



RESEARCH CURRENTS

Research News from the U.S. Department of Veterans Affairs



VA medical foster homes: What does the research show? 6

Photo by Robert Turtil

WHAT'S INSIDE

Fast Findings 2



Decline in antibiotic use for older Vets with urinary infections 9



Researchers piloting nerve stimulation for amputation pain 10



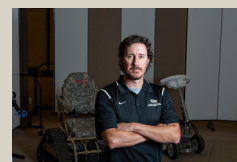
MVP study pinpoints genes tied to PTSD flashbacks 13



Gaining insight into Parkinson's 14



New VA program helping inventors turn ideas into viable products 16



VA Researchers Who Served: Josh Marino 20



Supported employment boosts functional outcomes in PTSD

Supported employment improves overall PTSD-related functioning, found a VA study. Individual Placement and Support is a VA program to help Veterans with PTSD find jobs. It uses individual-centered job development and employment specialists. Past studies have showed that IPS is more effective than transitional work programs at helping Veterans find sustained employment. The new study of 512 Veterans shows that IPS also improves PTSD-related functions in other areas. In addition to greater work functioning, Veterans given IPS had greater improvement in school, relationship, and lifestyle functioning, compared with those given transitional work. The results show that IPS has benefits beyond helping Veterans with PTSD find work. (*Psychiatric Rehabilitation Journal*, September 2019)




Photo: ©iStock/shironosov

Cover photo: A powered stair climber provided by VA helps James Burgess get to his second-floor bedroom in the home of registered nurse Anita Wilkens (background), who runs a VA medical foster home where she cares for Burgess and two other Veterans. Read more on page 6. (Photo by Robert Turtill)

The print edition of
VA Research Currents
 is published quarterly by:
VA Research Communications
U.S. Department of Veterans Affairs
 31 Hopkins Plaza, Ste. 102
 Baltimore, MD 21201
 443-759-3456
 varesearchcurrents@va.gov

Read the expanded online edition of
 VA Research Currents at www.research.va.gov

 [facebook.com/VAResearch](https://www.facebook.com/VAResearch)

 twitter.com/VAResearch

Editor/writer: Mitch Mirkin

Writers: Mike Richman, Tristan Horrom

Layout: Robert Williams

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.

VA

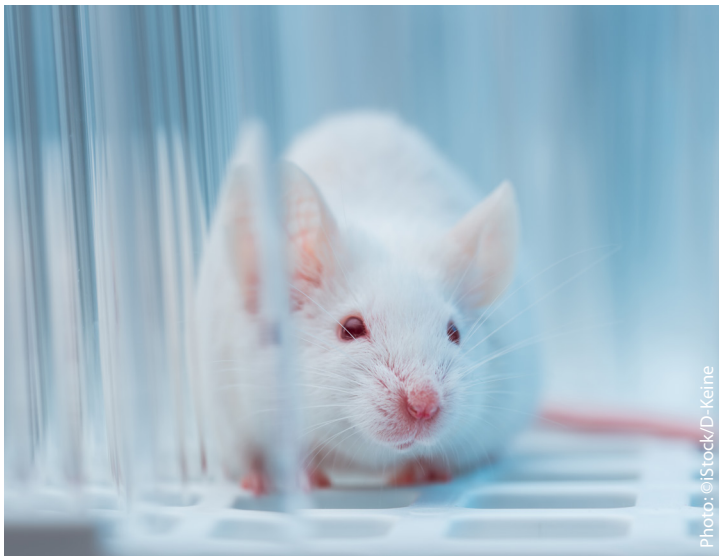


U.S. Department
of Veterans Affairs



Early deployment could increase suicide risk

Early first deployment may increase the risk of suicide attempt, according to a study of U.S. enlisted soldiers. VA San Diego researchers and colleagues looked at data on a large number of soldiers, including 1,700 who attempted suicide. Soldiers who deployed within 12 months of beginning their Army service were 70% more likely to attempt suicide, compared with soldiers who deployed later. The early deployers' risk was elevated both during and after deployment. More study is needed to understand how training and preparedness affect suicidal behavior, say the researchers. (*Suicide & Life-Threatening Behavior*, Sept. 23, 2019)



Mouse study: Potential stroke treatment effective only in males

In a mouse study, a potential stroke therapy was found to be effective in males but not females. A team of VA Portland Health Care System researchers and colleagues gave stroke-affected mice a drug called anti-PDL2. An inflammatory immune response can lead to brain tissue death during stroke. Anti-PDL2 potentially block this immune response. The team found that giving anti-PDL2 significantly reduced the amount of brain cell death, but only in male mice. It had no protective effects in female mice. The difference may be due to changes in cell production in the spleen that occurred in males but not females. The results suggest that anti-PDL2's potential as a stroke treatment may

be limited to men, say the researchers. (*Metabolic Brain Disease*, Aug. 13, 2019)



Many VA providers unaware of corticosteroid risks

Many providers are unaware of guidelines on corticosteroid use for COPD, according to a survey of VA primary care providers. Inhaled corticosteroids are recommended for chronic obstructive pulmonary disease (COPD) only in severe cases. Their use can lead to pneumonia, fracture risk, cataracts, and poor diabetes control. However, more than 50% of COPD patients in VA are prescribed the drugs. According to the survey, many providers are not aware of the current evidence and recommendations regarding corticosteroids.

For example, 46% were unaware of the risk of pneumonia. Participants said it was hard to keep up with current guidelines because of the broad scope of primary practice. Many were also reluctant to change prescriptions made by other providers. More efforts are needed to limit the use of this potentially harmful drug class in VA, say the researchers. (*Journal of General Internal Medicine*, Aug. 2019)



Menopause linked to more opioid prescribing

VA researchers in San Francisco looked at prescribing data from over 100,000 mid-life women Veterans with chronic pain. They found that menopause symptoms were linked with higher opioid prescribing. Women with symptoms had higher odds of being prescribed long-term opioids, high-dose opioids, and opioids co-prescribed with central nervous system depressants such as sedatives or muscle relaxants, compared with symptom-free women. Another study by the team found that women with menopause symptoms were twice as likely to have chronic pain

than those without symptoms. The researchers say more awareness of the links between menopause and pain could help curb risky prescribing. (*Journal of General Internal Medicine*, Aug. 14, 2019)



Telephone goal-setting may ease depression in diabetic patients

Telephone-delivered collaborative goal-setting can help reduce depression in patients with diabetes, found a Michael E. DeBakey VA Medical Center study. One in three patients with diabetes also have depression symptoms. Patients with both uncontrolled diabetes and clinical depression were enrolled in the Healthy Outcomes Through Patient Empowerment (HOPE) program. HOPE includes nine telephone sessions with health care professionals, focusing on collaborative goal-setting to improve health and behavior. Twelve months after participating in HOPE, patients had lower

depression symptom scores, compared with patients receiving usual care. HOPE did not lead to improved diabetes control, as measured by HbA1c levels. The results show that HOPE has potential to improve depression in patients with diabetes, say the researchers. (*JAMA Network Open*, Aug. 2, 2019)



