Promising new osteoporosis drug not cost-effective

Anyone who has fractured a hip, wrist or spinal vertebrae due to osteoporosis can attest to the debilitating impact of the disease, and would no doubt welcome a new kind of osteoporosis drug that prevents fractures by rebuilding lost bone rather than merely halting bone loss as most therapies do.

But CHP/PCOR researchers have found that the first such medication now available, called teriparatide (brand name Forteo), is not cost-effective compared with the most commonly prescribed osteoporosis drug, alendronate (brand name Fosamax), because of teriparatide’s much higher price. While the average wholesale price of alendronate is about $900 a year, teriparatide costs nearly eight times as much at about $6,700 annually.

The findings, published in the June 12 Archives of Internal Medicine and covered by several news media outlets, suggest that teriparatide should be given only to the highest-risk patients and to those who don’t tolerate standard treatments.

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Centers brimming with research activity on health, aging

Aside from their similar-looking acronyms, CADMA (the Center on Advancing Decision Making in Aging) and CDEHA (the Center on the Demography and Economics of Health and Aging) have much in common. Both are multidisciplinary research centers based at CHP/PCOR that support promising early-stage projects focused on health, economics and aging.

Both centers are also brimming with activity; CADMA has three upcoming projects for the 2006-07 academic year and three underway, while CDEHA has two upcoming projects and four underway (see box on p. 12). Leaders of CADMA and CDEHA say they’re pleased with the centers’ progress over the past year and are looking forward to next year’s projects, presentations, publications, and continuing collaboration.

“Both centers have seen a lot of collaboration this year and are very active,” said Tamara Sims, CHP/PCOR project manager for CADMA and CDEHA. “We’ve been successful in supporting good early-stage projects that might not have been funded otherwise.”

CHP/PCOR director Alan Garber, who is principal investigator for both centers, said, “CADMA and CDEHA are devoted to...”
Evidence lacking to recommend ultrasound for osteoporosis screening

Calcaneal quantitative ultrasound — a diagnostic test that assesses the density and quality of bone in the heel using high-frequency sound waves — is attracting increased interest as a screening tool for osteoporosis, and has been suggested as a potential improvement over the most commonly used test, known as DXA, because of ultrasound’s greater accessibility and lower cost.

If ultrasound were found to be as accurate as DXA in detecting osteoporosis, it could significantly expand screening and identify the disease in millions of people who have it but don’t know it.

For now, however, that’s still a big if, according to a study led by CHP/PCOR trainee Smita Nayak and published in the June 6 Annals of Internal Medicine. The study — the first to synthesize all published research on the accuracy of heel ultrasound vs. DXA — found current evidence indicates that heel ultrasound results are insufficient to rule in or rule out osteoporosis as defined by World Health Organization criteria.

Calcaneal ultrasound still holds promise, Nayak said, but further research is needed before it can be recommended for widespread use. “Until we have more information, we should stick with what we know,” she said. “DXA may not be perfect, but it’s a good standard for determining who is most likely to benefit from osteoporosis treatment.”

According to a 2004 study, an estimated 10 million Americans have osteoporosis, but only half of them have been diagnosed. DXA, short for dual-energy x-ray absorptiometry, detects osteoporosis by measuring bone mineral density (BMD). In 1994, when DXA was one of the few osteoporosis screening tests available, the WHO developed an operational definition for osteoporosis of a BMD 2.5 standard deviations (T-scores) or more below the mean for healthy young women. Since this definition was developed in the context of DXA, DXA has become the de facto gold standard for diagnosing osteoporosis.

While DXA is considered a good screening test for osteoporosis, there are reasons why heel ultrasound might be a better option. Ultrasound costs four times less, about $36 per test compared with $139 for DXA. Ultrasound is also small and portable, so it can be brought to hard-to-reach populations such as homebound individuals or those in remote areas. That portability confers a significant advantage over DXA, a large, expensive piece of equipment typically found in hospitals or large clinics.

“People who don’t live near a referral center may have to travel many miles for a DXA test. That can be a substantial barrier to screening,” Nayak said. “With ultrasound, more patients could get screened right in their doctor’s office, or the machine could be brought to them.”

To determine whether heel ultrasound might be a viable alternative for osteoporosis screening, Nayak and colleagues (including CHP/PCOR investigators Ingram Olkin, Hau Liu, Michael Gould, Douglas Owens and Dena Bravata) reviewed all published studies on the subject, selecting 25 that met their inclusion criteria. Analyzing the studies was challenging due to a few factors. First, while there is a standard cutoff threshold for DXA to determine who has osteoporosis (T-score of -2.5 or below), calcaneal ultrasound has no such standard. Thus, the studies evaluating ultrasound for osteoporosis detection used different thresholds, making it difficult to determine the accuracy of ultrasound machines versus DXA.

The researchers overcame this hurdle by developing regression models that allowed them to determine the relationship between the sensitivity and specificity of the ultrasound machines studied and the cutoff thresholds used. Using these models, “We were able to make sense of a body of literature that had findings that seemed to be all over the map. Much of the variation between study findings was related to the use of different ultrasound thresholds,” Nayak said.

