VA health care providers who treat hepatitis C patients, at three different VA medical centers. Interview subjects were randomly chosen from a list of all hepatitis C patients who received their care from VA or the Choice Program.

The interviews were semi-structured and asked Veterans about their hepatitis C care, their experiences with the Choice Program, and perceived barriers to treatment. VA providers were asked about their experiences with the Choice Program, the hepatitis C treatment process, and funding shortages for hepatitis C medications.

Four themes were identified:

1. Difficulties in enrollment, support, and billing with third-party administrators.
2. Lack of choice about the location of hepatitis C care (VA providers vs. community providers).
3. Fragmented care that led to care coordination challenges between VA and community providers.
4. Uncertainty about referring care to community providers among VA providers.

“The Choice Program has the potential to increase Veteran access to HCV treatment, but Veterans and VA providers have described substantial problems in the initial years of the program,” the researchers wrote. “Enhancing care coordination, incorporating shared decision making, and establishing a wide network of community providers may be important areas for further development in designing community-based specialist services for needy Veterans.”

Veterans who seek health care through the Veteran Health Administration (VHA) have three times the rate of hepatitis C, compared with the general U.S. population (9.5 percent vs. 2.4 percent). The volume of patients who need care for hepatitis C and the cost for newer, but significantly more expensive, drugs to treat the virus have placed a greater demand on the VHA to provide and pay for appropriate care for this population.
Editorials from VA Research Scientists

“Medicare could learn a thing or two from VA: A well-functioning formulary lets Veterans get the medications they need with low copayments”


VA researcher Dr. Walid Gellad published an op-ed in the Wall Street Journal that proposed using the VA drug formulary as a national model to address runaway prescription drug prices in the United States. According to Gellad, who is co-director for the Center for Pharmaceutical Policy and Prescribing at the University of Pittsburgh and an investigator at the VA Center for Health Equity Research and Promotion (CHERP), the VA formulary system has much to commend it.

Given that VA employs a single electronic health record across all 152 health care centers, there is ease of communication and transparency for prescribing physicians and pharmacists. Because VA is able to negotiate drug prices, a course of treatment with a high-cost drug like Harvoni (used to treat hepatitis C) means a Veteran could pay just $33 out of pocket, not the roughly $6,000 that a patient using Medicare Part D could. And just as in most private insurance plans, VA patients are generally prescribed lower-cost medications first that are part of the VA formulary, but have the option to use a non-formulary drug if it is appropriate and recommended by their physician.

“Management of chronic pain in the aftermath of the opioid backlash”


The United States has reached a crisis state in opioid medication overuse and dependency. In response, the medical community has severely restricted prescribing guidelines for physicians who treat chronic pain, suggesting that only a limited number of opioids should be prescribed to patients. Dr. Kurt
Kroenke, a physician and VA researcher at the Center for Health Information and Communication (CHIC) in Indianapolis, said there still remains an urgent need to appropriately address pain management for the more than 25 million Americans who live with daily, chronic pain.

He and his colleague Dr. Andrea Cheville, a physician with the department of physical medicine and rehabilitation at the Mayo Clinic, have written an editorial in JAMA that highlights the necessity for continued research into pain management and the development of new treatments. The authors go on to caution that the use of opioid medications should not be eliminated entirely. There are select patients for whom opioid pain management works well, they said, given the limited effectiveness of analgesics like acetaminophen and NSAIDs for lower-back pain. Together with nondrug approaches like cognitive behavioral therapy, mindfulness or meditation, and yoga, opioids still have a place in the physician’s armament.

“Claudication: pay for structured exercise or go take a hike”


Claudication quite literally means “a pain in the leg” that happens during exercise when blood flow is obstructed to a lower limb. Often, it can be a symptom of peripheral artery disease (PAD), said Dr. Neal Sawlani, a cardiologist and researcher with the VA Boston Healthcare System. Together with his colleague Dr. Scott Kinlay, a VA investigator in the cardiology division at the West Roxbury Campus, Sawlani advised patients to “take a hike” when it comes to their leg pain, in an editorial published in the July issue of JACC.

