

VA RESEARCH & DEVELOPMENT

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A Message from the Chief Research and Development Officer

Together, the four services of VA research cover the spectrum of research from basic biomedical science to the delivery of health care. One way the Office of Research and Development provides synergy to these efforts is by organizing the research enterprise into nine Designated Research Areas (DRAs) that cut across traditional research boundaries and represent health issues of concern to the veteran population. While pursuing the common goal of improving health care for veterans and the nation, each service brings unique strengths to our endeavor.

The Cooperative Studies Program that I have the privilege of directing determines the effectiveness of new therapies through large-scale, multicenter clinical trials. VA investigators-with collaborators across the country and sometimes around the world-improve survival and quality of life for patients with heart disease, lung disease, cancer and many other illnesses.

The Medical Research Service, led by **Paul Hoffman, M.D.**, focuses on the causes, development, diagnosis and treatment of disease. Its recent achievements include establishment of a new program to support novel research strategies in specific disease areas and advances in understanding and treat-



ing chronic pain, infectious diseases, liver disease, neurological disorders, and mental illness.

Mindy Aisen, M.D., directs the Rehabilitation Research and Development Service, which dedicates its efforts to minimizing loss and restoring function for veterans with chronic impairment. Its research program includes nine special centers, where investigators concentrate on specific rehabilitation questions, including disabilities associated with aging, hearing loss, and the testing and development of better wheelchairs.



The Health Services Research and Development Service, led by **John Demakis, M.D.**, identifies effective and cost-effective ways to organize and deliver health care. For example, its Quality Enhancement Research Initiative is improving patient and system outcomes by implementing research results, assessing physician practice behavior, and reducing unnecessary practice variations.

Increasingly, our four services find common interests and opportunities for collaboration across disciplines. Even as they conduct research within their own specialties, they are bound by the unifying goal ensuring that our veterans receive the best possible care. This document highlights some of VA's recent accomplishments in each of our Designated Research Areas. I am pleased to share it with you.

John R. Feussner, M.D.
Chief Research and Development Officer

1

Aging and Age-Related Changes

Research in this area represents VA's efforts to identify the unique characteristics of the aging process and develop strategies to treat or prevent age-related health problems. Scientists have focused, for example, on the different nutritional needs of older adults; treatment and prevention of frailty, immobility and falls; and end-of-life issues. Following are a few examples of our recent research achievements in this area.

Age-associated memory loss may be reversible

A VA team and colleagues have identified a process by which the normal primate brain degenerates with aging and showed that this degeneration can be reversed by gene therapy. In a study of normal monkeys, the researchers found that aging was accompanied by significant shrinkage and loss of function in nerve cells of the brain's cholinergic system, which regulates the brain's cortex and hippocampus, allowing the cortex to process information. Equally important, these nerve cells were not dead, only atrophied, and returned to nearly normal function and appearance after gene therapy that delivered nerve growth factor to the impaired cells. In addition to implications for cognitive function in normal aging, the findings also may offer a new approach against the cognitive decline in conditions such as Alzheimer's disease, in which this same system of cells degenerates and dies. [Medical Research Service](#)

Smith DE, Roberts J, Gage FH, Tuszynski MH. Age-Associated Neuronal Atrophy Occurs in the Primate Brain and is Reversible by Growth Factor Gene Therapy. Proc Natl Acad Sci USA;96(19): 10893-8, 1999.

Study evaluates VA hospice care

VHA's National Health Plan includes access to an organized and coordinated program of hospice care for all eligible veterans who need and want such care. This study assessed the effectiveness and efficiency of programs providing hospice care to veterans. It found that hospice programs are common throughout VA and are expanding. VA medical centers have adopted two major approaches to providing services: Referring patients

to non-VA community hospice for home care (65 percent), or providing inpatient care at VA medical centers (35 percent). Satisfaction with VA hospice care is high and has similar satisfaction levels to those of the non-VA population. VA has used these findings to expand or change hospice programs that will continue to improve the quality of end-of-life care. [Health Services Research and Development](#)

Hickey, EC, Berlowitz, DR, Anderson J, Hankin C, Hendricks A, Lebner L. The Veterans Hospice Care Study: an evaluation of VA hospice programs. Final Report. February, 1998. Report Number MRR-97-004.

Study focuses on nutrition for the hospitalized elderly

Many studies have shown a strong correlation between the severity of nutritional deficits and an increased risk of adverse outcomes among the hospitalized elderly. This study examined the nutritional intake of 497 elderly patients, without cancer or other terminal conditions, who were hospitalized at VA facilities. Findings showed that 21% of these patients had an average daily in-hospital nutrient intake that was less than 50% of the calculated requirements. While this group did not differ from the other subjects in the reason for their hospital admission or the length of their hospital stay, they did lose more weight while in hospital and they had a higher mortality rate. A few of the factors contributing to the problem of inadequate nutrient intake were the ineffective utilization of both canned supplements and nutrition support. These results show that given the difficulties of reversing nutritional deficits in elderly patients, greater attention must be paid to preventing this problem during periods of hospitalization. [Health Services Research and Development](#)

Sullivan DH, Sun S, Walls RC. Protein-energy undernutrition among elderly hospitalized patients. Journal of the American Medical Association;281: 2013-2019, 1999. IIR 92-112.

Outcomes of specialized care for elderly patients evaluated

The proportion of veterans over age 65 will increase from 26 percent in 1990 to 46 percent in 2020, and VA must be prepared to serve the needs of this growing population. A large, multi-outcome study will determine whether specialized inpatient and outpatient units are the best way for VA to care for elderly patients. The impact of this study will extend far beyond VA, as mil-

lions of older Americans come under managed care. No other study is likely to provide the conclusive and incontrovertible evidence needed to guide policy in this critical area. [Cooperative Studies Program](#)

Evaluation of Geriatric and Management (GEM) Units and Geriatric Follow-up. CSP #6. Palo Alto.

Improving long-term care for aging veterans

VA has one of the most comprehensive long-term care (LTC) programs in the nation. Nearly 30 percent of veterans are age 65 or older. A substantial number of these veterans will have LTC needs. This study sought to identify existing data on LTC and document any limitations in providing this type of care. This study compiled a three-volume Resource Guide: VA Long Term Care Programs and Services (VALTC) that is now being maintained and updated by the VA Information Resource Center (VIREC). The dissemination of the VALTC will help researchers use available VA data and guide policy makers as they make decisions about long-term care, especially for our growing elderly population. [Health Services Research and Development](#)

Weaver F, Guiban M, Cowper D, Nydam T, Miskevics S. VA Guide to Long Term Care Program and Services. <http://www.virec.research.med.va.gov/SDR/93-113>.

Study links periodontitis with higher risk of heart disease and stroke

Oral conditions are important factors in general health and well-being. A study using data from the VA Normative Aging Study (NAS) and the VA Dental Longitudinal Study (DLS) found that subjects with advanced periodontitis were more likely to develop chronic heart disease and were at higher risk for stroke. This information helps clinicians identify patients at risk. [Health Services Research and Development](#)

*Garcia, RI, Krall EA, Vokonas PS. Periodontal disease and mortality from all causes in the VA Dental Longitudinal Study. *Ann Periodontol*;3(1):339-349, 1999. RCD 93-310.*

2

Acute Illness and Traumatic Injury

The field of acute and traumatic injury is comprised of injuries due to blunt force, temperature extremes, electric shock, pressure, or diseases such as diabetes and cancer. Specific focus areas within this field include amputation, bone fractures, brain injury, multi-organ failure, stroke, and shock. Researchers are also investigating the physical, psychological, cognitive and behavioral effects of acute and traumatic injuries, and the health services and procedures required to treat them. In this section we describe selected research findings that are advancing care for acute and traumatic injury.

Improving amputee mobility and independence

VA researchers in Seattle are developing new prosthetic limbs that will provide unprecedented mobility for veteran amputees. Many individuals with amputations across the shin or thigh lack endurance because of the extreme effort simply to walk with today's prosthetic limbs. To combat this problem, researchers developed an artificial muscle and tendon to replace the lost musculature of the lower limb. The resulting powered prosthetic limb, which will enter clinical testing soon, is expected to reduce patient fatigue and produce greater propulsive forces for walking. [Rehabilitation Research and Development](#)

*Klute GK, Hannaford B. Fatigue characteristics of McKibben artificial muscle actuators, *Proceedings of the IEEE/RSJ 1998 International conference on Intelligent Robotic Systems (IROS '98)*, Victoria BC, Canada:1776-1781, 1998. A0806-C.*

Practices identified with improved outcomes for patients with stroke

With the emergence of effective drug therapies for the treatment of stroke, interest has increased in identifying effective practices for these patients. This study sought to describe the full array of patient outcomes associated with stroke and identify those practices associated with improved patient outcomes. Researchers studied 1,073 patients with acute stroke from nine VA medical centers. Of these patients, 10 percent died during their hospital stay and 69 percent were discharged to the community, with 79 percent on

antiplatelet or antithrombotic agents. Measures of physical function and psychological health indicate that the greatest improvement took place during the first six months after stroke. Through the identification of practices associated with improved outcomes, health care providers will be able to increase the cost-effectiveness of care provided to acute stroke patients hospitalized in VA and non-VA facilities. [Health Services Research and Development](#)

Horner RD. Commentary on "Factors Contributing to Practice Variation in Post-Stroke Rehabilitation." *HSR: Health Services Research*;32: 223-227, 1999. SDR 93-003.