According to the researchers’ analyses, “the sensitivity and specificity of calcaneal ultrasound at commonly used cutoff thresholds seem to be too low to conclusively rule out or rule in DXA-determined osteoporosis” for the kind of patients typically seen in clinical practice. Those who test positive with ultrasound, therefore, would still require a DXA test to confirm their diagnosis, and ultrasound would fail to identify some individuals who would meet the DXA criteria for osteoporosis.

Complicating matters further, while studies have shown that heel ultrasound predicts an individual’s risk of fracture nearly as well as DXA, it is unknown whether patients identified as having high fracture risk by ultrasound would benefit from treatment as much as those identified by DXA. That’s because all clinical trials of osteoporosis drugs in patients without previous osteoporotic fractures have studied patients selected by DXA criteria.

CONTINUED ON PAGE 3
Drugs widely prescribed without scientific evidence, study finds

In choosing which drugs to prescribe for their patients, doctors often select medications despite a lack of conclusive medical evidence of their effects and safety, according to a study led by Randall Stafford, associate professor of medicine at the Stanford Prevention Research Center and a CHP/PCOR fellow.

Of a wide sampling of prescriptions dispensed to patients in 2001, the study found, 21 percent were prescribed for medical conditions for which the drugs lacked specific approval from the U.S. Food and Drug Administration, though other published research suggested possible benefits. Furthermore, about 75 percent of those prescriptions were for conditions for which there was little or no evidence of the drugs’ effectiveness.

This practice of “off-label prescribing” offers doctors flexibility and innovation in treating patients, but it also carries risks, Stafford explained. The findings, published May 8 in the Archives of Internal Medicine, are based on a large database of the number of off-label prescriptions among the 100 most-used drugs and 60 other randomly selected, commonly used medications.

The results show that scientific evidence plays only a partial role in physicians’ treatment decisions, said Stafford. Indeed, many doctors might be unaware of whether a drug has been FDA-approved for a specific use or how much research supports its use, he added.

It is unclear how off-label uses become established within the medical community in cases where little or no scientific evidence backs up their use. Informal communication between physicians, promising or preliminary scientific studies, and marketing by the pharmaceutical industry could play roles, Stafford said.

The FDA approves drugs for treating specific indications only, and there are many reasons why a drug might not have been approved for treating a particular condition, Stafford said. Undergoing the trials necessary for approval, for instance, can be time-consuming and expensive.

What’s more, many drugs belong to classes of medications that work in similar ways, though each might have different side effects. It would be logical to assume that a drug in a particular class would have the same effect as others in that class. Other off-label uses represent an extension of labeled uses or evolving new uses that have not been stringently evaluated. Greater caution is advised in such circumstances, Stafford said.

In collaboration with researchers at Dartmouth Medical School and the Massachusetts Institute of Technology, Stafford compiled data taken from the 2001 National Disease Therapeutic Index, a continuing survey of U.S. physicians. The survey compiles data from 3,500 physicians who report information about patient care during two consecutive workdays every quarter.

According to the data, the 160 drugs selected for the study accounted for an estimated 725 million in annual prescriptions. Off-label prescriptions accounted for 150 million. Of those, 27 percent were for indications supported by scientific evidence, while the remaining 73 percent, or 109 million prescriptions, had little or no evidence. The team considered a drug’s use scientifically supported if the indication appeared with an evidence rating of “good” or “excellent” in DRUGDEX, a nationally recognized pharmaceutical compendium.

Stafford said better communication and education for physicians and patients about off-label use is crucial to good health care. “Patients and physicians need to ask what’s the level of evidence for using a specific drug for a specific condition,” he said. “Empowering patients to ask about the supporting evidence and having the physicians respond to these questions will improve patient care.”

This article was produced by the Stanford School of Medicine’s Office of Public Affairs. The study findings were covered by numerous news media outlets, including USA Today, United Press International, the New York Times, the Washington Post, the Los Angeles Times, the Wall Street Journal, Forbes.com, the San Jose Mercury News, the Miami Herald, National Public Radio’s “All Things Considered,” and in several TV news segments around the country.
For the first two weeks in April, CHP/PCOR research assistants Meghan Fay and Raina Mahajan went with core faculty member Paul Wise on his latest trip to San Lucas Toliman, Guatemala, where for 30 years he has been making working trips each year to provide much-needed medical care for the region’s underserved people. A Mayan community in the highlands of southwestern Guatemala, San Lucas Toliman has few doctors and just one clinic serving the region, so many residents rarely if ever see a doctor. The residents are generally poor, and many can’t afford even basic treatments.

Fay and Mahajan — who speak Spanish and are interested in international health — went to Guatemala as part of a global health training program Wise has established, in which he leads small groups of medical students and other trainees who assist him with various medical treatment and health promotion activities. These include setting up makeshift clinics in nearby villages; making house calls to care for seriously ill or homebound individuals; giving simple talks to villagers about key health topics; and working with volunteer health promoters, or promotores de salud. The promotores are local villagers (generally women) who receive training on the prevention and treatment of common health conditions and who then provide health information, advice and referrals for their communities.

Aside from assisting with these activities, Fay and Mahajan worked on another project in Guatemala: They conducted tape-recorded interviews with about a dozen of the health promoters, asking about their experiences and motivations. Fay and Mahajan used the interviews to create educational materials for future participants in Wise’s global health training program.

