



Kaiser Permanente Southern California



Mapping Paths to Real-World Health



From Left: Dr. Steven Jacobsen and Sac Carreathers, director of research administration, outside of the Department of Research & Evaluation in Pasadena, California.

“What drew me here was the opportunity to do research that could be translated into patient care, to make a difference for our patients tomorrow.”

— Steven Jacobsen, MD, PhD, director of research

How can we encourage patients to take medication that can potentially improve their health? If a child is obese, what additional diseases should pediatricians screen for? How can we fine-tune cancer treatments to extend survival and quality of life?

These questions are just a few examples of the kind of research currently underway in Southern California. The opportunity to participate in this kind of research—asking and answering questions that have a real-world impact on health care—is what drew me here from Mayo Clinic in 2006.

It has been an exciting time. We now have more than 200 team members, compared with 60 just five years ago. We’ve also added new areas of research, including hospital and health services research. And we’re seeing more physicians and clinical staff from Kaiser Permanente Southern California get involved in research.

Collaborations, both within Kaiser Permanente and with others in the traditional academic and health care community, have played an important part in expanding our research portfolio. Clinician partners within Kaiser Permanente help us identify questions with real-world implications for care. Outside collaborators provide scientific expertise that complements our own.

Grants from the National Institutes of Health and other federal sources, along with funding from industry partners, have supported rapid growth in our research program. We also receive continued support from the Southern California Permanente Medical Group and Kaiser Permanente’s Community Benefit Initiative. The pages that follow offer a sampling of research conducted by scientists in the Department of Research & Evaluation and physician researchers throughout Kaiser Permanente Southern California. We look forward to new, mutually beneficial partnerships in the coming years.

Be well and thrive.

Steven Jacobsen, MD, PhD

● Guiding Patients Towards Prescriptions for Better Health



From Left: Pharmacist Dr. Craig Cheetham, Research Scientist Dr. Stephen Derose, and Research Associate Teresa Harrison, part of the team studying medication adherence.



Statins are commonly prescribed to lower cholesterol and reduce the risk of cardiovascular events. But a large number of patients don't take their medications as instructed.

In Kaiser Permanente Southern California, almost 20 percent of patients who have been newly prescribed statins don't pick up their first prescription.

“We wanted to understand why some patients don't fill their new prescription to find out if there was something we could do differently,” said Research Scientist Kristi Reynolds, PhD, MPH, whose research focuses on cardiovascular health, including medication adherence. “There hasn't been a lot of research on these patients. Most research regarding medication adherence has been on patients who have been on medication for a while and take it incorrectly or stop taking it altogether.”

The Department of Research & Evaluation, Pharmacy Analytical Services, and Clinical Operations have teamed up to conduct research into primary non-adherence for statins, with funding from Merck. Studies to date include:

GAINING INSIGHTS

- A study identifying characteristics of patients who did not pick up their first statin prescription within 60 days of the order date.
- An intervention study exploring whether automated phone calls and letters to patients who hadn't picked up their new statin prescription within a few weeks increased the number who ultimately filled the prescription.
- A survey of patient perceptions to better understand the reasons they did not pick up their new statin prescription.

“This kind of research is a good example of translational research. It helps us get people on medication that has been proven effective,” said Research Scientist Stephen Derose, MD, MS, the principal investigator for the statin primary non-adherence research project. “We were also able to gain insights by leveraging Kaiser Permanente’s population-based care and electronic medical records.”



Using Findings to Improve Health

Insight into patients’ perceptions is particularly useful in clinical practice, according to Ronald D. Scott, MD, regional co-lead of Complete Care for Cardiovascular Conditions for the Southern California Permanente Medical Group.

“One of the things we uncovered through this research is that many patients who don’t pick up their first statin prescription fear the medication will do more harm than good,” said Dr. Scott, who practices in the Family Medicine Department in the Culver Marina Medical Offices in West Los Angeles. “As I talk to other clinicians, one of the points I make is that a lot of people have this pre-conceived notion. We need to address this fear and clearly explain the preventive benefits.”

To shift these perceptions, Kaiser Permanente Southern California’s Medication Adherence team has created educational tools, including a flyer for patients with graphics showing how statins work. Additionally, prescription labels for statins include the phrase “to keep arteries open.”

“Results of the pilot study revealed significantly more patients came to pick up their prescription after getting a call than members who did not get the intervention,” said Kelley Green, RN, PhD, senior consultant in the Clinical Operations department. “So we will institute an ongoing Regional Outreach program to provide our members with this relatively inexpensive, but very effective, intervention to support their adherence to statins and decreased risk for cardiovascular events.”

Detailed results from the primary non-adherence studies will be published in forthcoming papers.

“Drugs don’t work in people who don’t take them.”

— C. Everett Koop, MD, ScD, former U.S. Surgeon General

Improving Medication Adherence for Other Conditions

Studies are underway to evaluate whether reminding members who are overdue for refills might also improve medication adherence for statins and other medication therapies including hypertension, diabetes, and cancer drugs.

“Integrating findings from this research into clinical practice will help us improve medication adherence, one of our top clinical priorities,” said Assistant Medical Director Joel Hyatt, MD, who co-leads the regional medication adherence efforts for Kaiser Permanente Southern California. “Studies on the effectiveness of automated outreach will help identify better ways to support physicians, especially in primary care.”

• Finding Ways to Help Women Thrive After Breast Cancer



Across the U.S., tens of thousands of breast cancer survivors take tamoxifen, an oral chemotherapy drug, to reduce their risk of recurrence. While effective, tamoxifen has a number of side effects, including hot flashes, night sweats, and depression. About half of the women on tamoxifen also take antidepressants, which can help manage these side effects.

Some studies suggest certain antidepressants--selective serotonin reuptake inhibitors, or SSRIs--interfere with tamoxifen's protection against breast cancer.

“There has been some evidence from laboratory studies showing that SSRIs reduce the effectiveness of tamoxifen,” said Reina Haque, PhD, MPH, who is the principal investigator of a new project, ‘ABC: Antidepressants and Breast Cancer Pharmacoepidemiology.’ “But previous studies involving women have been small in scale, and findings have been contradictory.”

