



RESEARCH CURRENTS

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

PTSD and heart disease: What's the connection?

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A Marine provides security during a training exercise in Camp Leatherneck in Helmand province, Afghanistan, in 2013.

Photo by Sgt. Tammy K. Hinline

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U.S. Department of Veterans Affairs
Veterans Health Administration
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Research suggests elite troops such as Navy Seals have higher levels of the anti-stress hormone neuropeptide Y, which also plays a role in the cardiovascular system.

Photo by Kyle D. Gahlau/USN



Unraveling the link between PTSD and heart disease

Researchers are exploring how exactly PTSD increases the risk of heart disease. The bottom line for Veterans: Seeking PTSD treatment may improve their mental *and* physical health.

Science is catching up with what many war Veterans have long sensed: Emotional trauma isn't about only the mind. It also affects the body—especially the heart.

“There’s now a large body of evidence that unequivocally links trauma exposure to poor physical health,” says Dr. Paula Schnurr of VA’s National Center for Posttraumatic Stress Disorder. She says an Israeli study published in 1989 was “one of the early studies suggesting PTSD was associated with impaired cardiovascular function.” Fast-forward a quarter-century, and the literature backing that link is robust. Much of it has come from VA authors.

A 2013 article by VA and UCSD researchers even posed the provocative question of whether PTSD is a “fast track to premature cardiovascular disease.”

Is there in fact the scientific equivalent of a smoking gun establishing a direct *causal* link between PTSD and heart disease? Not quite. But the research seems to be moving in that direction. Dr. Stephen Sidney, with Kaiser Permanente, wrote in a recent editorial in the *Journal of the American College of Cardiology*: “Overall, there are considerable data supporting an association that is likely causal between PTSD and coronary heart disease outcomes.”

Still, plenty of questions remain: How exactly does PTSD play out in the cardiovascular system? Is it strictly a cause-and-effect relationship, or is the link more complex? Could there be pre-existing risk factors—say, gene variants—that raise someone’s risk for both PTSD and heart disease? And how do poor health behaviors, such as smoking, and

accompanying psychiatric conditions, such as depression, jumble the equation?

AN INCENTIVE TO SEEK MENTAL HEALTH CARE

The answers are important for America's war Veterans. PTSD is estimated to affect between 11 and 20 percent of Afghanistan and Iraq Veterans. And VA cares for tens of thousands of Vietnam Veterans who are still coping with PTSD after four decades. About 3 in 10 Veterans from the Vietnam era have struggled with the condition.

PTSD by itself is a major health challenge. Higher rates of heart disease drive down quality of life even more—and drive up the risk of an earlier death. There are treatments for both conditions. But the better that doctors understand the nexus between them, the more they can focus on therapies likely to have a huge impact—and maybe prevent some problems from occurring in the first place. For example, if inflammation linked to PTSD turns out to be a key catalyst of heart disease, dietary changes could target that factor.

Just as important, hard proof of the impact of PTSD on cardiac health could be the extra push some Veterans need to seek mental health treatment.

"We can show Veterans there's an opportunity here. If we can work on reducing their PTSD symptoms, it could improve how they are feeling both mentally and physically," says Dr. Beth Cohen, an internist at the San Francisco VA Medical Center who studies the link between PTSD and heart health.

RECENT STUDIES SUPPORT LINK

Cohen's group recently provided robust evidence of the PTSD-cardiac link, as part of their work on the Mind Your Heart Study. Published Dec. 1, 2013, in *Biological Psychiatry*, the study involved 663 Veterans at two VA sites in California. The patients walked on a treadmill while hooked up to an electrocardiogram, or EKG, which traces the heart's electrical activity as it pumps blood. Those who met the criteria for PTSD—about a third of the patients—were more likely to have EKGs showing reduced blood flow to the heart, or ischemia. The condition was present in 17 percent of the PTSD group, compared with 10 percent of the non-PTSD group.

The findings were in line with those from a study led by Dr. Viola Vaccarino of Emory University. She worked with

KEY POINTS

- **Many studies over the past quarter-century** show that Veterans and others with chronic PTSD are at higher risk for heart disease, along with other physical illnesses.
- **Trauma exposure by itself**, even when PTSD doesn't develop, may also raise the risk of heart disease.
- **It's not clear how exactly PTSD leads to heart disease.** Most experts believe it's a combination of factors: biological (for example, stress hormones and inflammation), behavioral (lack of activity, poor diet, smoking, social isolation), and psychological (accompanying conditions such as depression and hostility, which themselves are linked to heart disease).
- There also may be **underlying genetic risk factors** that increase the risk of both PTSD and heart disease.
- **Veterans with PTSD who seek treatment** may be helping not only their mental health, but their physical health as well.

VA investigators to analyze data from the Vietnam Era Twin (VET) Registry. The VA-run registry includes some 7,000 middle-aged male twin pairs, all of whom served in the U.S. military during the Vietnam War.

The study looked at 562 Veterans—281 twin pairs—who had been followed an average of 13 years. It found that heart disease was more than twice as common among those with PTSD—about 23 versus 9 percent. When the researchers then conducted imaging tests with a radioactive tracer that shows blood flow to the heart, they found reduced flow among those with PTSD, even after adjusting for traditional cardiovascular risk factors and depression. The group reported its findings in the Sept. 10, 2013, *Journal of the American College of Cardiology*.

Heart disease was one of several health problems that VA researchers found to be more common among those with PTSD in another study of Vietnam-era Veterans that appeared online in *Quality of Life Research* in December 2013. Like Vaccarino's study, this one involved the Vietnam Era Twin Registry. But it relied only on mail surveys and



Research shows Veterans who were exposed to the intense stress of combat may be at higher risk for heart disease and other physical health problems later in life, regardless of whether they ever developed full-blown PTSD.