After smokers quit, heart risk declines, but slowly

Former heavy smokers had lower risk of cardiovascular disease five years after quitting but were still at greater risk than people who had never smoked, in a study including VA Tennessee Valley Healthcare System researchers. The study followed nearly 9,000 people for several decades. Heavy smokers who had quit about half the risk of cardiovascular disease five years after they stopped smoking, compared with current smokers. However, they were still at significantly

higher risk than people who had never smoked. Former smokers had about the same cardiovascular risk as nonsmokers 10 to 15 years after quitting. The results show that while quitting smoking lowers risk of cardiovascular disease, it may take a decade or more for the risk caused by smoking to totally decline. (*JAMA*, Aug. 20, 2019)



Registered nurse Anita Wilkens has turned her home into a VA medical foster home, in which she provides 24/7 skilled care for James Burgess and two other Veterans.

No place like home: Studies on VA medical foster homes show good outcomes for Vets

VA medical foster homes are a sensible way to deliver 24/7 long-term care for Veterans, says Dr. Cari Levy of the Denver VA Medical Center. Her research has shown cost and mortality benefits, compared with conventional nursing home care.

Having served stateside as an Army medic during the Vietnam era, James Burgess knows a thing or two about caring for others. But nowadays, the 79-year-old stroke survivor is in need of care himself.

Many older people with Burgess' medical needs would end up in a nursing home. Burgess and his daughter opted, instead, for him to receive long-term care in a VA medical foster home.

JB, as he likes to be known, lives in the cozy, well-maintained home of registered nurse Anita Wilkens. He occupies one of three upstairs bedrooms in the compact townhouse, on a quiet suburban street outside of Baltimore. The other bedrooms house two other Veterans, each with his own health care needs.

JB, who ran a plumbing business for more than three decades and drove a cab after he retired, seems content, despite his health challenges. On a recent summer day, he was getting ready to go out on a fishing trip with a VA

Photo by Robert Turtill



recreational therapist and a few other Veterans. He enjoys playing with Wilkens' toy poodle, Wiggles, and watching sports on the large-screen TV in the living room. Two days a week, he goes to a VA-contracted adult day health center, where he likes to play cards and checkers.

If there's something on the menu not to his liking, that can be easily adjusted, more so than in a conventional nursing home. Wilkens says she tries to arrange it so her three residents eat together whenever possible. "That way they can talk with each other."

Research backs cost-effectiveness, quality

As typical as JB's experiences might be in the VA medical foster home program, there's more than anecdotal evidence backing the effectiveness of this model of care.

The program is a sensible way to deliver 24/7 long-term care, says Dr. Cari Levy, who has published studies on it. Levy heads palliative care at the Denver VA Medical Center and is the associate director of the Center of Innovation for Veteran-Centered and Value-Driven Research.

For example, a study her group published earlier this year found medical foster homes to be less costly than traditional nursing home care. The difference was

about \$71 per day per Veteran. Even when the monthly fees paid by Veterans were factored in, the foster home model was no more expensive.

The study also showed a trend toward better survival among Vets living in such homes, relative to Vets with similar health and demographic profiles living in nursing homes.

Her team concluded that "efforts to expand the medical foster home program appear warranted given that the program adds to the array of long-term-care options for persons in need of nursing home care while achieving cost-savings and a mortality advantage when compared to traditional community nursing home care."

Program linked to VA Home-Based Primary Care

The program has been around since 2008. Levy says that to understand how VA medical foster homes work, you first have to understand VA's home-based primary care program, or HBPC. The two programs are closely linked.

"HBPC is essentially for Veterans who are too sick to go to clinic," she says. "Clinic can be a burdensome activity because of functional disability or just the physical and medical issues that are going on. It can be quite taxing—being driven to the clinic, waiting for appointments, the drive back home.

"HBPC wraps all of the primary care around the Veteran in their own home. It involves all the disciplines that are needed. The idea is to bring most of that primary care to the home. Technology can also help—a tablet, phone calls."

She calls it "Cadillac care" because of the quality. "These are dedicated, highly qualified clinicians coming to your home."

With the medical foster home, she says, "instead of bringing all of that care to the Veteran's home, we're bringing it to a foster home."

"There was a very consistent theme that they [the Veterans] were part of the family."



were at dinner. They were at breakfast. They kids were in the household and the dog was there. All the events that happened with the family were involving the Veterans. There were all the lovely conversations. The highs and lows that happened with families were happening for these Veterans because they were in the home.”

The caregivers in the MFH program get paid—it’s a fulltime job for the primary caregiver, in fact—but they also do it as a calling, says Trimble.

“The money helps, but this is not easy work. They enjoy caring for people, and for Veterans

especially. One of our caregiver teams, it’s a man and a woman, and the gentleman is a Korean War Veteran wanting to give back and take care of his fellow Veterans.”

Wilkins, for her part, says the MFH program is an extension of her nursing career. “I worked with Alzheimer’s patients. I was in geriatrics my whole career. Taking care of people is something I like doing.”

Ask JB how he came to live at Wilkens’ home, and he’ll tell you how his daughter and her daughter grew up together and remained friends. There was already a family bond.

“I took care of both my parents before they passed away,” shares Wilkins. “His daughter called me and said, ‘I watched how you took care of your Dad, and I was wondering if you could take care of mine.’ That made me feel real good.”

Read more at www.research.va.gov/currents ★

Foster caregivers approved by VA can care for up to three individuals in their home. No more. The goal is to maintain a homelike atmosphere.

VA social worker Nicole Trimble oversees the MFH in six Maryland counties and Baltimore City.

She emphasizes that “you’re never going to have any more than three residents in the home, really keeping with the mission of the program, which is to provide a homelike atmosphere where you’re getting the extensive care you need to maintain yourself in the community, versus being in a nursing home or in a more institutionalized assisted-living facility.”

Foster caregivers: It's a calling

Levy's qualitative studies, which have included interviews at several MFHs with residents and caregivers, paint a picture of warm, family-style care.

“There was a very consistent theme that they [the Veterans] were part of the family,” says Levy. “They

Study finds decline in antibiotic use for older Veterans with urinary infections—a positive result from stewardship efforts

A new study finds a significant drop in antibiotic use at VA community living centers treating older Veterans with urinary tract infections—a positive sign in efforts to limit the health problems that can result from the improper use of antibiotics.

The findings appear in the October 2019 edition of the journal *Infection Control & Hospital Epidemiology*.

