

### Dedicated to Barry Miller, PhD



The Division of Research (DOR) lost a colleague and dear friend in 2008. We want to acknowledge the work over the past 14 years of Barry Miller, PhD, who joined The Permanente Medical Group in 1994 and

became the DOR's administrative director in 2003. Barry died suddenly in October. He brought a level of energy, an exemplary professionalism, a sense of humor, and a passion for living that enriched all of us. We will deeply miss Barry and have named a conference room after him to keep his memory alive.

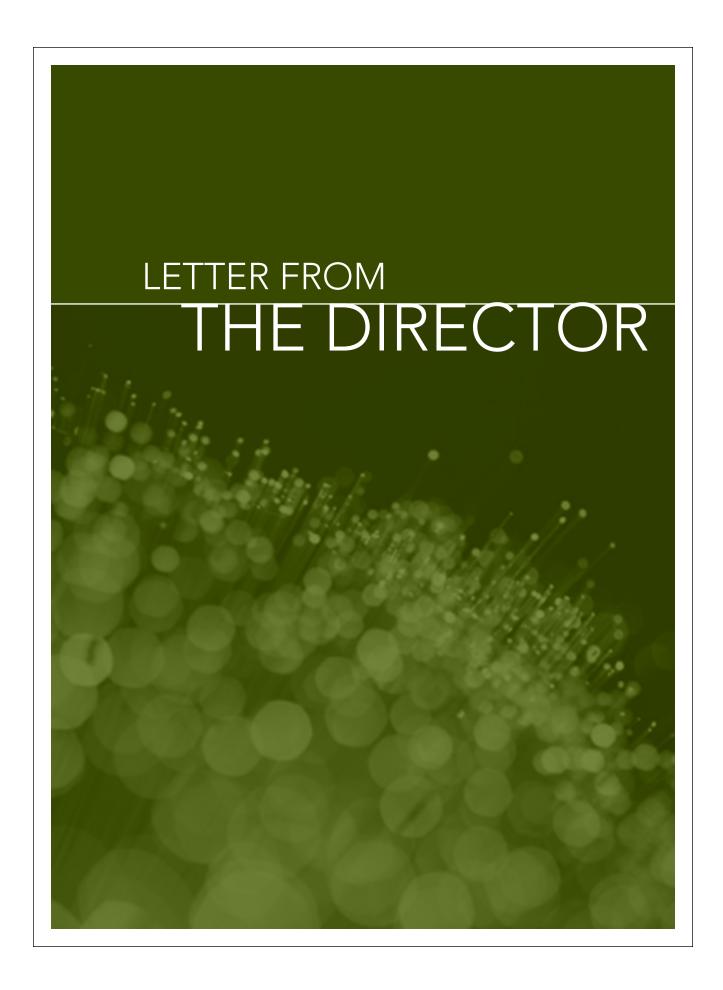
## WELCOME

The Division of Research (DOR) conducts, publishes, and disseminates high-quality epidemiologic and health services research to improve the health and medical care of Kaiser Permanente members and the society at large. It seeks to understand the determinants of illness and well-being and to improve the quality and cost-effectiveness of health care. To accomplish these goals, the DOR is committed to providing a supportive research environment that fosters independent thinking, creativity, continued learning, and adherence to the highest scientific standards.



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Joe V. Selby, MD, MPH, has served as director of the Division of Research since 1998.

## DEAR FRIENDS AND COLLEAGUES,

On behalf of Kaiser Permanente Northern California's Division of Research (DOR), I am pleased to present the 2008 Research Report. In the last two years, we have experienced continued growth and several noteworthy new directions within the Kaiser Permanente Northern California (KPNC) research enterprise.

Like other resource-conscious organizations, the DOR is concerned about its impact on the environment. With that in mind, we are making a few changes to this year's report. We will be providing information about our researchers and their research interests, previously presented within this paper report, on our Web site: www.dor.kaiser.org/researchreport. We hope you'll go to the site and take the time to explore and learn more about the DOR and its researchers.

The DOR's 47-year-old research program is built on a foundation of rigorous epidemiologic investigation in a large, well-characterized population. Many of the DOR's major contributions have been in the areas of risk factor identification, prevention, and drug safety. However, this is an exciting time in biologic, medical, and health services research, and the DOR is contributing to progress in many new areas.

We are particularly pleased with the progress of Kaiser Permanente's Research Program on Genes, Environment and Health (RPGEH), led by Catherine Schaefer, PhD, in reaching its goal of building a world-class genetic epidemiology resource. Launched in February 2007, the RPGEH will become one of the world's largest biorepositories for conducting studies that examine how genes and the environment affect our health. Nearly 400,000 KPNC members have completed the RPGEH health survey and approximately 70,000 have already contributed saliva samples for the biorepository. Important research projects have begun. Schaefer, executive director of the RPGEH, was funded to participate in one of the largest studies on bipolar disorder and Stephen K. Van Den Eeden, PhD, will conduct a study of the causes of prostate cancer in African-American men (pg. 32).

We have also recognized KPNC's remarkable potential for conducting strategically important clinical trials through partnerships between the DOR and clinicians from The Permanente Medical Group (TPMG). In 2008, the DOR established the Comprehensive Clinical Research Unit (CCRU), led by Alan S. Go, MD, and supported by KPNC's Community Benefit Program, to support clinical trials conducted by DOR research scientists and TPMG clinicians across a variety of specialties (pg. 14).

As the nation comes to grips with the dilemma of rising health care costs and decreasing health care coverage, Kaiser Permanente is also in a remarkable position to help answer the critical questions of how to implement and use health informatics, manage chronic illness, motivate self-care and disease prevention, and optimize design of health care benefits.

With support from Kaiser Permanente's Institute for Health Policy, John Hsu, MD, MBA, MSCE, and the DOR have established the Kaiser Permanente Center for Health Policy Studies at the DOR to focus our health services efforts on key policy questions and disseminate those findings to policy makers within and outside Kaiser Permanente (pg. 38).

The most important healthrelated research today is done through inter-institutional collaboration.



New technologies create new frontiers in research and new opportunities to innovate in health promotion and health care delivery. DOR researchers are currently studying the use of several new technologies, including innovations in population management made possible by Kaiser Permanente HealthConnect, Kaiser Permanente's electronic health record; e-mail-delivered interventions for health promotion; and Web-based programs to assist patients in managing chronic conditions. On page 28, we describe eCare for Moods, an intervention program led by Enid M. Hunkeler, MA, that assists patients with major depression or bipolar disorder communicate with their providers and manage their condition.

With Kaiser Permanente's diverse Northern California population, the DOR has been home to many studies that investigate the causes of socioeconomic and racial/ethnic disparities in conditions such as diabetes, heart disease, and cancer, to name just a few. On page 42, we share projects from Andrew J. Karter, PhD, Alyce S. Adams, PhD, and other DOR researchers who are focusing on understanding and eliminating health disparities.

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The most important health-related research today is done through inter-institutional collaboration. On page 20, we describe some of our valued collaborations, including our partnership with the University of California, San Francisco (UCSF), which was awarded one of the first 12 Clinical and Translational Science Awards (CTSA) from the National Institutes of Health, and our close ties with researchers in 14 other HMO-based research centers through the HMO Research Network.



The DOR's direction can be traced back to our founder, Morris "Morrie" F. Collen, MD, to whom we owe a debt of gratitude. In 1961, Morrie became founding director of the

Department of Medical Methods Research, later renamed the Division of Research.

In November 2008, we celebrated Morrie's 95th birthday by naming the DOR's conference center and library after Morrie in recognition of his vision and his contributions to the public's health, clinical medicine, and health care delivery.

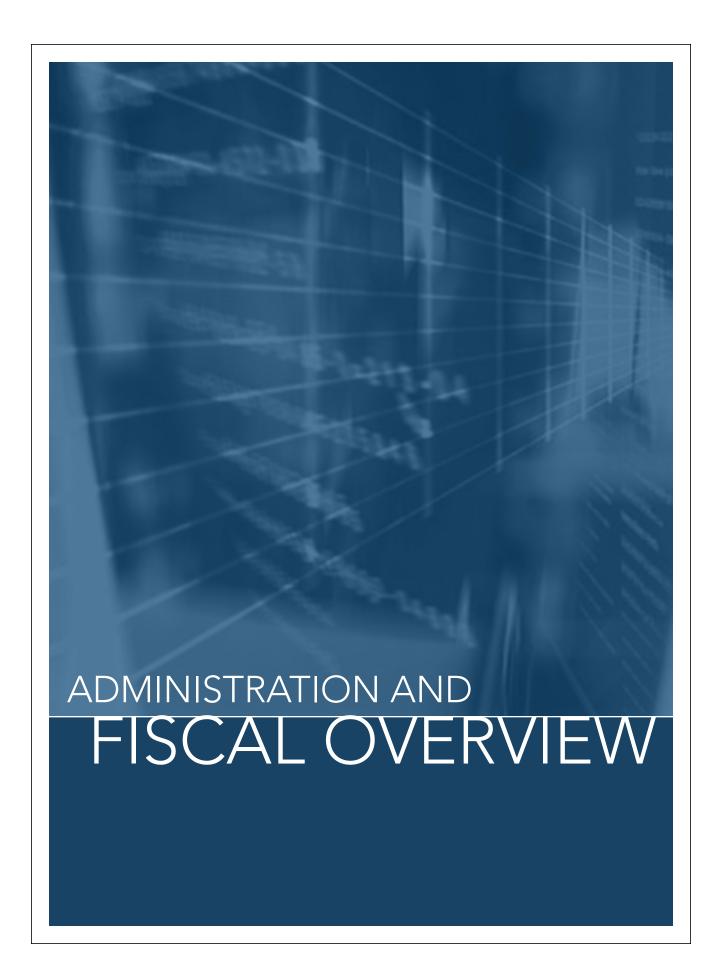
Morrie continues working on his trademark blockbuster projects. Currently, he is teaming with Joseph F. Terdiman, MD, PhD, the DOR's director of IT, to launch what we call the "Research Database." This database is a highly efficient and accessible relational database that captures all Kaiser Permanente electronic data from KP HealthConnect and earlier legacy systems, as well as important data from many other sources to facilitate large-scale drug safety research (pg. 31).