Popular arthritis drugs proven dangerous for ulcer sufferers

A new class of painkillers, COX-2 inhibitors, used to treat arthritis, may prove dangerous for some individuals. These drugs differ from conventional nonsteroidal anti-inflammatory drugs (NSAIDs) in that they block the enzyme involved in pain and inflammation (COX-2) and do not harm COX-1, which protects the stomach. However, recent VA research shows that these drugs may block the body's natural ability to heal stomach ulcers by inhibiting angiogenesis, the formation of tiny blood vessels that are essential to wound and ulcer healing. Researchers treated rat and human cells with indomethacin, a conventional NSAID or NS-398, a COX-2 inhibitor. Results showed a significant decrease in angiogenesis with the COX-2 inhibitor. [Medical Research Service](#)

Jones MK, Wang H, Peskar BM, Levin E, Itani RM, Sarfeh IJ, Tarnawski AS. Inhibition of angiogenesis by nonsteroidal anti-inflammatory drugs: Insight into mechanisms and implications for cancer growth and ulcer healing. *Nature Medicine*;5(12):1418-1423, 1999.

VA patients receive high quality care for heart attacks

As part of the Quality Enhancement Research Initiative (QUERI), the Ischemic Heart Disease group, recently assessed VA treatment for patients suffering from heart attack (acute myocardial infarction, AMI). The study found that VA has comparable or superior quality of care for veterans with AMI compared to the private sector in three main areas: key validated quality measures (including the use of aspirin, beta-blockers and ACE inhibitors and in avoiding the use of calcium channel blockers); guideline compliance, and; cardiac procedure use. The study also found that VA

needs to decrease the time between a patient's arrival at a treatment facility and the administration of a thrombolytic agent. [Health Services Research and Development](#)

QUERI IHD Group. *The Treatment of Acute MI in the Veterans Health Administration: Quality Assessment. Acute Myocardial Infarction Report, Quality Enhancement Research Initiative Ischemic Heart Disease Group, May 21, 1999. QUERI IHD.*

Study establishes national baseline measures to evaluate cardiac care

Acute myocardial infarction (AMI), a type of heart attack, is a leading cause of mortality and morbidity among veterans and the general population. Information from the Center for the Study of Practice Patterns in Veterans with AMI has helped policymakers, clinicians, and administrators better understand patterns of care for veterans hospitalized with AMI. Analyses of a national database that includes all VA hospitalizations for AMI between 1988 and 1997 have yielded several important findings: 30 day mortality rates for veterans with AMI decreased by 23 percent between 1988 and 1997; cardiac catheterization increased by 30 percent, bypass surgery by 50 percent, and coronary angioplasty by 176 percent between 1988 and 1995; and mortality rates for veterans with AMI were similar between those initially hospitalized in VA vs. Medicare-financed hospitals between 1992 and 1996. Study publications have addressed issues related to access, effectiveness and cost of cardiac care in the VA and have helped establish national baseline measures that can be used to evaluate the effectiveness and quality of current and future cardiac care for veterans. [Health Services Research and Development](#)

Petersen LA, Wright SM, Normand SL, Kluiber S, Daley J. Positive predictive value of the diagnoses of acute myocardial infarction in the VA patient treatment file. *J Gen Intern Med, 14(9):555-558, 1999. PPR 94-001.*

Improved design and function of upper limb prostheses

A VA research initiative involving microcomputer technology will modernize the design of electric-powered upper limb prostheses. VA researchers are developing a position-sensitive controller that will improve functional performance, fitting flexibility, and ease of operation. The new controller provides sensory feedback from the prosthesis to the ampu-

tee, thus giving the amputee a better “feel” for the position of his prosthetic limb in space. This important research by VA will help assure better prostheses and better controllers for all upper-limb amputees. [Rehabilitation Research and Development](#)

Weir RF, Childress DS, and Heckathorne CW. Towards Achieving the Goal of Meaningful, Coordinated, Subconscious, Multi-Functional, Control of Prostheses. Proceedings of the VA Rehabilitation Research & Development Service 1st Annual Meeting, “Enabling Veterans: Meeting the Challenge of Rehabilitation in the Next Millennium,” Washington, 1998.

Bertos YA. The Design and Development of an Embedded Microcontroller System for an E.P.P. Based Position Controller for Upper-Limb Prostheses. Master’s Thesis, Dept. Electrical Eng., Northwestern University, 1999. A2087-RA.

Implants may be future innovations for prostheses

Directly anchoring prostheses to bone using titanium implants produces better sensory perception than traditional socket prostheses. This phenomenon, called osseoperception, facilitates improved feedback control of the prosthesis and enhances psychological acceptance of the artificial limb. It is believed to be associated with increased sensory nerve fiber density in bone as well as structural and functional changes in sensory and sympathetic neurons.

Researchers at the VA San Diego Health Care System have developed an experimental model in which titanium implants are installed in the thigh bones of rats. Preliminary results show changes in expression of the neuropeptide parallel increases in the neuropeptide CGRP, which helps regulate bone remodeling. [Rehabilitation Research and Development](#)

Ysander M, Brånemark R, Meyers RR. Nerve fiber density and neuropeptide expression, especially CGRP related to osseointegration of the experimental fixture. Journal of the Peripheral Nervous System;4(2):207, 1999.



Military Occupational and Environmental Exposures

Military Occupational and Environmental Exposures are a unique concern to veterans. Researchers working in this field are investigating the chronic health effects of events veterans experience during military service. This includes contact with foreign substances, such as toxins, irritants, or emerging pathogens, extreme temperatures, and post-traumatic stress disorder (PTSD). Gulf War veterans are a particular focus as we learn more about their special health concerns. Following are descriptions of selected studies in the areas of Gulf War Veterans Illnesses (GWVI), PTSD and Infectious Agents.

GULF WAR VETERANS ILLNESSES

Amyotrophic Lateral Sclerosis (ALS) among Gulf War veterans

The Durham Epidemiologic Resource and Information Center has initiated an epidemiological investigation of the incidence of ALS (Lou Gehrig’s disease) among veterans of the Gulf War. The study will focus in particular on three areas: defining the natural history of ALS; determining whether there is a higher-than-expected occurrence of ALS among Gulf War veterans; and ascertaining the possible or probable cause(s) of ALS if above normal event rates are determined.

Through a national survey of veterans and follow-up examinations, the study will increase understanding of ALS among Gulf War veterans by developing descriptive epidemiology of cases. It will also compare the rate of ALS among Gulf War veterans with that of military personnel on simultaneous active duty but not deployed to the Gulf. Researchers will also investigate possible etiologic factors (with focus on environmental factors) in the Gulf and possible genetic-based susceptibilities to neurodegenerative disorders. [Cooperative Studies Program](#)

An Investigation into the Occurrence of ALS Among Veterans of the Gulf War. CSP# 500, Durham.

Testing antibiotic treatment for patients with Gulf War Veterans Illnesses (GWVI)

In this CSP study, VA researchers are testing a possible treatment for Gulf War Veterans Illnesses (GWVI). Although the cause of GWVI is unknown, one explanation that has received fairly wide attention holds that infection with the microorganism *Mycoplasma fermentans* may be responsible. The purpose of this study is to determine the effectiveness of a one-year course of an antibiotic called doxycycline in patients with GWVI who test positive for mycoplasma species. If doxycycline is shown to be effective, this relatively inexpensive and easily delivered drug could improve symptoms and possibly cure many veterans with GWVI. [Cooperative Studies Program](#)

Collaborator: Pfizer Pharmaceuticals. Antibiotic Treatment of Gulf War Illnesses. CSP #475, Perry Point

Assessing new approaches for treating veterans with Gulf War Veterans Illnesses (GWVI)

There is no definitive therapy for treating GWVI, and veterans suffering from this symptom complex are frequently frustrated by continued pain, fatigue or cognitive difficulties. VA researchers are trying to determine whether cognitive behavioral therapy and aerobic exercise, two approaches that have provided relief for people with fibromyalgia and chronic fatigue syndrome, can be used to help veterans with GWVI. The study is enrolling 1,356 GWVI patients in one of four treatment groups: cognitive behavioral therapy plus aerobic exercise, aerobic exercise alone, cognitive behavioral therapy alone, and usual and customary care. Treatment will be provided for three months and patient outcomes will be tracked for one year. This research may provide needed answers for veterans who suffer from these mysterious and often disabling illnesses. [Cooperative Studies Program](#)

A Randomized, Multi-Center, Controlled Trial of Multi-Modal Therapy in Veterans with Gulf War Illness. CSP #470, West Haven

VA survey assesses health of Gulf War veterans and their families

A large-scale survey by VA of Gulf War veterans and their families will help guide future policy regarding the appropriate care and support of these veterans,

many of whom have complained of a variety of symptoms collectively known as Gulf War Veterans Illnesses. The study will compare the prevalence of physical and psychological conditions among deployed and non-deployed Gulf War veterans, their spouses and their children. To date, researchers have surveyed veterans by mail and by telephone for this legislatively mandated study. Researchers are now conducting clinical examinations of veterans, spouses and children from each group. [Cooperative Studies Program](#)

National Health Survey of Gulf War Veterans and Their Families - Phase III Physical Examinations. CSP #458, Hines.

POST-TRAUMATIC STRESS DISORDER

Toward better treatments for post-traumatic stress disorder

Post-traumatic stress disorder (PTSD) is characterized by flashbacks, nightmares, startled reactions, depression and withdrawal from family and friends. VA researchers have made tremendous progress in efforts to advance understanding of neurological changes that may underlie these debilitating symptoms. In one recent study, investigators used positron emission tomography imaging to measure cerebral blood flow in groups of Vietnam veterans while they were watching pictures and sounds of combat and neutral situations. Results suggest that functional alterations in specific brain areas involved in memory, visuospatial processing and emotion may underlie the symptoms of patients with PTSD. Findings in this and other studies may ultimately allow researchers to design better treatments for the disorder. [Medical Research Service](#)

Bremner JD, Staib LH, Kaloupek D, Southwick SM, Soufer R, Charney DS. Neural correlates of exposure to traumatic pictures and sound in Vietnam combat veterans with and without post-traumatic stress disorder: a positron emission tomography study. Biol Psychiatry;45(7):806-16, 1999.