The researchers found that much of the decline in antibiotics stemmed from a reduced use of fluoroquinolones during the five-year study period. The fluoroquinolone class of antibiotics is often used to treat illnesses, such as respiratory and urinary tract infections (UTIs), and includes agents like ciprofloxacin (commercial name Cipro) and levofloxacin (commercial name Levaquin).

“Antibiotic stewardship efforts across VA community living centers should be applauded and should continue to be an ongoing effort,” the researchers write. “Antibiotic stewardship can be used to reduce inappropriate use of antibiotics and ultimately improve the care of residents with UTIs.” Antibiotic stewardship also refers to efforts to promote the right antibiotic, dose, and duration of use.

Dr. Haley Appaneal, a clinician scientist at the Providence VA Medical Center in Rhode Island, led the study. With expertise in infectious diseases, antibiotic stewardship, and pharmacy practice, she’s interested in improving the quality of Veteran care at community living centers through a reduction in inappropriate antibiotic use. Such facilities, which are similar to nursing homes, provide services to Veterans who need



A VA study has documented a drop in the use of antibiotics to treat urinary tract infections at VA community living centers.

a medically skilled environment to assist with short- and long-term stays.

Antibiotics could potentially do more harm than good

The findings in the study are important, Appaneal says, because antibiotics are among the most commonly used drugs at all VA and non-VA long-term care facilities, they are often used for urinary tract infections, and they are often used the wrong way.

“All antibiotic use, both appropriate and inappropriate, can lead to problems,” says Appaneal, who is also an adjunct assistant professor at the University of Rhode Island. “However, when antibiotics are used inappropriately, they may cause more harm than good. Problems that antibiotics can lead to include adverse drug effects, allergic reactions, serious diarrhea due to a bacteria known as *Clostridium difficile* or *C. diff*, hospitalizations, and an increased risk of infections because of bacteria that resist the effects of antibiotics and are harder to treat.”

Read more at www.research.va.gov/currents ★



A Veteran who uses a lower-limb prosthesis takes part in the 2016 National Veterans Summer Sports Clinic.

(VA photo)

Researchers piloting nerve stimulation for amputation pain

VA researchers are testing whether nerve stimulation can help Veterans with post-amputation pain. A small pilot study involving 16 Veterans is now underway.

Researchers at the Hunter Holmes McGuire VA Medical Center in Richmond, Virginia, are testing whether nerve stimulation can help Veterans with post-amputation pain. A small pilot study involving 16 Veterans is now underway.

Limb loss is often associated with post-amputation pain that can be challenging to treat and may require the use of opioids, painkilling drugs that can become addictive.

The discomfort could be in the form of acute pain, which is sudden and typically lasts for up to three months post-surgery, or chronic pain, which can persist for six months or more.

Advances in neuromodulation—which involves implantable and non-implantable technologies that impact the transfer of information such as pain signals through the nervous system—have led to the development of a peripheral nerve stimulation system (PNS) that has shown promising results for chronic post-amputation pain. Studies involving the minimally invasive Sprint PNS system have found that it reduced residual (stump) pain, which is at or just above the incision site, and phantom pain, which is pain that originates in the brain and spinal cord and feels like it's from a limb that was removed.

In peripheral nerve stimulation, a form of neuro-modulation, electrodes are placed along peripheral nerves, which are located beyond the brain or spinal cord, to control pain. An electrical current sent to the nerves tricks the brain into turning off or reducing painful signals.

What about the acute post-amputation period? Dr. Denise Lester, an anesthesiologist at the Richmond VA, is exploring that question. She's leading a pilot study on the feasibility and effects of the Sprint PNS system in the acute pain period following amputation. It's the first study of its kind, she says.

The U.S. Food and Drug Administration (FDA) has approved the Sprint PNS device for treating acute and chronic pain.

"Currently, there's no convincing evidence regarding the role of PNS in the acute post-amputation period," says Lester, who's also an assistant professor at Virginia Commonwealth University. "That may be a critical time to control pain, as those with high pain appear to be at greater risk of developing persistent post-procedural pain."

A prosthesis can possibly be fitted faster on patients with little or no pain—maybe about two months after amputation if all goes well, she notes.

"Yes, definitely," she says. "Earlier and better and worn more often, more and more hours a day. One of the biggest barriers to prosthesis fitting and use is pain."

"The problem is many of these patients can't get pain control," Lester adds. "So you're looking at the possibility that the pain can lead to opioid addiction, disability, divorce, or suicide. All of these possibilities are very concerning. We want to help Veterans avoid them within our community."

A 'bridge' between hospital and home

Lester is pursuing her pilot study knowing that

post-amputation pain lacks what she calls a "non-opioid, non-local anesthetic, non-destructive option." The latter refers to the possibility of damaging nerves, for instance, by treating the pain with heat, ice, or burning chemicals. She also understands that prior to the FDA's approval of Sprint PNS for acute pain, patients would be discharged from the hospital with nothing but opioids or a local anesthetic catheter, which brings the risk of infection.

She explains that the Sprint PNS technology can thus be a "bridge" between hospital pain control methods and the home. "That means patients would get amputated in the hospital with excellent pain care," she says. "They would feel great but would go home with just opioids. They'd be in severe pain for up to months until the surgical site heals or for years and years later. There'd be no bridge in pain management

between the acute post-surgical time and the period long after surgery. So this 60-day device can be a bridge between great hospital care and pain control needs that occur later on."

Lester was also curious to see if the Sprint PNS device, when applied at the time of amputation, would lead to earlier fitting of the prosthesis. She wanted to learn, too, if it would help with wound healing, minimize the potential for pain in the transition from acute to chronic stages, and decrease other possible post-operative problems of pain management, such as opioid addiction and catheter infection.

Results 'very encouraging' thus far

Lester's pilot study includes 16 Veterans who have undergone non-traumatic lower-limb amputation above the knee (transfemoral) or below the knee (transtibial). The amputations were needed because of such conditions as critical limb ischemia, a severe blockage in the arteries of the lower extremities that reduces blood flow; Charcot joint disease, a progressive

"The pain can lead to opioid addiction, disability, divorce, or suicide. All of these possibilities are very concerning. We want to help Veterans avoid them..."

Continued on next page

degeneration of a weight-bearing joint; or gangrene, which occurs when tissue dies due to a loss of blood supply.

The participants have been randomized evenly, with patients in the treatment group undergoing placement of the Sprint PNS system within seven days of surgery. Patients in both groups are eligible to be treated with opioids and non-pharmacologic pain therapies, such as acupuncture, ice, heat, a massage, mindfulness, or meditation. They are evaluated weekly for the first eight weeks post-amputation, then at three, six and 12 months.

Lester and her team have collected three months of data thus far, with evaluations of the average percent reductions in stump pain and phantom pain at the 60-day mark. She says the results have been “very encouraging.” The Sprint PNS device has helped reduce both stump and phantom pain in the treatment group, with the difference in average pain relief between both cohorts being the largest for phantom pain.