In an interview excerpted below, Fay and Mahajan discussed their experiences and insights from the trip.

What were your impressions of Guatemala and San Lucas Toliman?

(Fay) It’s a beautiful area, on a lake [Lake Atitlan] and surrounded by volcanoes. The people know how to relax and have fun, but they also work very hard. You’ll see a 7-year-old selling mangoes on the street, or carrying buckets of stones to help with a construction project. Then you’ll see 70-year-old men and women carrying wood on their backs, walking barefoot uphill.

(Mahajan) I was struck by how open the people are, especially the family we stayed with. In just two weeks, they opened up to us and were willing to talk about personal hardships that would generally be considered private here.

What kinds of medical conditions did you see?

(Mahajan) We saw a variety of problems. We saw a lot of children with scabies, which shows up as a bad rash. A lot of kids had intestinal problems caused by amoebas. Many of the women had back aches and muscle pains from doing physical work. We saw a family with AIDS and a woman who they thought had leukemia. A lot of the care we provided was pretty basic, like giving antibiotics or over-the-counter medications.

Was there anything surprising to you about the patients you saw?

(Fay) I spent a day with a nurse practitioner, doing at-home prenatal visits with pregnant women. One of the routine questions we asked was, “Have you lost any children?” Without fail, every woman we talked to had had at least one child die, from various illnesses. It was striking to see how common that was — how fragile life is there.

(Mahajan) A lot of what we saw was preventable or curable if treatment had been given earlier. There was a baby in the hospital who was covered with scabs, which were caused by cradle cap all over her body. In the U.S. that wouldn’t be a big deal, but this baby’s parents couldn’t bring her in for two weeks, so the problem became severe. You could really see the disparities in access to care.

Since the health promoters don’t get paid, why do they do it? What’s their motivation?

(Mahajan) In our interviews we asked them this. They all said, “We love helping our neighbors.” Some of the women have five or six kids, and it’s amazing how they find time to take care of them, work to support their families, and make time to be a health promoter. They’re such an important health resource for their communities.
CHP/PCOR in the news, spring 2006 quarter

• MRI breast cancer screening is cost-effective for certain women aged 35 to 54 years who carry the BRCA1 and BRCA2 gene mutations, according to a study co-authored by CHP/PCOR associate Sylvia Plevritis and director Alan Garber, published in the May 24 Journal of the American Medical Association.

Using a computer model to weigh the costs of the tests against the lives saved at various ages, researchers evaluated the cost-effectiveness of screening women with BRCA1 or BRCA2 mutations with mammography plus breast MRI vs. mammography alone. Researchers found that screening strategies that incorporate annual MRI as well as annual mammography have a cost per quality-adjusted life-year (QALY) gained ranging from less than $45,000 to more than $700,000, depending on the ages of the women and the BRCA mutation.

Specifically, the study found that, “At a cost-effectiveness threshold of $100,000 per quality-adjusted life-year gained, adding annual MRI to mammography from the ages of 35 to 54 years is cost-effective among all BRCA1 mutation carriers” and “for BRCA2 mutation carriers who have mammographically dense breasts.” The study findings were covered by several news media outlets, including the Washington Post, Reuters, WebMD.com, and Forbes.com.

• An article in Stanford Report discussed a study co-authored by CHP/PCOR associate Brian Knutson that examines the link between the brain’s reward circuits and its memory system. For the study, published May 4 in Neuron, subjects were given a list of pictures to remember for a test the following day. Prior to seeing the images, the subjects were told how much money they would get for recognizing each of them correctly. The subjects’ brain activity was monitored throughout the experiment, using functional magnetic resonance imaging (fMRI). Researchers found that the subjects were better able to recall the pictures worth more money. The results of the study show that brain activity can predict what people will remember, even before the experience they will remember occurs.

• In an article in the April 3 issue of The New Yorker, titled “Relatively Deprived: How poor is poor?” core faculty member Victor Fuchs discussed the merits of using a relative poverty line to determine who is poor in America. Fuchs asserted that using a relative scale (which looks at how a family’s income and material goods compare with others in their community, not their absolute living standards) “is the right way to think about poverty, especially from a policy point of view.”

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GUATEMALA TRIP, FROM PAGE 4

What was the best part of the trip?
(Fay) It felt good to know that you can make such a big difference in people’s lives by doing simple things like setting up a clinic in a town hall and giving out medications. You realize there’s a lot you can do at a basic level, without hospitals or high-tech equipment.

What was the most challenging part?
(Fay) It was hard to see cases where a person was seriously ill and there wasn’t much we could do for them because of a lack of resources. We saw a family where two of the members had HIV. They were getting their medicines covered by Doctors Without Borders, but they couldn’t afford to get their CD4 counts done, which shows how severe the disease is and helps the doctors adjust their treatments. The test is expensive, and there was no way they could pay for it.

How did Paul explain what you were seeing, and how did he interact with patients?
(Fay) It was incredible to see his way with patients, especially since we’d never seen him in a clinical setting. He’s always looking at the whole situation, and considering things from the patient’s point of view.

(Mahajan) One thing about Paul: He seems to know everyone in the town. You can’t walk down the street with him, without people stopping and saying, “Hola Pablo, ¿Cómo estás?” He has a great connection with the community.