Researchers look to group-treatment model for relief of PTSD

Despite the often devastating effects of post-traumatic stress disorder (PTSD) on veterans, there is no proven, effective method to treat this condition. This randomized clinical trial will test what VA considers to be the most promising approach for treating PTSD, trauma focus group therapy (TFGT). This study is evaluating the efficacy of TFGT for

treating PTSD symptoms and its effect on other psychiatric symptoms, functional impairment, physical health and utilization of medical and mental health services. If this intervention is found to be effective and feasible, VA will have at least one proven therapy for veterans with this debilitating combat-related illness. [Cooperative Studies Program](#)

Group Treatment of PTSD. CSP #420, Palo Alto

INFECTIOUS AGENTS

VA care for HIV is at least as cost-effective as non-VA care

VA is the nation's largest provider of care to HIV-infected individuals. This study examined data from two projects that included more than 2,000 HIV-infected patients receiving care at VA facilities, non-VA facilities, or patients who used both VA and non-VA health care providers. Findings show that even after considering patients' clinical and socioeconomic characteristics, there were no differences among VA-only users, dual VA and non-VA users, and only non-VA users for most of the health care utilization measures. Further, overall results indicate that for HIV-infected patients, care provided at VA settings is at least as cost-effective as care provided at non-VA settings. [Health Services Research and Development](#)

Menke TJ, Rabeneck L, Soucek J, Wray NP. Comparison of Department of Veterans Affairs (VA) and non-VA health care utilization and outcomes among HIV-infected men. Annual meeting of the Association for Health Services Research (AHSR). Chicago, 1999. IIR 95-107.

Emerging pathogens: The search for unrecognized microbes

AIDS, drug-resistant tuberculosis, hepatitis C and other emerging diseases underscore that the fight against infectious diseases continues despite antibiotics and other 20th century advances. Previously unrecognized organisms threaten new epidemics, and scientists now believe that microbes may trigger an array of disorders without currently known causes. As leaders in the effort to thwart new diseases, a VA team has developed new molecular techniques based on polymerase chain reaction amplification, which can turn a tiny shred of microbial genetic material into millions of copies that can then be analyzed and compared to genetic makeup of known organisms. The

VA researchers already have characterized several bacterial agents causing disease and identified a previously unknown parasite that killed a patient with HIV infection. They have also shown that a region of the normal human mouth contains many more kinds of bacteria than had been detected with traditional culture techniques. [Medical Research Service](#)

Relman, DA. The search for unrecognized pathogens. Science;284(5418):1308-10, 1999.

Kroes I, Lepp PW, Relman DA. Bacterial diversity within the human subgingival crevice. Proc Natl Acad Sci USA;96(25):14547-52, 1999.

Santamaria-Fries M, Fajardo LF, Sogin ML, Olson PD, Relman DA. Lethal infection by a previously unrecognized metazoan parasite. Lancet;347(9018):1797-801, 1996.

Flesh-eating bacteria studies point to better treatments

VA researchers have conducted landmark studies on the so-called "flesh-eating" group A streptococcal bacteria that can destroy body tissues and trigger fatal shock and organ failure. This team was the first to describe a group of patients who had suffered toxic shock syndrome caused by these strains of streptococci, the bacteria best known as the cause of strep throat. The researchers showed that toxins produced by these virulent strains cause the release of body chemicals that trigger the shock and organ failure. The team has also done critical work showing that penicillin, the antibiotic traditionally used to treat group A streptococcal infections, is ineffective against the flesh-eating strains and that patients must be treated with antibiotics that suppress toxin production. [Medical Research Service](#)

Stevens DL, Bryant AE, Hackett SP, Chang A, Peer S, Kosanke S, Emerson T, Hinshaw L. Group A Streptococcal bacteremia: The role of tumor necrosis factor in shock and organ failure. J Inf Diseases 173:619-626, 1996.

Stevens DL. The flesh-eating bacterium: what's next? J Infectious Diseases;(3)179:Suppl 2:S366-74, 1999.

4

Chronic Diseases

VA research focuses on the range of chronic diseases and conditions that are highly prevalent among veterans, including life-threatening conditions and less severe problems that affect quality of life and the need for health services. The disease may be a primary ail-

ment or a complication resulting from another disease. Specific areas of emphasis include bone and joint disorders, cancer, vascular diseases, chronic infectious diseases, lung and renal diseases, dementias, diabetes, gastrointestinal disorders and spinal cord dysfunction. Below are short descriptions of VA Research studies in some of these areas.

HEART DISEASE

Non-invasive approach works better at managing patients with non-Q-wave infarctions

Most patients who suffer a certain kind of heart attack known as a non-Q-wave infarction can be managed with a non-invasive approach that improves their survival and reduces treatment costs, according to results from VA's VANQWISH (VA Non-Q-Wave Intervention Strategies in Hospital) trial. This study evaluated two competing diagnostic and clinical care approaches in treating patients with non-Q-wave heart attacks. Under the conventional approach, coronary angiography is the essential first step, followed by additional non-invasive tests or therapeutic interventions. However, this invasive strategy is costly and poses additional risk to the patient. Alternatively, the patient may undergo non-invasive tests, followed by whatever procedures are deemed necessary by the physician. This approach proved to reduce mortality, an unexpected and important finding. These results have significant implications, both for the improved survival of patients who suffer non-Q-wave infarctions and for avoiding unnecessary invasive procedures. [Cooperative Studies Program](#)

Collaborator: Marion Merrell Dow Pharmaceuticals.

Boden WE, O'Rourke RA, Crawford MH, et al. Outcomes in patients with acute non-Q-wave myocardial infarction randomly assigned to an invasive as compared with a conservative management strategy. New England Journal of Medicine; 338 (25):1785-1792, 1998. CSP #368, Palo Alto.

Gemfibrozil is cost-effective therapy for heart disease

Groundbreaking VA research demonstrated the effectiveness of the drug gemfibrozil in reducing coronary heart disease (CHD) among certain patients. About 25 percent of (CHD) patients have a lipid abnormal-

ity characterized by low HDL-cholesterol ("good" cholesterol) in the absence of high-risk LDL-cholesterol. The VA HDL Intervention Trial (HIT) is the first study to show significant reduction in the risk of major cardiovascular events by raising HDL, lowering triglycerides and not changing LDL levels. HIT was a seven-year, double-blind trial comparing the use of gemfibrozil with a placebo in 2,531 men. Daily use of gemfibrozil reduced CHD risk by 22%, with significant reductions in CHD death, heart attack, stroke, and transient ischemic attacks. Gemfibrozil is off patent (available as a generic drug) and since there were no major adverse events associated with it, use of this medication is likely to reduce costs as well. [Cooperative Studies Program](#)

The VA HDL Trial (HIT): Secondary prevention of coronary heart disease in men with low HDL-cholesterol and desirable LDL-cholesterol. New England Journal of Medicine; 341(6):410-8, 1999. CSP #363, West Haven.

Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE)

Heart disease affects more than 7 million people in the United States and is the leading cause of death among Americans. The COURAGE study is a large-scale, multi-center, randomized controlled trial comparing the effectiveness of angioplasty with medical therapy to medical therapy alone in patients with coronary heart disease. Investigators are testing whether angioplasty with intensive medical therapy is superior to intensive medical therapy alone, using the combined endpoint of all-cause mortality or non-fatal myocardial infarction. This international 6.5-year study involves 37 hospitals—12 VA, 12 US non-VA, and 13 Canadian—and more than 3,000 patients. [Cooperative Studies Program](#)

Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE. CSP #424, West Haven.

Warfarin and Antiplatelet Therapy Study in Heart Failure (WATCH)

Congestive heart failure (CHF) remains an important clinical and societal problem. In the United States alone, it is estimated that more than 4 million patients suffer from CHF, with an annual incidence of more than 400,000 new cases, resulting in 40,000 deaths and

875,000 hospitalizations. Although there have been important advances in the pharmacologic treatment of CHF over the past two decades, CHF remains a very lethal condition.

The use of anticoagulant therapy to prevent thromboembolic complications in patients with dilated cardiomyopathy has long been advocated, but little is known about the efficacy of this therapy, the optimal therapy, and for whom the therapy will be effective. Current practice guidelines reflect this uncertainty. This study will compare the effect of three antithrombotic therapies in patients with congestive heart failure. Eligible patients will be randomized to treatment with aspirin, warfarin or clopidogrel. This international study will enroll 4,500 patients over three years at up to 150 centers, with all patients followed for a minimum of two years. Non-VA centers in the United States as well as Canadian and United Kingdom centers will participate. [Cooperative Studies Program](#)

Warfarin and Antiplatelet Therapy Study in Heart Failure (WATCH). CSP #442, Perry Point.

Researchers evaluate use of beta-blockers for chronic heart failure patients

This major study, jointly funded by the National Heart, Lung and Blood Institute and the Intercardia Corporation, found that the beta-blocker bucindolol did not reduce death from heart failure. The Beta-Blocker Evaluation and Survival Test (BEST) involved 2,800 patients with moderate to severe heart failure. Earlier studies found that beta-blocker treatment improved survival. BEST's results may be related to its use of a different medication and its greater number of African American participants and patients with severe heart failure. Although unexpected, the study's results point the way to further research to determine which patients are most likely to benefit from beta-blocker therapy and the need to examine gender, racial and ethnic differences in studies of cardiovascular disease. [Cooperative Studies Program](#)

Collaborators: National Heart Lung & Blood Institute; Intercardia Pharmaceuticals

Beta-Blocker Evaluation of Survival Trial. 72nd Scientific Sessions of the American Heart Association, Atlanta, GA, 1999. CSP #395, Palo Alto.

PROSTATE CANCER

Landmark prostate cancer trial will illuminate treatment options

The management of localized prostate cancer in older men has generated considerable debate due to the risks and potential benefits associated with different treatment options. Prostate cancer is the second most frequent cause of cancer deaths in men. Research shows patients' treatment preferences vary significantly, depending on the risk associated with surgery, life expectancy, symptoms and tolerance for their symptoms. As a result, patient preference and experience are critical factors in making treatment decisions for prostate cancer.