Pain levels are still being periodically assessed. The study team will have evaluated all of the participants for one year by March 2020.

Read more at www.research.va.gov/currents ★

For an overview of the latest VA research on high-priority topics affecting Veterans' health, visit www.research.va.gov/topics/default.cfm.

VA research on POSTTRAUMATIC STRESS DISORDER (PTSD)

In earlier wars, it was called "soldier's heart," "shell shock," or "combat fatigue." Today, clinicians recognize the issues described by each of these terms as a distinct medical condition called posttraumatic stress disorder, or PTSD.

ABOUT PTSD

- PTSD can occur after a traumatic event like combat, assault, or disaster. While stress is common after a trauma, for those with PTSD reactions such as reliving an event in their mind and feeling distant or angry do not go away over time, and can even get worse.
- While PTSD can affect people who have experienced a wide range of life-threatening events, in Veterans the condition is commonly associated with combat trauma. It has taken a significant toll on many war Veterans who currently use VA health care including Iraq and Afghanistan Veterans. Military sexual assault or harassment can also lead to PTSD.
- The disorder can lead to distressing and persistent symptoms, including re-experiencing the trauma through flashbacks or nightmares, emotional numbness, insomnia, relationship problems, sudden anger and drug and alcohol abuse. Recently, reckless and self-destructive behavior has been added as a PTSD symptom.

VA RESEARCH ON PTSD: OVERVIEW

- VA has a continuing commitment to fund efforts to understand, prevent, and treat PTSD. The wide-ranging nature of current PTSD research includes studies of Veterans at large, subgroups of Veterans, families, and couples. Veterans of all ages are included in these studies.
- Ongoing studies range from investigations of the genetic or biochemical foundations of the disorder to evaluations of new or existing treatments.
- VA's [National Center for PTSD](#) (NCPD) is a world leader in research and education programs focusing on PTSD and other psychological and mental consequences of traumatic stress. It currently consists of seven VA academic centers of excellence across the United States, with headquarters in White River Junction, Vermont.
- VA's [National PTSD Brain Bank](#) is a brain tissue repository that supports research on the causes, progression, and treatment of PTSD. The bank is responsible for tissue acquisition and preparation, diagnostic assessment, and storage. Most of the brains stored in the bank are from people who died of PTSD. Others are from donors who had major depressive disorders. Other brains are from healthy controls. The goal is to help to pinpoint how PTSD affects brain structure and function.
- In 2013, VA and the Department of Defense (DoD) announced that the two departments together were committing more than \$100 million to fund [top new](#).

SELECTED MILESTONES AND MAJOR EVENTS

- 1989 - Created the [National Center for PTSD](#).
- 2007 - [Confirmed](#) the value of prolonged exposure therapy.
- 2013 - Funded, along with the DoD, two [contracts](#) to improve treatment for PTSD and mTBI.
- 2014 - [Found](#) that cognitive processing therapy by individualized tailoring is as effective for PTSD as in-person therapy.
- 2014 - [Found](#) that Veterans who sought and received care soon after their service had lower rates of PTSD than those who waited to get treatment.
- 2016 - Announced the [PTSD Exposure and Coping Initiative](#) to foster work on identifying, testing, and confirming the most effective PTSD medications for Veterans.

(Continued on back)

VA research on TRAUMATIC BRAIN INJURY

VA research related to TBI is wide-ranging. Among the goals of VA researchers working in this field are to shed light on brain changes in TBI, improve screening methods and refine tools for diagnosing the condition, and develop ways to treat brain injury or limit its severity when it first occurs.

ABOUT TRAUMATIC BRAIN INJURY

- The CDC defines a TBI as "a disruption in the normal function of the brain that can be caused by a bump, blow, or jolt to the head, or penetrating brain injury."
- After a TBI, the person may experience a change in consciousness that can range from becoming dazed and confused to loss of consciousness. The person may also have a loss of memory for the time immediately before or after the injury.
- The DoD estimates that 22 percent of all combat casualties from Iraq and Afghanistan are brain injuries. TBI is a significant cause of disability outside of military settings, most often as the result of assaults, falls, automobile accidents, or sports injuries.
- TBI can include a range of consequences, from headaches, irritability, and sleep disorders to memory problems, slower thinking, and depression. These symptoms often lead to long-term mental and physical health problems that impair Veterans' employment and family relationships, and their reintegration into their communities.
- While most people with mild TBI have symptoms that resolve within hours, days, or weeks, a minority may experience persistent symptoms that last for several

VA RESEARCH ON TRAUMATIC BRAIN INJURY: OVERVIEW

- Beyond studying how to better treat TBI, researchers are also developing improved methods to assess the effectiveness of treatments and learning the best ways to help family members cope with the effects of TBI and support their loved ones.
- VA's [TBI Model System](#) (TBMMS) is a longitudinal multisite research program that examines the recovery course and outcomes of Veterans and active-duty service members with TBI. The goal of the system is to conduct research that contributes to evidence-based rehabilitation interventions and practice guidelines that improve the lives of people with TBI.
- VA's [Translational Research Center for TBI and Stress Disorders](#) (TRACTS) conducts studies to understand the complex changes in the brain, thinking, and psychological well-being that result from TBI and posttraumatic stress disorder (PTSD). These studies will lead to more understanding and better treatment options for returning Veterans with TBI and PTSD.
- The [Chronic Effects of Neurotrauma Consortium](#) (CENC) serves as a comprehensive research network for DoD and VA that focuses on the long-term effects of combat and military-related TBI. The CENC is designed to conduct research that provides clinically relevant answers and interventions for service members and Veterans and to develop long-term solutions to the chronic effects of TBI.

SELECTED MILESTONES AND MAJOR EVENTS

- 2008 - Established a [Brain Bank](#) to collect and study post-mortem human brain and spinal cord tissue to better understand the effects of trauma on the human nervous system.
- VA's [TBI Model System](#) (TBMMS) is a longitudinal multisite research program that examines the recovery course and outcomes of Veterans and active-duty service members with TBI. The goal of the system is to conduct research that contributes to evidence-based rehabilitation interventions and practice guidelines that improve the lives of people with TBI.
- VA's [Translational Research Center for TBI and Stress Disorders](#) (TRACTS) conducts studies to understand the complex changes in the brain, thinking, and psychological well-being that result from TBI and posttraumatic stress disorder (PTSD). These studies will lead to more understanding and better treatment options for returning Veterans with TBI and PTSD.

(Continued on back)

VA research on MULTIPLE SCLEROSIS

Multiple sclerosis is a complex neurologic disease that affects the central nervous system, including the brain, spinal cord, and vision pathways.