From Left: Research Associate Chantal Avila, Assistant Medical Director Dr. Joanne Schottinger, and Research Scientist Dr. Reina Haque are part of a large group of researchers and clinicians who are working to find better treatments for breast cancer.

ADVANCING TREATMENT

The ABC project, which is funded by the National Institutes of Health/National Cancer Institute, will follow nearly 17,000 breast cancer survivors over 10 years. The research team includes investigators from Kaiser Permanente Southern California, Kaiser Permanente Northern California, and Harvard Medical School.

“As a physician, it is hard to know what to tell my patients when one study involving a thousand patients says one thing, and another with almost two thousand suggests something else,” said Joanne Schottinger, MD, assistant medical director of Clinical Analysis for the Southern California Permanente Medical Group and a practicing oncologist. “A study like this one will give me the information I need to tell my patients with confidence whether taking these drugs together is a risk or not.”

“What we’re looking at is how to increase survival rates for women with breast cancer.”

— Joanne Schottinger, MD, assistant medical director of Clinical Analysis, Southern California Permanente Medical Group

Translating Breast Cancer Research into Treatment

As new findings related to breast cancer treatment are discovered, clinicians are eager to take them back into practice.

“As a medical group, we’ve done a tremendous amount to improve screening for breast cancer. Our 5-year survival rate is about 95 percent. Fine tuning the treatments we offer patients may push that rate even higher,” said Dr. Schottinger. “We’ll take the findings that come out of this study and others and make it happen in practice. That’s the exciting part of being a clinician here.”

Another recent study looked at when to intervene to increase use of adjuvant hormonal therapy among women with hormone-sensitive breast cancer. Researchers found that monitoring and intervention for use of adjuvant hormonal

therapy needs to begin by one year after breast cancer diagnosis and continue through the five years of recommended therapy to ensure women receive optimal benefit from this life-saving treatment.

“There is growing recognition that improving utilization of adjuvant hormonal therapy may be a key strategy in improving breast cancer prognosis,” said Virginia Quinn, PhD, MPH, principal investigator for the study. “At Kaiser Permanente Southern California, we have a unique opportunity to test innovative ways to improve care and quality of life among cancer survivors.”

Advancing Breast Cancer Treatment Through Clinical Trials

The Kaiser Permanente Southern California Cancer Clinical Trials Program is also extremely active in breast cancer research. The program emphasizes prevention, adjuvant treatment to prevent relapse after surgery, and novel treatments for metastatic cancer.

Recent successes include studies leading to Food and Drug Administration approvals of raloxifene for breast cancer prevention,

Herceptin® as an adjuvant treatment, and Eribulin® in treating metastatic cancer. Kaiser Permanente often ranks as one of the top recruiters nationally for these studies.

One recently closed trial used a genetically based, tumor-specific assay to precisely determine prognosis and identify who would benefit from postoperative chemotherapy. More than 200 Kaiser Permanente Southern California members have participated in the trial, known as the TAILORx trial, or Clinical Trial for Assigning Individual Options for Treatment. If the study succeeds, it could spare many more women with early stage breast cancer from going through chemotherapy.

“In the near future, breast cancer treatments will be personalized—based on the characteristics of a patient’s individual cancer,” said Jonathan Polikoff, MD, director of the Cancer Clinical Trials Access Program. “This will increase effectiveness and decrease toxicity. We anxiously await the results of the Tailorx study that hopefully will allow us to further refine our present care.”

● Pinpointing Risks of Childhood Obesity



From Left: Research Associate Mayra Martinez, Research Scientist Dr. Corinna Koebnick, Biostatistician Dr. Ning Smith, and Pediatrician Dr. Amy Porter are among those working to better understand the health implications of childhood obesity.

SEEKING LONG, HEALTHY LIVES



Obesity at an early age puts children at greater risk for other health conditions, including diseases normally seen in

adults. Researchers in Kaiser Permanente Southern California are discovering new links through a childhood obesity study funded by the National Institutes of Health/National Institute of Diabetes and Digestive and Kidney Diseases.

“Childhood obesity, especially extreme childhood obesity, raises risk for a number of other conditions,” said Research Scientist Corinna Koebnick, PhD, MSc, principal investigator for the childhood obesity study. “What we are finding points to a need to evaluate the benefit of screening children who are extremely obese for diseases not normally seen as pediatric conditions.”

Potential health consequences of obesity include cardiovascular risk factors such as high blood pressure and elevated cholesterol, as well as common conditions such as asthma, psoriasis, and functional digestive disorders. Findings to date include:

- Extreme obesity affects about 7 percent of boys and 6 percent of girls, with the highest frequency among Hispanic and African American children. (*Journal of Pediatrics*)¹
- Extremely obese children have a 40 percent higher risk of gastroesophageal reflux disease than normal weight children. (*International Journal of Pediatric Obesity*)²
- Extremely obese children were almost 80 percent more likely to have psoriasis than normal weight children. (*Journal of Pediatrics*)³

The study involves more than 920,000 children. Kaiser Permanente Southern California's large and diverse population, as well as its integrated care delivery model, offers a unique opportunity to study the health consequences of obesity, particularly for children who are extremely obese.

"This is about health, not what a child looks like or what kind of person the child will be. Children who are obese or extremely obese can grow up to be anything they want to be—judges, lawyers, doctors. But the one thing they can't be is healthy," said study co-investigator Amy Porter, MD, a Kaiser Permanente Baldwin Park pediatrician who leads the Pediatric Weight Management Initiative for Kaiser Permanente's Southern California Region.



Healthy ONES Encourages Healthy Habits

Over the past four years, the Healthy Options for Nutrition Environments in Schools (Healthy ONES) program has tested and implemented interventions designed to encourage healthier eating and increased fitness activity in the Lemon Grove School District in San Diego.

The community intervention program is funded as part of a study conducted by Research Scientist Karen Coleman, PhD, MS.