Important questions remain concerning long-term outcomes for prostate cancer treatment. VA, in collaboration with the National Cancer Institute (NCI) and the Agency for Healthcare Research and Quality (AHRQ), is addressing these questions through a landmark study that compares the two most widely used treatment methods: radical prostatectomy, in which the prostate is surgically removed, and "watchful waiting" in which only the disease symptoms are treated. The Prostate Cancer Intervention Versus Observation Trial (PIVOT) is a 15-year, randomized study involving 2,000 men from approximately 80 VA and NCI medical centers throughout the country. All patients will be followed for at least 12 years. The results will supply information on treatment-specific survival rates, complications and quality of life.

When completed, this study will provide more definitive answers on the best treatment for early-stage prostate cancer. If watchful waiting is as effective as surgery, million of health care dollars could be saved every year by avoiding unnecessary surgery. On the other hand, results favoring surgery would highlight the need for early detection and treatment of this disease. [Cooperative Studies Program](#)

Collaborators: National Cancer Institute; Agency for Healthcare Research and Quality

*Wilt TJ, Brawer MK. The prostate cancer intervention versus observation trial (PIVOT). *Oncology*;11(8):1133-1143, 1997. CSP #407, Perry Point.*

Patients and clinicians rate quality of life

Prostate cancer is the most common cancer among veterans today. This study evaluated changes in veteran patients' quality of life for 12 months following diagnosis, and compared patients' and VA clinicians' ratings of several aspects of health, such as pain, mood, energy, bladder and bowel function, and appetite. Patients and clinicians were asked to rate symptoms in terms of severity and order of importance. Results of this study showed that there was a high concordance between the clinician and patient ranking of the overall current state of the patient's health. However, while 69 percent of clinicians ranked sexual function as least important, 37 percent of the patients ranked it as one of their three most important considerations. The results of this study help health care providers better understand quality of life-related concerns of patients. [Health Services Research and Development](#)

Kim S, Knight S, Chan C, Chmiel J, Falcone D, Smith J, et al. Prostate cancer quality of life and outcomes research among patients with low socioeconomic status: An Overview of the VA CaPOS Project. Oncology;13(6):823-32, 1999. IIR 95-120.

Selenium and Vitamin E Cancer Prevention Trial (SELECT)

Prostate cancer is the most common malignant tumor (excluding non-melanoma skin cancer) among men in the United States. Until now, emphasis has been on screening for early detection and intervention after diagnosis. However, the ideal method to reduce mortality and morbidity of prostate carcinoma is through primary prevention. Studies have suggested that dietary factors may be the most important modifiable risk factors for prostate cancer. The VA is collaborating with Southwest Oncology Group and the National Cancer Institute on a trial of Vitamin E and Selenium in the primary prevention of prostate cancer. SELECT is a randomized, double-blind, placebo-control, trial to assess the effect of selenium and vitamin E alone, and in combination, on the reduction of prostate cancer incidence as detected by annual visits and routine care. Cooperative Studies Program

Selenium and Vitamin E Cancer Prevention Trial (SELECT) CSP #499, Perry Point.

NEUROLOGICAL DISORDERS

New treatment for chronic pain

In a study that may lead to relief for millions of chronic pain sufferers in the United States, researchers at the Minneapolis VA Medical Center have discovered a way to deplete the spinal nerves (neurons) that transmit chronic pain signals to the brain. Using a natural chemical messenger and a neurotoxin, they successfully shut down pain-associated neurons while leaving those needed for the normal pain responses intact. Rats receiving this treatment showed a marked reduction in chronic pain response and their analgesia (absence of pain) did not diminish with time (200 days). They also showed no side effects and the treatment did not affect morphine analgesia, the bedrock of pharmacological treatment for chronic pain.

Further research will evaluate the toxicology of this treatment in large animals, with the goal of easing chronic pain in terminally ill human patients. The same group of researchers has also developed a model of cancer pain that will enable researchers to create new, more effective therapies than the general-target narcotics currently used. [Medical Research Service](#)

Nichols ML, Allen BJ, Rogers SD, Ghilardi JR, Honore P, Luger NM, Finke MP, Li J, Lappi DA, Simone DA, Mantyh PW. Transmission of chronic nociception by spinal neurons expressing the substance P receptor. Science;286(5444):1558-61, 1999.

Improving outcomes for stroke patients: A psychoeducational program for family caregivers

Most stroke survivors return home after initial hospitalization and are assisted in the recovery process by a primary family caregiver, usually the spouse. A pilot study funded by the VA's Houston Rehabilitation Research and Development Center of Excellence on Healthy Aging with Disabilities tested an intervention program to improve post-hospitalization rehabilitation for stroke survivors and decrease the physical and psychological demands on family caregivers.

The psychoeducational intervention program was developed based on the Clinical Practice Guideline, Post-Stroke Rehabilitation, developed by the U.S. Agency for Healthcare Research and Quality (AHRQ, 1995). Preliminary results of this pilot study suggest that the intervention reduces depression and caregiver burden

among individuals caring for a family member following stroke. Caregivers receiving the intervention also reported being better prepared for their caregiving role. Given the vast literature on the negative psychosocial and physical effects of long-term caregiving, these results are quite promising. It also appears that a telephone intervention may be as beneficial for caregivers as the in-home program. Benefits have not been demonstrated on patient outcome variables, but follow-up data from the study are not yet available.

Rehabilitation Research and Development

Ostwald SK, Lim P, Protas E, Hersch G, Robinson-Whelen S, Turle J. Three approaches to assisting family caregivers with in-home rehabilitation of stroke survivors. Gerontologie and Geriatrie, Band 32 (supplement 2), 782, 1999.

Constraint-induced movement therapy: A new family of treatments in neurorehabilitation

A new family of therapies is greatly increasing use of extremities affected by a stroke. For the arm, the therapy involves two or three weeks of restricting movement of the unaffected extremity for up to 90 percent of waking hours and intensely training the affected arm during the trial period. Treatment for the leg involves concentrated training for three weeks. Both procedures result in greatly improved motor ability, and have met with almost 100 percent treatment success. Since stroke is becoming increasingly prevalent among WWII and Korean War veterans, this constraint-induced movement therapy has strong and increasing relevance to the VA mission. It is also receiving increasing attention internationally and has become part of successful clinical research program in the United States and several other countries.

Rehabilitation Research and Development

Taub E, Uswatte G, Pidikiti R. Constraint-induced movement therapy: a new family of techniques with broad application to physical rehabilitation—a clinical review. J Rehabil Res Dev;36(3):237-51, 1999. B95-975R, W 98 0410.

Uncovering clues to the language of movement

Scientists have long debated whether the motor cortex, a region of the brain that helps control muscle movement throughout the body, operates by stimulating select muscles into action or works on a more abstract level by sending complex commands for goal-

directed movement. Researchers at the Syracuse VA Medical Center recorded electrical activity of single cells in the motor cortex of a monkey trained to perform tasks involving a wide variety of wrist movements. They identified two groups of neurons, one corresponding to the activity of muscles and another to the independent muscle activity necessary to achieve a task. This is the first study to document the existence of both types of neurons in the motor cortex.

Deciphering the language of the motor cortex has wide-ranging implications in the rehabilitation field. For people who have suffered stroke or spinal cord injury, these findings may lead to new technology that can reconnect the damaged region or communication pathways of the brain and possibly restore lost functions. [Medical Research Service](#)

Kakie S, Hoffman DS, Strick PL. Muscle and movement representations in the primary motor cortex. Science;285(5436):2136-9, 1999.

New area of brain shown to be involved in thinking

VA researchers recently determined that the motor cortex, an area of the brain previously believed to be limited to controlling voluntary movements, plays a role in the thought process. Their finding is an important step in the quest to understand how the brain's higher functions work and perhaps ultimately identify new approaches to brain disorders such as cognitive problems. The research team taught monkeys a serial order task and rewarded animals with juice snacks for making the right decisions. After learning that light spots would appear in a certain order on a dark computer screen, the monkeys were shown one of the spots and rewarded if they pointed at the spot on the screen where the next should appear. A burst of nerve cell activity took place as the monkeys observed the signal and remembered the sequence, before they made any movement to point. The finding shows that the motor cortex is involved in planning those movements as well as carrying them out. Identifying the mechanisms behind these actions is a first step in advancing the treatment of movement disorders, such as spinal cord injury and stroke.

Medical Research Service

Carpenter AF, Georgopoulos AP, Pellizzer G. Motor cortical encoding of serial order in a context-recall task. Science;283(5408):1752-7, 1999.

OSTEOPOROSIS

Working to understand and prevent osteoporosis

Researchers at the Little Rock VA Medical Center, supported under the Research Enhancement Awards Program (REAP), are advancing understanding of osteoporosis, a bone disease affecting more than 28 million Americans. Specifically, the multidisciplinary effort focuses on identifying the mechanisms of bone loss in patients with metabolic, orthopedic, and cancer-related diseases, and the development of novel therapies for their management. Six VA investigators, led by Stavros C. Manolagas, M.D., Ph.D., are combining expertise in geriatrics, orthopedics, surgery, biochemistry and pharmacology. The REAP funds will also be used to create new training opportunities and to launch novel research initiatives that will translate basic research findings into clinical applications. [Medical Research Service](#)

Jilka RL, Weinstein RS, Bellido T, Roberson P, Parfitt AM, Manolagas SC. Increased bone formation by prevention of osteoblast apoptosis with parathyroid hormone. J Clin Invest;104(4):439-46, 1999.

