

Study suggests rise in wars' mental toll

Among nearly 290,000 veterans of the wars in Iraq and Afghanistan who used VA health care for the first time between April 2002 and March 2008, 37 percent received a mental-health diagnosis.

That's the main result of a database study by a team with VA and the University of California, San Francisco. The findings appeared online July 17 in the *American Journal of Public Health*.

An earlier study by the same group looked at 100,000 veterans of operations Enduring Freedom and Iraqi Freedom who were first seen in VA between 2001 and 2005. The study found that a quarter of

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Photo by Staff Sgt. Andrew Smith

Troops with the 25th Infantry Division operate in Paktika province, Afghanistan, in July 2009.



Photo by Jerry Ludwig

VA physician-researcher Dr. Melina Kibbe (background) talks with Army veteran Author Bragg as he undergoes a check of the blood pressure in his legs, performed by technician Justine Phagan.

White House awards for VA scientists

VA scientists Melina Kibbe, MD, and Alex Sox-Harris, PhD, will receive Presidential Early Career Awards for Scientists and Engineers at the White House this fall, along with researchers from eight other federal agencies.

The awards were established in 1996 as America's highest honor for early-career researchers. They are given each year for "innovative research at the frontiers of science and technology" and a commitment to community service. Winners receive up to five years in continued research funding from their respective agencies.

"These extraordinarily gifted young scientists and engineers represent the best in our country," President Obama said in a White House statement. "With their talent, creativity and dedication, I am confident that they will lead their fields in new breakthroughs and discoveries and help us use science and technology to lift up our nation and our world."

Kibbe is a vascular surgeon and biomedical researcher at the Jesse Brown VA Medical Center in Chicago. Her lab studies how a body chemical called nitric oxide promotes healthy blood vessels. The work aims to improve patient outcomes after procedures such as bypass surgery or balloon angioplasty and stenting. These procedures

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Researchers probe strategy to make flu drugs go further

During this year's outbreak of swine flu, or H1N1, the treatment of choice—outside of vaccination—has been oseltamivir, sold as Tamiflu. The oral drug blocks an enzyme that allows the virus to reproduce and spread.

Stockpiles of the drug are considered adequate as of now. But the outbreak was upgraded to pandemic status back in June, and the virus continues to spread worldwide. Will there be enough oseltamivir to go around?

VA researchers have been studying one way to make the drug go further: Combine it with another drug that keeps it in the bloodstream longer.

A trial led by Mark Holodniy, MD, an infectious disease specialist at the VA Palo Alto Health Care System, showed that such an approach could be safe and feasible. Volunteers who took probenecid capsules four times daily, along with oseltamivir, over two weeks were able to take the flu drug every other day, instead of daily, and still keep enough in their bloodstream.

Probenecid has been used in a similar way for decades to extend the effects of penicillin and other antibiotics, so safety concerns with the drug are minimal. But one potential hitch with the regimen tried in the VA clinical trial is that getting people to take a drug four times a day can be an uphill battle. “It doesn't seem sustainable,” says Holodniy. “We know that adherence to drug regimens in HIV and other diseases is a critical point. Are people able to sustain this for two weeks? We don't know. Some people have trouble just taking a vitamin once a day.”

Developing a sustained-release pill

Enter VA's Clinical Research Pharmacy Coordinating Center. The Albuquerque facility serves as a pharmacy for large VA clinical trials. Now, with partners at the University of New Mexico, research pharmacists at the site are developing a sustained-release version of probenecid. The idea is for patients to be able to take that drug only once daily.

“We've done some proof-of-concept piloting in test tubes and shown that we can get a fair amount of probenecid in a pill that can be designed for sustained release, such that we might be able to back it down to twice a day or even once a day,” says Holodniy. “This has not been previously developed or marketed, so it would be a new concept. This could allow people to be more adherent and make it a more viable regimen.”

Holodniy points out that the strategy is far from being ready for prime time. The oseltamivir-probenecid combination would still have to undergo further clinical trials and receive approval from the Food and Drug Administration. But if it proves viable, says Holodniy, it could be of value in future flu pandemics. —



On the line—Production at VA's Clinical Research Pharmacy Coordinating Center.

VA following H1N1 closely

VA's Office of Public Health and Environmental Hazards provides updates to VA leadership and staff—weekly, or more often if needed—on H1N1. The updates cover U.S. government activities, scientific and clinical information, and VA-specific initiatives regarding the virus, such as surveillance and educational outreach. VA patients can find information, including tips for preventing infection, at www.publichealth.va.gov/h1n1flu.