Morris F. Collen, MD, director emeritus

And finally, we want to thank our parent organization, The Permanente Medical Group, and its Associate Executive Director Philip Madvig, MD. The opportunity to work within such a remarkable organization is the reason we exist and thrive. Equally, we thank Kaiser Foundation Hospitals and Health Plan (KFH/HP), its Community Benefit Program, and its Kaiser Foundation Research Institute (KFRI). The support of KFH/HP has been pivotal in many areas, including provision of major funding to the RPGEH, the CCRU, the Center for Health Policy Studies, and our research in health disparities. The collegial administrative support provided by KFRI is, as always, greatly appreciated.

I hope this report gives you a fuller picture of the accomplishments of DOR research and the direction in which we are headed. Don't hesitate to contact us with questions or suggestions.



The Division of Research (DOR) is home to 41 investigators and 10 staff scientists who served as principal investigators or co-investigators on 353 research projects in 2008. In addition, DOR Administration provides support to 28 adjunct investigators from other academic institutions and to 35 clinician investigators from The Permanente Medical Group. The DOR was awarded 56 new grants and contracts in 2008. Extramural funding for research activities in 2008 totaled \$58.3 million, an increase of 18.2 percent from fiscal year 2007.

DOR research projects include epidemiologic and health services studies, clinical trials, and program evaluations covering a wide range of topics, including cardiovascular disease, cancer, diabetes, substance abuse, mental health, maternal and child health, women's health, drug safety, health care policy and health services, health and health care disparities, and genetic influences on health and illness.

DOR researchers contributed nearly 200 scientific articles to the medical and public health literature in 2008.



The majority of DOR studies involve collaborations with researchers from other regions of Kaiser Permanente, and from other health plan-based centers affiliated with the HMO Research Network. We also collaborate with academic institutions across the country. Of particular note are our rich collaborative relationships with academic centers in the Bay Area, including the University of California, San Francisco (UCSF), Stanford University School of Medicine, and the School of Public Health, University of California, Berkeley. The DOR is a founding partner with UCSF of its Clinical and Translational Science Institute.

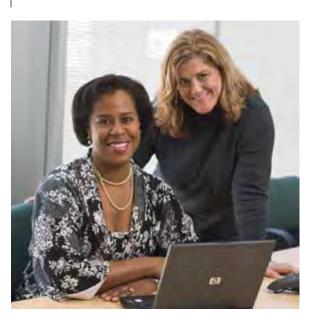
The DOR Administration team provides a wide range of services that include:

- Grants and contracts (pre-award support)
- Fiscal operations (post-award services)
- Human resources
- Communications/public affairs
- Research compliance (Institutional Review Board)
- Facility operations

DOR Administration also oversees medical records analysis, data entry services, administrative assistance, and the Morris F. Collen Research Library at the DOR.

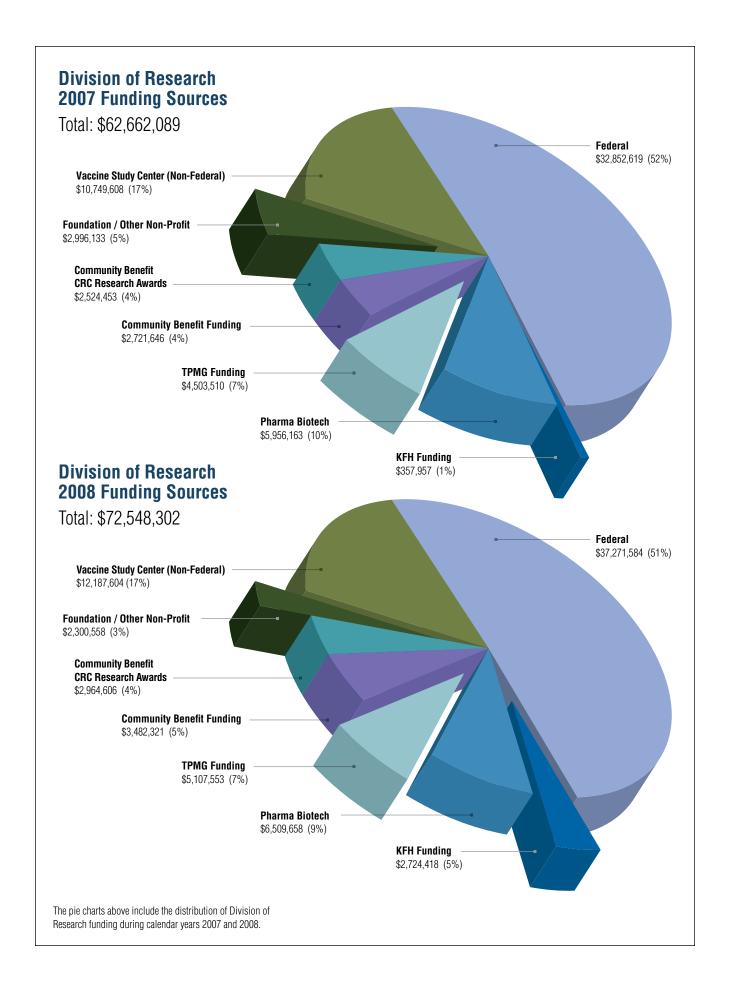
DOR's IT services, led by Joseph F. Terdiman, MD, PhD, provides comprehensive computing and informatics support to DOR investigators and staff. The strategic programming group, led by Jamila Gul, maintains many of the DOR's key databases and supports training and career development for more than 70 programmers/analysts at the division. The common goal of these two groups is to provide an IT infrastructure along with resources that offer rapid, accurate and cost-effective data retrieval. In addition, the strategic programming group is focused on transitioning the DOR to the new electronic health record system, Kaiser Permanente HealthConnect.

DOR Administration has been led by Barry Miller, PhD, for the past nine years. He died suddenly in October of 2008 and is missed particularly by those in Administration. The Administration team is being led on an interim basis by Elize Brown, DrPH, JD, acting administrative director, and Alison Truman, MHA, associate administrative director.



Elize Brown, DrPH, JD, and Alison Truman, MHA

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Forty-seven years ago, with the concept of integrated care just taking off and technology promising to forge new paths in medical research and medical care, the Division of Research (DOR) began its journey to becoming a leader in epidemiologic and health services research.

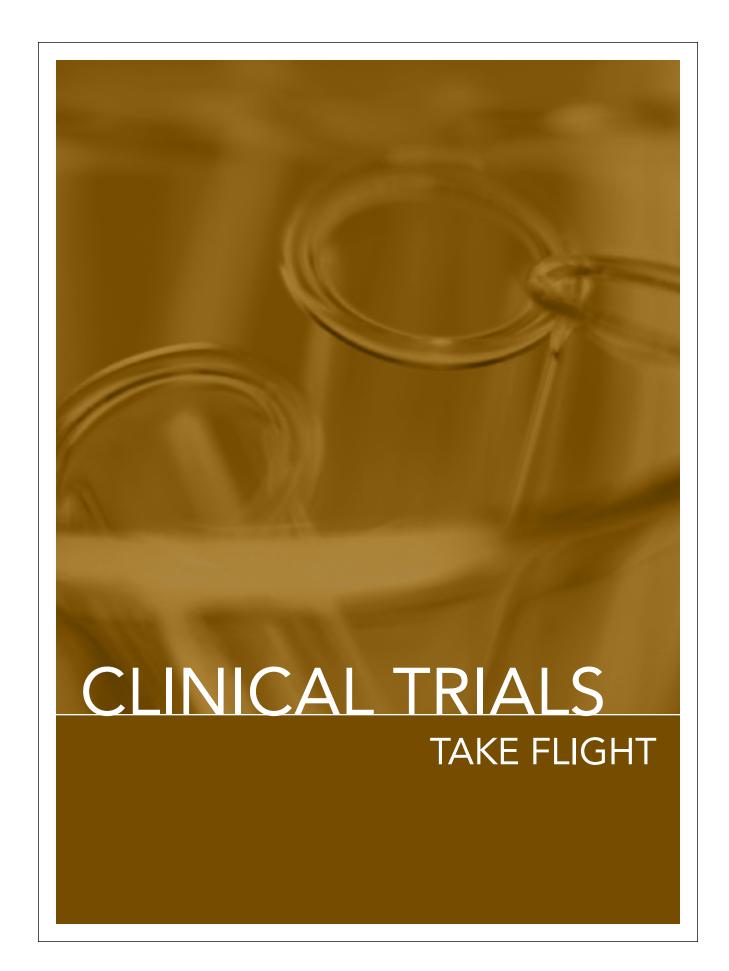
Today, as it increases its research collaborations and pursues growth in numerous areas, including genetics, health policy, technology, health disparities, and clinical research, the DOR and its investigators are relying on that solid bedrock of epidemiological expertise.