New methods for analyzing densitometry results can improve osteoporosis diagnosis

Dual-energy X-ray Absorptiometry (DXA) is currently the method of choice for measuring bone density and identifying individuals with low bone mass and osteoporosis. Results can be misleading, however, because different-sized bones of the same density can produce different readings. Researchers at the VA Palo Alto Rehabilitation R&D Center have developed a simple method for adjusting DXA scans of the heel bone for bone size. This new method provides an accurate determination of volumetric bone density. In addition, this group of researchers has developed a new DXA-based index for estimating fracture risk in normal and osteoporotic patients. These new methods have immediate clinical applicability in helping to identify individuals at risk for osteoporotic fractures. [Rehabilitation Research and Development](#)

Wren TAL, Yerby SA, Beaupre GS, Carter DR. Interpretation of calcaneus DXA measurements in the assessment of osteopenia and fracture risk. Journal of Bone and Mineral Research; Submitted August 1999. A2058-2RA.

LIVER DISEASE

Cellular On-off Switch Provides New Tactics Against Liver Disease

VA researchers in San Diego have discovered a cellular pathway that may offer a way to encourage liver cell growth in people with liver damage or to block growth of liver tumors. They found that a gene cloned in the laboratory was a powerful regulator of development when they stimulated mouse liver cells with a hormone known to trigger cell growth. The key step was a single change in the protein product of that gene.

This finding may also point the way to better artificial livers for people needing a transplant and may even suggest ways to restore lost cells in the brain and other tissues. The researchers now hope to learn more about the mechanics of the protein change so they can use it as an “on-off” switch for cell growth, possibly developing drugs or other techniques to flip that switch. [Medical Research Service](#)

Buck M, Poli V, van der Geer P, Chojkier M, Hunter T. Phosphorylation of rat serine 105 or mouse threonine 217 in C/EBP beta is required for hepatocyte proliferation by TGF alpha. Mol Cell, 4(6):1087-92, 1999.

Improved blood testing for Hepatitis C

A VA team has developed a sensitive test to detect hepatitis C virus (HCV) genetic material in whole blood of people with no antibodies detectable by routine testing. Using this method, the group has shown that many people with elevated liver enzymes, but no detectable antibodies are actually infected with HCV. The researchers are studying the virus' molecular biology and patient immune responses to determine how and why HCV can infect and cause disease but remain undetected by current standard diagnostic tests. [Medical Research Service](#)

Stapleton JT, Klinzman D, Schmidt WN, Pfaller MA, Wu P, LaBrecque DR, Han JQ, Phillips MJ, Woolson R, Alden B. Prospective comparison of whole-blood and plasma-based hepatitis C virus RNA detection systems: improved detection using whole blood as the source of viral RNA. J Clin Microbiol;37(3):484-9, 1999.

Schmidt WN, Wu P, Caderna J, Mitros EA, LaBrecque DR, Stapleton JT. Surreptitious hepatitis C (HCV) infection detected in the majority of patients with cryptogenic chronic hepatitis and negative HCV antibody tests. J Infect Dis;176(1):27-33, 1997.

Hepatitis C in chronic infection and liver transplantation

Under the Medical Research Service Research Enhancement Award Program (REAP), investigators at the Portland VA Medical Center are looking at the critical problem of recurring hepatitis C in patients who have had a liver transplant to replace an organ severely damaged by the virus. The researchers are attempting to determine how immune systems of some patients prevent the virus from infecting their new liver, while in other cases a new cycle of liver destruction begins. Other teams are analyzing rapid mutations that seem to keep the virus one step ahead of the immune system, attempting to design a vaccine, and looking at whether HCV alone causes liver disease or if the body's immune response to the organism harms liver tissue. [Medical Research Service](#)

Rosen HR, Lentz JF, Rose SL, Rabkin J, Corless CL, Taylor K, Chou S. Donor polymorphism of tumor necrosis factor gene: relationship with variable severity of hepatitis C recurrence after liver transplantation. Transplantation;68(12):1-5, 1999.

Rosen HR, Hinricks DJ, Gretch DR, Koziel MJ, Chou S, Houghton M, Rabkin J, Corless CL, Bouwer HG. Association of multispecific CD4(+) response to hepatitis C and severity of recurrences after liver transplantation. Gastroenterology;117(4):926-32, 1999.

OTHER CHRONIC CONDITIONS

Anti-anemia drug for dialysis patients may be administered subcutaneously

More than 90 percent of hemodialysis patients experience severe anemia. A new drug, recombinant human erythropoietin, is very effective at combating this anemia, but its cost is \$5,000 to \$10,000 per patient annually when administered intravenously. However, a randomized, multi-center trial by VA with 208 patients found that recombinant human erythropoietin can be administered just as effectively subcutaneously (under the skin), with a dosage reduction of 32 percent and no substantial increase in patient pain or discomfort. The Cooperative Studies Program is working with the Health Care Finance Administration to estimate potential savings to Medicare from subcutaneous administration of epoetin. [Cooperative Studies Program](#)

Collaborator: AMGEN Pharmaceuticals

Kaufman JS, Reda DJ, Fye CL, et al. [The Department of Veterans Affairs Cooperative Study Group on Erythropoietin in Hemodialysis

Patients.] Subcutaneous compared with intravenous epoetin in patients receiving hemodialysis. New England Journal of Medicine; 339(9):578-83, 1998. CSP #392, Hines.

Major trial testing new vaccine against shingles

Shingles in older people is extremely painful and can be disabling. Shingles is caused by the herpes-zoster virus that causes chickenpox in young people. After chickenpox is treated, the virus remains dormant in the body until late adulthood, when it may reactivate and cause shingles. There is no effective treatment for people who suffer from shingles lasting more than a month; nor is there an effective method to prevent shingles. This study will test a promising new vaccine for its ability to prevent shingles or reduce its severity and complications. This randomized, controlled trial will enroll 37,000 older veterans for a minimum of three years. If the vaccine proves successful, it will supply a safe and cost-effective means for reducing the severe impact of shingles and its complications on the health of older veterans. [Cooperative Studies Program](#)

Collaborator: Merck Pharmaceuticals

Trial of Varicella Vaccine for the Prevention of Herpes Zoster and its Complications. CSP #403 West Haven.

Effect of custom orthosis on foot kinematics and forefoot pressure distribution

Foot ulcers related to conditions such as diabetes pose significant problems to patients and a vexing challenge to health care providers. Gaining an understanding of potential causes of foot ulcers, including increased pressures across the forefoot, bony malalignment, and changes in relative motions between bones can lead to a more systematic approach to treatment and prevention of this problem. An experimental flatfoot model is being used to determine the effects of rigid and compliant (flexible) orthoses on the movement of the foot. Computerized scans delineate the bone architecture of each foot and are used to create three-dimensional images for design of customized orthoses. Early results show that the rigid orthosis can correct eversion (outward turning) of three foot bones. [Rehabilitation Research and Development](#)

Sangeorzan BJ, Czerniecki JM. Rehabilitation Research and Development Center for Amputation, Prosthetics, Limb Loss Prevention. A0806-C.

Mechanical stimulation gives human arthritic cartilage cells a boost toward health

Research at the VA Palo Alto Rehabilitation Research and Development Center has yielded new insights into the response of human osteoarthritic cartilage cells to physical force or pressure. As a joint surface is damaged by disease, a specialized form of the structural protein, collagen, is lost from the cartilage, exposing the bone surface, causing pain and reducing freedom of movement. Researchers at the Palo Alto Rehabilitation Research Center showed that a short daily application of hydrostatic pressure, followed by a period with no pressure, increased expression of molecules essential to formation of collagen. Future studies will try to determine which loading conditions produce the best responsiveness and to assess whether mechanical stimulation will provide a viable way to regenerate health cartilage in diseased joints. [Rehabilitation Research and Development](#)

Smith RL, Lin J, Kajiyama G, Shida J, Trindade MCD, Yerby S, van der Meulen MCH, Vu T, Hoffman AR, Schurman DJ, Beaupre GS, Carter DR: Hydrostatic pressure and cartilage repair: analysis of chondrocyte collagen gene expression. Transactions of the 18th Annual Meeting of the Society for Physical Regulation in Biology and Medicine, 1998. A857-RC.

VA researchers honored for nitric oxide discoveries

Ferid Murad, M.D., Ph.D., who shared the Nobel Prize for Medicine in 1998, was honored in part for research he conducted at the Palo Alto VA Medical Center. Dr. Murad and the other laureates received the prize for their discoveries of the role played by nitric oxide in a number of body functions, such as relaxing blood vessels and regulating blood pressure. He was cited for work including the finding that nitroglycerin and related heart drugs act by releasing nitric oxide gas. His studies of cyclic GMP, another small messenger molecule that plays a role in blood vessel dilation, proved important in later work to tease out the workings of nitric oxide.

Another VA researcher well known for contributions to this field is John Hibbs, Jr., M.D., of the Salt Lake City VA Medical Center. Dr. Hibbs was co-recipient of the 1993 William S. Middleton Award, one of VA's highest scientific honors, for research discovering and mapping the production of nitric oxide by macroph-

ages, immune system cells that are among the body's key defenders against cancer and intracellular microbes. He and colleagues also discovered an inhibitor of this process. His findings paved the way for the entire field of nitric oxide study, leading to major advances in knowledge of how the gas mediates many body functions. Dr. Hibbs is continuing studies of the immunological functions of nitric oxide, work that may lead to ways to augment the body's defenses against tumors and infection. [Medical Research Service](#)

Murad F. Discovery of some of the biological effects of nitric oxide and its role in cell signaling. Biosci Rep;19(3):133-54, 1999.

Granger DL, Hibbs JB, Jr. High-output nitric oxide: weapon against infection? Trends in Microbiology 4(2):46-47, 1996

5

Sensory Disorders and Loss

Humans rely on sensory perception to interact with and interpret their surrounding environment. Loss or impairment of a sense, such as sight or hearing, can be a traumatic event, causing mental and emotional anguish. VA researchers are working toward understanding the biological causes of sensory loss, restoring or improving lost function for affected individuals, and improving the health services and rehabilitation aids that are available. Below are examples of our research in vision, language and hearing.