ABOUT MULTIPLE SCLEROSIS

- In MS, the immune system attacks the myelin sheath, the fatty tissue that surrounds and protects nerve fibers, as well as the nerve fibers themselves. Damage from these attacks is called demyelination. When any part of the myelin sheath or nerve fiber is damaged or destroyed, nerve impulses traveling to and from the brain and spinal cord are distorted and interrupted, causing a wide variety of symptoms.
- Sometimes the myelin can repair itself and the MS symptoms go away after the immune attack. Over time, however, the myelin and underlying nerve fibers cannot recover and suffer permanent damage. The cause of MS is currently unknown.
- Symptoms vary depending on the location of the lesions in the brain and spinal cord. They may include tingling, numbness, painful sensations, slurred speech, and blurred or double vision. Some people experience muscle weakness, poor balance, poor coordination, muscle tightness or spasticity, tremor, or temporary or permanent paralysis. Problems with bladder, bowel, sexual function, or mood are also very common.

VA RESEARCH ON MULTIPLE SCLEROSIS: OVERVIEW

- Fatigue is a major concern for most people with MS, as are challenges with memory, attention, and concentration. Symptoms may come and go, appear in any combination, and be mild, moderate, or severe.
- Many symptoms—such as fatigue, insomnia, mood, cognition, mobility, spasticity, and bowel function—are very responsive to self-care lifestyle changes such as increased activity. In addition, medication therapies and other interventions are available to help manage MS symptoms.
- VA has also established a national integrated network of dedicated MS health care professionals for care and referrals within the VA health care system.

VA RESEARCH ON MULTIPLE SCLEROSIS: OVERVIEW

- Medical care for Veterans with MS, whether or not their illness was service-connected, can include disease-modifying therapies, other medications, physical and occupational therapy, and other health care services and medical equipment.
- Current VA research includes investigations into the biology of MS, targets for interventions, impacts of spasticity, fatigue and fall management programs, health services and the care delivery to evaluate and improve mood

SELECTED MILESTONES AND MAJOR EVENTS

- 2003 - Founded the [Multiple Sclerosis Center of Excellence](#).
- 2014 - [Determined](#) that military deployment to the first Gulf War was not a risk factor for developing MS.
- 2017 - [Discovered](#) that high dosage of folic acid can significantly slow brain atrophy, reduce falls, and improve walking times in some MS patients.

(Continued on back)



Photo for illustrative purposes only. ©iStock/tommaso79

In PTSD, re-experiencing refers to intrusive thoughts, nightmares, and flashbacks of the traumatic event.

A VA Million Veteran Program study has identified multiple locations in the human genome related to the risk of re-experiencing traumatic memories, the most distinctive symptom of posttraumatic stress disorder. Researchers from the VA Connecticut Healthcare System and Yale University School of Medicine and the VA San Diego Healthcare System and University of California San Diego collaborated with colleagues on this large genome-wide association study of more than 165,000 Veterans.

In addition to providing valuable information on genetic factors that may put people at risk for PTSD, the study also demonstrates “the immediate utility of the MVP sample for disorders prevalent in U.S. Veterans,” say the researchers.

The results appear online July 29, 2019, in the journal *Nature Neuroscience*.

Flashbacks, nightmares among ‘re-experiencing’ symptoms

PTSD is usually considered to have three main clusters of symptoms: re-experiencing, avoidance, and hyperarousal. Avoidance and hyperarousal are common to other anxiety conditions as well, but re-experiencing is largely unique to PTSD. Re-experiencing refers to intrusive thoughts, nightmares, and flashbacks of the traumatic event.

MVP study identifies genes linked to re-experiencing symptoms in PTSD

Using the vast genetic and health record data available through MVP, the research team set out to identify gene variants that increase the likelihood of PTSD re-experiencing. This study was considerably more powerful than previous PTSD genome-wide association studies (studies that look at the genomes of a large group of people for connections between shared gene variations and medical conditions or other traits) because of a larger sample size.

The researchers compared the genomes of 146,660 white Veterans and 19,983 black Veterans who had volunteered for MVP.

The study revealed eight separate regions in the genome associated with re-experiencing symptoms among the white Veterans. It did not show any significant regions for black Veterans, considered separately as a group, because there were far fewer black study participants available, making it harder to draw conclusions. The association between PTSD re-experiencing and common variants in three of these genome regions were highly significant: gene *CAMKV*, a region near genes *KANSL1* and *CRHR1*, and gene *TCF4*.

Key results were replicated using the UK Biobank sample, which has about 500,000 participants.

The results also showed genetic overlap between PTSD and many other psychiatric, behavioral, and medical conditions. Two genes previously associated with schizophrenia and bipolar disorder were found to be linked to re-experiencing in PTSD. This could mean that the hallucinations experienced in schizophrenia may share common biochemical pathways with the nightmares and flashbacks of people with PTSD, say the researchers.

Read more at www.research.va.gov/currents ★



Drs. Cameron McIntyre (center) and Aasef Shaikh (right) study brain pathways through the HoloLens with neurology colleague Dr. Camilla Kilbane. The photo shows what is seen through the HoloLens glasses.

Gaining insight into Parkinson's

A set of research projects at the Cleveland FES Center is using deep brain stimulation, virtual reality, and other technology to better understand how Parkinson's disease affects walking and balance.

During his training as a neuroscientist, Dr. Aasef Shaikh studied eye movement and the vestibular system—the sensory system that contributes to balance and spatial orientation. Afterward, Shaikh wanted to apply what he learned to complex movement disorders. He decided to focus his research on Parkinson's disease, a neurodegenerative disorder that causes gait and balance impairment. An estimated 1 million people in the U.S. have Parkinson's disease, with an additional 50,000 people diagnosed each year.

As an investigator at the Cleveland FES Center—a consortium of the Louis Stokes Cleveland VA Medical Center and several partner organizations— Shaikh is now involved in three research projects related to Parkinson's. In broad strokes, they examine how patients perceive the environment in which they walk, how they perceive their own motion through an environment, and how they navigate any given environment.

All three projects use high-frequency deep brain stimulation (DBS). In 2016, Shaikh teamed with Dr. Cameron McIntyre, a fellow investigator and associate director of industry relations at the FES Center. Shaikh's experience as a

vestibular and eye movement scientist, combined with McIntyre's expertise in DBS, provided "the perfect model" to study gait impairments in participants with Parkinson's disease, says Shaikh.

"Through our research, we are beginning to understand more and more about which particular pathways and structures are responsible for perception of motion and heading perception in humans," says Shaikh, who is a neurologist at both the Cleveland VA and University Hospitals Cleveland Medical Center. "In the future, we hope the much broader application of our work beyond Parkinson's will be to use similar concepts and strategies to treat balance function or navigational problems in patients with any condition."