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Study will boost role of electronic records in care, research

Humans are unique in their ability to use language. But machines are gaining ground.

Think of search engines such as Google or Yahoo. Type in even a careless entry such as “chicogp Movie theters” and amazingly the computer figures out what you want.

Such is the power of “natural language processing” (NLP). Search engines demonstrate only one aspect of this branch of computer science, which involves teaching computers to recognize and make sense of free text or speech.

Now, a new VA research project seeks to harness NLP’s power to squeeze more value out of electronic health records for researchers, clinicians and managers.

Changing free text into structured data

The project is called the Consortium for Healthcare Informatics Research (CHIR). According to lead investigator Matt Samore, MD, the main goal is to change free text in the electronic medical record—doctors’ notes, for example—into structured data. That will make the information more useful for research and other purposes.

“It’s basically a matter of converting information of one form into information of a different form that has all kinds of new uses,” says Samore, a clinician and epidemiologist at the Salt Lake City VA Medical Center.

Webmasters and database architects typically use checkboxes, pull-down menus and other tools to structure the information they want to collect. From their perspective, the less free text, the better. Free text—for example, a couple of sentences about why you visited a store—can’t be easily

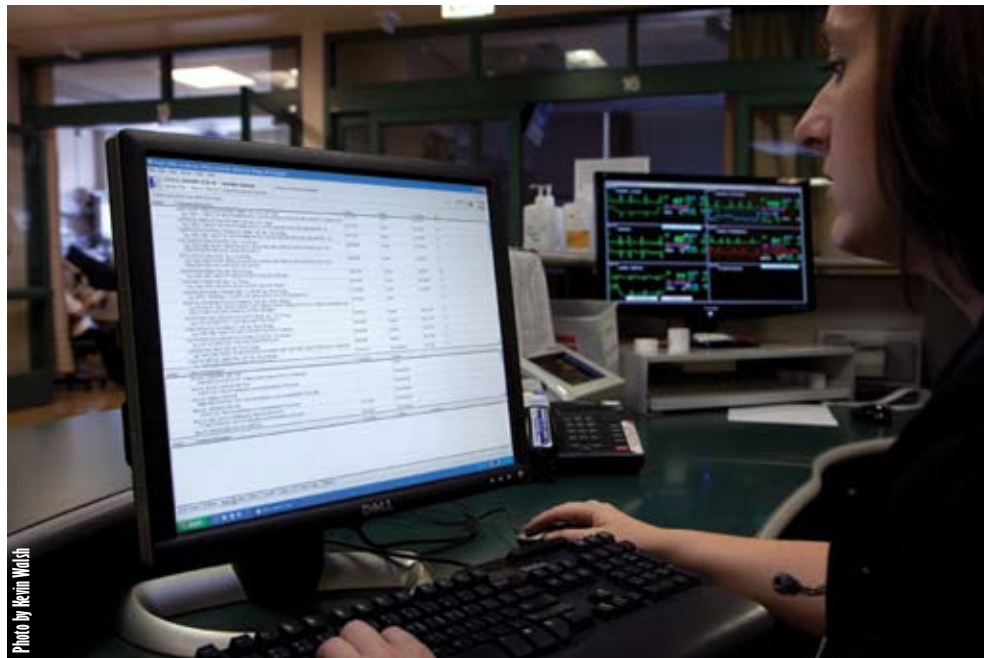


Photo by Kevin Wlach



Photo by Janet Litman

Clinical data galore—VA’s electronic medical record is used by nurse LeAnn Shipp in San Diego (above) and radiology technician Thomas Bielenda in New York City.

analyzed by computers. Electronic health records are a bit different. They use structured data and templates wherever possible, but there’s also an unavoidable need for free text. VA’s electronic records, first implemented in the 1990s and still

considered state-of-the-art, were designed to give doctors ample opportunity to record their thoughts and decisions.