How does this work in Guatemala relate to our research work at CHP/PCOR?
(Mahajan) Here at Stanford, Paul writes papers about health disparities, but the work he does in Guatemala actually helps sick kids and reduces those disparities in a concrete way. So there is a real connection to the work at CHP/PCOR. And, Paul has said that in the future he plans to do research in Guatemala.

CHP/PCOR said a fond farewell to Raina and Meghan in mid-June. Raina will be starting medical school in August at the University of Florida, Gainesville. Meghan moved to Saint Louis, where she will work for a year in the research field and then attend nursing school.
CHP/PCOR Profile: Shoutzu Lin

**Research interests:** analyzing data to examine health issues including patient safety, coronary heart failure in the elderly, and the impact of HMO ownership on hospital costs and revenues

**Where she’s from:** born and raised in Taiwan

**Education:** received an undergraduate degree in microbiology from Soochow University (Taiwan), and an MS in health policy from the School of Public Health at the State University of New York-Albany campus.

**Her work at CHP/PCOR:** Lin joined CHP/PCOR in 2000 as a research analyst. Based at the National Bureau of Economic Research office on Alta Road, she currently manages and analyzes data using SAS and STATA, for three projects: “Improving Safety Culture and Outcomes in Health Care,” led by Laurence Baker and Sara Singer; “Trends in Health Care Expenditures and Outcomes for Elderly Patients with Heart Failure,” led by Paul Heidenreich; and “Effect of Organizational and Market Changes on Hospital Behavior,” led by Yu-Chu Shen.

**Early career path:** As a young adult, Lin was interested in biology and considered being a biology teacher. After earning her undergraduate degree in microbiology, she did bench-side work in some government research laboratories in Taiwan. In one of these positions, she worked at a children’s hospital with a pediatrician who was researching treatments for leukemia. That experience gave her a broader perspective and sparked her interest in improving public health. As a graduate student in public health at SUNY, she began exploring the power of statistical analysis software to uncover patterns and relationships relevant to complex health-care questions.

**Research and professional experience:** During her graduate study, Lin worked on a project at SUNY-Albany evaluating the quality of New York state’s regional trauma-care system. She later participated in research on occupational safety and environmental monitoring, for the New York State Health Department, and evaluated the costs and effectiveness of mental health treatment, as a data analyst in the quality improvement department of Magellan Health Service.

**Aspect of work she likes best:** “I like working with Medicare data because it’s challenging to work with such a huge data source. Although the questions we’re asking might be straightforward, the strategy to process and analyze the data can be very complicated. When I finally make it work, I feel good.”

**Hobbies:** swimming, gardening, making Chinese arts and crafts

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Announcements from the spring quarter

**Douglas Owens** was promoted to professor of medicine, effective June 2. According to CHP/PCOR director Alan Garber, “please join me in wishing Doug the best on this important honor. It attests to his many accomplishments and to the esteem with which he is held by colleagues at Stanford and throughout the nation. We are very fortunate to have him as a colleague.”

CHP/PCOR director **Alan Garber** received the Clinician-Investigator Award from the Society of General Internal Medicine’s California Region. The award is given to an individual with excellent skills in original investigation; excellence in teaching of research skills, design, and methods; and demonstrated leadership in research areas relevant to general internal medicine.

Core faculty member **Grant Miller** received the Student Paper Award at the American Society of Health Economists’ inaugural conference, held June 4-7 at the University of Wisconsin-Madison. Miller was honored for his paper on “Contraception as Development? New Evidence from Family Planning in Colombia,” which he wrote for his PhD dissertation. The award is given for the paper judged to have made the greatest contribution to health economics.

CHP/PCOR fellow **Laurence Baker**, associate professor of health research and policy, was awarded the 38th annual Kaiser Foundation Award for Excellence in Preclinical Teaching — an honor chosen by students in preclinical medicine.

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ANNOUNCEMENTS, FROM PAGE 6

CHP/PCOR associate Donald Barr, associate professor of sociology and human biology, recently received three awards for his work advocating housing, health care and other services for the homeless. Barr received the Miriam Roland Volunteer Service Prize from Stanford’s Haas Center for Public Service; the Tall Tree Award from the Palo Alto Chamber of Commerce; and Santa Clara County’s Human Services Award.

As founder in 1998 of the Community Working Group on Homeless Services, Barr spearheaded the creation of the Opportunity Center, now under construction in Palo Alto, which will provide housing and social services to homeless people in the Midpeninsula area. He also recently founded Opportunity Health Partners, a nonprofit that will provide medical and mental health services to clients of the Opportunity Center.

Congratulations to VA Palo Alto project manager Catharine Fenn and the rest of the research team for the Group Visits to Improve Hypertension Management project (led by Mary Goldstein), on bringing the intervention phase of that project to a successful close.

Hellos and goodbyes:
In the spring quarter, CHP/PCOR welcomed these new staff members and affiliates:

Celeste Brown, our new administrative associate, has worked in a variety of roles, including serving as medical programs coordinator for Kaplan Test Preparation, and financial aid assistant and medical education coordinator at Stanford’s School of Medicine. She received a BS in biology from UC-San Diego.