New scanning laser ophthalmoscope promises breakthroughs in assessing visual impairment

VA researchers in Kansas City and Atlanta are conducting a series of studies to hone a state-of-the-art scanning laser ophthalmoscope that will improve the assessment of visual function in people with visual impairments. Among the assessments under way with the new ophthalmoscope: the relationship between basic eye movements and the ability to carry out complex tasks, the ability to find visual information in a visual field, face recognition ability, and an outcomes evaluation project. Ultimately, defining the relationships between visual function as assessed by the scanning laser ophthalmoscope and activities of daily living will help refine diagnosis and training methods used

in vision rehabilitation services. [Rehabilitation Research and Development](#)

Schuchard RA. Fixation/macular binocular perception characteristics in low vision subjects with macular scotomas. *Investigative Ophthalmology & Visual Science*;39:S398, 1998.

Fletcher DC, Schuchard RA, Walker JP, Wing GL, Raskauskas PA. The effect of visual impairments on ADLs and well being as identified by the NEI-VFQ. *Investigative Ophthalmology & Visual Science*;39:S841, 1998.

Successful mobility rehabilitation in patients with medical eye conditions

Investigators at Chicago Westside VA Medical Center recently completed a project to evaluate the effectiveness of three different optical enhancement systems on driving rehabilitation for patients with peripheral or central vision loss. Patients with peripheral visual field loss who were given amorphic lenses and training in their use showed increased visual functioning skills in the areas of recognition, mobility, peripheral detection, scanning, tracking, and visual memory. Patients with central vision loss who were given bioptic telescopes and training showed improvement in nearly all visual skills categories. Training in the use of the lenses resulted in greater improvement in nearly all of the visual skill areas compared to the performance of patients who received lenses but no training. Patients with hemianopic loss, the loss of half the vision field, showed smaller improvements than other patient groups. From these findings, customized training programs have been developed for different types of vision loss. [Rehabilitation Research and Development](#)

Szlyk JP, Seiple W, Laderman DJ, Kelsch R, Stelmack J, McMahon T. Measuring the effectiveness of bioptic telescopes for patients with central vision loss. *Journal of Rehabilitation Research and Development*, 37, 2000.

Szlyk JP, Fishman GA, Grover S, Revelins BI, Derlacki DJ. Difficulty in performing everyday activities in patients with juvenile macular dystrophies with a comparison to patients with retinitis pigmentosa. *British Journal of Ophthalmology*;82:0-4, 1998.

Szlyk JP, Seiple W, Laderman DJ, Kelsch R, Ho K, McMahon, T. The use of bioptic amorphic lenses to expand the visual field in patients with peripheral loss. *Optometry and Vision Science*, 75, 518-524, 1998

Szlyk JP, Fishman GA, Aslan RJ, and Grover S. Legal blindness and employment in patients with juvenile-onset macular dystrophies or achromatopsia. *RETINA*, 18, 360-367, 1998 C754-4RA.

Computer program quantifies language handicap in patients with aphasia.

A computer software assessment tool developed by VA researchers has far-reaching clinical applications for the assessment and treatment of language impairment in patients with aphasia, a disorder affecting the generating and understanding of speech. The new program measures the effort expended by listeners who are attempting to understand aphasic speakers. This information can be used to yield a measurement of spoken language handicap, encompassing both the impairment of the speaker and the effects of language impairment on normal listeners. This new tool ultimately will allow clinicians to measure the severity of communication disorder in patients with aphasia, monitor their treatment outcomes, and devise training modules for patients' primary partners. [Rehabilitation Research and Development](#)

Doyle PJ, McNeil MR, Goda AJ, Spencer KA, Cottrell K, Lustig A. The effects of concurrent picture presentation on retelling of orally-presented stories by adults with aphasia. *Aphasiology*;12:561-574, 1998. C894-2RA.

Preventing hearing loss due to ototoxic drugs

Hearing loss is a common side effect of drugs used to treat many medical conditions. Early detection of this side effect, known as ototoxicity, allows physicians to minimize hearing loss.

VA researchers in Portland have shown definitively that ototoxic hearing loss begins primarily in the high-frequency range (above 8000 Hz) that is not normally tested during routine audiologic evaluation. Furthermore, the data have revealed a sensitive range for ototoxicity that is specific to each patient according to their degree and configuration of hearing loss. This research suggests that testing in this range only, requiring only about one-third the time of testing all frequencies, would detect about 90 percent of ototoxic hearing loss relative to full-frequency testing. This sensitive-frequency range is currently being studied to determine its actual effectiveness in patients receiving ototoxic drugs. [Rehabilitation Research and Development](#)

Fausti SA, Henry JA, Helt WJ, Phillips DS, Frey RH, Noffsinger D, Larson VD, Fowler CG. An individualized, sensitive frequency range for early detection of ototoxicity. *Ear Hear*;20(6): 497-505, 1999. CO227RA.

Mental Illness

VA research in mental illness focuses on cognitive conditions, from anxiety disorders and depression to advanced schizophrenia. Investigators in the field have made great strides toward identifying the underlying causes of these disorders and are currently working to identify improved treatment methods and better health service systems to care for those with mental illness. Following are brief descriptions of important studies that illustrate VA's research in this important area.

Award winning sleep studies may help mentally ill

Eminent sleep researcher Robert McCarley, M.D., Deputy Chief of Staff for Mental Health Services at the Brockton/West Roxbury VA Medical Center, won the 1998 William S. Middleton Award, one of VA's highest scientific honors. Recognized as an authority on REM (rapid eye movement) sleep, Dr. McCarley was honored for his important contributions to our understanding of sleep and dreaming. For example, he was the first to systematically develop quantitative methods for testing hypotheses on cellular control of sleep states. He and his colleagues have identified control mechanisms for non-REM sleep and demonstrated that certain brain stem cells that use the neurotransmitter (chemical messenger between nerve cells) acetylcholine are critical for promoting REM sleep. In contrast, they found that other brain cells using the neurotransmitters serotonin and norepinephrine act to inhibit REM sleep. McCarley's work has helped set the stage for new approaches to sleep abnormalities, including sleep disruptions in psychiatric disorders.

Medical Research Service

Porkka-Heiskanen T, Strecker RE, Thakkar M, Bjorkum AA, Greene RW, McCarley RW. Adenosine: a mediator of the sleep-inducing effects of prolonged wakefulness. Science;76(5316):1265-8, 1997.

Study contributes to medication guidelines for schizophrenia management

Antipsychotic medication is an essential component of treatment for schizophrenia; the second most common discharge diagnosis in VA. A study examined the relationship between patient outcomes and the man-

agement of medication for schizophrenia. Results showed that 49 percent of patients receiving care through a VA medical center or state psychiatric hospital were prescribed doses outside the range recommended by practice guidelines for schizophrenia. This study also showed that patients who were prescribed medication within practice guidelines had significantly less severe symptoms. Findings from this study have contributed to the selection of national performance measures for the VA that will improve the quality of medication management and better patient outcomes.

Health Services Research and Development

Kirchner JE, Owen RR, Nordquist C, Fischer EP. Diagnosis and management of substance use disorders among inpatients with schizophrenia. Psychiatr Serv;49:82-85, 1998. IIR 95-020.

QUERI research shows VA networks and facilities follow practice guidelines for treating depression and schizophrenia

Mental health is one of eight diseases prevalent in the veteran population that are the focus of the Quality Enhancement Research Initiative (QUERI). The Mental Health QUERI group examines major depressive disorder and schizophrenia. Major depressive disorder costs the nation \$44 billion per year in direct (e.g., medical treatment) and indirect costs (e.g. lost productivity). Schizophrenia costs exceed \$30 billion per year. Medications reduce symptoms in a large percentage of patients with these illnesses but unfortunately, medication management for both of these is often lacking.

With treatment concerns in mind, the Mental Health QUERI recently conducted a survey to elicit information about clinical practice guideline implementation efforts for major depression and schizophrenia at the VA network and facility levels. The survey found that the majority of network and facility mental health leaders reported guideline implementation efforts for these illnesses. Results also suggest that additional efforts could be made to implement and evaluate mental health guidelines and address any barriers to implementation. Mental Health QUERI continues to monitor these activities, and will develop and disseminate tools, such as mental health clinical reminders and pocket cards, to promote guideline implementation. [Health Services Research and Development](#)

Survey of Mental Health Guidelines Implementation. Preliminary results are available on the Mental Health QUERI website at <http://www.va.gov/resdev/queri.htm> or <http://vaww.mentalhealth.med.va.gov/mbq/>

Clinical and economic impact of olanzapine in treating schizophrenia

Currently marketed antipsychotic drugs are useful in treating psychotic disorders, but opportunities exist to improve upon their efficacy and safety. Olanzapine is a novel antipsychotic agent for the treatment of psychotic disorders, including schizophrenia, and is associated with only a few mild and often transient side effects. This study will assess the cost effectiveness of olanzapine with that of a standard antipsychotic medication, haloperidol, in the treatment of schizophrenia as measured by clinical outcome. Secondary objectives will be to compare olanzapine with haloperidol for safety and efficacy and for improvements in social and vocational functioning in schizophrenic patients. [Cooperative Studies Program](#)

Collaborator: Eli Lilly and Company

The Clinical and Economic Impact of Olanzapine Treatment on Refractory Schizophrenia. CSP #451, West Haven.

Manic-depression treatment aims to improve functional outcome and quality of life

Based on promising preliminary data, researchers are comparing a high-intensity ambulatory treatment program for bipolar disorder against standard, office-based, physician-centered care. This devastating disorder affects many veterans and millions of Americans and their families. The intervention seeks to improve manic and depressive symptom scores, as well as reduce total treatment costs compared to usual care of bipolar patients focusing on the particular issues of relapse-prevention that are critical for the VA. [Cooperative Studies Program](#)

Reducing the Efficacy/Effectiveness Gap in Bipolar Disorder. CSP #430, Palo Alto.