Since our last report, the DOR has launched several exciting new programs and centers, including the Research Program on Genes, Environment and Health, which seeks to understand how genes and the environment affect health.

The DOR has also created the Comprehensive Clinical Research Unit to centralize its growing clinical trials program. As the DOR plays a greater role in national health policy discussions, the new Kaiser Permanente Center for Health Policy Studies at the DOR will serve as an important clearinghouse for key research. Moreover, as interdisciplinary collaborations have become increasingly important in creating more powerful research, the DOR has joined with the University of California, San Francisco in the Clinical and Translational Science Institute (CTSI) to expand inter-institutional collaborative clinical research as well as training of students, residents, fellows, and faculty in clinical and translational research. And this is only the start. Expect to see announcements of additional collaborations in the coming year.

As the DOR launches new research endeavors, we continue to rely on our unique assets—the ability to tap into millions of Kaiser Permanente electronic health records, our strong research team, close ties with physicians in The Permanente Medical Group and, ultimately, a unique and collaborative relationship with many institutions across the nation.







Alan S. Go, MD; Nanette H. Hock, RN, MSN, FAHA; and Phenius V. Lathon, CCRC

#### NEW COMPREHENSIVE CLINICAL RESEARCH UNIT SUPPORTS GROWING PROGRAM

The latest cancer drugs, vaccines, and other treatments all go through rigorous clinical research before they ever reach the broad patient population. In the last two decades, Kaiser Permanente Northern California (KPNC) clinicians and researchers have conducted a large body of clinical trial research in areas such as vaccine safety, HIV/ AIDS, oncology, and in many other clinical specialties. Currently, hundreds of clinical trials are being conducted in Northern California. The Permanente Medical Group (TPMG) physicians, based in KPNC medical centers, typically lead these trials. A growing number of clinicians are also getting involved in observational clinical research.

As clinical research has grown within the region, so too, has the need for more centralized support, especially for solo clinician researchers embedded in medical centers. With that in mind, the Comprehensive Clinical Research Unit (CCRU) was launched in early 2008. The CCRU's major purpose is to improve the design, implementation, and reporting of clinical research studies—both interventional clinical trials and clinical trials throughout KPNC, says Alan S. Go, MD, founding director. "Centralizing support for researchers at the individual and group levels helps to ensure that the research gets done efficiently and safely while taking some of the burden off the individual clinician."

As clinical research has grown within the region, so too has the need for more centralized support, especially for solo clinician researchers embedded in medical centers.



Alan S. Go. MD

Go, who is currently working on his own clinical research studies of new investigational medications for stroke prevention in atrial fibrillation and secondary prevention of coronary heart disease, says the new

research unit also provides an opportunity for more effective networking and collaboration among researchers and with external colleagues and research sponsors.

The CCRU offers operational support and consultation, expanded biostatistical and data analytic support, and online training on how to conduct clinical research studies. In early 2009, the CCRU launched a centralized research collaboration Web portal for any clinician or researcher who is considering doing a research project within KPNC.

The new research unit provides an opportunity for more effective networking and collaboration among researchers.

"Researchers can enter information about their proposed research project and we will provide a rapid evaluation of their ideas and approach and then connect them with potential collaborators," says Go. For example, he notes, a gastroenterologist in Santa Clara who wants to participate in a new clinical trial can request a project consultation, ask for pilot data with people at their facility, or possibly connect with other gastroenterologists in the region. Similarly, for a federal or industry sponsor looking for partners to help develop or enroll into clinical research studies, the CCRU can quickly connect that group with interested clinical experts within TPMG, says Go.



#### **ONCOLOGY CLINICAL TRIALS**

The CCRU will work closely with larger TPMG clinical trial groups such as Kaiser Permanente Oncology Clinical Trials (KPOCT), which began 20 years ago. KPOCT currently participates in more than 200 ongoing cancer studies, the majority of which are multicenter clinical trials. KPOCT, which does mostly Phase 2 and 3 clinical outcome trials, enrolls almost 400 Kaiser Permanente patients a year at KPNC's 26 medical centers. "Support from Kaiser Permanente's Community Benefit Program and the Kaiser Foundation Research Institute have helped continuous expansion of the program since its start from a small group to one of the largest national programs," says Louis Fehrenbacher, MD, medical director of KPOCT and an oncologist at Kaiser Permanente Medical Center, Vallejo.

KPOCT has participated in several key practice-changing clinical trials in the last decade. Between 2000 and 2005, KPOCT was the highest enroller in the nation for a key study on the breast cancer drug Herceptin, which showed a dramatic decrease in the recurrence of HER2 positive breast cancer in women who were treated with the drug.



In addition to its renowned Herceptin trials, KPOCT has participated in clinical trials from the 1990s to the present. The trials looked at the effects of the drug Avastin for advanced colon, lung, and breast cancer, finding that the drug was effective at advanced stages of disease. More recently, KPOCT researchers began a National Surgical Adjuvant Breast and Bowel Project (NSABP) trial to determine if the combination of Avastin and Herceptin is effective in preventing breast cancer from recurring.

### STUDYING BARRIERS TO ENROLLMENT

While clinical research is critically important in improving cancer treatments, only 3 percent of cancer patients participate in clinical trials and researchers are eager to learn why. Carol P. Somkin, PhD, a research scientist and sociologist at the Division of Research (DOR), is working with Fehrenbacher on a study looking at barriers to patient enrollment in oncology trials and ways to increase participation. The study offers patients in the intervention group a telephone counseling session with a nurse educator who discusses clinical trials as one possible treatment option.

The goal of this intervention is to engage patients in talking about clinical trials with their oncologist. Doctor-patient interactions are likely to be more productive if the patient comes to the oncology visit prepared to ask questions about clinical trials.



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Carol P. Somkin, PhD

"By using our electronic medical record, we can identify patients who are potentially eligible for ongoing clinical trials and tailor education specifically for them."

"Most studies about barriers to clinical trials have asked people to respond to hypothetical scenarios, or attempted to increase recruitment with community advertising," Somkin says. "But using our electronic medical record, we can identify patients who are potentially eligible for ongoing clinical trials and tailor education specifically for them in real time to see what works."

Somkin, who has partnered with Fehrenbacher on several trials, says "You can't do this kind of study without a collaboration between physicians and researchers. Dr. Fehrenbacher has been instrumental in many ways, including helping to choose the trials we work on, getting buy-in from the oncologists, and providing crucial feedback on the intervention."

#### **VACCINE STUDY CENTER**

The Kaiser Permanente Vaccine Study
Center was established in 1984 to conduct
vaccine clinical trials and epidemiological
research. Since then, there have been
numerous large and pivotal clinical trials that
have led to the licensure of many of the
current vaccines used in children, including
whooping cough and chicken pox, says
Nicola P. Klein, MD, PhD, co-director of the
center and research scientist at the DOR.

The center has built a trial network of research staff at 20 KPNC pediatric clinics and, at any one time, has several active Phase 2 or 3 studies that involve thousands of children. The center also conducts trials in other Kaiser Permanente regions, including Colorado and Hawaii.

"A major focus of our current efforts is on the efficacy of meningitis vaccines for toddlers and infants, which is important because while meningitis peaks both in infancy and during young adulthood, the currently licensed vaccine is only available for those over the age of two years," says Klein.



Bruce H. Fireman, MS, and Nicola P. Klein, MD, PhD

#### **FAST TRACK TO GROWTH**

In recent decades, the Division of Research has expanded from being a stellar epidemiology research group into new areas such as health policy, health services research, and genetics, says Go. The next major step will be to continue growing the DOR's expertise in and oversight of clinical trials, he says. "The DOR brings a unique mix of methodological and content expertise and often adds complementary clinical expertise by partnering with TPMG chiefs groups across a wide range of medical and surgical specialties," adds Go. "We believe we will very quickly become a model of how you can do this on a larger scale in a community-based setting."





## STRENGTHENING RESEARCH THROUGH COLLABORATION

"The power of collaboration is ultimately the power to improve patient care," says Joe V. Selby, MD, MPH, director of Kaiser Permanente Northern California's Division of Research (DOR). Selby's own experience as both a family physician and a clinical epidemiologist convinces him that the quickest route to better prevention and treatment often lies in research carried out in alliance with other HMOs and universities.