"By working closely with the schools, we were able to change many things that people said could never be changed," said Dr. Coleman. "We even managed to get rid of cupcakes for birthday celebrations, cake walks for fundraising, and chips and cookies for snacks."



Research Associate Magda Pomichowski is part of the Healthy ONES team.

Kaiser Permanente's Project Coordinator for Healthy ONES Maggie Shordon, MPH, led the team and worked with teachers, parents, principals, and nutrition services at four schools to implement a new Wellness Policy.

The Healthy ONES program significantly reduced the amount of unhealthy foods and beverages on school campuses. Results of the study will be published in a forthcoming paper.

Funding for this study was provided by the United States Department of Agriculture (USDA) National Research Initiative.

"What we want for children is for them to live long and healthy lives."

— Amy Porter, MD, Pediatric Weight Management Initiative lead for Kaiser Permanente Southern California

• Giving Mothers and Babies a Healthier Start



From left: (Front) Research Scientist Dr. Anny Xiang and Associate Investigator Dr. David Sacks. (Middle) Research Scientist Dr. Jean Lawrence and Biostatistician Dr. Mary Helen Black. (Back) Research Scientist Dr. Darios Getahun and Maternal-Fetal Medicine Specialist Dr. Michael Fassett.



Health during pregnancy can have short- and long-term consequences for both the mother and child.

One common condition is gestational diabetes—glucose intolerance first recognized during pregnancy.

“Identifying and managing gestational diabetes may prevent complications for both the mother and child,” said David A. Sacks, MD, who practiced in the Obstetrics/Gynecology department at Kaiser Permanente’s Bellflower Medical Center from 1975-2010 and is now an associate investigator with the Department of Research & Evaluation.

“For the mother, potential complications include higher frequency of preeclampsia, c-sections, and a higher propensity of maternal obesity,” he added. “Babies are often oversized at birth, and a greater proportion of their weight is from fat, which can increase risks for metabolic syndrome later in life.”

REDUCING RISKS

Assessing Risks for Complications

According to new criteria developed by the International Association of Diabetes in Pregnancy Study Groups, a woman can be diagnosed with gestational diabetes if just one glucose test value is abnormal. This can be a fasting blood test or the test value after consuming a beverage with a specific amount of sugar.

Risks for adverse pregnancy outcomes, however, vary significantly depending on which tests showed abnormal results, according to a December 2010 study published by Kaiser Permanente Southern California researchers in *Diabetes Care*.⁴ The retrospective study of 8,700 women showed that:

- Women who had normal fasting levels but elevated values following an oral glucose tolerance test were at higher risk for preterm delivery, gestational hypertension, and having an infant with jaundice.
- Women with elevated fasting and normal values after an oral glucose tolerance test were at higher risk of

“My hope is that through research we can refocus care before, during, and after pregnancy on areas that affect long-term health for the mother and child.”

— David A. Sacks, MD, associate investigator, Department of Research & Evaluation

having a large-for-gestational-age infant, compared with women without gestational diabetes.

“What the results of this study tell us is that risks are not the same for all women diagnosed with gestational diabetes. Clinicians need to consider a combination of test results to fully assess and manage the risks with their patients,” said Biostatistician Mary Helen Black, PhD, lead author of the study.

Glucose Testing After Pregnancy

Women who have had gestational diabetes are at increased risk for type 2 diabetes. Postpartum glucose testing can identify women who may be at risk or need treatment.

In a group of almost 12,000 women identified as having gestational diabetes, only about half received a fasting blood glucose or oral glucose tolerance test within six months after pregnancy,

researchers at Kaiser Permanente Southern California found. Among those tested, more than 1,000 women were at increased risk for diabetes.

“This provides a critical opportunity to work with women to reduce their risk of developing diabetes through increased physical activity and dietary changes to promote healthy weight loss,” said Research Scientist Jean M. Lawrence, ScD, MPH, MSSA, lead author of the study, which was published in the March 2010 edition of *Diabetes Care*.⁵

Risk of Recurring Gestational Diabetes

Women who developed gestational diabetes during their first or second pregnancies have an increased risk for recurrence, according to a study published in the November 2010 edition of *The American Journal of Obstetrics and Gynecology*.⁶

“Our study found that women who developed gestational diabetes during their first but not second pregnancies had a 630 percent increased risk for developing gestational diabetes during their third pregnancy,” said Research Scientist Darios Getahun, MD, MPH, lead author of the study.

This risk was even more pronounced in the third pregnancy for women who had gestational diabetes in their first and second pregnancies.

“Understanding this risk of recurrence identifies a group of women we can target more specifically for prevention efforts,” said Michael Fassett, MD, study co-author and a maternal-fetal medicine specialist who practices at Kaiser Permanente’s West Los Angeles and Kern County facilities. “What this study did was really underscore the magnitude of the risk in subsequent pregnancies.”

Building the Future of Hospital Care



From left: Medical Director of Quality and Clinical Analysis Dr. Michael Kanter, Senior Vice President of Quality and Risk Management Patti Harvey, and Research Scientist Dr. Jason Jones.

ASSEMBLING EVIDENCE



Kaiser Permanente's integrated care delivery model provides a unique environment to build evidence for better

hospital care and put that knowledge to use. Recognizing this, the Garfield Foundation provided funding in 2010 for a new hospital research program in the Department of Research & Evaluation.

"Most hospitals today are islands—information about a patient's health before admission or after discharge is limited at best," said Research Scientist Jason Jones, PhD, who focuses on hospital research. "At Kaiser Permanente, we see the complete continuum of care. As researchers, we also have the opportunity to work directly with the clinicians and patients we serve to improve quality of care."

Finding the evidence is just one part of what's needed to improve patient care. Dr. Jones is partnering with clinicians and organizational leaders to help get relevant evidence into the right hands at the right time, an essential step in translating new findings into better care.

“Clinician time is especially valuable in the hospital, where patients have complex illnesses,” said Patti Harvey, RN, senior vice president of quality and risk management, patient care services, and clinical operations support for Kaiser Foundation Health Plan/Hospitals. “We need to develop systems to deliver new and relevant findings to physicians and nurses at the frontline, so we can better support their decisions.”