He is actually being quite serious: When compared to endovascular surgery, structured exercise is an effective treatment for PAD, with equivalent patient outcomes. Sawlani cited a meta-analysis that compared the benefits of surgical intervention to structured exercise. When compared to the latter, surgery improved the ratio of blood pressure between the lower legs and
Editorials from VA Research Scientists

upper arms, he said, but did not improve walking impairment or the need for repeat surgery. However, structured exercise is rarely used in clinical practice because it is not covered by health insurance and many patients find it difficult to attend three classes a week. In lieu of a formal exercise program, Sawlani suggests a structured home-based exercise program could be used as an initial or adjunct therapy for PAD.

“Will strict limits on opioid prescription duration prevent addiction?”


In 2016, the Centers for Disease Control and Prevention published the “CDC Guideline for Prescribing Opioids for Chronic Pain,” in an attempt to address the growing problem of opioid dependence and addiction in the U.S. The guideline recommended that opioids prescribed for acute pain should be given for no more than seven days. In an editorial published in Substance Abuse, Dr. Stefan Kertesz, a primary care physician at the Birmingham VA Medical Center in Alabama, and his co-authors pointed out that an across-the-board restriction of opioid duration could harm patients with acute or chronic pain, and that available research data do not show such initiatives would prevent addiction.

In order to better define the correlation between initial opioid prescription and long-term use, Kertesz and his colleagues recommended assessing several factors. They said it is necessary to identify physician prescribing intent (short- vs. long-term) and factors that influence prescribing, like patient diagnosis and mental and/or physical comorbidities. They further caution that some regulatory efforts focused on prescription control have stigmatized pain patients while neglecting rising harm from heroin and fentanyl addiction.

*Listen as Dr. Kertesz* discusses the CDC’s latest guidelines on opioid prescribing in a VIDEO by WVTM Channel 13.
Awards & Career Milestones

2017 Middleton Awards go to antibiotic resistance, heart failure researchers

Dr. Robert A. Bonomo (left), a researcher at the Louis Stokes Cleveland VA Medical Center, and Dr. H. Kirk Hammond (right), a researcher with the VA San Diego Health Care System, have been awarded the 2017 William S. Middleton Award. 08-07-2017

Dr. Frank Lederle Receives 2017 Barnwell Award

Clinical research scientist Dr. Frank A. Lederle has been selected to receive the 2017 John B. Barnwell Award. It is the VA Clinical Science Research and Development Service’s highest honor. The award is given to senior VA investigators in recognition of outstanding contributions to clinical research that ultimately benefit the health of U.S. Veterans and others. 07-31-2017

VA Nobel laureate honored by Carnegie Foundation as ‘Great Immigrant’

Dr. Andrew V. Schally, Nobel laureate and VA distinguished medical research scientist, was recognized July 4, 2017, as a “Great Immigrant” by the Carnegie Corporation of New York. The tribute honors “outstanding naturalized U.S. citizens and their contributions to American society, culture, and economy.” 07-07-2017

VA research scientist receives prestigious Charles C. Shepard Science Award

Dr. Katie Suda and her colleagues have received the Centers for Disease Control and Prevention’s Charles C. Shepard Science Award for their research article on inappropriate antibiotic use in the U.S. 07-05-2017
Awards & Career Milestones

Internationally recognized VA investigator receives Under Secretary’s Award in Health Services Research

Dr. Eve A. Kerr, a physician researcher with the VA Ann Arbor Healthcare System, has received the 2016 Under Secretary’s Award for Outstanding Achievement in Health Services Research. It is the highest honor that VA’s Health Services Research and Development (HSR&D) bestows. 05-19-17

VA adaptive technology pioneer recognized for lifetime of public service

Senior VA research career scientist Dr. Rory A. Cooper, director of the Human Engineering Research Laboratories (HERL), was named one of 26 finalists for the 2017 Samuel J. Heyman Service to America Medals. The awards are given by the Partnership for Public Service to recognize exceptional federal employees who have distinguished themselves through singular efforts to improve the health and welfare of Americans. 05-11-17