The drive to collaborate is accelerating nationwide, as the federal government increasingly demands that researchers break out of the silos of their own organizations and begin working in larger, inter-disciplinary and inter-institutional teams. In some instances, pooling data across institutions allows for more statistically powerful analyses or for studies in more representative populations.

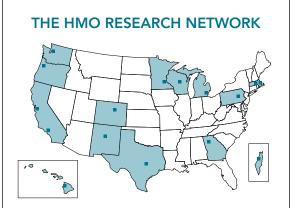
Pooling can also capture variations in treatment patterns that are valuable for answering certain questions. More often, though, it is the collaborative, intellectual capacity that makes the study more powerful. Researchers collaborating across a broader span of the clinical research spectrum can increase the "translational" impact of their work and speed potentially life-saving findings into clinical practice.

With the ability to pull from the medical records of nearly 11 million patients, the network's potential research power far surpasses that of typical research studies done by single institutions.

#### **HMO PARTNERSHIPS**

To accelerate collaboration, Kaiser Permanente Northern California (KPNC) and eight other HMOs around the country formed the HMO Research Network in 1994. The network. which includes six of Kaiser Permanente's regional research centers, now has 15 research centers located in not-for-profit health plans and draws from a patient population that spans from Hawaii to New England. With the ability to pull from the medical records of nearly 11 million patients, the network's potential research power far surpasses that of typical research studies done by single institutions. HMO Research Network studies are helping define what is the best care for patients with such diseases as hypertension, diabetes, cardiovascular disease, and cancer.

"Having a robust electronic health record and in-depth clinical information allows us to answer important research questions about why certain people suffer from various cardiovascular diseases."



For example, the HMO Research Network conducted important research regarding cervical and breast cancer screening through its Cancer Research Network (CRN). Carried out between 1995 and 2000 at seven HMO Research Network member sites, these two studies aimed to identify persisting challenges in the cervical and breast cancer screening programs of these health plans. Researchers wanted to know if the screenings were not as effective as they could be, or if some women were simply failing to go in for screenings. "Within these health care systems, mammography and Pap smears were essentially free. Nevertheless, our linked cancer registries were telling us that a number of women were still presenting with advanced-stage breast or cervical cancer," says Selby, who recently served as the network's governing board chair.

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Network scientists concluded that for both types of cancer, the explanation in more than 50 percent of cases appeared to be that women had simply failed to get screened. This research was important because it pointed to the need for more intense outreach to enrolled women members who have not been screened in several years or at all. "It is also important on a broader scale because if this problem exists within these high-quality health plans, it is almost certainly worse in the more fragmented US health care system," says Selby. Two papers on the research appeared in the Journal of the National Cancer Institute in 2004 and 2005. "The studies have really made an impact, both inside and outside these systems," Selby says.

## COLLABORATING ON HEART DISEASE RESEARCH

The Cardiovascular Research Network (CVRN) is a powerful new research arm of the HMO Research Network that was formed at the end of 2007 in partnership with the National Heart, Lung and Blood Institute. The collaboration includes 15 HMO Research Network sites and provides a rich source for very large studies of common cardiovascular risk factors, conditions, and treatments, while also offering a patient pool large enough for studies involving rarer cardiovascular diseases.

CVRN research success, as well as that of the HMO Research Network overall, depends a great deal on the volume and thoroughness of linkable patient medical records. Alan S. Go, MD, is director of the CVRN and also the director of the Comprehensive Clinical Research Unit at the DOR. He praises the network's ability to conduct population-based research studies by using database and electronic medical information across member research sites. "Having a robust electronic health record and in-depth clinical information allows us to answer important research questions about why certain people suffer from various cardiovascular diseases and how to prevent and treat these conditions more effectively. We are also able to track the epidemiology of cardiovascular risk factors and diseases over time," says Go.



A CVRN-leveraged study initiated in 2006 focused on the optimal duration of use of the antiplatelet drug clopidogrel in people with coronary disease treated with drug-eluting intra-coronary stents. As it turned out, the health plans in the CVRN were the only ones that possessed longitudinal individual-level medication data comprehensive enough to find the answer. The study clarified that the short-term risk of failure of drug-eluting stents was low and that some patients were not taking clopidogrel long enough. Go says the research informed the US Food and Drug Administration's decision to recommend keeping patients who receive drug-eluting stents on clopidogrel for at least a year after their stent is implanted.

Go currently leads a five-health plan CVRN study looking at the use of the blood thinner warfarin in patients with atrial fibrillation or venous thromboembolic disease. The study seeks to determine the risks of bleeding and blood clot formation associated with taking the drug.



## CLINICAL AND TRANSLATIONAL SCIENCE AWARDS

Another type of collaboration is demonstrated by the partnership of KPNC and the DOR with the University of California, San Francisco (UCSF) through its Clinical and Translational Science Institute (CTSI). The CTSI is an award from the NIH that aims to strengthen inter-disciplinary research and speed translation across academic research campuses and between academic institutions and their community partners. As part of the ambitious new effort, the DOR has established the KP CTSI Clinical Research Center.

The DOR's outpatient clinical research unit has joined with UCSF and other community-based clinical research centers in a network that supports inter-institutional clinical research as well as the training of students, residents, fellows, and faculty in clinical and translational research.

"Multidisciplinary collaboration is the future of medical research."

The KP CTSI Clinical Research Center hosts a wide range of collaborative studies on everything from kidney and pulmonary disease to women's health, osteoporosis, and diabetes. Current studies include research pertaining to chronic obstructive pulmonary disease outcomes, type 2 diabetes risk among women with gestational diabetes, and the epidemiology of chronic kidney disease.

KPNC is also a partner with UCSF in the CTSA Community Engagement Program. Together, the two institutions develop ways to ensure full, two-way exchanges between researchers at the DOR and at UCSF, while also exploring ways to strengthen research partnerships with Bay Area patient groups, schools, community-based organizations, safety net clinics, and other affected community members. In one project, a KPNC medical team is working with UCSF scientists to find new ways to increase colorectal screening. In another study, scientists are recruiting families in which two or more siblings have epilepsy for research to identify possible genetic markers for the disease.



"Research benefits if the community is engaged," says Selby. "This means that community members understand and agree with the ethics and logistics of the research, they participate in designing some of the research, and, ideally, they help to determine what research gets done. I think the NIH deserves credit for recognizing the importance of community involvement, and we are proud to be a partner with UCSF in the Community Engagement Program."

Selby concludes, "Multidisciplinary collaboration is the future of medical research. It makes sense and, frankly, it is more exciting, too."



## RESEARCH SCIENTISTS STUDY THE INTERSECTION OF TECHNOLOGY AND HEALTH

How does technology change the practice of medicine? Does it create more or fewer patient visits? Can it prevent adverse events or help patients manage their chronic conditions better? These are just a few of the questions researchers and clinicians at the Division of Research (DOR) and Kaiser Permanente Northern California (KPNC) are exploring through a robust technology research program that aims to determine the benefits and potential drawbacks of technology.

"Part of technology research is seeking to understand the consequences of technology and part of it is harnessing it for new uses," says Joe V. Selby, MD, MPH, director of the DOR. He points to diverse research projects underway, including studies that examine the ways in which Web-based programs help patients better manage conditions such as bipolar disorder and others that look at population management tools for improving care for the chronically ill.

"The program uses information from consumers to individualize care, update symptom profiles, add new coping strategies, and automatically alert the nurse when a patient needs help."



Selby credits Kaiser Permanente's electronic health record system, KP HealthConnect, for making much of this research possible, and, of course, Morris Collen, MD, founding director of the DOR, and a pioneer in medical informatics. Kaiser Permanente has been heralded as the vanguard in health care technology for creating the largest civilian electronic health record system in the nation, which includes all of its 8.7 million members. 3.4 million of whom reside in Northern California. "Technology and the electronic health record are particularly useful in that they allow us to look at populations of patients who meet very complex sets of descriptive requirements," says Selby. "In turn, this allows us to do research that we couldn't do before."

## MANAGING CHRONIC CONDITIONS OVER THE INTERNET

In 2000, Acting Associate Director Enid M. Hunkeler, MA, Joseph F. Terdiman, MD, PhD, director of information technology, and Yvonne Porterfield, RN, MSN, led a team of clinicians, researchers, and consumers to develop and evaluate two interactive, Internet-based care management programs for those with recurrent depression or bipolar disorder, eCare for Moods (patent pending), aims to improve a patient's ability to manage his or her moods, enlist the aid of a care partner, and keep in regular contact with mental health providers, says Hunkeler. She and William A. Hargreaves, PhD, conducted a randomized trial to evaluate the programs. The findings were promising.

Among other things, eCare for Moods allows patients to monitor their personal symptoms and early warning signs, daily functioning, and medication adherence and side effects. Program patients receive education, 24/7 advice, personalized action and emergency plans, and have regular online exchanges with a psychiatric nurse who monitors the Web site daily, says Hunkler. "The program uses information from consumers to individualize care, update symptom profiles, add new coping strategies, and automatically alert the nurse when a patient needs help."