Implementing these kinds of systems takes collaboration across Kaiser Permanente Southern California, involving frontline clinicians, regional leadership, researchers, and operational groups, such as the Management Information & Analysis team and the Clinical Analysis Department.

“Through research, we can find innovative ways to improve care, achieving even greater health outcomes for our patients.”

— Ben Chu, MD, MPH, president, Kaiser Foundation Health Plan/Hospitals, Southern California

Current projects seek to improve hospital care and outcomes starting before admission and extending beyond discharge. Examples span from an initiative to support early identification of emergency department patients with sepsis, to tools that identify patients at risk for readmission after discharge.

“One of the strengths we have as an integrated system is the ability to bring together people with a wide range of expertise,” said Michael Kanter, MD, medical director of quality and clinical analysis, Southern California Permanente Medical Group. “Working together we can build the tools that will guide us toward a better future for hospital care.”

Charting a Strategic Course in Clinical Research

Evidence-based care is a cornerstone of Permanente Medicine in both inpatient and outpatient settings. But there are many gaps in knowledge, and filling those gaps through traditional approaches to research can take years.

To accelerate that timetable, clinicians and scientists at Kaiser Permanente Southern California are embarking on a new strategic clinical research initiative focused on clinical questions with potentially significant organizational impact.

“Strategic research gives us a means of learning how to care for our members in a more efficient and effective way when there is no published literature to guide us,” said Dr. Kanter.

Research projects are getting underway to address strategically important clinical questions. A few examples include the following studies:

What factors are associated with an increased risk of lower-limb amputation in patients with diabetes? (*Principal Investigator: Annette Adams, PhD, MPH*)

Is adherence to the Surgical Care Improvement Program (SCIP) infection measures associated with fewer post-surgical infections in total hip and knee replacement patients? (*Principal Investigator: Annette Adams, PhD, MPH*)

Does treatment of depression and subsequent lowering of a patient’s score on the Patient Health Questionnaire result in better outcomes for chronic diseases as well as lower emergency department and hospital utilization? (*Principal Investigator: Karen Coleman, PhD, MS*)

Does improving hypertension control slow progression of chronic kidney disease? (*Principal Investigator: Stephen Deroose, MD, MS*)

How well does Archimedes IndiGO—a decision-support tool that calculates health risks—predict cardiovascular disease outcomes? (*Principal Investigator: Stephen Deroose, MD, MS*)

Which types of hysterectomy are best for patients with specific characteristics? (*Principal Investigator: Neal Lonky, MD*)

• Clinical Trials Pave Ways to Better Care



From left: Research Associate Myleine Flojo, Director of Clinical Trials Research Dr. Donald Fong, and Research Associate Nydia Soler



Across Kaiser Permanente Southern California, more than 300 clinical trials are underway. These trials provide

Kaiser Permanente members with access to promising therapies that would otherwise not be available to them, from new drugs to treat HIV to promising cancer treatments.

“We want our patients to have access to the latest advances in medicine,” said Donald Fong, MD, MPH, director of the regional clinical trials research program. “Physicians participating in clinical trials have the opportunity to participate in the development of new therapies and treatments, ensuring we are practicing cutting-edge medicine.”

Physicians who participate in the Southern California Permanente Clinical Trials Research Program learn about new therapies before they are approved by federal regulators. Through investigator meetings, they have the opportunity to network with other researchers and learn about new therapies that could potentially become treatment options well before findings are published.

A background image showing three medical professionals in white coats, overlaid with a semi-transparent yellow filter. The text 'Kaiser Permanente' is visible in small letters on the middle person's coat.

PROMISING THERAPIES

“Another reason it is important to participate in clinical trials is that we have a very ethnically diverse population,” said Dr. Fong. “When results are published, we want to make sure that findings are applicable to our population. The best way to ensure they do is to participate in the process.”

More than 30 specialty departments offer access to clinical trials. In addition, the Southern California Permanente Medical Group funds five ongoing clinical trials programs.

Cancer Clinical Trials Access Program

Principal Investigators: Jonathan Polikoff, MD, and Han Koh, MD

This program provides access to research trials for the prevention and treatment of cancer. It offers a wide range of oncology clinical trials, providing Kaiser Permanente members access to new therapies for lung cancer, leukemia, myeloma, and more. Physicians are taking part in studies that could change practices in treatment of colon and breast cancer. They are also participating in trials that contribute to the development of new cancer therapies for prostate cancer. In 2010, there were 53 active oncology trials, with another 96 open for follow up.

HIV/AIDS Research Trials

Principal Investigator: William Towner, MD

This program supports high-quality care for patients with HIV by providing access to new investigational drug therapies. In 2010, patients in the program accessed seven different investigational drug treatments including a novel one-pill, once-a-day therapy. The program is expanding in new areas, including hepatitis, infectious disease, and vaccines. The program conducted 17 active clinical trials in 2010 and has enrolled over 675 patients to date.

Kaiser Permanente/City of Hope Bone Marrow Transplant Clinical Trials

Principal Investigators: Neil Kogut, MD; Firoozeh Sahebi, MD; and Ricardo Spielberger, MD

This program provides Kaiser Permanente members with access to bone marrow and stem cell transplant treatment protocols at City of Hope Medical Center, where their care is provided by physicians from the Southern California Permanente Medical Group. These protocols include trials that are changing the way we prevent treatment-related complications, promoting better care for our members, and improving outcomes. Nearly 150 Kaiser Permanente members received

“The glory of medicine is that it is constantly moving forward, that there is always more to learn.”

— William J. Mayo, MD, co-founder of the Mayo Clinic

transplants in 2010. More than a thousand members are in long-term follow up in Kaiser Permanente facilities. In 2010, there were more than a hundred studies in progress, including 45 open to accrual. Southern California Permanente Medical Group physicians are active principal investigators or co-investigators in these trials.