Robert Chess, a new CHP/PCOR adjunct fellow and a longtime center collaborator, is acting CEO and chairman of Nektar Therapeutics and is chairman of BIO Ventures for Global Health, an industry collaboration aimed at creating favorable market conditions for the development of drugs largely affecting poor countries. He was co-founder and president of the dermatology company Penederm Inc., and in 1990-91 he was associate deputy director in the White House Office of Policy Development. He is also a lecturer in Stanford’s Graduate School of Business. He received a BS in engineering from the California Institute of Technology and an MBA from the Harvard School of Business.

Allison Gienger is a research assistant working on projects with the Stanford-UCSF Evidence-based Practice Center. Her experience includes working with professors and graduate students at the UC-Berkeley Optometry/Health Sciences Library and serving as an editor for the Berkeley Medical Journal. She earned a BA in molecular and cell biology from UC-Berkeley.

Noemi Pace, a second-year PhD student in the Economic Theory and Institutions program at the University of Rome-Tor Vergata, is spending six months at CHP/PCOR, taking economics courses and doing research on obesity and wage differences in Europe and the U.S. She is working with Jay Bhattacharya and with adjunct associate Vincenzo Atella, a professor in the Department of Finance at the University of Rome.

Haya Rubin, a new CHP/PCOR adjunct associate, is director of the Palo Alto Medical Foundation Research Institute. She has published research in areas including reducing healthcare disparities for minorities, preventing cardiovascular disease, improving patient safety, and studying physicians’ attitudes about clinical practice guidelines. She was previously a professor of medicine at Johns Hopkins University. She received a BA in chemistry from Oberlin College, an MD/PhD in medicine and pathology from Case Western Reserve University, and an MS in public health from UCLA.

Sean Tunis, a new adjunct associate, is director of the Center for Medical Technology Policy. From 2002-2005 he was chief medical officer and director of the Office of Clinical Standards and Quality for the Centers for Medicare and Medicaid Services. He was previously a senior research scientist at The Lewin Group, director of the Congressional Office of Technology Assessment’s Health Program, and a Congressional Science Fellow. He received an MD and an MS in health services research from Stanford, and completed a residency in medicine at the University of Maryland Hospital.

Congratulations to recently graduated CHP/PCOR trainees Smita Nayak and Kaleb Michaud. Smita will be leaving Stanford in late August to begin her new position as a clinician-investigator at the University of Pittsburgh’s Division of General Internal Medicine. Kaleb will be working this summer with the National Data Bank for Rheumatic Diseases based in Wichita, Kansas.

CHP/PCOR said a fond farewell last quarter to RAs Meghan Fay, Raina Mahajan and Robyn Lewis. Meghan is moving to Saint Louis, where she will work for a year in the research field and then attend nursing school. Raina will start medical school in August at the University of Florida, and Robyn will be attending law school at the University of Michigan.
Presentations from the spring quarter

**Jay Bhattacharya**
“Prospects for future health and health care spending among the elderly.” Hong Kong Hospital Authority 2006 Convention, May 8-9 in Hong Kong, China.


**Kate Bundorf**


**Stirling Bryan**
“Use of cost-effectiveness information in coverage policy decisions in the U.S. and the U.K.” Joint Meeting of the Trudeau Foundation and the Commonwealth Fund, May 2, 2006 in Montreal.


“Health technology coverage decisions in the U.K. and the U.S.” Veterans Health Administration invited seminar, June 1, 2006 in Washington, D.C.

**Ruth Cronkite**

**Sheryl Davies**
“Development of the AHRQ Pediatric Indicators.” Presented on behalf of the Pediatric Quality Indicators team, at the Academy Health Annual Research Meeting.

**Alain Enthoven**

**Mary Goldstein**
“Health preferences are not equal to the sum of their parts: older adults’ valuations of states of functional dependency.” Bay Area Health Care Quality and Outcomes Annual Research Conference, May 25, 2006 in San Francisco.


**Kathryn McDonald**

“Asessing pediatric healthcare quality in U.S. hospitals and regions using readily available administrative data.” Presented on behalf of co-authors Patrick Romano, Corinna Haberland, Sheryl Davies, Jeff Geppert and Amy Ku, at the Bay Area Health Care Quality and Outcomes Annual Research Conference, May 25, 2006 in San Francisco.

**Rudolf Moos**

**Douglas Owens**


**Tamara Sims**

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PRESENTATIONS, FROM PAGE 8


Sara Singer
“Patient safety climate in healthcare organizations survey: a psychometric journey.” Institute for Health Policy, Massachusetts General Hospital, April 6, 2006 in Boston.

“Why don’t experts seek more help?” Leadership Research Seminar, Center for Public Leadership at the Kennedy School of Government, April 28, 2006 in Cambridge, Mass.


“Safety climate, individual characteristics and clinical outcomes.” Presented with Laurence Baker at the Agency for Healthcare Research and Quality’s Patient Safety and Health Information Technology Annual Conference, June 5, 2006 in Washington, D.C.

“Hospital safety climate by management status, clinical status, and work area.” Poster presentation on behalf of co-authors Alyson Falwell, Tobias Rathgeb, Shou-tzu Lin and Laurence Baker, at the AcademyHealth Annual Research Meeting, June 26, 2006 in Seattle.