Enid M. Hunkeler, MA

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Following the success of eCare for Moods, eCare for Health was developed and beta tested. This Internet-based program helps patients manage their diabetes and provides primary care physicians with evidence-based treatment recommendations for individual patients. Patients can enter their blood sugar and blood pressure numbers at any time and receive online clinical assessments and advice on next steps. "Both eCare programs significantly advance our patients' abilities to manage their conditions and to communicate quickly and easily with clinicians," says collaborator Robin Dea, MD, Kaiser Permanente Northern California regional director, mental health services.

"When you know about medications and lab results, and know it for thousands of people, you have the ability to direct organizational attention to those patients who can benefit the most."

## IMPROVING DIET AND PHYSICAL ACTIVITY THROUGH E-MAIL

Similarly, the ALIVE (A Lifestyle Intervention Via E-mail) program, led by Barbara Sternfeld, PhD, seeks to promote physical activity and healthy eating using e-mail and a Web-based tool. Developed in the fall of 2006, the yearlong ALIVE program was offered to KPNC regional employees and included a randomized controlled study in which half of the group received 12 individually tailored e-mail messages about healthy food and lifestyle choices. The intervention group had a personal Web page and was measured on physical activity and dietary changes.

"The results were very positive. We saw improvements in all measures," says Sternfeld, noting that publication is pending. Overall, she says, compared to the control group, employees in the intervention group increased on all measures of physical activity, while showing a drop in sedentary behavior. Furthermore, the intervention group ate less saturated fats and transfats and more fruit and vegetables. "We saw the greatest improvement in those who needed to improve the most," says Sternfeld. The program, she adds, has the potential to work well in the work setting because it is offered via e-mail and encourages social support. "The greatest thing about this is that it's very cost effective and can be widely disseminated."



Julie Schmittdiel, PhD

## MANAGING CARE FOR LARGE POPULATIONS

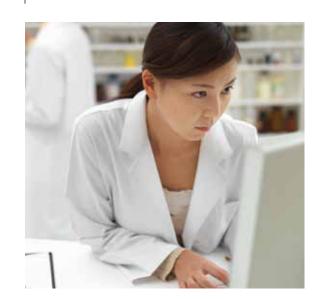
One of the obvious benefits of an advanced information technology system is the clinical data it generates. Yet, having the data in raw form doesn't mean it always gets to the clinician in a way that is useful. "We have huge databases but the question for me is how can we arrange these vast quantities of information in ways that are helpful to the people who use it," says Julie Schmittdiel, PhD. Schmittdiel and Selby are working to change this through the INFO (Intensification and Feedback of Outcomes) trial, which aims to leverage pharmacy and electronic health record data to improve care for patients with cardiovascular disease.

"We are well positioned to publish our findings because they are based on large numbers of patients, with bigh-quality data."

INFO, a two-year cluster-randomized trial, begun in 2007 and funded by AHRQ, is conducted in collaboration with Kaiser Permanente's Quality and Operations Support (QOS) Department. INFO generates new information and adds it to Kaiser Permanente's Panel Management Tool (PMT), a database for patients at high risk of cardiovascular disease. These 300,000 Kaiser Permanente patients are part of the PHASE program (Preventing Heart Attacks and Strokes Everyday).

The INFO study processes pharmacy data to calculate medication adherence and identifies patients who are adherent to their medications but need the doses to be modified. INFO research staff place this new information in the PMT and work with staff in intervention facilities to make it useful, notes Schmittdiel. "The INFO study will evaluate whether providing this new information enables PHASE teams in facilities to help more people reduce risk factor levels in the population." While the study has another year to go, Schmittdiel says if results are positive, the goal will be to offer these tools to all KPNC facilities.

Over the next several years as Kaiser Permanente continues to hone its technology capabilities, the DOR hopes to participate further with operational and clinical leadership in this rich research area. "When you know things such as a person's medications and lab results, and know it for thousands of people, you have the ability to direct organizational attention to those patients who can benefit the most," says Selby. "At the same time, we are well positioned to publish our findings because they are based on large numbers of patients, with high-quality data."



### THE ULTIMATE RESEARCH DATABASE



Inspired by the medical information system developed by Morris F. Collen, MD, in the late 1960s, Joseph F. Terdiman, MD, PhD, director of information technology, has

had a vision of creating a

research database that would provide "one-stop shopping" for researchers.



Terdiman, who joined the DOR in 1969, is finally seeing his dream turn into reality. With the help

director emeritus



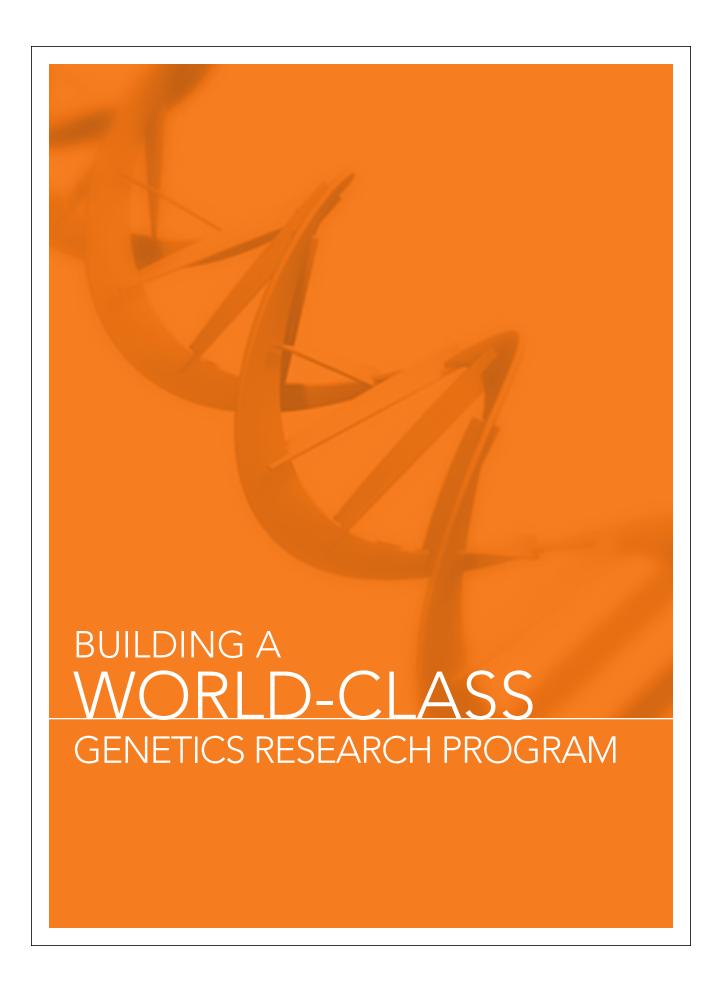
of Collen and two other computer programmers, Terdiman is working to merge all Kaiser Permanente Northern California clinical data from the past 40 years into a single data warehouse. This means moving everything from medical data collected on an electronic Joseph F. Terdiman, MD, PhD punch card system developed by Collen in the

1960s to information that now resides on KP HealthConnect into an Oracle database.

The project started in 2005 and involves 13 million current and past medical records. "The data is scattered and the process is complicated, but in the end it will bring tremendous value to analysts and researchers for decades to come," says Terdiman.

Once the research database is fully up and running in 2009, researchers will be able to deploy data mining techniques in a multitude of areas, says Terdiman. "A big focus will be to mine the data for adverse drug reactions."





With new funding and a growing biorepository, the Research Program on Genes, Environment and Health (RPGEH) is developing into an important resource to study the genetic and environmental causes of common diseases, such as heart disease, cancer, diabetes, high blood pressure, Alzheimer's disease, asthma, and many others. The research program is already supporting new research projects.

In the spring of 2007, RPGEH researchers began a survey of Kaiser Permanente members in Northern California. This health survey, completed by nearly 400,000 members, was a critical benchmark in establishing the program, because it provided important information about the background, lifestyle, and health behaviors of members.

In 2008, RPGEH researchers began re-contacting the 400,000 survey volunteers to collect saliva samples to obtain DNA for genetic analyses. By reaching out to various groups of Kaiser Permanente members, including participants in other large cohort studies, the RPGEH hopes to build the largest and most diverse population-based biobank in the United States.

The RPGEH ultimately plans to collect samples of saliva or blood from 500,000 members. In March 2009, nearly 70,000 saliva samples had already been collected.

The RPGEH was initially funded by grants from the Wayne and Gladys Valley Foundation and the Ellison Medical Foundation. Kaiser Permanente's Community Benefit Program has also provided important financial support for the program during the first several years. In December 2008, the RPGEH received an \$8.5 million grant from the Robert Wood Johnson Foundation Pioneer Program to support development of the biorepository through the collection of genetic samples. The grant will also support the continued development of the program's infrastructure and readiness to function as a resource for research projects on many common diseases.



## AN ENVIRONMENTAL DATABASE LIKE NO OTHER

RPGEH's infrastructure includes an environmental database that will hold a comprehensive array of data on the social and physical environment. "From the very beginning we have known that environment plays a very important role in common diseases. Genes are only part of the picture," says RPGEH Executive Director Catherine Schaefer, PhD.