Pediatric Oncology Investigational Trials

Principal Investigator: Robert Cooper, MD

This program provides access to promising new treatments for children and adolescents with cancer. Through investigational trials sponsored by the Children's Oncology Group, researchers in Kaiser Permanente Southern California collaborate with clinicians across the nation to develop and refine cancer treatments. In 2010, the group had 95 trials open, including 10 new trials opened within the year.

Surgical Radiation Oncology Clinical Trials Access Program

Principal Investigator: Steve Vasilev, MD

This program manages clinical trial protocols for patients with cancer where treatments involve surgical procedures and/or radiation treatments in addition to chemotherapeutic regimens. It includes multiple principal investigators from the specialties of surgery, radiation oncology, and obstetrics/gynecology. The program works with cooperative research networks and industry funded trials. In 2010, the program had 22 open protocols.

Exploring Vaccine Safety and Effectiveness



From left: Biostatistician Jeff Slezak, Research Scientist Dr. Hung-Fu Tseng, Director of Research Dr. Steven Jacobsen, and Research Scientist Dr. Virginia Quinn, four of the co-authors of a May 2010 JAMA article that examined the association between the pneumonia vaccine and cardiovascular events.

UNDERSTANDING PREVENTION



Vaccines are a powerful tool for preventing the spread of disease and reducing risks of complications. Researchers in Kaiser Permanente Southern California are conducting a number of studies to better understand the effectiveness and safety of vaccines.

Pneumonia Vaccine and Cardiovascular Events

Respiratory infections, including influenza and pneumonia, have been linked to heart attacks and stroke. Studies have suggested that the influenza vaccine can reduce these risks. But research on the protective benefit of the pneumococcal vaccine has been more controversial.

Scientists at the Department of Research & Evaluation followed 84,000 men over a 5-year period, looking for a link between the pneumococcal vaccine and reduced risk for heart attack and stroke. They found none. The results were published in *JAMA* in May 2010.⁷

“This study is important because a previous study found that there was a protective effect,” said Research Scientist Hung-Fu Tseng, PhD, the lead author of the study. “The biggest difference between our study and the previous study is that we were able to control for other important factors that could lead to differences.”

The study included members from Kaiser Permanente Southern and Northern California. Researchers gathered demographic and lifestyle information from surveys, obtained vaccination records from the Kaiser Immunization Tracking System, and looked at outcomes using electronic health records.

“This is a great example of the kind of study that can be done at Kaiser Permanente,” said Steven Jacobsen, MD, PhD, senior author of the study. “We were able to link vaccination records to outcomes in a large and diverse population to provide important insights for patients and physicians.”

This study is part of the California Men's Health Study, which is funded by the California Cancer Research program.

“When meditating over a disease, I never think of finding a remedy for it, but, instead, a means of preventing it.”

— Louis Pasteur, French scientist

Shingles Vaccine Effectiveness

A retrospective study of 300,000 men and women age 60 years and older found that the herpes zoster vaccine was associated with a 55 percent reduced risk of getting shingles.

These findings, published in *JAMA* in January 2011, added to the evidence of vaccine efficacy for herpes zoster as reported in the largest clinical trial of the vaccine, the Shingles Prevention Study.⁸

“In many ways, our study reinforces the findings of the earlier clinical trial, but there were differences,” said Dr. Tseng, lead author of the study. “In the clinical trial, the vaccine appeared to be less effective for people over 75. Our study, however, showed that people over 75 also had a 50 percent reduced risk if they received the vaccine.”

Pneumovax and Shingles Vaccine

The administration of both the pneumococcal and the herpes zoster vaccines to patients during the same visit is beneficial and does not appear to compromise the protective effect of the zoster vaccine, according to a study published by Kaiser Permanente Southern California researchers in the May 2011 edition of *Vaccine*.⁹

“This was a particularly relevant study,” said Jim Nomura, MD, chief of infectious disease at Kaiser Permanente’s Los Angeles Medical Center. “The manufacturer had put out a statement that you shouldn’t give the vaccines concurrently because of attenuated response to the zoster vaccine. The CDC, on the other hand, said it was okay.”

Kaiser Permanente Southern California’s clinical guidelines for vaccines mirror the CDC’s recommendations.

“This study helped to resolve a discrepancy within the medical community,” said Bruno Lewin, MD, chair of Kaiser Permanente Southern California’s Regional Immunization Practice Committee. “Within our region, it reaffirmed the usual standard of care, which supports administering both vaccines in the same visit.”



Additional Vaccine Studies

Additional vaccines that researchers in Kaiser Permanente Southern California are studying include those for chicken pox (varicella), whooping cough (pertussis), shingles (herpes zoster), rubella, hepatitis B, human papillomavirus, and encephalitis.

Kaiser Permanente Southern California is a partner in the Vaccine Safety Datalink, a collaborative network spearheaded by the Centers for Disease Control and Prevention’s Immunization Safety Office.

Supporting Clinician Researchers in Quest for New Evidence



From left: Research Project Manager Dr. Sharon Hudson with Administrator of Graduate Medical Education Felice Klein.

LIFE-LONG LEARNING



The Regional Research Committee provides funding for clinicians within Kaiser Permanente Southern California who want to pursue research.

“The cornerstone of evidence-based medicine is research,” said Donald Fong, MD, MPH, chair of the Regional Research Committee. “We provide funds to physicians and staff whose research can contribute to the evidence-base necessary for medical care.”

In 2010, the committee awarded nearly \$500,000 in funding for projects initiated by Kaiser Permanente Southern California physicians, residents, and employees.

“The application process has gotten quite competitive,” said Sharon Hudson, PhD, senior research project manager, who works with many of the applicants. “To be successful, applicants need a strong proposal based on a research idea that is feasible, interesting, ethical, and relevant.”

The full committee, which includes Area Research Chairs from each of Kaiser Permanente Southern California local

areas, meets twice a year to consider new applications. Priority is given to projects that might be difficult to fund externally but have the potential to lead to better practices and outcomes.

“A lot of the questions applicants want to investigate have direct applications to care, not just for our patients, but for the whole country,” said Patrick Van Winkle, MD, area research chair for Orange County and a pediatric hospitalist. “Externally, there is often a mismatch between the research being done and the problems we need to solve in real-world practice.”