Photo by Staff Sgt. Staci Miller

telephone interviews and did not include any physical exams or imaging tests.

The study included 5,574 Veterans in all. Among those with PTSD, about 25 percent reported cardiovascular disease. For those without PTSD, the figure was 17 percent.

Similar gaps in health status between those with and without PTSD were found across a range of physical and mental conditions, besides heart disease: diabetes, lung disease, depression, anxiety, alcohol use disorder. Those with PTSD also reported more disability.

The researchers also found that combat exposure increased the risk of poor health and disability later in life, even in the absence of PTSD. The findings “have potential

implications for all combat-exposed Veterans,” wrote the authors. “Physical and mental health treatment programs should consider both PTSD and combat experience.”

Similar findings emerged from a VA and Naval Health Research Center study published in March 2014 in *Circulation*, a journal of the American Heart Association. The study used data on more than 60,000 service members who took part in the Millennium Cohort Study. Among troops who had deployed, those who saw combat were more likely to develop heart disease—even at their relatively young age—than those who had not been involved in combat.

The implication is that for warfighters, the experience of combat may register in the brain and nervous system as a



Ischemic heart disease—reduced blood flow to the heart—is the top cause of hospitalization among Veterans who use VA health care. Research has linked chronic PTSD to higher rates of ischemia, along with other heart conditions.

Photo by Warren Park

trauma, even if the person never develops full-blown PTSD. And that trauma experience—like PTSD—may be enough to set in motion some physical disease processes.

In fact, according to Cohen, while some studies look at trauma exposure and others at PTSD, both approaches tend to produce similar findings in terms of links to physical disease. One example is research tying trauma or PTSD to inflammation—a key factor in heart disease.

“There’s enough evidence demonstrating that each is independently associated with inflammation,” she says. “In addition, some studies show associations between early life trauma and inflammation many years later.”

SO HOW EXACTLY DOES PTSD AFFECT THE HEART?

While most experts agree there’s a strong link, maybe even a causal one, between PTSD and heart disease, theories abound as to how exactly that disease process works. Is the main culprit stress hormones that damage blood vessels over time? The bad health habits that tend to go along with PTSD,

such as smoking and not exercising? Or poor sleep quality, which can thwart the immune system? In all likelihood, it’s all of these and more, all interacting in complex ways.

Another question: Is there something unique about PTSD’s effects on the heart, or is the same impact seen with related emotional problems, such as depression, anxiety, and hostility?

The links between those mental conditions and heart disease are well-documented. One recent study looked at the records of more than 236,000 Veterans and found a higher incidence of heart failure among those with depression or anxiety alone, or the combination of both. Past studies have found similar links to heart attack. Teasing out the impact of those conditions, versus that of PTSD alone, can be difficult. The consensus so far is that PTSD exerts an effect independent of any other conditions.

Dr. Mary Whooley, at the San Francisco VA Medical Center and UCSF, leads the Heart and Soul Study, which followed more than 1,000 heart patients for a decade. Her

research has focused mainly on depression, not PTSD, but there are clear parallels.

She calls the relationship between depression and heart disease “complex and bidirectional,” and suggests the same could be said of PTSD.

What’s getting the most attention now as a factor in heart disease, says Whooley, is the behavioral dimension of depression. A few of her studies have suggested that poor health habits “strongly contribute” to the development of heart disease—habits such as inactivity, poor diet, social isolation, smoking, and not sticking to medication regimens.

“The emphasis is now on, well maybe this is a health behavior issue that can be modified, rather than a biological consequence we can’t do anything about,” says Whooley.

A similar dynamic, she notes, may apply in PTSD, with some key differences.

“Certainly there are different things that cause PTSD versus depression. And each may have different physiological responses that contribute to cardiovascular disease in different ways. At the same time, says Whooley, “There is likely to be significant overlap as far as how the two conditions are linked with heart disease. PTSD patients also have poor health behaviors, and these behavioral changes are linked to elevated inflammation and norepinephrine.”

Norepinephrine, also called noradrenaline, is a hormone released in response to stress.

‘FIGHT OR FLIGHT’

Others emphasize how the emotional state of PTSD itself may *directly* vex the cardiovascular system.

One hallmark of PTSD is hyperarousal—feeling keyed up, on the lookout for danger. Another is mentally reliving the trauma, through flashbacks or nightmares. These symptoms, along with others, might set in motion the body’s stress response, starting in the brain and orchestrated by the autonomic nervous system. Norepinephrine and other hormones are secreted, triggering changes throughout the tissues and organs of the body.

It’s the “fight or flight” response, which is how the body responds to danger and threats. The heart beats faster, arteries constrict, blood pressure increases. The platelets in the blood become stickier, in preparation for clotting a potential wound. More glucose is pumped into the bloodstream, for quick energy. This can all save your life if you’re being chased by a tiger. But when the process happens repeatedly over time, in response to chronic emotional stress, the lining of the arteries gets damaged. The heart muscle weakens. The effect is destructive, not protective.



In one study of Iraq and Afghanistan Veterans, those with combat experience were almost twice as likely to have a new diagnosis of heart disease within a few years after their return home, versus those who had deployed but not seen combat.

Photo by Cpl. Sean Searfus/USMC



Every time the body goes through changes to adapt to stress, it adds to the overall wear and tear on the organism.