Research carried out by the RPGEH will link environmental data to the neighborhoods where Kaiser Permanente members live. These maps of environmental data will allow researchers to measure the exposure of members to environmental factors and determine whether such exposures might be related to different health conditions. To accomplish this, Senior Investigator Stephen K. Van Den Eeden, PhD, is heading an ambitious effort to collate data from various sources, including the RPGEH survey and California public databases. "When this is complete, we will have some of the most comprehensive environmental databases available," says Van Den Eeden. "Nobody else can bring these things fully together like Kaiser Permanente, partly because we are a very large integrated health system."



Sarah Rowell, MPH; Catherine Schaefer, PhD; Stephen K. Van Den Eeden, PhD; and Lisa A. Croen, PhD

The environmental database will include data on air pollution, water quality, pesticide use, and Superfund sites. "We have an advantage in California because it has some of the richest databases," adds Van Den Eeden. Additionally, data is being gathered on Bay Area neighborhood characteristics, such as a community's proximity to parks, grocery stores, and healthy foods. Other individual health-related data such as weight, prescription drug use, physical activity, and smoking habits will be collected as the project moves forward. The RPGEH is also collaborating with researchers at the University of California, San Francisco (UCSF) and the University of California, Berkeley, which have expertise in mapping environmental data and linking these data to better understand the environmental influences on health.

"We want to create a biorepository resource that is unique in terms of its size and composition and its ability to link large numbers of people with any type of disease or exposure," adds Croen. Over time, RPGEH researchers hope to collaborate with Kaiser Permanente's Regional Laboratory, which processes about 30,000 blood samples a day.

## NEW BIOREPOSITORY AN EARLY SUCCESS

The RPGEH biorepository includes saliva samples from survey participants, and in the future will also include blood specimens. "Those specimens will allow us to do genetic research into the causes and outcomes of disease and will also allow us to look at things like drug reactions," says research scientist Lisa A. Croen, PhD, who heads up the biorepository effort. Eventually each participant's DNA sample will be combined with their individual health data and lifestyle information from the survey.

The nearly 70,000 saliva samples collected thus far already exceed numbers at established national biobanks. Schaefer notes that member information, whether it is from the survey, medical record, or DNA sample, is always obtained with the person's informed consent, and the privacy and security of data are carefully protected.



The program will move beyond basic science and the discovery stage to perform research that looks at how to translate findings to the bedside.



#### PROSTATE CANCER RESEARCH FOCUSED ON AFRICAN-AMERICAN MEN

One of the first studies through the RPGEH is a genome-wide association (GWA)\* study, led by Van Den Eeden and researchers from UCSF. The study, begun in early 2009 and funded by the National Cancer Institute, examines the genetic factors and risk of new prostate cancer in African-American men in Northern California. The study is designed to look across the human genome to understand the genetic influences on this disease. The study includes 1,500 African-American men and 1,500 controls, all Kaiser Permanente Northern California members.

## SUPPORT AND GUIDANCE FROM KAISER PERMANENTE LEADERSHIP

A governance group that includes leadership from The Permanente Medical Group (TPMG) and Kaiser Foundation Health Plan at both the regional and national levels helps to guide the RPGEH and provide institutional support.

The RPGEH Scientific Advisory Panel includes worldwide experts. To ensure that the program continues to meet the needs of the community, the RPGEH meets quarterly with a 30-member Community Advisory Panel, led by Elize Brown, DrPH, JD, director of community research collaborations and acting administrative director at the DOR. The panel is representative of the racial, ethnic, and geographic diversity that comprises the Bay Area.

"Kaiser Permanente is an excellent place to do pharmacogenetic studies because of our high-quality, long-term prescription and clinical data."

#### **BRIGHT OUTLOOK**

The next two years call for many exciting changes. Program leaders are currently



Mary Henderson, MPH, MBA

planning to build permanent space for the program's biorepository, while also focusing on developing a more robust administrative structure. In 2008, Mary Henderson, MPH, MBA, joined the team as managing

director. With 21 years of experience at Kaiser Permanente overseeing large-scale programs, Henderson will be responsible for directing nonscientific aspects of the program. In addition to Henderson, Larry Walter has joined the program as the associate director for IT and informatics, and Sarah Rowell, MPH, is the new associate director of research operations.

Schaefer says that as the infrastructure is built, the RPGEH will seek to do research in a number of areas, including pharmacogenetic studies. "Kaiser Permanente is an excellent place to do pharmacogenetic studies because of our high-quality, long-term prescription and clinical data," she says. There is much work ahead to make such discoveries available to members and the community at large, says Schaefer, adding that the program will move beyond basic science and the discovery stage to perform research that looks at how to translate findings to the bedside. "It is ambitious, but it separates us from some of the other biobank research programs focused primarily on the discovery phase of research."

## FEATURED STUDY RPGEH STUDY ON BIPOLAR DISORDER

#### Multiethnic Genome-Wide Association Study of Bipolar Disorder

Principal Investigator.
Catherine Schaefer, PhD
Executive Director, RPGEH

Funding: \$12.7 million over five years from the National Institute of Mental Health Conducted in collaboration with the UCSF Institute for Human Genetics, this study will involve 6,000 Northern California members with bipolar disorder and a matched control group of 6,000 members who don't have bipolar disorder. "This genome-wide association study is one of the new variety of studies enabled by a new genetic technology that allows researchers to look across the entire genome to try to find new genes associated with bipolar disorder," says Schaefer. "This will be the largest study in the world done so far on bipolar disorder."

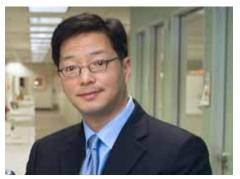
<sup>\*</sup>A genome-wide association study is an approach that involves rapidly scanning markers across the complete sets of DNA, or genomes, of many people to find genetic variations associated with a particular disease. Courtesy: National Human Genome Research Institute.



## GROWING RESEARCH PROGRAM ATTRACTS POLICYMAKERS WORLDWIDE

Before Medicare Part D passed in 2003, a doughnut hole was only fried dough. Today it is also a metaphor for a complex coverage gap in prescription drug benefits for seniors, something that is of increasing interest to the health policy research team at the Division of Research (DOR). John Hsu, MD, MBA, MSCE, for one, wants to understand the impact this gap has on the health of seniors and their interactions with the health care system. Hsu, a physician and health policy research scientist, serves as director of the new Kaiser Permanente Center for Health Policy Studies at the DOR.

The center, launched in 2008, shares its findings on Medicare Part D and other health policy and health services research both internally and with policy makers worldwide. "The center was created to capture the ongoing policy discussions at the international, national, state, and organizational levels that look at how we pay for health care, and how we structure and get better value out of the delivery of care," says Hsu. "There is very little empirical evidence that supports policy decisions and Kaiser Permanente is one of the few places that can do this kind of research."



John Hsu, MD, MBA, MSCE

Hsu notes that Kaiser Permanente is an excellent environment to study health policy challenges because of its large population, excellent data, and long history of innovation with respect to health care delivery and financing. "The question health policy researchers are constantly trying to answer is how does one improve the value of care, including gathering better information and using it to insure that the right things happen to the right people at the right time."

Over the last decade, health policy and health services research at the DOR has examined issues around the financing of health care, including the impact of Medicare and cost-deductible insurance on patients, and has taken a close look at Medicare risk adjusting and physician pay-for-performance.

"The question health policy researchers are constantly trying to answer is how does one improve the value of care."

DOR researchers have also produced many studies evaluating the effectiveness and cost effectiveness of health services, including chronic disease management and alcohol and drug treatment programs. By virtue of its size, integration and data systems, Kaiser Permanente is typically among the first to launch innovative new approaches to health care delivery.

By providing information on what works and how well it works, DOR researchers help policymakers and other health systems understand and incorporate the costeffective elements into services elsewhere.

## SOLVING HEALTH POLICY CHALLENGES

Medicare reform, a centerpiece of national politics in recent years, has provided researchers numerous issues for exploration. Hsu has conducted several studies evaluating Medicare policy and changes in patient cost sharing. "The Kaiser Permanente experience provides a window on what may be happening nationally. We have been particularly interested in the thoughts and behaviors of Medicare beneficiaries as they cope with these changes," says Hsu. In a study published in April 2008, Hsu and other investigators examined knowledge and behavior among 1,040 Kaiser Permanente Northern California Medicare Advantage prescription plan beneficiaries who experienced a gap in their drug coverage.

"We found that people who had less understanding about how their benefits were structured experienced more financial burden compared to those with better knowledge and who were doing things like talking to their physicians about which medications they really needed," says Hsu.

Currently, Hsu is working on a study of how the Medicare Part D coverage gap impacts clinical events and the health of 400,000 Kaiser Permanente members in Northern California. In addition to health care financing, Hsu is also evaluating delivery system issues such as the impact of information technology and care coordination. He and other investigators are conducting a study called **IMPACT** (Information Technology Ramifications for Patients with Chronic Medical Conditions), which examines how clinical care for people with chronic conditions changes over time with the use of information technology such as KP HealthConnect, Kaiser Permanente's electronic health record system.