The Regional Research Committee provides significant funding for clinician research projects—up to \$60,000—and also helps connect researchers to additional support. Applicants frequently work with staff from the Department of Research & Evaluation to complete their project.

“Kaiser Permanente has an amazing support system for clinician research,” said Dr. Van Winkle. “That’s the great thing about this organization—there are people who have expertise in many different areas who can be brought together to research important questions.”

Research by Residents and Fellows

Research is an important component of residency and fellowship programs. Even those who decide not to pursue research later in their career acquire valuable skills by performing research during residency.

“One of the basic tenets of residency is committing to an investment in life-long learning,” said Felice Klein, RN, administrator of graduate medical education for Kaiser Permanente Southern California. “Participating in research helps develop physicians who are able to read studies with a critical eye, discerning which findings are credible and useful to their practice and which are not.”

Scientists and staff from the Department of Research & Evaluation provide mentoring and other support.

“The research scientists and staff have always been very willing to help,” said Klein. “They provide basic guidance about

developing research questions and walk people through the research process.”

Urology residents, for example, meet with Director of Research Steven Jacobsen, MD, PhD, on a weekly basis, during a six-month period of their residency dedicated to research.

“The weekly meetings gave us a good structure to develop research projects and see them all the way through,” said Melanie Wuerstle, MD, a urology resident at Kaiser Permanente’s Los Angeles Medical Center.

“We learned everything from the basics—how to conceive a research idea, how to get funding— through statistical analysis and manuscript preparation,” she added. “For a lot of us, that kind of experience and resultant publications are really helpful when we’re applying for fellowships or jobs.”

Services to Support Research

The Department of Research & Evaluation provides support to Kaiser Permanente Southern California physicians and staff interested in the conduct of research, including the following services:

- Critiquing written hypotheses and research questions.
- Assisting with study design and written study protocols.
- Suggesting funding sources.
- Providing guidance on study implementation and data collection plans.
- Consultation on study design and choices/application of statistical methods.
- Performing power and sample size calculation.
- Providing programming and data management.
- Using statistical software for data analysis and interpretation of results.
- Consultation on Kaiser Permanente Southern California electronic data systems and data-quality issues.
- Formatting, submitting, and tracking manuscripts for publication.

Sponsored Programs Administration and the Research Finance Office provide grant development and submission support as well as the fiscal and programmatic management of external and internal research projects for medical center researchers as well as scientists within the Department of Research & Evaluation.

“Once you know the inner workings of a research project, you are better able to critically analyze the research you’ll be reviewing in your clinical practice.”

— Melanie Wuerstle, MD, urology resident, Los Angeles Medical Center

● Growing Department Supports Expanding Research Portfolio



Front: Senior Contracts and Grants Administrator Monty Adams. Middle, from left: Research Scientist Dr. Kristi Reynolds, Research Scientist Dr. Annette Adams, Research Associate Karin Liu, Research Scientist Dr. Karen Coleman, Natural Language Processing Specialist Dr. Chengyi Zheng, Research Administrative Analyst Nora Kasparian, Back: Research Associate Alex Carruth.



The Department of Research & Evaluation continues to grow rapidly, more than tripling in size in the past

five years. The growing team supports an expanding research portfolio, with an increasing focus on translational research—research that can be translated into improved patient care.

“The research group is an eclectic and energized group that wants to do important research with a real-world impact,” said Director of Research Steven Jacobsen, MD, PhD. “We partner with clinicians who practice state-of-the-art medicine, and know what the important clinical questions are. That makes this an ideal environment for translational research.”

In 2009 and 2010, the department added six new scientists. These scientists broadened the diversity of research interests in the department, adding new scientific expertise in areas ranging from orthopedics to neuroepidemiology. Six additional scientists are expected to join the Department by early 2012.

TRANSLATING RESEARCH

As the scientific team has expanded, so has the Department of Research & Evaluation as a whole. It now includes more than 200 individuals, including scientists, biostatisticians, programmers, clinical trials support staff, research support staff, grant administrators, finance staff, information technology personnel, administrative support, and operations staff.

“Each of our business units plays a critical role in supporting the expansion of our research portfolio,” said Director of Research Administration Sac Carreathers. “We bring together diverse expertise, from statistical analysis to desktop support, in support of the scientific work of the department.”

New Scientific Partnerships

The Department of Research & Evaluation has joined forces with other Kaiser Permanente research institutes to develop a new center for trans-regional research. The Kaiser Permanente Center for Effectiveness and Safety Research (CESR) will make it easier to bring together the varied scientific interests and expertise from different Kaiser Permanente research centers to study important clinical questions.

“What’s exciting for me is to be at the heart of a learning organization where research can be translated directly into best practices that are taken up rapidly in the care delivery system,” said Beth McGlynn, PhD, director of the Kaiser Permanente Center for Effectiveness and Safety Research.

Another new partnership is with the Southern California Clinical and Translational Science Institute (SC CTSI), a consortium spearheaded by the University of Southern California. This will facilitate access to educational and core facilities there, as well as enhance the number and quality of Kaiser Permanente Southern California’s collaborations with affiliated investigators in addressing important translational research questions.

In 2010, the Department of Research & Evaluation also forged new partnerships with the following collaborative networks and multi-center studies:

Mental Health — Karen J. Coleman, PhD, MS, is the site principal investigator for the Mental Health Research Network, a national network involving 10 health systems funded by the NIH/National Institute of Mental Health. The network is designed to conduct population-based mental health research that can be effectively translated into clinical practice. Several projects are ongoing as a part of this effort, including an Autism Spectrum Disorder registry and studies of how mental health practices vary across medical settings.

Diabetes — Jean M. Lawrence, ScD, MPH, MSSA, is the site principal investigator for SUPREME-DM (Surveillance, Prevention, and Management of Diabetes Mellitus) study, a multi-institutional consortium for comparative effectiveness research in diabetes prevention and treatment. Bringing together researchers from 12 integrated health care systems with more than 11 million members, including 750,000 people with diabetes, the consortium aims to link clinical and administrative information to conduct cutting-edge research.