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Naps boost creativity—Daytime naps that include Rapid Eye Movement (REM) sleep—the stage of sleep when dreams occur—can boost the ability to solve problems that require creative thinking, according to a study by a team with VA and the University of California, San Diego. Volunteers were shown groups of three words—for example: cookie, heart, sixteen—and asked to name a fourth word related to the other three—sweet, in this instance. The volunteers took the problem-solving test in the morning and again in the afternoon, after either a nap with REM sleep, one without REM sleep, or a quiet rest period. Only those who got REM sleep improved their performance. VA-UCSD researcher Sara Mednick, PhD, author of a book titled *Take a Nap! Change Your Life*, says that during REM sleep, information flows freely among different brain networks. “During REM sleep, you have this loose, associative mind that can be very conducive to coming up with new and useful solutions to problems.” (*Proceedings of the National Academy of Sciences*, June 23, 2009)

Vision and traumatic brain injury—In a Palo Alto VA study involving 68 veterans with moderate to severe traumatic brain injury and 124 with mild TBI, most of the veterans in both groups—78 and 98 percent, respectively—had normal or near-normal visual acuity—that is, they could read the letters or numbers on eye charts or cards. About three-quarters of the veterans in both groups, however, reported vision complaints, and high numbers of them tested positive for vision problems. For example, more than 4 in 10 veterans in both groups had convergence insufficiency, which affects how the eyes work at close distances. Often missed on basic eye exams, the condition causes eye strain, blurred or double vision, and headaches. Most of the brain injuries in both groups were the result of blasts. The authors concluded that “the visual consequences of such injuries necessitate further study and support the need for appropriate evaluation and treatment in all severities of TBI.” (*Optometry and Vision Science*, July 2009)

PTSD links to specific physical ailments prove elusive—A VA review study found mixed results in past research looking at ties between PTSD and specific physical illnesses. Data conflicted in studies on PTSD in connection with diabetes, coronary heart disease and stroke. The findings were slightly more consistent with regard to arthritis and digestive disorders. “A lot of people assume that something as stressful as PTSD—a chronic stress—will be linked to physical illness. But when you look at specific disorders, there’s relatively little there [in the medical literature],” said Mark Kunik, MD, MPH, senior author of the study. “We were expecting to find more studies and stronger associations.” Lead author was Salah Qureshi, MD. Both researchers are with VA’s Houston Center for Quality of Care and Utilization Studies. Qureshi is also a psychiatry fellow with VA’s South Central Mental Illness Research, Education and Clinical Center. (*Psychiatric Quarterly*, June 2009)



Photo by Jeff Miller, UC of Wisconsin

Cutting calories slows aging—VA scientists and colleagues found that restricting caloric intake to about 30 percent of normal can slow aging and prevent disease in primates. Caloric restriction had shown similar effects in countless animal studies, but never in primates. The researchers, led by Richard Weindruch, PhD, of the Madison VA and the University of Wisconsin, reported findings from a 20-year study that involved, at one point, 76 rhesus monkeys. At the 20-year mark, half of the regular-diet monkeys survived, versus 80 percent of those eating fewer calories. Caloric restriction reduced the incidence of diabetes, cancer, cardiovascular disease, and brain atrophy, as measured by brain scans. (*Science*, July 10, 2009)

Canto (left), 27, has eaten a calorie-restricted diet while Owen, 29, has been on an unrestricted diet.



Robotic stroke rehab—Above, research volunteer Madeline Pillinger watches as Jamie Lush of the Human Motor Performance Lab at the Baltimore VA fits an “Anklebot” to her leg. Researchers with VA and the University of Maryland are studying whether the device, invented at the Massachusetts Institute of Technology, can improve gait and balance following stroke. They reported on the work in June in *IEEE Transactions on Robotics*.

The Anklebot helps as needed when the user cannot complete a movement. This type of assisted movement has been shown to help the brain relearn to move a limb paralyzed or weakened by stroke. The Anklebot also resists movement, helping to build ankle strength, and records data on ankle movement. In one phase of the research, Anklebot users move their ankle in response to visual cues on a video screen. “This device has the potential to evoke positive changes in walking speed, reduce ankle stiffness and improve ankle motor control, as indicated by increased smoothness and speed of targeted ankle movement,” said researcher Anindo Roy, PhD. “In fact, some of these benefits are gained and retained even after a single session of playing the video game with the robot engaged.”

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“There’s a real limitation to asking clinicians to input only structured data when they are evaluating patients, recording those evaluations, describing what’s happening with the patient, documenting their decisions,” says Samore. “There’s a richness to free text, a communication benefit. It allows people to express themselves.” Merry Ward, PhD, who is overseeing CHIR for VA’s Office of Research and Development, agrees: “That narrative is very important for health care providers. Radio buttons, pull-downs, yes-no and other forced choices can only go so far in describing the patient’s condition. It’s much more complex than that.”