“Relationship of organizational characteristics to hospital safety culture.” Poster presentation on behalf of co-authors Alyson Falwell, Tobias Rathgeb, Shou-tzu Lin and Laurence Baker, at AcademyHealth Annual Research Meeting.

“Relationship between hospital safety climate and outcomes.” Presented on behalf of co-authors Alyson Falwell, Shou-tzu Lin, Tobias Rathgeb and Laurence Baker, at AcademyHealth Annual Research Meeting.

Mark Smith
“Economics of implementation: moving beyond traditional cost-effectiveness analysis.” American Society of Health Economists’ first annual conference, June 5-7 at the University of Wisconsin-Madison.

Todd Wagner
“Tiered co-payments and cost-related medication underuse?” American Society of Health Economists’ first annual conference, June 4-7 at the University of Wisconsin-Madison.

New CHP/PCOR grants from the spring quarter

Grants submitted:

“Support for Quality Indicators” (National Quality Forum Support)
AHRQ, with Battelle
Principal investigator: Kathryn McDonald
Project period: 7/1/06 - 9/30/07

“The Causes and Behavioral Foundations of Mortality Decline in Developing Countries”
NIH/National Institute of Child Health and Human Development
Principal investigator: Grant Miller
Project period: 4/1/07 - 3/31/11

Grants awarded:

“The HIV/AIDS Pandemic and Africa’s Orphaned-Elderly (CDEHA seed award)”
NIH/National Institute on Aging
Principal investigators: Bhattacharya/Miller
Project period: 7/1/06 - 6/30/07

“Automated Construction of a Gene-Environment-Disease Interaction Network” (pilot project)
Stanford Bioethics/NIH
Principal investigator: Paul Wise
Project period: 5/1/06 - 7/31/06

“Indoor Air Pollution and Health in Developing Countries: An Intervention Study in Bangladesh”
Woods Institute for the Environment (Stanford SIE)
Principal investigator: Grant Miller
Project period: 7/1/06 - 6/30/07

“Health Insurance Provision for Vulnerable Populations”
NIH/National Institute on Aging
Principal investigator: Jay Bhattacharya
Project period: 6/1/06 - 5/31/11
We’re not saying you shouldn’t use this new drug at all, but, given that we have limited healthcare resources, we need to consider whether we as a society are prepared to pay the additional cost of the drug, given the effectiveness of existing therapies,” said lead study author Hau Liu, a postdoctoral trainee at CHP/PCOR.

A disease most prevalent in postmenopausal women, osteoporosis causes bones to become porous and weak, making them vulnerable to fractures even with minor falls. An estimated 10 million Americans have osteoporosis, though studies find that fewer than half of them know it. People with osteoporosis have higher mortality rates and a lower quality of life than the general population, due to fractures which can bring on complications and restrict daily activities. Patients with hip fractures, in particular, are often hospitalized and may require subsequent nursing-home care.

Approved by the Food and Drug Administration in 2002, teriparatide is the first available drug in a new class of osteoporosis medications called anabolic agents, which stimulate new bone growth by increasing the function of osteoblasts, the body’s bone-forming cells. This is potentially a significant advance over the most commonly used class of osteoporosis drugs, called bisphosphonates (of which alendronate is the market leader), which halt bone loss and increase bone density but don’t build new bone. Still, no studies have directly compared teriparatide and alendronate in terms of their effectiveness in preventing fractures.

Teriparatide is given through daily injections, while alendronate is taken as a once-a-week pill. According to drug-industry analysts, an estimated 600,000 prescriptions were written for teriparatide in 2005, generating more than $350 million in revenue, and sales are projected to reach $750 million by 2008.

Liu’s research team — including CHP/PCOR investigators Kaleb Michaud, Smita Nayak, Douglas Owens and Alan Garber — sought to find out whether teriparatide was worth its hefty price tag when compared with alendronate. Using a computer simulation model, they evaluated the impact of four treatment strategies in a population of 200,000 hypothetical postmenopausal women who were white, had severe osteoporosis as defined by World Health Organization criteria, and had not previously been treated.

The four treatment strategies evaluated were “usual care” (taking vitamin D and calcium but no medication); alendronate alone for five years; teriparatide alone for two years; and two years of teriparatide followed by five years of alendronate. The Stanford study is the first to evaluate the cost-effectiveness of this last approach, known as sequential therapy, which is advocated by a growing number of osteoporosis experts to first build new bone and then maintain it.

The researchers looked at six elements for their hypothetical patients: treatment strategy chosen; number and type of pre-existing fractures; death or survival during the simulation period; entrance (or not) to a nursing home; adverse reactions from treatment; and new fractures during the simulation period. Then the researchers calculated the cost-effectiveness of each therapy in terms of the cost per quality-adjusted life-year gained.

Teriparatide alone cost $11,600 per QAL Y compared with usual care and did not produce benefits as great as those of alendronate, prompting the authors to write that the new drug “is not a rational choice.”

Alendronate alone cost $11,600 per quality-adjusted life-year gained in comparison with usual care, making it solidly cost-effective, according to the researchers. Teriparatide alone cost $172,300 per quality-adjusted life-year compared with usual care and, despite its high cost, did not produce health benefits as great as those of alendronate, prompting the authors to write that the therapy “is not a rational choice.” They noted, however, that teriparatide may be a reasonable option for patients who are unable to use alendronate.