Schnurr believes these direct biological links have a lot to do with PTSD's role in heart disease and other medical problems. But she doesn't discount the other mechanisms: poor health habits, for example, or related psychological conditions, such as depression or hostility.

The bottom line is, no one single mechanism seems to account for the relatively huge impact of PTSD on heart health and mortality. "We have links between stress and health," says Schnurr, "but we don't have the type of direct one-to-one links you might expect. And so it's hard to get from point A to point B."

To tie it all together, she likes to cite the "allostatic load" theory, first proposed in the late 1980s. "It seems like a good way to connect the dots," says Schnurr. Allostatic load refers to the cumulative burden of stress. Every time the body goes through these many physiological changes to adapt to stress—some of them small and subtle—the experience adds

to the overall wear and tear on the organism. It's like adding miles on your car and all its parts. Eventually, says Schnurr, "We pay a price."

She adds: "For the most part, the biological changes we see are not clinically remarkable. So it's hard to argue that any by themselves could lead to the types of physical health changes we see in PTSD. So conceptually, this theory makes sense." ★



This article has been condensed from its original version. For the full version, visit www.research.va.gov/currents/spring2014/spring2014-1.cfm



Error messages

A VA researcher in Chicago is studying the brain's "error messages" as a potential key to understanding PTSD.



Read more at www.research.va.gov/currents/spring2014/spring2014-13.cfm.

Photo by Jerry Daliege

Can magnetic coil ease tinnitus? VA trial aims to find out

“Sometimes I hear it in both ears, sometimes only in one ear. Sometimes it seems to be right in the middle of my head. It’s not predictable.”

John Emmons, 67, a retired police officer in Oregon who served as an Army medic in Vietnam, is talking about the tinnitus he has lived with for the past three decades. It keeps him up many a night, and during the day can be a “severe distraction.”

Some people with the condition hear whistling. Others hear ringing or buzzing. Emmons says the tone he hears is “hard to describe.”

For some it’s a mild annoyance—for others, a life-shattering disability.

TARGETING BRAIN CELLS MAY ALTER PERCEPTION OF NOISE

Regardless of the intensity, tinnitus appears to involve overactive neurons in a part of the brain called the auditory cortex. They light up on MRI brain scans of people with the condition.

That’s why VA researcher Dr. Robert Folmer and others believe that a treatment called transcranial magnetic stimulation (TMS) may help. In TMS, clinicians hold a magnetic coil, usually in the form of a figure eight, against the skull. The coil emits repetitive electromagnetic pulses that reach the brain cells under the scalp and change their activity pattern. This, says Folmer, may help reduce the abnormal perception of sounds.

The Food and Drug Administration approved the painless treatment for depression a few years ago, and researchers have been studying its use in a variety of other conditions. German researchers first used it with tinnitus about 10 years ago. Folmer is one of the researchers pioneering the therapy in the U.S.

Emmons and some 70 others with tinnitus have taken part so far in a trial of TMS that Folmer is heading at the National Center for Rehabilitative Auditory Research (NCRAR), based at the Portland VA Medical Center. About 100 more patients are expected to enroll. Folmer’s group ran a small pilot trial a few years ago that showed promising results, and the new VA-funded trial, he says, is “the largest clinical trial of TMS for tinnitus ever conducted in the U.S.”

IF SUCCESSFUL, TMS WOULD COMPLEMENT OTHER THERAPIES

Volunteers in the study get TMS treatments over 10 days. Folmer says there is evidence the short-term regimen may

TINNITUS AND VETERANS

- **Tinnitus has been one of the top service-connected disabilities** for Veterans during all periods of service, including war deployments and peacetime.
- **Veterans are at high risk** because of their exposure to aircraft, gunfire, and other loud noise in battle zones and on training bases.
- **VA and Department of Defense research** has also linked tinnitus to traumatic brain injury and post-traumatic stress disorder.
- **The American Tinnitus Association** estimates that as of 2014, VA disability claims for the condition will top \$2 billion annually.

Source: American Tinnitus Association 2012 report



Veteran John Emmons undergoes a TMS treatment with Dr. Robert Folmer as part of a study at the Portland VA Medical Center.

Photo by Michael Moody

produce some relief that holds up to six months or more. But his team won't have formal results until all the data are compiled and analyzed. Patients in the study are being followed up to 26 weeks, and Folmer has applied for funding to do longer-term follow-up, up to a year. He and his colleague Dr. Sarah Theodoroff are also seeking funding to do brain imaging to see if the exact anatomy of people's brains affect how they respond to the coil, which must be held over a specific region of the skull to be effective.

One of the strengths of the current trial is that it's placebo-controlled. Some patients are getting real TMS,

while others are getting sham treatments, from a coil that makes clicking sounds like the real one but emits lower-intensity pulses.

Folmer says even if TMS proves effective, it would be used along with, and not instead of, other effective treatments already in place. "TMS could augment existing therapies and provide a valuable option for patients who do not respond favorably to other treatments," he says.

Among the other treatments audiologists often recommend are cognitive behavior therapy, mindfulness, self-hypnosis, and relaxation therapy. These approaches

OTHER VA STUDIES ON TMS

A handful of VA studies in recent years have tested the benefits of transcranial magnetic stimulation. Here are three that are currently underway:

- **PTSD biomarkers**—Dr. Zhewu Wang in Charleston, S.C., is using TMS as an aid in eliciting certain brain-wave patterns that may be a biomarker for posttraumatic stress disorder.
- **Severe brain injury**—A small pilot study by Dr. Theresa Pape in Hines, Ill., is testing whether TMS may hold any benefit for comatose patients.
- **Chronic pain**—More than 200 Gulf War Veterans with chronic pain are taking part in a trial of TMS by Dr. John Wesson Ashford in Palo Alto.

can help patients take their mind off the noise in their ears, thus making it less of a distraction and annoyance. Another treatment is sound therapy: Patients wear a small device in the ear that makes white noise to mask the buzzing, ringing, or whistling of the tinnitus, or that makes other soothing or relaxing sounds that can help shift their focus from the troubling sound.