Exploring why Parkinson's patients veer to the side

One project focuses on motion perception. "We are studying how participants with Parkinson's perceive their own directional heading—whether they are going straight ahead or veering to the side," says Shaikh. "In addition, we're also interested in understanding why

"We will have three separate pieces of information, and in the future we will be able to fuse them to get the big picture about a patient."

they veer and which particular neural pathways are involved in perception of their self-motion." Using that information, the researchers hope to discover how to tweak those pathways with DBS to eliminate veering.

Shaikh's team is conducting behavioral experiments in the lab with motion simulators like the Moog Chair. These are similar to those used by NASA to train astronauts. In the pilot study, Parkinson's patients with DBS implantations are placed in

the simulator, where experiments are performed with the DBS turned on and off to determine if it makes a difference in perception of motion. That information is then combined with MRI images of the participants' brains, and with bioelectric field stimulation models created by McIntyre.

"Together, this gives us a sort of 3D picture of everything involved in the process," says Shaikh. "That allows us to understand how participants with Parkinson's perceive their own directional heading." Shaikh and McIntyre can view these models using the HoloLens. The device is a self-contained, holographic computer that allows users to interact with digital content and holograms in the environment around them.

"You see holographic objects in the context of the real world as opposed to virtual reality, where you are 100 percent immersed in a digital environment," says McIntyre. "When you are able to still see the real world, you can see people's faces and communicate with people around you." He says this makes HoloLens technology an ideal teaching tool, particularly for understanding something as intricate as the human brain and its exquisite network of interconnected neurons.

Read more at www.research.va.gov/currents ★



Dr. Fatema Ghasia (right), an ophthalmologist and eye surgeon, is leading a study on the role of abnormal brain circuits in eye misalignment and lazy eye in Parkinson's. Here she works with medical student Sarah Kang.



Respiratory therapist Catherine Abee displays her invention, the heat-enhanced pulse oximeter, while in the company of colleagues at the VA Pittsburgh Healthcare System.

New VA program helping inventors turn ideas into viable products

The Technology Transfer Assistance Project (TTAP), part of the VA Technology Transfer Program, aims to bring worthy VA discoveries closer to public use.

The idea was fresh in the mind of respiratory therapist Catherine Abee when she joined the VA Pittsburgh Healthcare System in 2008.

Abee envisioned a device that would warm an area on the body of patients being tested for the amount of oxygen in their bloodstream. The human body requires and regulates a specific balance of oxygen in the blood. Warming the measurement site, she thought, would improve blood flow and thus provide a more accurate reading. The device, a heat-enhanced pulse oximeter, could be attached to one's fingers, forehead, foot, ears, or toes.

While working with colleagues to make the concept a reality, Abee came in contact with VA's Technology Transfer Program, which assists researchers and other VA employees by licensing protected VA technologies to companies able to make and sell the inventions to the public. The program's lawyers help patent VA's inventions, which gives the owner the right to prevent others from making, selling, using, and importing the patented item or method. A U.S. patent on Abee's invention

was issued in 2017. Canadian and European patents are pending.

In 2018, Abee's invention was adopted as one of the seven first-year products in the newly formed Technology Transfer Assistance Project (TTAP), an initiative of the Technology Transfer Program. TTAP aims to bring worthy VA discoveries closer to public use by supporting the creation of a working prototype and by consulting on pathways for commercialization. TTAP funded its main partner, the Human Engineering Research Laboratories (HERL), a large VA facility that does research, development, and testing on a myriad of technologies, to build a second-generation prototype of Abee's device.

HERL engineers have since produced a viable device that's ready for licensing. Thus far, two companies have approached VA with an interest in licensing it, says Dr. John Kaplan, director of the Technology Transfer Program.

"Once HERL was brought on board, I met with them to discuss what I wanted the pulse oximeter to look like and what was needed to make it perfect," Abee says. "They developed a better heat source that will plateau and maintain a warmth for hopefully eight hours.

Thus, in a clinical care setting for long-term patients, clinicians know that one probe may last eight hours, so that would be one per shift. That means the product is economically sound. When HERL had a prototype ready, we met again and discussed any changes I wanted. They also adapted their equipment to keep the packaging in an enclosed environment to make sure the heat source was not activated."

Abee is fortunate that she's had TTAP and HERL to help bring her invention to the cusp of the marketplace. Over the years, many VA scientists, clinicians, and researchers have conceived of ideas for technologies that can help Veterans and others with their needs. But they've often lacked the means and guidance to convert

those ideas into products with commercial potential.

That's why TTAP was formed. The VA initiative takes bench-top or early prototype inventions and develops them—in collaboration with the inventor—so the product will be more attractive for licensing. The VA researcher is named on the patent application as the inventor, as is the case with Abee and the heat-enhanced pulse oximeter, giving more exposure to VA and its inventors. If the product is licensed to a company, VA gets royalties on the sales and possibly preferred pricing.

"Abee created a working model using commercially available components, with the idea that adding heat to the patient's finger would thereby produce an improved blood oxygen reading," says attorney David Marks, a VA technology transfer specialist who has worked with Abee on patenting her product. "Her original idea was the basis for the patent application. But HERL under TTAP has tried to develop a second-generation device that would be more appealing to a manufacturer to license."

"The Technology Transfer Program and TTAP...worked diligently to guide me and to make sure I've followed all of the steps necessary to reach the point where we are."

Three TTAP projects have received patents

Abee's device is one of three first-year TTAP projects that has received a patent. The other two are the cord caddy,

which prevents the tangling of a patient's multiple IV (intravenous) lines and can be used during surgery and in other phases of a patient's hospital stay; and the RX-1 label applicator, which attaches labels to pharmaceutical packages of various sizes and shapes faster than a person can, thus increasing efficiency in a pharmacy dispensary.

Patent applications are pending on three of the other technologies:

- sterile-tip catheter: keeps the tip of a scope protected when it goes into a person's lung, improving the chances of getting a good sample for diagnosing pneumonia.
- hand pedal: a hand-powered pedal for people with lower-limb impairment; it can be used with

Continued on next page

equipment, such as a stationary bike, to promote arm exercise and is also useful for people with partial paralysis and those who are temporarily immobilized and are trying to rehabilitate from an injury.

- prosthetic hook mouse: a modified computer mouse for people with an upper-limb, hook-type prostheses; it's made to permit easier movement of the mouse and to improve clicking in the desired position on a computer screen.

The other first-year TTAP project is the oxygen burn-back valve cover, a thermal fuse cover that is designed to reduce the risk of a fire in and around an oxygen gas line.

“The Technology Transfer Program and TTAP have helped me take my idea from a possibility and create a device that has been needed since pulse oximetry began in 1972,” Abee says. “Without those folks, there would be no heated pulse ox probe ready to market. They’ve worked diligently to guide me and to make sure I’ve followed all of the steps necessary to reach the point where we are. I’ve been working on this for a decade, and things have progressed amazingly over the past year.”