Samore and colleagues—a consortium involving experts within VA and at several universities—want to unleash the wealth of free-text information within VA’s electronic medical records, in a secure manner, so VA can use it to improve veterans’ care.

“If you can convert narrative text into structured data,” says Samore, “you can improve your measurement of quality, improve surveillance [of infectious diseases and adverse drug events], create new decision-support systems, and help clinicians improve documentation of problems in the medical record. There are a huge number of applications.”

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Electronic-records project tackles MRSA, PTSD

As part of CHIR, VA investigators have launched two multi-year studies to help advance the development of natural language processing and its clinical applications.

One will look at methicillin-resistant *Staphylococcus aureus*, known as MRSA. The tough-to-treat germ has long been the nemesis of infection-control experts in hospitals. It causes tens of thousands of serious infections each year. The project will aim to capture more MRSA-relevant information in the electronic medical record, beyond standard coded data, so surveillance and control can be improved.

A second project, on posttraumatic stress disorder, will examine whether free text can shed light on how the disorder progresses and how symptoms may vary from one patient to the next.

Other CHIR projects, of shorter duration, will look at several clinical topics that figure largely in care for heart disease, cancer and other diseases.



Veteran Louis Romm receives a nasal swab from Dr. Eli Perencevich, with the Baltimore VA Medical Center, to test for MRSA.



In a healthier vein—Dr. Melina Kibbe, one of two VA winners of a White House award for early-career scientists and engineers, performs an ultrasound on the carotid artery of veteran Calvin Ellis. Kibbe’s research focuses on the role of nitric oxide in promoting healthy blood vessels and helping patients heal after procedures such as bypass surgery or balloon angioplasty.

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injure the inner lining of blood vessels. This thwarts production of nitric oxide. The result is unwanted tissue growth inside the vessels, leading to new blockages. In one project, Kibbe’s group is developing a prosthetic vascular graft that releases nitric oxide. If the device proves successful in humans, it would be used in place of a standard vein graft and could improve recovery after bypass surgery.

In addition to her VA role, Kibbe conducts research at the Institute for BioNanotechnology in Medicine at Northwestern University and is a surgeon at Northwestern Memorial Hospital. Outside of her research and clinical duties, she developed a DVD movie library for veterans at the Chicago VA and for children at the local Shriners Hospital. She also raises money for the American Vascular Association to help provide scholarships for young investigators.

Sox-Harris is a researcher at VA’s Center for Health Care Evaluation, in Palo Alto. He has led efforts to study how well quality measures used widely by VA and other U.S. health systems predict outcomes for patients treated for drug or alcohol addiction. Based on his research, he has proposed a new strategy that would “pre-validate” quality measures to make sure they actually correspond to improved patient outcomes. “This would give



Dr. Alex Sox-Harris

administrators a means to identify high- and low-performing facilities, monitor the effects of system-wide initiatives, and incentivize particular practices,” he said.

In related research, Sox-Harris has probed other issues in alcohol screening, counseling and treatment, and topics such as suicide attempts after addiction treatment and the impact of spirituality and religion on health. He is also a statistician with VA’s Center for Bone and Joint

Rehabilitation and is noted for his expertise in research methodology, often consulting for other research groups within VA. A recent article of his in the *Journal of Psychiatric Research* outlined common statistical and research-design problems in papers submitted to prominent psychiatry journals.

Aside from his VA role, Sox-Harris is a member of the Washington Circle Public Sector Workgroup for Substance Use Disorder Treatment. He is active in his community as a Cub Scout volunteer. —

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One key application, says Samore, is research. For instance: Doctors often enter free-text notes about why they are prescribing certain drugs or how patients are responding. The only way for researchers to study the notes would be to manually review each chart. In studies involving thousands of charts, this would chew up countless hours of time. The effort would be laborious, inefficient and perhaps inaccurate.

With NLP, computers could scan tens of thousands of patient records, find and extract the relevant notes, and convert the information into a structured format. Researchers could use computers to analyze it in huge batches. This could reveal new insights about the drugs that would otherwise remain hidden.

According to Ward, such studies could reveal nuances—as expressed by doctors in free text—about the comparative benefits of one treatment over another. “If we can look at large numbers of patients, large amounts of data, we might be able to get a better sense of what is it about some patients that made them respond better to one treatment over another.”

Genomic studies could benefit

The technology would also boost genomic research—studies that link patients’ genetic information with their health risks, needs or outcomes. Ward says CHIR will allow the electronic medical record to be a “very powerful” tool in this regard—for example, by enabling researchers to analyze free text about clinical traits tied to certain genes.