TREATING HEARING LOSS OFTEN HELPS

Hearing aids are often useful, as well. Many patients with tinnitus also have significant hearing loss, and amplifying incoming sounds can lessen the perception of the tinnitus.

Emmons is one such patient. His hearing loss likely began during his Vietnam service. “I think the aircraft noise

was probably the worst,” he says. Then came his years in law enforcement. “You can’t believe how loud that siren is when you’re inside the car.”

The Oregon man shares that toward the end of his career, he would often have trouble hearing radio calls and would have to turn up the volume to hear certain voices. “At the end of a shift, my ears would be buzzing big-time.”

His care team at the Portland VA has now recommended he try hearing aids, to help both his hearing and possibly the tinnitus. Says Folmer, “His pattern of hearing loss is typical of someone who has been exposed to loud sounds repeatedly over time.”

In VA, clinicians use an approach called progressive tinnitus management, spearheaded a few years ago by the NCRAR’s Dr. Jim Henry, to sort out and prioritize treatment options for those complaining of tinnitus. Everyone gets proper assessment. Some then need only basic education. Others need that plus treatment for their hearing loss. A relatively small percentage of patients—those with more intense, disabling tinnitus—end up needing further individualized treatment to deal with the problem.

Emmons says he realized relatively late in life—after developing significant hearing loss and tinnitus—how important it was to protect his hearing.

“At one point, I finally got the idea that to protect what I had was important. So anytime I was around loud noise—on the firing range, for example—I would go to extremes to protect my ears.”

At any rate, he says he feels optimistic because of everything he has now been learning from the audiologists at the Portland VA. “My experience there has been very positive—and very encouraging.” ★



Fuel findings

Those who work around jet fuel—or other hydrocarbon fuels—may be at higher risk for problems with how the brain interprets incoming sound, suggests research at the Loma Linda VA.

Read more at www.research.va.gov/currents/spring2014/spring2014-11.cfm.

Photo by Airman 1st Class Tom Brading



A nationwide clinical trial will generate evidence to guide providers in choosing the best medications to help people with diabetes control their blood sugar.

Photo: iStock

VA enrolling participants for **groundbreaking diabetes study**

Study will compare four widely used medications

A landmark trial to determine the long-term effectiveness of drugs used to treat type 2 diabetes will involve nine VA centers, along with 37 other clinical sites.

The Glycemia Reduction Approaches in Diabetes (GRADE) trial, funded by the National Institutes of Health, aims to learn which of four widely used, well-established diabetes drugs is most effective for which patients. The study is expected to include some 5,000 participants nationwide.

“It’s the first time these drugs have been compared head to head,” says Dr. Sophia Hazel Hox, an osteopathic endocrinologist who will help lead the trial at the VA Pacific Health Care System in Hawaii. “The hope is that we’ll be able to

gather information on which drug or drug combination is best for a given population—not just on treatment, but as far as avoiding adverse side effects as well.”

The other VA sites are Atlanta, Cincinnati, Cleveland, Denver, Miami, Omaha, San Diego, and Seattle. Each clinical center in the study has a target enrollment of 150 participants.

DIABETES AFFECTS ONE IN FIVE VA PATIENTS

Type 2 diabetes affects nearly 30 million Americans nationwide. About one in five VA patients has the condition.

The GRADE study is open to patients over age 30 who have been diagnosed with type 2 diabetes in the past five years.



Nurse manager Kelly Johnston of the Ann Arbor VA checks the blood pressure of Allen Shuh, who took part in a diabetes study at the site.

Photo by Scott Soderberg

The four medications to be compared are sitagliptin (sold as Januvia), glimepiride (Amaryl), liraglutide (Victoza), and glargine (Lantus). Participants will take one of the four drugs in concert with metformin (Glucophage), a drug typically used as a firstline treatment.

Researchers will examine the participants and collect data quarterly over the next four to seven years. Participants will be advanced to insulin therapy if the initial combination is not adequate.

EVIDENCE TO GUIDE CARE

The randomized, controlled study is expected to yield evidence to help providers make educated, fact-based decisions on diabetes care.

Several physician societies have developed guidelines for the management of diabetes based on the available data. Doctors have typically used these guidelines to determine what medications to prescribe to patients with type 2 diabetes. Researchers are hoping GRADE will provide data for more robust algorithms.

Hazel Hox: “Some of these drugs have been on the market for 10 years or more, and while we know they work, we don’t know if one is better than another or if there is a

particular scenario where one is more optimal. There are many options for doctors today as far as what treatment option they choose. It often comes down to the circumstances and health issues at the time the patient is in the office and what medications they are familiar with.”

She adds that GRADE should move VA and other providers one step closer to personalized medicine for patients with diabetes.

“Knowing that we have a large and growing population of people suffering from diabetes, we need to be doing our best to treat them with the most effective care. Part of that is giving them the right medication,” she says. “This is one piece of that puzzle. The results of this study will get us closer to the kind of tailored, personalized medicine we need to provide.” ★



For more information about the study, contact the study team at (216) 231-3240 or visit the website at <https://grade.bsc.gwu.edu>.



Dr. Machelie Pardue is with Emory University and the Atlanta VA Center for Visual and Neurocognitive Rehabilitation.