The thinking behind the creation of TTAP is that if a working prototype or a second- or third-generation device can be developed, instead of just something on paper, “we could have a better chance of gaining more

interest from companies in licensing the technology,” Kaplan says.

“VA does a lot of research and doesn’t do too much development,” he adds. “So this is getting at more of the developmental side. It’s a team effort to prepare the product for patenting. The HERL engineers and scientists, the original inventor, and the technology transfer specialists work together to refine the invention in order to build the best prototype and submit the strongest patent application to the U.S. Patent and Trademark Office.”

U.S. government officials can issue a patent before a working prototype is created. But applying for a patent after the prototype is completed can get the inventor a stronger one that can withstand scrutiny from potential competitors, Kaplan notes.

Technologies were once 'back of the envelope' concepts

HERL, a collaborative effort between VA Pittsburgh and the University of Pittsburgh, has a strong team of engineers and perhaps the best fabrication and standards testing facilities in VA. HERL's projects include wheelchair technologies, advanced prostheses, and other innovative systems that improve the quality of life for people with disabilities, such as lost limbs and spinal injuries. The facility is home to the VA Center for Wheelchairs and Associated Rehabilitation Engineering and is based in a state-of-the-art research and development park that includes government, academic, and private industry innovators.

HERL director Dr. Rory Cooper notes that most of the first-year TTAP products were just “back-of-the-envelope concepts” before they became part of the program.

“Now, they’re real working prototypes,” Cooper says. “You can’t really provide a Veteran an envelope, and it’s hard to license something that’s just more or less a paper concept. So we made them real.”

Cooper, who has a doctorate in electrical and computer engineering with a concentration in bioengineering, has been credited with at least 25 patents that have advanced assistive technology. He and other HERL engineers have developed each of the seven first-year



Dr. Rory Cooper, director of the Human Engineering Research Laboratories, displays a couple of the products being developed through the Technology Transfer Assistance Project.

TTAP technologies into a more refined prototype. He played a role in designing two of the technologies: the prosthetic hook mouse and the hand pedal. They are the only first-year TTAP innovations being manufactured at HERL.

The other five projects were invented by researchers at VA medical centers and are more “orphan” products, Cooper says, pointing out that they aren’t similar to the work that HERL normally does. “We took them in because they were what Dr. Kaplan’s group identified as areas of greatest need,” he says. Those five devices are in the pipeline to be marketed to companies via TechLink. The non-federal entity, in partnership with VA Tech Transfer and its Department of Defense (DOD) counterpart, markets VA and DOD inventions and guides businesses and entrepreneurs through the licensing process.

Number of TTAP projects expected to grow

The development of TTAP stemmed from a visit to HERL by Kaplan to learn more about the facility and the technologies that HERL develops. He and Cooper discussed the need to build more working prototypes from research and ideas.

VA’s Office of Research and Development (ORD) first approved funding for TTAP for fiscal year 2018. ORD provides funds for TTAP that go to HERL to perform

work on products that are chosen by the Technology Transfer Program.

In Kaplan’s opinion, HERL is the perfect facility to transform the technologies from concepts and designs into working prototypes.

“HERL is a unique VA resource,” he says. “It’s the only VA facility I’ve seen or heard about that has an extensive manufacturing capability across a wide range. It can do material stuff, it can do electronics, it can do a whole host of different things. In conjunction with that manufacturing capability, it has an engineering and technician staff that uses a lot of equipment and capability to build prototypes.

The TTAP-HERL partnership, Cooper notes, is a way to solve some of the health challenges that clinicians and Veterans face.

“A lot of brilliant clinicians in VA have ideas for solutions,” he says. “They just don’t necessarily have the means to turn them into reality. What we’re doing should improve VA care and demonstrate to the public even greater value of VA, because VA will be introducing solutions that not only help Veterans but in general will help the medical community. What’s also cool is because we’re building these prototypes and trying them in VA first, that in some ways will continue to establish VA as a provider of cutting-edge care.”

Want to hear about the latest in VA research, *direct* from the experts?

Listen to the Voices of VA Research podcast series:

www.research.va.gov/podcasts





Photo by Bill George

Josh Marino is an education and outreach coordinator and a Veteran peer mentor at the Human Engineering Research Laboratories (HERL) in Pittsburgh.

VA Researchers Who Served: Josh Marino

Josh Marino, an Army Veteran, is an education and outreach coordinator and a Veteran peer mentor at the Human Engineering Research Laboratories (HERL), a joint project between the VA Pittsburgh Healthcare System and the University of Pittsburgh. He counsels and mentors Veterans who take part in testing HERL's projects, which include wheelchair technologies, advanced prostheses, and other innovative systems that improve the quality of life for people with disabilities like lost limbs and spinal injuries. He also oversees HERL's internship program, which exposes science, technology, and engineering students to real-world concepts and challenges. He was originally recruited to participate in HERL's ELeVATE program, which is designed to re-integrate Veterans into college. He earned a bachelor's degree in social science and a master's degree in clinical rehabilitation and mental health counseling at the University of Pittsburgh.

What motivated you to join the military?

Service to my community and country has always been a part of my life, and my family members have served in the armed forces. That sense of duty became even more important to me during my years in the Boy Scouts of America. As an Eagle Scout, I wanted to make a career out of serving my country.

What inspired your research career?

After I sustained a traumatic brain injury (TBI) while serving in the Army and was later diagnosed with PTSD, I saw a glaring disconnect between the providers and those seeking treatment. Few, if any, providers had first-hand

military experience comparable to [that of] their patients. Given my background, I saw this as a niche that I was meant to fill.

Did you have mentors who inspired you in life, the military, or your research career?

We all have those who pass through our lives at different times, influencing our decisions and our world view. I look back on my interactions with educators, leaders, friends, and family, and I see how much I carry myself based on the examples that they have set. Platoon sergeants and commanders whose faith in my abilities pushed me to excellence have taught me to lead with patience and trust. Scout leaders showed me how to remain considerate of others and their needs, and to act thoughtfully and purposely rather than impulsively. Academics who have spent their valuable time ensuring that I grasped complex concepts proved that due diligence is its own reward.

When and where did you serve in the military? Describe your military experience.