The Department of Research & Evaluation is involved with a number of collaborative networks. The following are a few examples:

- Cancer Research Network
- Cardiovascular Research Network
- Center for Education and Research on Therapeutics
- Coordinated Clinical Studies Network
- Developing Evidence to Inform Decisions about Effectiveness (DEcIDE-2) Network
- HMO Research Network
- Kaiser Permanente Center for Effectiveness and Safety Research
- Mental Health Research Network
- Southern California Clinical and Translational Science Institute
- SUPREME-DM (Surveillance, Prevention, and Management of Diabetes Mellitus)
- Vaccine Safety Data Link

2010 Grants in Brief



The Department of Research & Evaluation receives funding from multiple sources, including federal and state agencies, industry contracts, and internal funding. Overall funding has increased significantly since 2006, with a substantial increase in funding from federal and industry sources.

The following are just a few examples of new 2010 federal awards with scientists from the Department of Research & Evaluation serving as principal investigators:

Antidepressants and Breast Cancer Pharmacoepidemiology — Reina Haque, PhD, MPH, is the principal investigator for a \$1.8 million grant from the NIH/National Cancer Institute to examine common drug interactions in a cohort of 17,000 breast cancer survivors. (For more details see page 4).

Childhood Obesity — Corinna Koebnick, PhD, MSc, is the principal investigator for a NIH/ National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)-funded study of childhood obesity involving more than 920,000 children. (For more details, see page 6).

Disparities in Progression to Renal Replacement Therapy — Stephen Derose, MD, MS, is the principal investigator for a NIH/ NIDDK-funded retrospective cohort study among members of Kaiser Permanente Southern California to study the clinical determinants of end-stage renal disease. Chronic kidney disease is now recognized as a major public health problem. Rates of end-stage renal disease are particularly high among African Americans. The insights gained from this study will help guide clinical interventions to reduce racial/ ethnic disparities and benefit patients with chronic kidney disease, regardless of race or ethnicity.

Renewed Grants

The Centers for Disease Control and Prevention (CDC) awarded more than \$3 million to support the next five years of the SEARCH for Diabetes in Youth Study, a multi-center observational study. Jean M. Lawrence, ScD, MPH, MSSA, is the principal investigator.

Industry Grants

In addition to federally funded grants, scientists from the Department of Research & Evaluation have been successful in obtaining funds from industry. Aniket Kawatkar, PhD, MS, is principal investigator for the following grants:

Oncology — This study, which spans a 10-year time horizon, will estimate the incidence rate, treatment management patterns, resource utilization and expenditure, and mortality outcomes associated with febrile neutropenia in Kaiser Permanente Southern California members with non-Hodgkin's lymphoma, breast cancer, and lung cancer.



ADVANCING SCIENCE

Diverticulitis — This study will set up a health-related quality of life assessment to inform a cost-effectiveness model comparing mesalamine and standard-of-care empirical treatment. This study is unique in that it evaluates changes experienced by diverticulitis patients within 48 hours of a patient presenting with an acute episode.

2010 Publication Highlights

In 2010, researchers from Kaiser Permanente Southern California published more than 200 articles in peer-reviewed journals. More than 90 were first-author articles. In addition to the studies previously mentioned, examples include:

Red wine consumption not associated with reduced risk of colorectal cancer (*Nutrition and Cancer*)¹⁰

Red wine consumption and risk of prostate cancer: the California men's health study (*International Journal of Cancer*)¹¹

Treatment of ductal carcinoma in situ among patients cared for in large integrated health plans (*American Journal of Managed Care*)¹²

Intravitreal bevacizumab and ranibizumab for age-related macular degeneration: A multicenter, retrospective study (*Ophthalmology*)¹³

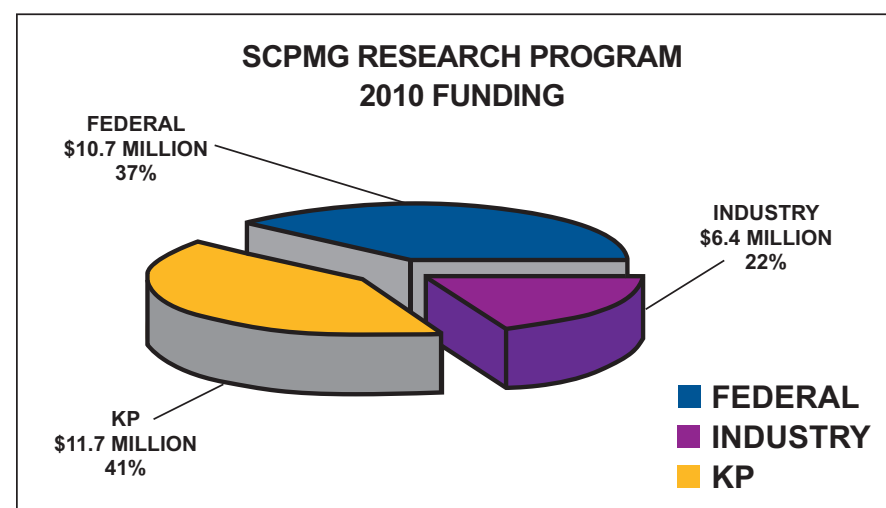
Body weight and height data in electronic medical records of children (*International Journal of Pediatric Obesity*)¹⁴

Kaiser Permanente National Total Joint Replacement Registry: aligning operations with information technology (*Clinical Orthopaedics and Related Research*)¹⁵