## HEALTH SERVICES RESEARCH LEADS TO EXCITING FINDINGS

Researchers know that drug and alcohol dependency cuts a wide path through a chemically dependent person's family. New research from the DOR Drug and Alcohol Research Team (DART) is pinpointing how. The DART study, which looked at the health care costs associated with people who received treatment for chemical addiction, found that family members have higher costs of health care and utilization and are more likely to be diagnosed with a medical or psychiatric condition than those who did not have a family member with alcohol or drug problems.

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Constance M. Weisner, DrPH, MSW, and Stacy A. Sterling, MPH, MSW

"The good news is that when chemical dependency is successfully treated, costs for family members also go down," says Constance M. Weisner, DrPH, MSW, investigator and director of DART.

Over the years, DART researchers have published key findings on chemical dependency, including studies showing the benefits of integrating primary care with chemical dependency treatment. Other DART research has found that older women receiving drug and alcohol treatment have particularly good outcomes compared to men. At the same time, adolescents being treated for alcohol and drug problems have better outcomes when they receive even the briefest of psychiatric services at the same time.

From the time DART started in 1993, the program has evolved into one of close collaboration with clinicians in the field, says Weisner. "In fact, many of our research questions have come from them," she says. "These close partnerships have brought depth to our findings and allowed the research to be more quickly translated into the care setting."

The DART team currently has 14 active studies following several large samples of Kaiser Permanente Northern California adult and adolescent members, most of whom are or were in treatment for substance abuse. In one study, a collaboration with the Kaiser Permanente Center for Health Research in Portland, Ore., researchers are studying the adoption of buprenorphine, an alternative to methadone, which can be administered to patients who suffer from an opiate addiction. In collaboration with Group Health of Seattle, the group is studying long-term use of opioids for chronic pain and adverse events, including substance abuse.

DART research scientists are also looking closely at the relationship between health care services and treatment for chemical dependency. The research shows a strong link between chemical dependency, mental health, and medical co-morbidities, says Weisner. This has led to a number of changes, adds Weisner, including earlier identification of chemical dependency problems. "Perhaps the most impactful result of the research is that Kaiser Permanente is moving toward a new model of integration."



Health disparities research seeks to identify, understand, and eliminate differences in health status between groups of individuals defined by racial or ethnic background, socioeconomic position, age, gender, or sexual orientation.

In many ways, Kaiser Permanente, with its highly diverse and representative member population, provides an ideal laboratory for studying the sources of disparities and the potential positive or negative impact of a health care system on disparities. Says Andrew J. Karter, PhD, a senior disparities researcher at the Division of Research (DOR): "At least in theory, all Kaiser Permanente members have uniform access to the same relatively high-quality services. So our research can examine potential reasons for observed health disparities that go beyond access and quality issues." In this way, adds Karter, "research conducted at Kaiser Permanente can complement the large national, population-based studies, which have clearly shown that differences in access to and quality of care are important causes of health disparities."

Current disparities research at the DOR includes studies in the areas of diabetes, cancer treatment, asthma, perinatal medicine, coronary artery disease, hypertension, viral hepatitis, and substance abuse.



Carlos Iribarren, MD, MPH, PhD, and Stephen Sidney, MD, MPH

If access and quality of care are comparable, that leaves a number of other potential explanations for health disparities. These explanations range from differences in social and environmental factors that influence patients' knowledge, beliefs, preferences or self-efficacy, to barriers induced by differential sensitivity to costs, communication barriers between patients and providers or systems of care, cultural differences between providers and patients, and, potentially, discrimination. These factors can cause de facto differences in access to or quality of health care even within systems such as Kaiser Permanente. In the case of gender and racial/ethnic disparities, biological factors such as genetics must also be considered.

As a national organization, Kaiser Permanente has recognized that understanding and eliminating disparities is a key ethical and fiscal responsibility. "There are few places in this country where you find a large health care system so closely partnered with a large research group toward the common goal of reducing health care disparities," says Alyce S. Adams, PhD, a new investigator at the DOR who is focusing on disparities research. Adams also works closely with Kaiser Permanente's Community Benefit Program in shaping the organization's approach to health disparities.

DOR researchers study disparities from a range of perspectives. Often, though not always, they observe a reduction in disparities at Kaiser Permanente relative to the general population. This may suggest that having health insurance enhances access and the quality of health care, which in turn reduces disparities. In many areas of study, Kaiser Permanente researchers find that there are no disparities in the processes of health care, such as rates of mammography or hemoglobin A1c testing. However, some differences in outcomes remain. It is these persisting differences that draw the attention of researchers.



Alyce S. Adams, PhD, and Elize Brown, DrPH, JD

Current disparities research at the DOR includes studies in the areas of diabetes, cancer treatment, asthma, perinatal medicine, coronary artery disease, hypertension, viral hepatitis, and substance abuse. Below are a few examples of compelling findings.

In studying racial and ethnic differences in coronary artery disease, research scientists Carlos Iribarren, MD, MPH, PhD, and Stephen Sidney, MD, MPH, discovered that societal factors, such as lower socioeconomic status rather than race and ethnicity, appeared to explain differences in certain health risks such as recurrence of acute coronary syndrome. Meanwhile, TRIAD (Translating Research into Action for Diabetes), a study led by Joe V. Selby, MD, MPH, director of the DOR, surveyed nearly 12,000 patients with diabetes from 10 managed care plans.

"The more you partner with diverse groups, the more you learn to identify disparities and understand how they affect people's lives."

In that study, both minority race/ethnicity status and lower educational level made independent contributions of comparable size to differences in cardiovascular risk factor control. Moreover, a host of possible explanatory factors, including communication with and trust in providers, depression, concerns about the costs of medications, and level of physical activity were also related to risk factor control, but they did not appear to explain either the racial/ethnic or socioeconomic differences.

The Diabetes Study of Northern California (DISTANCE) is an ongoing study led by Karter and funded by the National Institute of Diabetes and Digestive and Kidney Diseases that has gathered survey and electronic data from 20,000 Kaiser Permanente Northern California members with diabetes. DISTANCE is a collaborative study that also involves researchers from several academic centers. It focuses on the role of education and race as two key social indicators in health outcomes. DISTANCE researchers will also study the relationships of neighborhood factors, health literacy, and medication adherence to disparities in diabetes control and complications.



"Thus far, our research shows a pretty steep gradient of worse outcomes associated with lower levels of education, regardless of the complication," says Karter. "But the picture is much less consistent for race and ethnicity. For several major outcomes in diabetes, white patients are at greater risk than any minority population, but for others, particularly renal disease, nonwhite members have higher rates of disease." This complex pattern raises the possibility of biological differences in susceptibility to various complications. The DOR's Research Program on Genes, Environment and Health (RPGEH) (pg. 32) provides a platform for studying biologic as well as environmental and social causes of a broad range of health conditions and, potentially, for understanding observed disparities in those conditions.

Pain management in diabetes is another area in which DOR researchers are focused. Adams, whose previous research has examined disparities in diabetes, will be focusing on disparities in management of pain for patients with diabetes and other chronic pain syndromes. "I hope to find out whether there are differences in how patients report pain, in how that pain affects their lives, and in their patterns for accessing health care services and seeking treatment," she says. "It's not just looking at the health system but also the patient perspective to understand where the disparities come from. A person's culture may influence how patients describe their pain or their treatment preferences. I will be looking at whether there are disparities in Kaiser Permanente as there have been identified in other settings."

#### **ENGAGING THE COMMUNITY**

The DOR's disparities research is strengthened through growing partnerships with communities to translate research evidence, define barriers to improved outcomes, and develop ideas for effective, sustainable interventions within the community and the health care setting. "The more you partner with diverse groups, the more you learn to identify disparities and understand how they affect people's lives," says Elize Brown, DrPH, JD, director of community research collaborations and acting administrative director at the DOR.



Brown led the formation of a 30-member Community Advisory Panel (CAP) for the RPGEH. Over the past two years, the CAP has met quarterly to provide advice on ethical, legal, and social implications arising from the RPGEH enterprise. "It has been really good to have a broad range of views and experiences around the CAP table. It keeps us humble and accountable and shows us that people beyond our walls do care about the work we do. The CAP also helps build alliances with other organizations in the community."

## FEATURED STUDIES IN DISPARITIES AT THE DIVISION OF RESEARCH

#### Lesbian, Gay, Bisexual and Transgender Tobacco Use

Principal Investigator: Elisabeth Gruskin, DrPH This project compares the tobacco use, cessation and secondhand smoke of a lesbian, gay, bisexual and transgender population in California to that of the general population.

#### Coronary Artery Risk Development in Young Adults (CARDIA)

Principal Investigator: Stephen Sidney, MD, MPH This study describes the distribution of coronary heart disease risk factors in a biracial cohort of men and women and their relationship to the development of subclinical and clinical heart disease.

### Ethnic Disparities in Perinatal Outcomes

Principal Investigator: Gabriel J. Escobar, MD This study aims to delineate the elements of communication, expectations, values, and interpersonal relationships that characterize the delivery, use, and outcomes of health care services for patients of different race/ethnicity.

### Prospective Study of Breast Cancer Survivorship

Principal Investigator.
Lawrence Kushi. ScD

This prospective cohort study is examining how lifestyle, clinical, and molecular factors are associated with breast cancer recurrence and survival in a diverse population. This study will eventually establish one of the largest prospective cohort studies of women with breast cancer.