Along with these applications, Samore says CHIR will also develop new ways to “de-identify” patient charts so researchers can access clinically relevant information but not patient names or other identifiers. He says protecting veterans’ privacy is a critical, overarching goal of the project.

‘Rolling up’ data nationwide

While CHIR will increase the number of data fields within the electronic health record that are available for research, a related project will greatly expand the number of patient records available for any given study.

As of now, the records from each of VA’s more than 1,400 care sites are gathered together only at the regional level. Most studies based on patient records use charts only from a facility-wide or region-wide sample—say, from the Southwest. Some administrative data are pulled out and made available in national databases, and VA researchers have been using these for years, but this represents only part of the data available in the actual records.

That will change, thanks to an initiative called Veterans’ Informatics, Information, and Computing Infrastructure. Known by the acronym VINCI, the project will “roll up” electronic medical records from VA sites nationwide into one secure, centralized data repository.

“VINCI will make all the data available for researchers in a highly secure fashion,” explains Samore. “The data will never be taken off the VINCI servers. And the tools to do natural language processing will be installed and available for use within the VINCI environment.”

Adds Ward, “Not only will the data that researchers have access to be much richer [because of the ability to analyze free text], but they’ll be able to include veterans everywhere.”

She notes that currently, veterans seen at medical centers with no research program are far less likely to be included in database studies by VA investigators at other sites. The new paradigm will allow for more representative sampling of veterans nationwide.

Between CHIR and VINCI, experts expect that VA researchers will be in a



VA's electronic medical record

VA's electronic medical record system is often referred to as the Computerized Patient Record System, or CPRS. Actually, CPRS is a Windows interface to the umbrella system known as VISTA (Veterans Health Information Systems and Technology Architecture), which contains more than 100 clinical, financial and administrative programs. Through VISTA, providers can securely access patient information at any VA care site nationwide. They can update a patient's history, place orders, review test results, and view X-rays and other images.

As of June 2006, VISTA contained:

- 839 million clinical documents, such as progress notes or discharge summaries (601,000 added each workday)
- 506 million images (755,000 added each workday)
- 1.02 billion vital-sign measurements (690,000 added each workday)

position to conduct large, nationwide studies—in some cases covering up to two decades of patients’ medical care, as documented in their electronic records—with unprecedented efficiency and precision. The end beneficiaries of the knowledge gained, notes Samore, will be veterans.

“VA research is always tied to care of veterans and efforts to improve care,” he says. “It’s not just research for research’s sake.” —

Inside: Enhancing the role of electronic health records in research and care

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them had at least one mental health diagnosis. “What’s really striking is the dramatic acceleration in mental health diagnoses, particularly PTSD, after the beginning of the conflict in Iraq [in 2003],” said lead author Karen Seal, MD, MPH, noting that no such trend was seen after U.S. forces began fighting in Afghanistan in 2001.

In the latest study, nearly 22 percent of the veterans had PTSD. Among veterans who had been on active duty, PTSD was nearly twice as common in the youngest cohort—those under age 25—as in those over age 40. Among National Guard and Reserve veterans, the trend was reversed: Older veterans were at higher risk than their younger peers for PTSD.

Active-duty veterans who were of enlisted rank, who served in the Army rather than other service branches, or who had multiple tours of duty—all factors linked with greater combat exposure—were more likely to have PTSD.

Other common diagnoses were depression, seen in 17 percent of the veterans, with women at higher risk than men; alcohol use disorder, affecting 7 percent of the veterans; and drug use



Photo by Roy Noltzschmidt

The Brain at War—Drs. Valerie Cardenas-Nicholson and Timothy Durazzo review MRI scans of the brain at the Neuroscience Center of Excellence at the San Francisco VA. For a research guide titled “The Brain at War,” based on a recent center symposium, visit www.ncire.org.

disorder, 3 percent. A third of those with mental health problems had three or more different conditions.

The study didn’t explore why there was a sharp uptick in mental health issues following the start of the Iraq war. But the authors say possible reasons include “waning public support and lower morale among troops, as occurred during the Vietnam war era,” along with a war zone

characterized by unpredictable threats, such as from roadside bombs. They also cite increasing media attention and multiple, longer deployments. To address the trends noted in the study, the authors recommend targeted screening for mental health problems and early interventions tailored to the problems of particular subgroups of veterans, such as women, young men under age 25, and Guard and Reserve members over 40. —