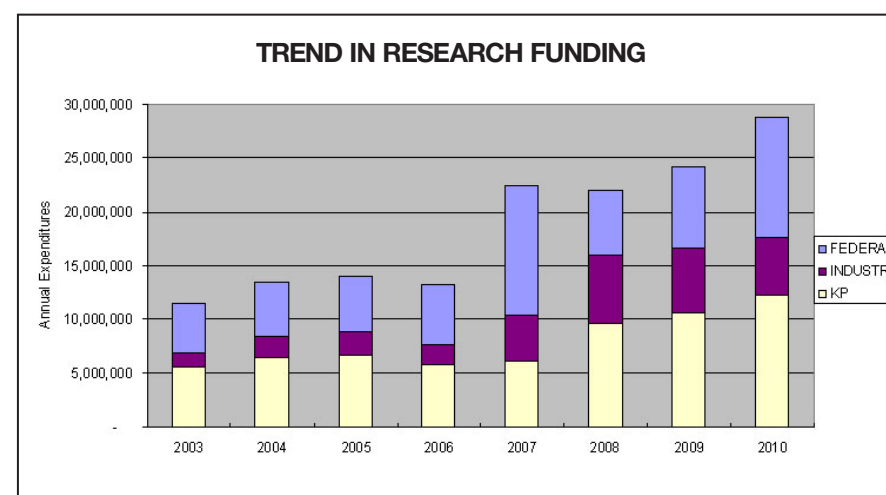
A prospective study of 80,000 total joint and 5,000 anterior cruciate ligament reconstruction procedures in a community-based registry in the United States (*Journal of Bone and Joint Surgery*)¹⁶

For the full citation, see references on page 24.

For more information about our studies and publications, visit the Department website at www.kp-scalresearch.org.



Funding for the research program in 2010 totaled \$28.8 million.



Research funding has increased significantly since 2006.

Research Program Overview



From Left: Dr. Kelley Green, from the Department of Clinical Operations, with Research Scientist Dr. Kristi Reynolds.

ENHANCING HEALTH



Our scientists and medical center investigators carry out a program of research and conduct program evaluations spanning a range of areas, including:

Clinical Research examines which treatments work, how well they work, and which work better than others. Treatments under study can range from vaccines to cancer screening tests, and include drugs and new medical devices.

Epidemiological Research examines possible causes of disease in specific populations. This research has focused on smoking and cancer, genetic defects, and other topics.

Health Services Research helps develop greater knowledge about the most effective ways to deliver and finance care, improve access to care, and enhance patient satisfaction.

Behavioral Research examines the role of behavioral interventions to improve health and prevent disease.

Department Overview

The Department of Research & Evaluation is structured into eight groups with specific disciplines that work as cross-functional teams to support scientific research:

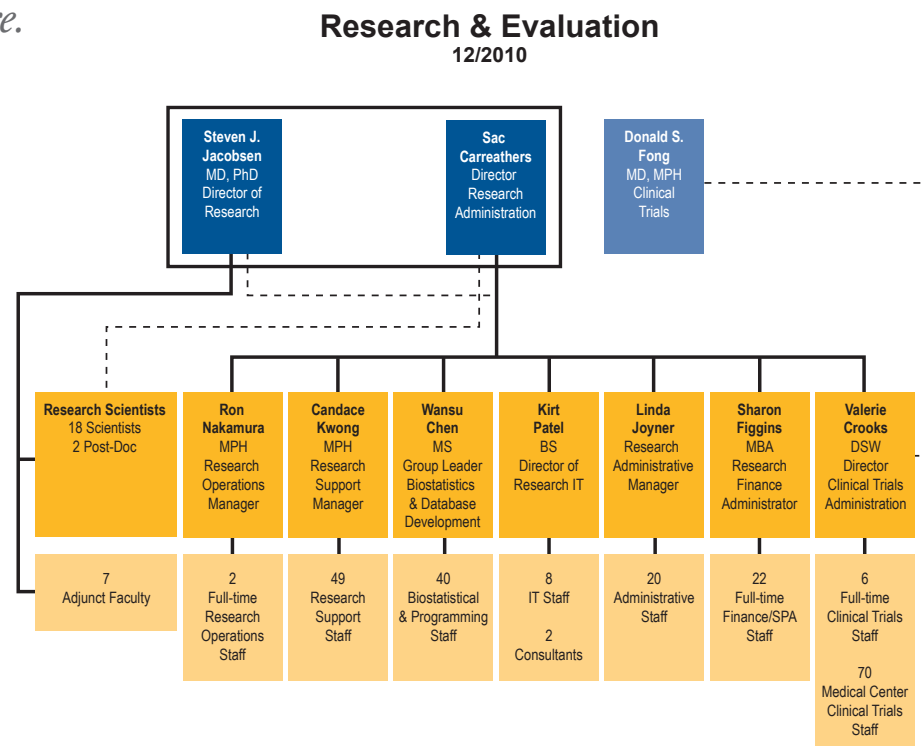
- Research Scientists
- Biostatistics and Database Development
- Clinical Trials
- Research Support
- Administrative Support
- Research Finance Office/Sponsored Projects Administration
- Research IT
- Research Operations

*“What has been true of our past must be true of our future.
We must go on building people...for the best is yet to be.”*

— Henry Kaiser, co-founder of Kaiser Permanente

Scientists and affiliated investigators in the Department of Research & Evaluation have expertise in the following research areas:

- | | |
|-------------------------------|------------------------------------|
| ■ Aging | ■ Injury |
| ■ Cancer | ■ Kidney Diseases |
| ■ Cardiovascular Disease | ■ Maternal and Child Health |
| ■ Child and Adolescent Health | ■ Medication Adherence |
| ■ Comparative Effectiveness | ■ Men's Health |
| ■ Diabetes | ■ Mental Health |
| ■ Digestive System Disorders | ■ Molecular Epidemiology |
| ■ Eye Research | ■ Neurological Disorders |
| ■ Genetics | ■ Obesity |
| ■ Gestational Diabetes | ■ Pharmacoepidemiology |
| ■ Health Economics | ■ Prevention and Behavior Change |
| ■ Health Equity | ■ Quality Improvement |
| ■ Health Informatics | ■ Vaccine Safety and Effectiveness |
| ■ Health Services Research | ■ Violence and Abuse |
| ■ HIV/AIDS | ■ Women's Health |



*To read more about our scientists and
their research interests, visit the Department
website at www.kp-scalresearch.org.*

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