Substance Abuse

Research on substance abuse encompasses all types of addiction, including alcohol, nicotine, and other drugs. VA scientists are working to identify the underlying causes of abuse and addiction, and the subsequent treatment and rehabilitation methods that prove most effective. Research also includes efforts to

understand the ramifications of substance abuse throughout the body, such as the liver disease resulting from alcohol abuse. Below are two examples of progress in this critical area.

Probing the genetics of alcoholism

VA researchers are among leaders in research devoted to teasing out the complex interplay between heredity and alcoholism. For example, one VA team recently reported that genetically engineered mice without a certain cell receptor consumed less alcohol than unaltered mice. Mice without the dopamine D2 receptor, a cellular docking site for the brain chemical dopamine, consumed half as much alcohol as “wild type” mice. The study illustrates a technique in which particular genes influence substance abuse. Researchers use molecular methods to delete, or ‘knock out’, a suspect gene and then study the effect in the ‘knock out’ mice. In an earlier study, the VA researchers discovered that mice without a gene containing the receptor for serotonin, consumed twice as much alcohol as unaltered mice. Although they are just beginning to understand the role played by receptor subtypes in alcohol consumption, VA researchers indicate these studies may ultimately lead to new pharmacological treatments or gene therapies. The researchers caution scientists who study how genes affect behavior that genetically identical mice behave differently in seemingly identical tests at three separate laboratories. They emphasize that genetic manipulation and effects should be replicated cautiously before drawing conclusions, especially when there are slight results in behavioral differences. [Medical Research Service](#)

Crabbe JC, Wablsten D, Dudek BC. Genetics of mouse behavior: interactions with laboratory environment, Science;284(5420):1670-2, 1999.

Phillips TJ, Brown KJ, Burkhart-Kasch S, Wenger CD, Kelly MA, Rubinstein M, Grandy DK, Low MJ. Alcohol preference and sensitivity are markedly reduced in mice lacking dopamine D2 receptors. Nature Neuroscience;1(7):610-15, 1998.

VA center targets alcoholic liver disease

The Omaha VA Medical Center’s Research Center for Basic and Clinical Studies of Alcoholism was established in 1990 to advance the understanding and treatment of alcoholism. One of two VA Centers of Excellence for the study of alcoholism, the Omaha center is well known for its advances in the understanding of alcoholic liver disease. For example, re-

searchers there are conducting studies to determine how certain chemicals are formed that may trigger an immune response that harms the liver and interferes with its vital functions when animals are fed alcohol. One project is looking at whether liver cells that play a major role in “turning on” the immune system contribute to liver damage. Unraveling this process may lead to halting misguided immune attacks and improve treatments for alcoholic liver disease. [Medical Research Service](#)

Thiele GM, Miller JA, Klassen LW, Tuma DJ. Chronic ethanol consumption impairs receptor mediated endocytosis of formaldehyde-treated albumin by isolated rat liver endothelial cells. Hepatology;29(5):1511-7, 1999.

Xu D, Thiele GM, Beckenhauser JL, Klassen LW, Sorrell MJ, Tuma DJ. Detection of circulating antibodies to malondialdehyde-acetaldehyde adducts in ethanol-fed rats. Gastroenterology;115(3):686-92, 1998



Special Populations

Demographic, socioeconomic, and health risk factors distinguish some groups of veterans from the general population. The VA Office of Research and Development is ensuring that these groups are fairly represented in the research program. Veteran populations identified for special attention include veterans with permanent disabilities, veteran cohorts defined by shared military experience, minority veterans, and homeless, institutionalized or homebound veterans. Examples of VA's research in this area follow.

Functional Electrical Stimulation

Functional Electrical Stimulation (FES) uses surgically implanted electrodes to activate paralyzed muscles. A consortium including the Cleveland VA Medical Center, Case Western Reserve University and MetroHealth Medical Center is producing promising results that have led to new applications and many advances in restoring function to paralyzed individuals.

Advances by VA in the implantation and control of functional electrical stimulation (FES) walking systems hold great promise for patients with paraplegia. A research participant with paraplegia is now testing a new 16-channel system that allows him to exercise and walk in a limited area around his wheelchair. An implanted

neuroprosthesis is helping individuals with high chest or low neck injuries to exercise their legs, stand, and perform standing transfers. Another FES device offers promise for improved bladder and bowel control for individuals with spinal cord injuries, giving them greater freedom and reducing the costs and inconvenience of bladder and bowel care.

FES is also helping patients with tetraplegia due to spinal cord injury to grasp and release objects with paralyzed hands. Researchers in Cleveland are developing and testing new hand-grasp systems that offer finer control and extend function to the elbow and forearm. Another type of implant stimulates the triceps muscle so that individuals with tetraplegia can reach overhead and grasp objects. These and other advances in FES may allow persons with paraplegia and tetraplegia to expand employment opportunities and work more independently. Rehabilitation Research and Development

Kobeti R, Triolo RJ, Ublir J, Bier C, Wibowo M, Polando G, Marsolais EB, Davis JA, Ferguson K, Sharma M. Implanted functional electrical stimulation system for mobility in paraplegia: a follow-up case report. IEEE Transactions on Rehabilitation Engineering (in press).

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B0681-3RZ, B011-7RA, B835-3RA, B804-2RA

Tissue engineering to replace lost nerves

Tissue engineering - combining living cells with synthetic materials - holds promise for repair and regeneration of skin, bone, cartilage, nerve and essential organs. Researchers at the VA Palo Alto Rehabilitation R&D Center are recruiting patients who require grafting of nerves in the hand, arm or leg. Rather than performing a whole-nerve autograft, the investigators will repair the damage with an artificial graft seeded with the patient's own cells from the sheath surrounding the nerve fibers. New biomaterials and techniques now being tested for reconstructing peripheral nerves may be applied to the more difficult problem of regeneration of the central nervous system after stroke or spinal cord injury. [Rehabilitation Research and Development](#)

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Transplantation of myelin-forming cells to the injured CNS

Researchers in West Haven are studying transplantation of Schwann cells that form a protein sheath around some neurons. Myelinated nerves conduct impulses more rapidly than those without myelin.

Using magnetic resonance imaging, the investigators hope to establish whether cells transplanted into the primate central nervous system (CNS) can produce myelin, the complex protein that makes up the sheath. These studies serve as a necessary prelude to human studies that may lead to use of cell transplantation as a treatment for injury to the CNS. Investigators have also successfully developed cell harvesting and preservation techniques that will further research on transplantation of myelin-forming cells. [Rehabilitation Research and Development](#)

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Better understanding of fracture risks and healing

Individuals with spinal cord injury frequently suffer long-bone fractures in the legs, because they have reduced bone mass, are unable to sense pressure or improper limb placement, and lack the muscle strength and coordination to prevent falls. Fractures in this population can result in grave secondary complications, especially as they are frequently not diagnosed immediately because of absence of sensation (pain).

Standard treatments used in able-bodied persons (casts and prostheses) cannot be used in this population because of elevated risk of skin breakdown and infection as well as reduced skeletal structure and strength. Al-

though the heightened risk for fracture has been acknowledged for over 30 years, there has been too little research in the area to establish a consensus on treatment in this population. VA researchers in Palo Alto have identified patterns between specific causes of fracture (e.g., fall from wheelchair) and location and type of fracture. In addition, these researchers have developed a unique Healing Index that helps identify the rate of healing can be determined for each fracture from consecutive radiographs. Healing rates may differ for different types and location of fracture, and decisions for care and intervention can thus be based on precise information and expected outcomes. [Rehabilitation Research and Development](#)

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Sodium Channels and Pain

Following nerve and spinal cord injury some spinal sensory neurons become hyperexcitable, generating impulses when they should not. Hyperexcitability of pain-signaling spinal sensory neurons occurs as part of this phenomenon, so it is important to understand the molecular basis for hyperexcitability of injured spinal sensory neurons. Investigators in West Haven have shown that a particular sodium channel, one of the molecular "batteries" that produce electrical impulses in nerve cells, is prevalent in spinal sensory neurons and not present at significant levels in other types of nerve cells. The channel acts as an amplifier, boosting depolarizing inputs and exciting other sodium channels.

In the past year, investigators have also discovered that two molecules control the expression of other sodium channels. Understanding the roles of these spinal sensory neuron-specific channels may lead to development of new, more effective therapies for hyperexcitability of injured spinal sensory neurons, thus providing more effective treatment for chronic pain in disorders of the nervous system. [Rehabilitation Research and Development](#)

Fjell J, Cummins TR, Fried K, Black JA, Waxman SG. In vivo NGF deprivation reduces SNS expression and TTX-R currents in IB4-negative DRG neurons. Journal of Neurophysiology, 81:803-811, 1999.

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Health Services and Systems

Health Services and Systems is a research effort focused on improving the health care provided to our nation's veterans, whether it be for a specific disease or a broad category of care, such as primary or mental health care. Research in Health Services and Systems addresses supply and organization of resources and services, evaluation of treatment methods currently in effect, health and safety of research participants, application of research findings to standard practice, and outcomes of care. The studies described below are part of our effort to ensure that our veterans receive the best possible care.

Research efforts put outcomes data into practice

HSR&D researchers are putting important information about patient outcomes into the hands of VA managers, where it can be used to evaluate and improve the quality of care received by veterans. The researchers studied outcome and utilization rates within the VA from 1995-97 and analyzed morbidity and mortality rates as screens for quality of care. Study findings are published electronically on a VA web site ensuring rapid dissemination to VA managers and clinicians. Some of the mortality rates computed for this study are posted on VA's electronic report card by the VA National Performance Data Resource Center so that VA managers and clinicians can use them for quality improvement purposes. [Health Services Research and Development](#)

Petersen NJ, Ashton CM, Soucek J, Menke T, Collins TC, Foster W, Wray NP. A Cohort-Based Analysis of Utilization and Survival Rates Across the VA Health Care System, 1994-1998: Findings in Brief. Houston Center for Quality of Care and Utilization Studies. May 1999. SDR 98-001.