Photo by Adam Hernandez

Lab study: Exercise wards off retinal damage

The equivalent of a brisk walk daily may thwart some causes of blindness

Exercising on a treadmill may prevent blindness—at least in mice. That’s the upshot of a lab study by vision researchers at the Atlanta VA Medical Center and Emory University. They reported their findings in the Feb. 12, 2014, issue of the *Journal of Neuroscience*.

The researchers exposed two groups of mice to bright white light, similar to full daylight. The light is harmful to the eyes of the nocturnal animals. It breaks down the retina’s photoreceptor cells, which detect light signals. The rest of the retina processes the signals and sends the image information to the brain, via the optic nerve.

The damage caused by the “toxic” light in mice is similar to that seen in people with age-related macular degeneration,

or a genetic eye disease called retinitis pigmentosa. Both can cause blindness due to the death of photoreceptors.

In the lab experiment, one of the two groups of mice was exercised. The rodents ran on a treadmill for an hour a day, five days a week, for four weeks.

The researchers found the exercise—which they say is “comparable to a brisk walk”—was enough to prevent about half the damage to photoreceptors that occurred in the unexercised mice.

That compares favorably with what drugs may have to offer, notes lead researcher Dr. Machelie Pardue. “This level of preservation is similar to many pharmaceuticals that have been tested in this and other animal models.”

Exercise boosts production of a chemical called BDNF, which appears to protect vision.

Her team also found that a protective protein known as BDNF—for brain-derived neurotrophic factor—was elevated in the exercised mice. When the researchers injected a compound into the retina to block the action of BDNF, the exercised mice showed the same eye damage as the unexercised mice.

Pardue and coauthors wrote, “The data suggest that exercise is neuroprotective for retinal degeneration and that this effect is [controlled] by BDNF signaling.”

‘IMPRESSIVE LEVELS OF PRESERVATION’

Researchers have tried to give BDNF directly, but without much success. “The challenge is that BDNF has a very short half-life,” explains Pardue, “so it’s hard to achieve sustained delivery. Exercise offers a noninvasive way to get the body to make more BDNF.”

She says findings from the new study “show impressive levels of preservation of the retina for a therapy that is inexpensive and noninvasive.”

Pardue adds that the benefits may potentially apply not only to macular degeneration and retinitis pigmentosa, but also to other conditions that affect the retina, such as glaucoma and diabetic retinopathy.

She says that in May, her group will present findings on “the positive effects of exercise on the retina in diabetic rodents.”

Diabetes affects some one in five VA patients, and retinopathy is a common complication of the disease. ★



Researchers found Skype to be an effective way to deliver psychotherapy to homebound older adults with depression.

Photo: iStock

Skype therapy works for low-income, homebound elderly

VA and university researchers found the popular video calling tool Skype to be an effective way to deliver psychotherapy to homebound older adults with depression. In fact, the approach was even more effective than in-home visits from a therapist.

The study appeared online Feb. 5 in the journal *Depression and Anxiety*.

The authors wrote that the approach has the potential for “easy replication and sustainability to reach a large number of underserved older adults and improve their access to mental health services.”

Senior author was Dr. Mark Kunik, a psychiatrist at the Michael E. DeBakey VA Medical Center and associate director of VA's Houston-based Center for Innovations in Quality, Effectiveness and Safety. Lead author was Dr. Namkee Choi at the University of Texas at Austin.

Nearly 160 older adults with depression took part in the six-week study. All were low-income and homebound.

A control group received weekly 30-minute phone calls offering only general support, with no specific therapy. A second group received psychotherapy via Skype, on laptops they had been given and taught how to use during an initial in-person meeting. A third group had a therapist visit them at home for all the treatment sessions.

The two treatment groups received a form of cognitive behavioral therapy called problem-solving therapy. Over

the course of six hour-long sessions, therapists worked with patients on evaluating their problems, and identifying and implementing solutions. They also tried to motivate them to take part in enjoyable activities.

SKYPE PARTICIPANTS MAY HAVE FELT MORE COMFORTABLE

Both groups that received the therapy—either in person, or via Skype—showed improvements in depression. They also reported decreasing disability. The improvements in the Skype group, though, remained stronger at a nine-month follow-up.

The control group, which received only “care” calls, also improved, but not as much as the two therapy groups.

Why did Skype therapy have an edge over in-person therapy? The researchers theorize that the volunteers may have felt more comfortable

with the video set-up than with having someone in their home. The therapists reported that the Skype patients appeared more focused on the work, whereas the in-person group seemed more distracted. They took more breaks during their therapy sessions—for example, to answer the phone, use the restroom, or get a glass of water.

Kunik and colleagues say most older people prefer to avoid antidepressants because they are already on several medications for other health problems. That makes psychotherapy especially valuable for them. But sending therapists into the homes of homebound older adults can be costly—and there is a shortage of geriatric mental health specialists. Delivering the therapy via video call, say the researchers, may be an ideal solution. ★



Children of deployments

Children with a deployed parent may be at increased risk for behavioral problems, maltreatment, and substance abuse, say researchers.



Read more at www.research.va.gov/currents/winter2013-14/winter2013-14-28.cfm.

Photo by Sgt. Jesse Houk



VA researchers aiming to improve end-of-life care

Dr. Amos Bailey knows something about death. As an oncologist, he began referring patients to home hospice shortly after it became widely available in the late 1980s. The experience changed his outlook on care for the dying.