The teriparatide/alendronate combination cost $156,500 per quality-adjusted life-year, relative to alendronate alone. Though this value is generally too high to be considered cost-effective, researchers found the strategy could become cost-effective under three conditions: if teriparatide’s price were reduced by 60 percent; if the drug combination were given only to women with exceptionally low bone density; or if a six-month course of teriparatide were proven as effective in preventing fractures as two years of treatment.

While it’s difficult to predict pricing for any drug, Liu noted that other anabolic agents for osteoporosis are being developed, which could be introduced at lower (and thus more cost-effective) prices than teriparatide. “Our study gives some idea of what a reasonable price for these products might be, assuming they’re as effective as teriparatide.”

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This study was funded by the Agency for Healthcare Research and Quality and by the Department of Veterans Affairs. Its findings were covered in news articles by United Press International, HealthDay News and Forbes.com. The study was also featured in an AHRQ podcast and was referenced in televised segments on WHO-TV (Des Moines, Iowa), KASA-TV (Albuquerque, N.M.), WATE-TV (Knoxville, Tenn.) and WIS-TV (Columbia, S.C.).
**CADMA & CDEHA Research Roundup**

**New CADMA projects for 2006-07**
*(projects begin August 1, pending NIA approval)*

- “Benefits and Costs of Health Insurance Choice among Older Adults: The Case of Medicare Prescription Drug Plans”
  Investigators: Kate Bundorf, Helena Szrek
- “Age, Affect Valuation, and Health-related Decision Making”
  Investigators: Jeanne Tsai, Tamara Sims
- “Choosing Not to Choose: Ambiguity Aversion in Younger and Older Adults”
  Investigators: Brian Knutson, Gregory Larkin

**Current CADMA projects**

- “Age Differences in Emotional and Cognitive Decision-Making”
  Investigator: Elaine Robertson
- “Risk Taking and Financial Decision Making in Older Adults”
  Investigators: Brian Knutson, Camelia Kuhnen, Gregory Larkin
- “Incorporating Health Preferences of Older Adults into the Electronic Medical Record”
  Investigator: Amar Das

**Recently completed CADMA projects**

- “Affective Forecasting and Decision Making in Older Adults”
  Investigator: Brian Knutson

**New CDEHA projects for 2006-07**
*(projects began July 1)*

- “The HIV/AIDS Pandemic and Africa’s Orphaned Elderly”
  Investigators: Jay Bhattacharya, Grant Miller
- “Increasing Physical Activity Among the Elderly: A Meta-Analysis of the Effectiveness of Pedometers”
  Investigator: Dena Bravata

**Current CDEHA projects**

- “Health Insurance and Well-Being among the Elderly in Colombia”
  Investigator: Grant Miller
- “Affective Forecasting Across the Lifespan”
  Investigator: Brian Knutson
- “National Trends and Practice Patterns of Detection and Treatment of Hypertension among the Elderly During Ambulatory Visits in the U.S.”
  Investigator: Jun Ma
- “Elder-care, Gender, and Son Preference: The Role of Cultural Transmission and Diffusion During the Process of Rural-urban Migration in China”
  Investigator: Li Shuzhuo

**Recently completed CDEHA projects**

- “Effects of Obesity on Employer-sponsored Health Insurance”
  Investigators: Kate Bundorf, Jay Bhattacharya

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**CADMA/CDEHA, FROM PAGE 1**

Some of the most important challenges facing an aging America. CDEHA, with its focus on the demography and economics of health and aging, addresses a wide range of issues, including changes in health and family structure of the aging, and health policy challenges. CADMA is devoted to decision making regarding aging.

A central aim of both CADMA and CDEHA is to help researchers jump-start less-developed projects, enabling them to gather pilot data that will help them apply later on for larger government grants. The centers typically fund projects for one year, though some CADMA projects may be funded for two years.

“Seed funding is a great way to give early-stage projects a leg up, so researchers can gather enough pilot data to show [future funders] they know what they’re doing,” said Laura Carstensen, professor of psychology and co-principal investigator of CADMA. Seed projects are also a good value, she said. “For a relatively small amount of money, we can bring attention to important, practical questions of health and aging.”

There are key operational and thematic differences between the two centers. CDEHA was first funded in 1999 by the National Institute on Aging and has produced many publications in recent years, including articles in medical and social science journals and, most recently, a book by CDEHA grantees Shuzhuo Li and Marcus Feldman, about the effects of rural-to-urban migration on elder care, marriage and the preference for sons in China. Each spring, CDEHA’s steering committee selects two projects to fund for the coming academic year.

CADMA, in contrast, is a relative newcomer. It was created in fall 2004 with a grant from the National Institute on Aging, as one of 10 U.S. entities known as Edward R. Roybal Centers for Research on Applied Gerontology. Each spring, CADMA’s steering committee funds three projects for the coming academic year.

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Since CADMA’s projects are still relatively new, their results haven’t been published yet, though several project manuscripts were recently submitted to journals. All CADMA investigators have presented their work at Stanford seminars, and several have submitted to present in other venues such as the Gerontological Society of America’s 2006 annual meeting.