Enhancing the Quality of Informed Consent (EQUIC)

Informed consent is the keystone of the protection of human rights in medical research, along with careful review of proposed projects. EQUIC is a Cooperative Studies program-wide project aimed at systematically improving the quality of informed consent, by testing and measuring the results of innovative approaches to

informed consent. Practitioners of clinical trials must ensure that patients' participation in research is informed and voluntary. This responsibility implies that we should strive continuously to improve the effectiveness of methods for informing prospective research volunteers about experimental studies, thereby enhancing the protection of their interests. We should test innovations in informed consent in realistic contexts such as clinical trials, and with the strongest scientific designs.

EQUIC will field and test a method to assess the capacity of a research volunteer to understand and consent to a study; a method for "tailoring" an informed consent encounter to the vulnerabilities uncovered by that assessment; and a direct assessment of the success of an informed consent process at producing a good result, defined in terms of the successful protection of the patient's rights. Once these are fielded and tested, it will be possible to study a wide range of innovations in informed consent in the full variety of patients studied in the Cooperative Studies Program. An important side benefit will be the ability to assess the true results of current practice in the VA CSP, and, potentially, other systems. [Cooperative Studies Program](#)

Enhancing the Quality of Informed Consent (EQUIC)CSP # 476, Palo Alto.

New flu vaccine may provide better protection for people with lung disease

VA researchers are trying to determine whether a new vaccine can protect patients who have chronic obstructive pulmonary disease (COPD) against influenza and its often dangerous complications. COPD, a serious type of lung disease, is common among VA patients. COPD patients are especially vulnerable to developing severe complications from influenza that include pneumonia, hospitalization, and even death. The standard flu vaccine, given by injection in the arm, prevents flu in only about half of patients with COPD. Recently, a new flu vaccine that is sprayed in the nose has been developed. This VA study, a randomized, multi-center trial that involves 4,000 people with COPD, will determine whether patients who receive both flu vaccines are better protected than those who receive only the standard flu vaccine. Researchers started vaccinating patients in the fall of 1998 to observe whether they develop flu. If successful, this new immunization regimen will save lives, prevent serious complications, and reduce treatment costs. This study

may have significant implications for changing VA policy on vaccinating individuals with COPD against flu. [Cooperative Studies Program](#)

Collaborator: AVIRON Pharmaceuticals

A Randomized, Controlled, Blinded, Multi-center Trial to Assess the Efficacy of Protection from Natural Influenza Virus Infection of Influenza Virus Vaccine, Trivalent, Types A and B, Live, Cold-Adapted (CAIV-T) and Inactivated Influenza Virus Vaccine in Patients with Chronic Obstructive Pulmonary Disease (COPD). CSP #448, West Haven.

NSQIP's new risk factor models help predict patient outcomes

Risk factor models developed by the National VA Surgical Quality Improvement Program (NSQIP) can predict hospitals that provide superior and inferior surgical care. NSQIP is an ongoing, prospective study involving 132 VA medical centers that gathers data on patient-specific factors affecting mortality and morbidity in the 30 days following major surgery. The study uses preoperative data to develop models of risk factors that predict surgical mortality and morbidity. The models can then be used to compute observed-to-expected mortality and morbidity ratios for each hospital, for surgical subspecialties, and for surgery as a whole. This unique program monitors the quality of VA's surgical care and provides important data for improving it. [Cooperative Studies Program](#)

*Khuri SF, Daley J, Henderson W, et al. [The National VA Surgical Risk Study.] Risk adjustment of the post-operative mortality rate for the comparative assessment of the quality of surgical care: results of the National Veterans Affairs Surgical Risk Study. *Journal of the American College of Surgeons*;185(4):315-327, 1997.*

*Chen AY, Daley J, Pappas TN, et al. Growing use of laparoscopic cholecystectomy in the National Veterans Affairs Surgical Risk Study. *Annals of Surgery*;227(1):12-24, 1998.*

*Longo WE, Virgo KS, Johnson FE, et al. Outcome after proctectomy for rectal cancer in Department of Veterans Affairs hospitals. A report from the National Surgical Quality Improvement Program. *Annals of Surgery*;228(1):64-70, 1998. SDR #91-007, Hines.*

Home-based primary care model goes under the microscope

This multi-site, randomized trial is evaluating the effectiveness of team-managed, home-based primary care (HBPC) in the VA system. Researchers are comparing this approach in terms of cost, satisfaction and patient outcomes with other types of post-acute care for veterans. Positive results could lead to the estab-

lishment of additional HBPC programs and expansion of existing programs, so that more patients may benefit from needed services.

*Hughes SL, Ulasevich A, Weaver FM, et al. Impact of home care on hospital days: a meta-analysis. *Health Services Research*;32(4):415-432, 1997. CSP #3, Hines.*

Veterans Health Study provides outcomes information critical for VHA's quality improvement efforts

The Veterans Health Study (VHS) followed 2,425 veteran patients for four years monitoring outcomes of care in VA and developing health status assessments. One of the measures used in this study was a 36 item short form health survey study (the SF-36V) that has proven to be an extremely valuable tool for measuring health status. Since this study, the SF-36V has been administered more than 200,000 times from 1996 to 1998 and is currently being used in a VA national demonstration project examining the use of this survey by clinicians in the routine care of patients. The Veterans Health Study provides critical tools and information necessary to evaluate the quality of care in the Veterans Health Administration. [Health Services Research and Development](#)

*Kazis LE, Wilson N, Rogers W, Lee A. Health outcomes of veterans using the SF-36V: 1998 national survey of ambulatory care patients. 17th Annual VA HSR&D Service Meeting, *Health Services Research at the Interface*, 1999. SDR 91-006.*

Teledermatology, using digital imaging technology, paves the way for better care for veterans with limited access to health-care delivery

Digital images of visual information can be transmitted within telemedicine networks. This study compared the reliability for the diagnoses and management plans given by clinic-based examiners to those of consultants using digital imagery. Preliminary results show that dermatologists agree on their diagnoses of skin lesions equally well whether evaluating the patient in person or reviewing the digital image. In addition, investigators found diagnostic accuracy to be comparable among clinic-based and digital image examiners. This study suggests that the clinical use of digital imaging is an appropriate alternative for patients with limited access to adequate clinical care. [Health Services Research and Development](#)

Whited JD, Hall RP, Simel DL, Foy ME, Stecbuchak KM, Drugge RJ, et al. Reliability and accuracy of dermatologists' clinic-based and digital image consultations. *J.Am.Acad.Dermatol*;41(5 Pt 1):693-702, 1999. IIR 95-045.

Ambulatory Care Quality Improvement Project promises to improve quality of care

The Ambulatory Care Quality Improvement Project is determining whether quality and outcomes of care improve when primary care providers have access to regular assessments of their patients' health along with routine clinical data and information about clinical guidelines. The project system collects patient reports on health status and satisfaction and links them with clinical data. It then packages all of this information into concise reports for primary care providers along with evidence- and guideline-based practice information. Instruments developed for this study, including the Seattle Angina Questionnaires (SAQ) and the Seattle Obstructive Lung Disease Questionnaire have been well received and are presently being used in ongoing clinical trials. The SAQ has been adopted by the Medical Outcomes Trust and translated into several languages. Data from the project are currently being used in VA's Quality Enhancement Research Initiative. [Health Services Research and Development](#)

Reiber GE, McDonell MB, Schleyer AM, Fibn SD, Reda D. A comprehensive system for quality improvement in ambulatory care. In: Assal J, Golay A, Jisser A, editors. *New Trends in Patient Education*, Amsterdam: Elsevier, 1999. SDR 96-001.

Researchers provide critical budgeting and forecasting information to VA managers

Medical care cost recovery - the process by which the VA bills private, third-party insurers for treatment of non-service connected conditions - is of great financial importance to VA. Accurate projections of future potential revenues require extensive analysis of VHA utilization patterns and insurance information for users of VA services. VA researchers are helping the Office of Medical Care Cost Recovery forecast these cost recoveries into Fiscal Year 2002. As a result, VA Headquarters has changed the way it sets goals for third-

party payment collections by the 22 Veterans Integrated Service Networks. These projections are also used in VA's budget negotiations with the Office of Management and Budget. [Health Services Research and Development](#)

Hendricks, AM. *A Model for MCCR Projections. Study reports from MRR 99-005 for the Chief Finance Office. 1997-1998. MRR 99-005.*

DNA bank demonstration project

The "DNA bank" is a program-wide genetic tissue databank for the VA Cooperative Studies Program (CSP). The aim of the DNA Bank is to ensure the protection of individual patient rights while enabling VA investigators to take advantage of exciting advances in human genetics that promise dramatic progress toward medical research and treatment goals. It will serve a wide range of studies in several disease areas.

The DNA bank is a collaboration among three institutions. The Palo Alto CSP Coordinating Center administers the tissue bank, coordinates the scientific and ethics oversight committees, maintains central access to clinical study data linked to the tissue bank, and provides statistical analysis. The Massachusetts VA Epidemiologic Research and Information Center (MAVERIC) provides a central repository for DNA and other genetic tissue specimens. The Human Genetics Center at Stanford University provides key scientific, legal, and ethical expertise to the DNA bank. The DNA bank will begin with a demonstration study, partnered with CSP #410, The Iron (Fe) and Atherosclerosis Study (FeAST), in patients with peripheral vascular disease. [Cooperative Studies Program](#)

DNA Genetic Tissue Banking. CSP #478, Palo Alto.