“I was struck that I could have two patients with the same illness, one in the hospital and another at home,” says Bailey, who today is director of the Safe Harbor Palliative Care Program at the Birmingham VA Medical Center and professor of gerontology, geriatrics, and palliative care at the University of Alabama at Birmingham School of Medicine. “When I visited the ones at home, they were so much more at peace than what I was seeing in the hospital. They had their medication at their bedside. Their families were there. There weren’t unnecessary dietary restrictions. Even something as simple as sitting in a recliner can make a difference. There were environmental things that made being at home much more comfortable than in the hospital.”

The experience eventually led Bailey to initiate a study called Best Practices for End-of-Life Care for our Nation’s Veterans, or BEACON, which took place at six VA medical centers from 2005 to 2011. The study, which included more than 6,000 patients, was published online Jan. 22 in the *Journal of General Internal Medicine*.

DYING AT HOME—PREFERRED, BUT LESS LIKELY

Polls consistently show that most Americans would prefer to die at home. Unfortunately, according to Bailey, that isn’t likely. “More than half of Americans die in an institution, either a hospital or a nursing home and it appears that those numbers are rising. We need to realize people are going to die in hospitals and we need to make it a better experience.”

Bailey is quick to point out that this isn’t necessarily a knock on hospital care. Hospitals, he says, are required to

follow certain guidelines. “You can’t just leave medication out by the bedside in the hospital, and they have to worry about you falling out of that recliner,” he says. “There have to be controls, but there can be a balance between home care and what’s feasible in the hospital. We only die once and there is only one opportunity to provide excellent care to a patient in the last days of life.”

When he came to the Birmingham VA, Dr. Bailey began to implement a comfort care order set for dying Veterans who were not able to be discharged to home or community hospice programs. This involved first identifying Veterans who were likely to die in the hospital, and then communicating with patients and families, and developing plans patterned on the best practices of home hospice care.

“It wasn’t a perfect match,” says Bailey. “It couldn’t be. But we were able to make some significant changes. For example, we changed to sublingual medicines that dissolved under the tongue.” Bailey also simplified the process for providing pain medication to dying patients, decreasing the time it took to provide relief to Veterans in pain.

He then teamed up with VA researcher Dr. Kathryn Burgio, a behavioral psychologist and also a professor at UAB. Together they studied the effects of Bailey’s comfort care project. By 2003 they were able to demonstrate what Bailey describes as “remarkable” changes in the process of care. Having established the program at Birmingham, they then set out to test the effectiveness at other VA medical centers.

CHANGING HOSPITAL CULTURE

The new sites—in Florida, Georgia, Mississippi, and South Carolina—were selected as much for their proximity to Birmingham as anything else. Bailey and his team underwent routine site visits, spending several weeks at a time conducting educational visits with VA staff and then observing the results.

“The keys to excellent end-of-life care are recognizing the imminently dying patient, communicating the prognosis, identifying goals of care, and anticipating and palliating symptoms,” says Burgio. To do this across multiple sites, the team developed training and education materials and leveraged the efforts of local champions to encourage culture change. The goal of the research, according to Burgio, was not just to change the practice

and behavior of individual providers, but also to change the culture of the hospital.

“It’s difficult to do and sometimes even harder to accept, but when a medical provider is in lifesaver mode, they’re not going to be focusing on the symptoms,” says Burgio. “The sooner you realize a patient is dying, the sooner you can focus on their comfort. That can mean medications for pain, delirium, or other issues.” It can also mean less use of intrusive techniques like nasogastric tubes or IV lines.

“We talked about things that weren’t necessarily helpful, like feeding tubes and IVs,” says Bailey. “We showed them that they didn’t have to stop treatment in order to model their care on what hospice does at home.”

The researchers looked at 16 care variables, from the use of medication for pain or confusion to pastoral visits. They encouraged providers to allow patients access to favorite food and drinks, tried to minimize invasive procedures, and allowed families to spend more time with loved ones.

FOCUS ON FAMILY

Part of the focus is on the family members, says Burgio. “We want the bereaved family members to feel like everything they want has been done and that their loved one had a comfortable death. The traumatic death of a family member can affect people for the rest of their lives and make it harder for them to deal with their grief.”

From improving access to pain medications to just letting patients sit up in a chair, BEACON led to improved rates for all 16 variables. “Every one of the outcomes we measured improved after implementation of BEACON,” says Burgio. Orders for pain medication went up 11 percent, while the use of feeding tubes and IVs went down. Prescriptions for death rattle went up nearly 19 percent.

The researchers hope to expand their training program and eventually disseminate the best practices they have developed not only throughout VA, but nationwide. “Only about 15 percent of Veterans who die each year do so at a VA facility,” says Bailey. “We need to be able to improve end-of-life care not just at VA facilities, but nationwide, and not just for Veterans, but for everyone.” ★



Marine Lance Cpl. Kyle Anderson underwent polytrauma care in 2010 at the Minneapolis VA Medical Center.

Photo by April Eilers

Researchers building **roadmap of OEF/OIF injuries**

For Dr. Mary Jo Pugh, a research scientist at the South Texas Veterans Healthcare System and a professor of epidemiology and biostatistics at the University of Texas Health Science Center in San Antonio, the study of “complex comorbidity clusters” is personal. Pugh suffered a head injury while serving in the Air Force, and her husband is a Veteran of the Iraq

war. While her early work focused on geriatric populations, the evolution of research on Afghanistan and Iraq war Veterans became increasingly compelling to her.

“My own experiences after head injury piqued my interest in the subject, but after my husband’s deployments, I began to see some things in his friends that made me want to explore how

different conditions manifest alongside one another,” says Pugh.

WHAT ARE COMORBIDITY CLUSTERS?