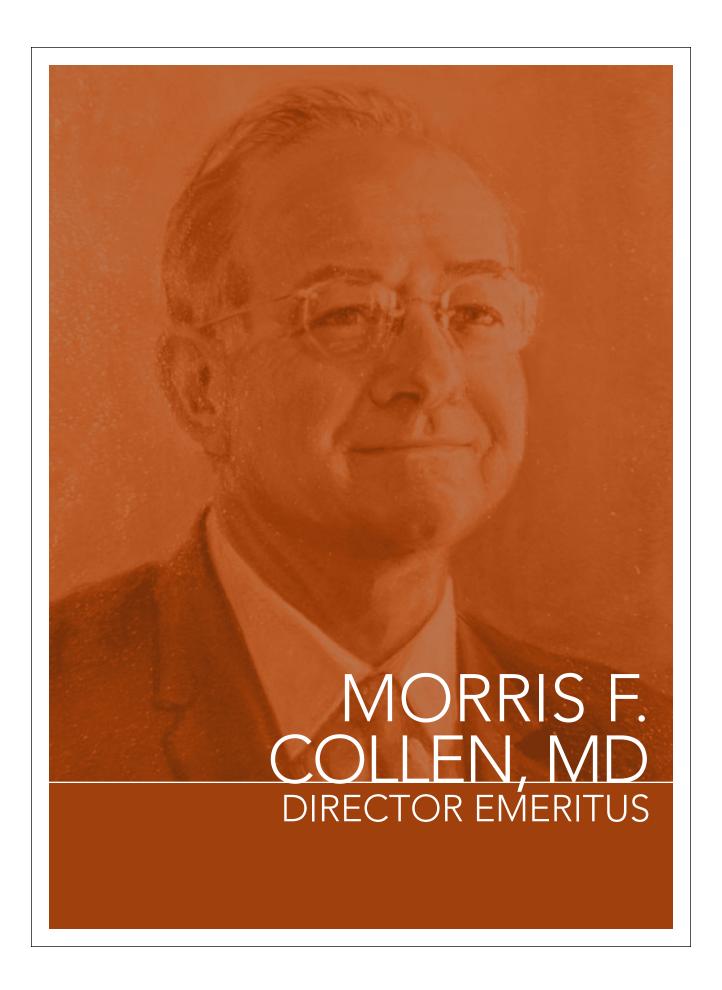
### The Kaiser Permanente Viral Hepatitis Registry

Principal Investigator:
M. Michele Manos, PhD, MPH, DVM

The Viral Hepatitis Registry work includes identification of, and electronic medical record data collection from, retrospective cohorts of chronic viral hepatitis cases. The Registry monitors trends in incidence and quality of care. Data are also used to update standards of care.

#### Identifying Sources of Disparities in Behavioral Health Risks and Health Status in the Adult Health Plan Membership

Principal Investigator: Nancy Gordon, ScD Using data from the Kaiser Permanente Northern California adult member health surveys, this study explores differences in behavioral health risks, chronic health conditions, and health service use associated with race/ethnicity, education, age, and gender.



#### SIXTY-SIX YEARS AS PHYSICIAN, RESEARCHER, AND MEDICAL INFORMATICS PIONEER—AND STILL GOING STRONG

From his time as a young doctor administering to Henry J. Kaiser's shipyard workers in Richmond, Calif., in 1942, to his present day work in research and medical informatics, Morris F. Collen, MD, has made many important contributions to Kaiser Permanente's Division of Research (DOR), to the field of medical informatics, and to the public's health. As founding director of the Department of Medical Methods Research, today's DOR, Collen grew the fledgling research operation, which opened in 1961, into a research institution renowned today as a trailblazer in drug safety, risk factor epidemiology, health services, and genetics research, among other areas.



Morris F. Collen, MD, with open binder, explains potential uses of the computer in medical care to a visiting delegation from Washington, D.C. in 1966.

In November 2008, Collen celebrated nearly 47 years with the DOR. A physician and electrical engineer by training, Collen says his greatest influence was his friend, mentor, and colleague Sidney R. Garfield, MD, founding physician of Kaiser Permanente. "Dr. Garfield had great vision. He wanted Kaiser Permanente to not only provide good, high-quality care that members could afford, but he also said research, education and training were important," recalls Collen. "He told me 'we need to use computers to help physicians give better care to our patients.' In the 1940s, he asked me to start a resident training program and in 1961 the Department of Medical Methods Research." One of the primary goals of the research program, says Collen, was to conduct research focused on the application of computer technology in the clinical care setting.

Kaiser Permanente's early electronic health record system became internationally known because of Collen.



"If there is such a thing as reincarnation, I am going to come back and be a Kaiser Permanente doctor."

During the 1950s, with a postwar shortage of physicians, one of Collen's first major achievements was the development of the multiphasic health checkup, a series of procedures and tests given to thousands of Kaiser Permanente members that screened for conditions such as heart disease, diabetes, and cancer. The tests were revolutionary in that they not only saved physicians' time but also constituted a significant experiment in preventive care. Collen eventually automated the multiphasic health checkups, moving them onto a punch card system in 1964. An early computer-based patient record and database followed using the multiphasic health checkup records. From this first computerized database, large-scale population research was born at the DOR.

Under Collen's leadership, Kaiser Permanente became one of a handful of places in the world to start this pioneering work in medical informatics. Over the next 40 years, the multiphasic database alone provided material for more than 500 papers published in more than 75 medical journals.

Kaiser Permanente's early electronic health record system became internationally known because of Collen, who predicted the computer would probably have "the greatest technological impact on medical science since the invention of the microscope." Collen has written five books on medical informatics and was honored by the American College of Medical Informatics (ACMI) in 1993 with the highest honor it bestows, the Morris F. Collen, MD Medal for Outstanding Contributions to the Field of Medical Informatics.



Rudolf Christofferson, at left, becomes the 1,000th longshoreman to go through an automated multiphasic examination in 1961.

"I keep saying to all the young people, you just have to live long enough and you will see wonderful things happen."

Although semiretired, Collen, age 95, continues his work today. He is currently working with his longtime colleague Joe Terdiman, MD, PhD, director of information technology, to create a national research database that will merge 13 million Kaiser Permanente Northern California electronic health records, going back to Collen's multiphasic health checkups, into one database. Once complete, Collen is particularly interested in the potential to detect adverse events associated with the use of multiple drugs in the elderly.





"You can do so much now with pharmacy data. Currently, there is not an adequate early warning system. But the beauty of our program is that we have access to all the data from our electronic health record and our pharmacy systems," notes Collen.

"I keep saying to all the young people, you just have to live long enough and you will see wonderful things happen. I just don't want to let it go because it is so exciting," he says. Reflecting on nearly seven decades of service to Kaiser Permanente members, Collen sums it up as this: "I have traveled the world and seen health care programs in Europe, Asia, and elsewhere, and if there is such a thing as reincarnation, I am going to come back and be a Kaiser Permanente doctor."

#### 2008 DIVISION OF RESEARCH

# SCIENTISTS & ADJUNCT SCIENTISTS

#### RESEARCH SCIENTISTS

Annette E. Aalborg, DrPH Lynn M. Ackerson, PhD Alyce S. Adams, PhD Ameena T. Ahmed, MD, MPH Mary Anne Armstrong, MA Maryam M. Asgari, MD, MPH Andrew L. Avins, MD, MPH Bette J. Caan, DrPH Cynthia Campbell, PhD, MPH Douglas A. Corley, MD, MPH, PhD Lisa A. Croen, PhD Gerald N. DeLorenze, PhD Gabriel J. Escobar, MD Assiamira Ferrara, MD, PhD Bruce H. Fireman, MA Vicki Fung, PhD Alan S. Go, MD Nancy P. Gordon, ScD Elisabeth P. Gruskin, DrPH Erica P. Gunderson, PhD Laurel A. Habel, PhD Monique M. Hedderson, PhD Lisa J. Herrinton, PhD Michael A. Horberg, MD, MAS John T. Hsu, MD, MBA, MSCE Enid M. Hunkeler, MA Carlos Iribarren, MD, MPH, PhD Andrew J. Karter, PhD Nicola P. Klein, MD, PhD Ai Kubo, PhD, MPH Lawrence H. Kushi, ScD Marilyn L. Kwan, PhD Theodore R. Levin, MD De-Kun Li, MD, MPH, PhD Joan C. Lo, MD M. Michele Manos, PhD, MPH, DVM Jennifer Mertens, PhD Nina Oestreicher, PhD Charles P. Quesenberry, Jr., PhD Mary E. Reed, DrPH, MPH Catherine Schaefer, PhD

Julie Schmittdiel, PhD
Joe V. Selby, MD, MPH
(DOR director)
Stephen Sidney, MD, MPH
Michael J. Silverberg, MPH, PhD
Carol P. Somkin, PhD
Barbara Sternfeld, PhD
Joseph F. Terdiman, MD, PhD
Stephen K. Van Den Eeden, PhD
Constance M. Weisner, DrPH, MSW
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