I joined the Army in May 2001 as a satellite communications systems operator and maintainer. My first duty station was a tactical post in South Korea. I loved being in South Korea so much that I extended my one-year tour to three years. That country has a beautiful culture, the friendliest people, and absolutely stunning sights. After that, I was placed at Fort Riley in Kansas with a unit that was in the early stages of formation but would soon be flagged as the 4th Brigade Combat Team, 1st Infantry Division. My unit deployed in early 2007 to the Iraqi capital, Baghdad, as part of the U.S.-led coalition's surge in forces. My fellow soldiers and I maintained a brigade-level communications suite for the next 14 months. My duties rarely required me to leave the base. But in June 2007, I was walking on one side of a concrete wall when mortars from an enemy attack hit the other side. The wall protected me from most of the debris and shrapnel. But the concussive waves compressed and shook my brain. I was diagnosed with a concus-

sion and shock. Later examinations would show a TBI with post-concussive migraines. My initial shock from the event would later be diagnosed as PTSD, and my condition deteriorated to where I couldn't perform my job as a communicator or as a leader. I was medically discharged in July 2009 due my combat injuries and resulting cognitive impairment. I moved back to Pittsburgh, where I had grown up.

What kinds of research are you involved in? How does it potentially impact Veterans?

We all wear many hats at HERL. In my work as an education and outreach coordinator, I've established and maintained great relations with many organizations from the greater Pittsburgh area. They include Veteran service organizations, the University of Pittsburgh's Office of Veteran Services, and Veteran support groups like PittVets and Operation StrongVet. In this role, I make sure to get educational information directly into the hands of those who need it most, including details on HERL internships and training sessions.

In addition, I've worked with many Veterans on navigating the VA Pittsburgh Healthcare System and the Pittsburgh vocational rehabilitation offices. With HERL's internship program in mind, I've published articles on making laboratories and machine shops more accessible to people who use mobility devices or have limited range of motion; on educating the next generation of researchers in the areas of advocacy, integration, and empowerment; and on counseling transitioning Veterans on educational and employment opportunities.

I've also taken the ELeVATE program under my wing to ensure that it stays as stellar a program as it was when I went through it. I have some great memories and have achieved incredible accomplishments since I began working with HERL.

Read more at www.research.va.gov/researchers_whoserved ★

Video Telehealth in Action



VA researchers studied the impact of video telehealth tablets for Veterans facing barriers to accessing care. **4 in 5 recipients** used their tablets during the evaluation period. Increases were reported in:



Psychotherapy encounters



Continuity of care



Medication management visits

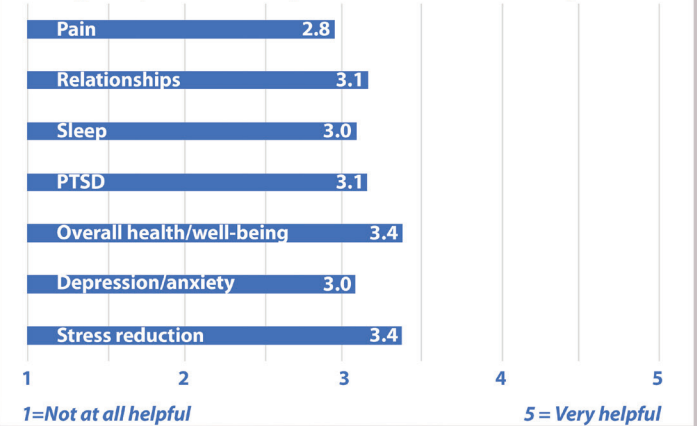
Follow the link below to see more findings:

"Virtual Care for High-Need Patients: Implementation and Effectiveness of a VA Nationwide Initiative to Distribute Video Telehealth Tablets to Veterans with Access Barriers" (<https://academyhealth.confex.com/academyhealth/2019arm/meetingapp.cgi/Paper/32018>). Presented at the AcademyHealth annual research meeting, June 2019. Infographic by VA Research Communications, August 2019. Photo: © iStock/BrianAJackson, simpson33, vittaya25, AJ_Watt.

Mindfulness meditation among Veterans

18% of Veterans reported using mindfulness in the past year

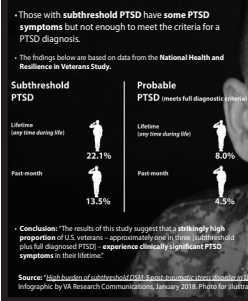
Average helpfulness ratings for various conditions (partial list)



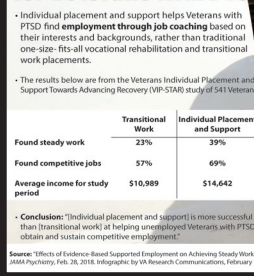
Based on a survey of 1,230 VA patients. From "Utilization and perceived effectiveness of mindfulness meditation in veterans: Results from a national survey," *Mindfulness*, online Sept. 11, 2019. Infographic by VA Research Communications, August 2019. Photo: © iStock/stray_cat.

www.research.va.gov/pubs/infographs

The high burden of 'subthreshold' PTSD



Individual Placement and Support for Veterans with PTSD



Firearm training among U.S. adults



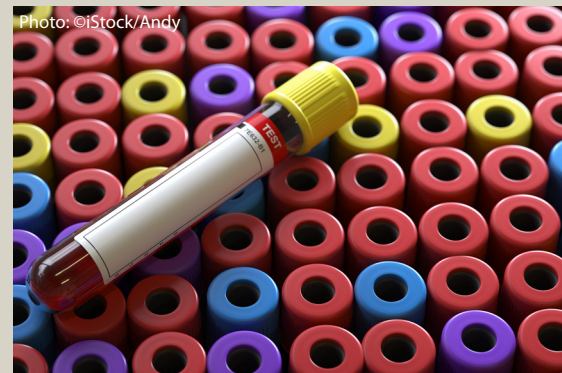


RESEARCH CURRENTS

Research News from the U.S. Department of Veterans Affairs

Biomarker to diagnose heart failure

Clinicians have a useful tool to quickly and easily test for heart failure thanks to VA researcher Dr. Alan Maisel and his colleagues at the VA San Diego Healthcare System and the University of California, San Diego. In the early 2000s, Maisel's team developed and promoted the use of the biomarker B-type natriuretic peptide (BNP) as an indicator of heart failure. Levels of the biomarker can be assessed with an easy blood test using immunoassay. Today, the BNP test is used around the world to diagnose heart failure.



In congestive heart failure, the heart does not pump strongly enough to provide enough blood flow to the body. BNP is a hormone secreted by heart muscle cells. When the heart muscles are under stress from heart failure, BNP secretion increases. Therefore, elevated levels of BNP in the blood can be a sign of heart failure.


While no one test can reveal heart failure with 100% accuracy, BNP is considered a gold standard biomarker for the condition. Maisel and his team continue working to refine the BNP test and to identify other biomarkers useful in evaluating cardiac health.

For more examples of VA research innovations being translated into everyday care, visit www.research.va.gov/research_in_action.



U.S. Department
of Veterans Affairs

VA Research Communications | 31 Hopkins Plaza, Ste. 102 | Baltimore, MD 21201
varesearchcurrents@va.gov | 443-759-3456

 Read the expanded online edition of
VA Research Currents at www.research.va.gov

 facebook.com/VAResearch  twitter.com/VAResearch