Comorbidity clusters sound more complicated than they are. Take the polytrauma clinical triad, or PCT. When Veterans are diagnosed with one illness, say a traumatic brain injury,



Pugh and her team studied the records of nearly 200,000 Iraq and Afghanistan Veterans and discovered six major injury clusters.

they're more likely to also have experienced posttraumatic stress disorder and pain. In the case of TBI, PTSD and pain tend to come in tandem. PCT is generally considered the signature complex comorbidity cluster found in Iraq and Afghanistan Veterans, but it's certainly not the only one.

On the surface it can seem obvious. If your foot is injured, you'll walk differently. If you walk differently, eventually our knee will also hurt. In reality, such as in the higher prevalence of cardiovascular disease in Veterans with PTSD, relationships are often less clear.

What is clear, however, are the benefits of identifying and treating conditions before they worsen. To do this, clinicians need a sense of when diseases are likely to co-occur, and at what rate. With this in mind, Pugh set out to create a roadmap of comorbidity clusters so care could be better coordinated and tailored to each Veteran's needs.

"Take chronic disease, for example," she says. "We found that individuals with PCT who were just a little older tended to develop chronic diseases. If clinicians could get a sense of who these people were beforehand, we might be able to

delay or alter the course of that disease altogether."

SIX MAJOR PATTERNS IDENTIFIED

Pugh and her team studied the records of nearly 200,000 Iraq and Afghanistan Veterans and discovered six major clusters:

1. PCT and chronic disease, such as diabetes or heart disease (4.6 percent)
2. PCT (8.6 percent)
3. Mental health and substance abuse (23.6 percent)
4. Sleep disorder, amputation, and chronic disease (4.3 percent)
5. Pain, moderate PTSD (5.6 percent)
6. Relatively healthy (53.5 percent)

The records were analyzed against 21 variables, from hearing loss to back pain to obesity. The results, published in the February issue of *Medical Care*, identified a number of trends. For example, Veterans from cluster 1 were more likely to be prescribed pain and psychotropic medications, while adverse outcomes were highest for those in clusters 1 and 3. Veterans in cluster 3 had the highest mortality rate, while those in 1 were more likely

to use health care services. Cluster 5 experienced higher than normal back pain, but much lower rates of homelessness and depression than cluster 1.

Interestingly enough, despite the prevalence of research focusing on PCT, Pugh found only about 13 percent of the Veterans studied fit into that category. According to Pugh, this is a hopeful sign. "We hear so much about PCT and all of these conditions, but what we found was that 53 percent of Iraq and Afghanistan Veterans actively seeking care fell into the 'relatively healthy' category."

"Knowing what these Veterans are faced with will allow us to better use our post-deployment health clinics," says Pugh. "Right now they tend to focus on PCT, but based on this data, we can say that PCT is only affecting a small percentage of Veterans. This could allow us to identify trends in patients so that those with more complex issues go to one place and those who are healthier go to another. It would be like a form of triage that would allow us to tailor our care to each Veteran so that they receive exactly the care they need from the moment they arrive." ★



Dr. Leslie Hausmann, a research psychologist at the Pittsburgh VA Medical Center, is using positive-psychology activities to help Veterans and others cope with chronic pain.

Photo by Bill George

Pain reduction, via positive psychology and the Web

Visitors to a positive psychology website who were given simple activities to do over six weeks—such as writing about three “good things” each day in a journal—reported less physical pain for up to six months after the study.

The VA study was published online Feb. 22 in the *Journal of Pain*.

There is growing scientific evidence for the idea that positive thinking can help thwart physical pain. But the new study is among the first to show how this can be achieved via the Internet. It is also among the first to report relatively long-lasting effects from such simple, low-cost methods.

“Our findings suggest that teaching people simple, evidence-based positive activities administered online can lead to lasting reductions in bodily pain,” wrote lead author Dr. Leslie Hausmann and colleagues. Hausmann is a research

psychologist with the University of Pittsburgh and VA’s Center for Health Equity Research and Promotion.

The study recruited volunteers through a website hosted by the University of Pennsylvania’s Positive Psychology Center. The study involved 417 volunteers, all reporting mild to moderate pain at the outset. Most were women, and most were college-educated.

The volunteers were randomly assigned to complete 0, 2, 4, or 6 positive activities over six weeks. The exercises, all shown to boost well-being when administered in person, centered on concepts such as gratitude, mindfulness, and identifying and using personal strengths.

The participants, on average, completed about half the activities they were assigned. In any case, those given at least four activities showed substantial improvements in pain scores relative to the other volunteers. The gains persisted when the participants were surveyed one, three, and six months after the completion of the study.

According to Hausmann’s team, the study was based on the idea that pain is a function of not only biological factors, but “psychosocial” ones as well. The effect has been seen in past studies. For example, one trial found that people in a nursing home who watched a funny movie reported less physical pain afterward—and needed less pain medication. Another found that a simple positive psychology exercise—having people write about their vision for their “best possible self” in the future—lowered their pain-intensity ratings.

The researchers say future studies should test methods that are more interactive, that “allow people to log their performance, reflect on their response to activities, and connect with others who are completing the activities.” They point to some popular phone apps that already incorporate such features.

Hausmann is also working on a version of the therapy that doesn’t rely on an Internet connection, for Veterans with chronic pain. She led a recent pilot in which Veterans with arthritis completed activities in a written workbook at home, with weekly support calls from a staffer. ★



Dr. Scott Grundy, seen here in a 2001 photo, is a longtime nutrition researcher with VA and the University of Texas Southwestern Medical Center.