Thematically speaking, CDEHA and CADMA differ in the aspects of health and aging they examine. CDEHA’s research takes a broader societal perspective with an emphasis on population trends, including an international component. At the inaugural conference of the American Society of Health Economists, held in June at the University of Wisconsin-Madison, CDEHA sponsored a panel session on “The Demography and Economics of Health and Aging,” showcasing the work of grantees Kate Bundorf, Jay Bhattacharya and Jun Ma (see “CHP/PCOR Presentations,” p. 8).

In contrast, CADMA examines healthcare decision making by the elderly with a focus on how individuals make decisions, taking into account their values, preferences, and cognitive processes. “CADMA is almost the mirror opposite of CDEHA, because CADMA looks at individual differences while CDEHA looks at populations,” Sims explained.

Carstensen described CADMA’s mission this way: “Older people today have to make tough healthcare decisions. Economists, psychologists and physicians think about those decisions in different ways. CADMA brings all the disciplines together, to improve our understanding of how older people make decisions and to develop tools to help them make better decisions.” Garber noted that the importance of this topic is illustrated by the reaction to the Medicare prescription drug benefit’s implementation, which some beneficiaries found confusing.

While CADMA’s projects to date have largely reflected collaborations among physicians, economists and psychologists, the center is seeking to forge connections with other disciplines, such as medical informatics, engineering and sociology. This fall, CADMA will host the first of a series of “Interdisciplinary Dialogues,” in which faculty from different departments are invited to discuss a specific theme. The first such dialog will be on “Obesity, Physical Activity and Aging.”

Applied research is a key component of CADMA, and a prime example is E-preference, a software tool developed by grantee Amar Das (assistant professor of medicine) that helps patients decide between two possible treatments, or no treatment, for atrial fibrillation. The Palo Alto Medical Foundation — a large multispecialty group practice — is incorporating E-preference into its online patient health service, PAMFOnline.

A promising body of work to emerge from both centers is that of Brian Knutson, assistant professor of psychology, who has research projects funded by CADMA and CDEHA. Knutson’s research examines the role of emotion in individuals’ decision-making, and his preliminary results suggest that emotion plays a larger role, earlier on in the decision making-process, than previously reported.

In Knutson’s studies, participants are asked to perform specific tasks — such as playing a video game or investing a hypothetical amount of money — that could earn them a monetary reward depending on how well they do the task. During the experiments, participants’ emotions are measured in various ways by monitoring, for example, their heart rate, skin temperature, facial expressions and brain-wave activity. “By looking at what’s happening in their brain before they make decisions, we can predict what decisions they’ll make and we can understand different styles of decision-making,” Knutson explained. “If we understand how people make decisions, we can help them make better decisions.”

Knutson said he is “very thankful” for the support from CADMA and CDEHA, because without it his research might not have been funded at all.

“If it weren’t for CADMA and CDEHA, we wouldn’t have been able to develop these tools and do these experiments,” he said. “We’re starting out really basic in trying to measure these things, and NIH isn’t going to make a major investment in something like that unless you’ve shown you can pull it off.” Using data from his CDEHA-funded work, Knutson recently published a paper in Neuron and has applied for an NIH grant.❖

Note that in July, Tamara Sims will step down as project manager for CADMA and CDEHA and will turn those responsibilities over to Sarah Songer, an RA who has been working on the FLAIR project. Sims will pursue a PhD in psychology at Stanford starting in September.
**Research in Progress seminars**

April 5: David Meltzer, “Learning by Doing and Network Effects in a Multicenter Trial of Academic Hospitalists”


April 26: Christopher Stave, “From EndNote to Meta-analyses: A Quick Review of Lane Library’s e-Resources, Tools and Services”

May 3: Laurence Baker, “Managed Care, Adoption of Cardiac Care Technologies, and the Health of Heart Attack Patients”

May 10: Amitabh Chandra, “The Economics of Treatment Disparities in Healthcare”

May 17: Elaine Robertson, “Emotion Regulation and Selective Attention in Older Adults”

May 24: Neeraj Sood, “HIV Treatment Breakthroughs, Law Enforcement and Risky Sexual Behaviors”

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**NEWS ROUNDUP, FROM PAGE 5**

- **Alan Garber** provided comment for a *U.S. News & World Report* article, “Five tips for surviving high-deductible healthcare.” Garber discussed the usefulness of Web sites to help those with consumer-driven health plans research their medical conditions and treatment options.

- United HealthCare recently launched a nationwide program encouraging its members to split pills to save money, when the patient and the medication are deemed clinically appropriate. CHP/PCOR fellow **Randall Stafford** provided comment on the program for articles by Bloomberg News and the *Fort Lauderdale Sun-Sentinel*. The articles referenced a 2002 study by Stafford that identified 11 medications considered medically appropriate for pill-splitting.

- **CHP/PCOR associate Lars Osterberg** — clinical assistant professor of medicine at Stanford, and chief of general internal medicine at VA Palo Alto Health Care System — provided comment for a *Stanford Daily* article about the merger of two free medical clinics (the Arbor Free Clinic in Menlo Park and the Pacific Free Clinic in San Jose) to form the Cardinal Free Clinics. Both clinics enlist Stanford medical school students to provide a variety of medical services to uninsured and underinsured individuals. Osterberg is medical director of the Arbor Free Clinic.