Photo by David Gresham

1988 STUDY

Title: Comparison of monounsaturated fatty acids and carbohydrates for reducing raised levels of plasma cholesterol in man

Journal: *American Journal of Clinical Nutrition* (June 1988)

Authors: Grundy, SM, Florentin, L, Nix, D, Whelan, MF

VA site: Bonham, TX (near Dallas)

What was studied: The authors tested three different diets, with different combinations of fats, cholesterol, and carbohydrates, on 10 men for six weeks to see the effects on their blood cholesterol levels.

What was learned: A diet rich in monounsaturated fat—the type found in olive oil—was superior to a low-fat diet because while both reduced overall cholesterol and LDL (so-called “bad”) cholesterol, the monounsaturated fats did not reduce HDL (“good”) cholesterol.

2014 VIEW:

“In the late 1980s we carried out a series of studies with monounsaturated fats that involved VA patients [including two that were published in the *New England Journal of Medicine*]. Prior to these studies, there was little interest in monounsaturated fats. These studies showed that monounsaturated fats are as good as polyunsaturated fats for lowering cholesterol levels, and they are potentially safer. They had a major impact on nutrition and thinking about the importance of monounsaturated fats for the diets of Americans and people in other countries. This led to a resurgence in interest in olive oil as a safe fat. It also increased interest in the Mediterranean diet as a healthy diet. There is no doubt that these studies opened a new field for nutrition. I checked Pubmed for clinical trials and meta-analyses with monounsaturated fats and found about 2,600 publications. This is just one indicator of the interest generated in the nutrition community by our early studies. I don’t want to overstate their importance, but I believe these studies were quite impactful.” ★

The Mediterranean diet: A look back at one VA group’s contribution

May is National Mediterranean Diet Month, a time to focus attention on a way of eating that has consistently been shown to help reduce the risk of heart disease and other chronic ailments. VA researcher Dr. Scott Grundy is among many in VA who have studied the topic. *VA Research Currents* asked him to take a look back at one of his group’s early studies in the area, and to comment on its relevance today. Grundy is chief of diabetes and metabolic diseases at the Dallas VA Medical Center. He also directs the Center for Human Nutrition and the Clinical and Translational Research Center at the University of Texas Southwestern Medical Center, and is a distinguished professor of internal medicine at the university.



Veterans who sign up for MVP provide health information and a blood sample that is used for DNA analysis.

Photos by Frank Curran and Jeff Bowen

Million Veteran Program hits quarter-million enrollment mark

MVP signing up Veterans at nearly 50 sites nationwide

VA's Million Veteran Program (MVP) enrolled its 250,000th volunteer research participant in early March.

A Korean War Veteran at the VA Loma Linda (Calif.) Healthcare System was the 250,000th person to sign up for the research program.

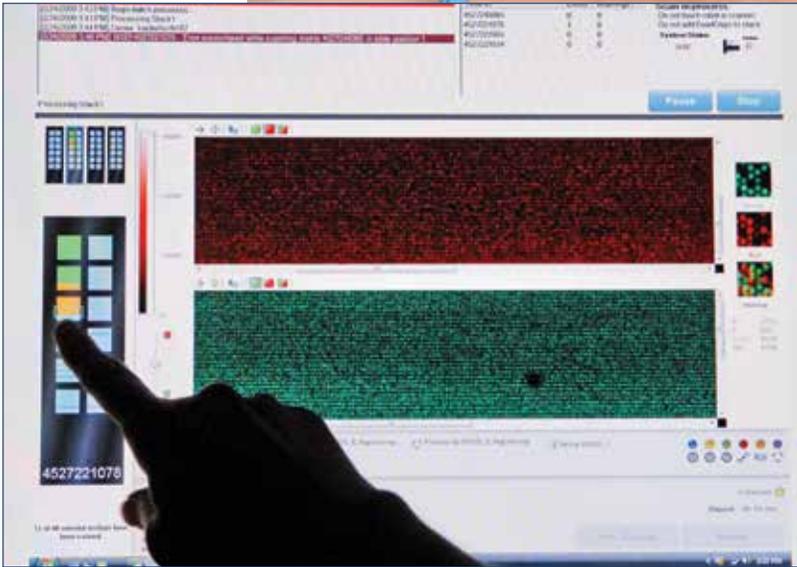
Launched in 2011, MVP aims to create one of the world's largest databases of health and genetic information. Up to a million Veterans are expected to be enrolled in MVP by

2018. The goal is to better understand how genes affect health.

Health information and genetic samples collected through MVP are stored securely and will be made available for studies by authorized researchers. The information is linked to Veterans' VA electronic health records, giving researchers more valuable data to study. Stringent safeguards are in place to protect Veterans' privacy.

MVP data will help researchers study a wide range of health conditions—from chronic diseases such as diabetes and schizophrenia, to post-deployment concerns such as PTSD and traumatic brain injury.

MVP is enrolling Veterans at nearly 50 VA medical centers nationwide. For more information, visit www.research.va.gov/MVP. ★



CARTOON CORNER

SLEEP DISORDER RESEARCH

Cartoon publication supported by navref.org



RESEARCH CURRENTS

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



DID YOU KNOW?

Dr. Rosalyn Yalow, a pioneering scientist who won the Nobel Prize for her work at the Bronx VA Medical Center on new ways to detect and measure substances in the blood, passed away on Memorial Day three years ago, at age 89. The 1977 Nobel announcement included this praise of her earlier achievements in science: "This was pioneering work at the highest level. It had an enormous impact. We were witnessing the birth of a new era in endocrinology, one that started with Yalow."



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