2015 Director’s Letter

Research: A pillar of a great health care organization

The idea that research is integral to a learning health care system has become au courant, but it’s far from revolutionary. Two of Kaiser Permanente’s founders, Sidney Garfield and Morrie Collen, considered research, clinical care, and teaching the three pillars of a great health care organization. Today, Kaiser Permanente is internationally respected for research that transforms health by discovering the key drivers of health and disease, and identifying effective and efficient ways to deliver health care.

In 2015, the Division of Research continued to grow as a national leader in epidemiology, clinical effectiveness research, and delivery science — which identifies the best ways to deliver health care to people in real life. We draw on rich resources in both colleagues and data. We have a growing community of physician-researchers throughout Northern California, and vast electronic records that we have made usable for clinical operations as well as research via our Virtual Data Warehouse.

One example of the power of our partnerships and our data was the collaboration between physicians at the Kaiser Permanente San Francisco Medical Center and investigators in our Division. Last fall, this team published the first evaluation of pre-exposure prophylaxis to prevent HIV infection in a clinical practice setting. Their findings — no new HIV infections among patients during more than two years of observation — drew global attention to a promising tool for HIV prevention.

We also expanded our leadership on prominent national projects with the receipt of a funding award from the National Institute on Drug Abuse for a new Addiction Research Network that integrates addiction treatment into medical settings in order to improve patient outcomes. And the National Cancer Institute substantially increased funding for Kaiser Permanente’s NCI Community Oncology Research Program for the next four years due to our success in high enrollment in cancer clinical trials across all regions.

Last year, Kaiser Permanente celebrated its 70th anniversary and the fact that we have grown to more than 10 million members nationwide. Our Division is very fortunate to be embedded in a vigorous and expanding organization that inspires our social mission to produce knowledge about health and health care that benefits society as well as our own members.

Warm regards,

[Signature]
2015 Research Highlights

Behavioral Health and Aging

**Oral steroids for acute sciatica:** For many years, physicians have given patients short courses of oral steroids to treat acute sciatica under the assumption that they are highly effective. We now know that may not be true. A study led by Harley Goldberg, DO, and Andrew Avins, MD, MPH, demonstrated that the treatment resulted in only modest improvement in function and no significant improvement in pain, and that most patients will do just as well with a placebo.

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**Screening for adolescent substance use:** Substance use is associated with the leading causes of death among adolescents and often is related to mental health and other medical problems. In the first trial to compare different approaches to delivering substance use and mental health screening in primary care for adolescents, Stacy Sterling, PhD, and Connie Weisner, DrPH, showed that training for physicians and embedding behavioral health clinicians produced better results than usual care.

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**Powering precision medicine for age-related diseases:** By volunteering to mail saliva samples to the Research Program in Genes, Environment and Health, thousands of Kaiser Permanente members have helped build one of the nation's most powerful medical research tools. In 2015, researchers published papers on the genetic ancestry and telomere lengths of a cohort of more than 100,000 volunteers, and described the innovative methods that allowed them to complete DNA analysis within 14 months.

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**Integrating addiction treatment into clinical care:** The National Institute on Drug Abuse has awarded Cynthia Campbell, PhD, and Connie Weisner, DrPH, funding for a new Addiction Research Network that includes 15 health care systems across the country. The network's focus is to conduct research that integrates addiction treatment into medical settings in order to improve patient outcomes. Prescription opioid use, marijuana use, and co-occurring health conditions are among the high-priority areas.

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**Identifying genetic susceptibility for hernia:** In the first large-scale genetic study of hernia risk in adults, led by Eric Jorgenson, PhD, researchers have identified genetic variations associated with inguinal hernia. Surgical repair of inguinal hernias is one of the most commonly performed operations in the world, yet little is known about the genetic mechanisms that predispose individuals to develop them.

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Biostatistics

Research consultations: Under the direction of Mary Anne Armstrong, MA, in 2015 the Biostatistical Consulting Unit provided support for 189 resident and fellow research projects, 33 miscellaneous funded projects, and 10 miscellaneous unfunded consultations (via funding from the Comprehensive Clinical Research Unit); and helped clinical partners develop 56 Community Benefit grant proposals. The unit also provided intensive consultations on 19 Community Benefit projects that were funded in 2015. Throughout the year, unit staff contributed to 16 publications and 38 conference presentations for their clients.

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Cancer

Breastfeeding and breast cancer recurrence: Women diagnosed with breast cancer who previously breastfed their babies had a 30 percent overall decreased risk of the disease recurring, according to new research by Marilyn L. Kwan, PhD, Bette J. Caan, DrPH, and colleagues in the Journal of the National Cancer Institute. Researchers also found that the protective effect of breastfeeding was more pronounced for tumors of particular genetic subtypes, including the most commonly diagnosed breast cancers.

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Evidence-based care in clinical practice: Kaiser Permanente and the Cancer Research Network, led by Lawrence H. Kushi, ScD, hosted the most recent Training Institute for Dissemination and Implementation Research in Health, which brought together over 40 attendees and more than 30 faculty and presenters in Pasadena, California to talk about designing research aimed at improving health and preventing disease in clinical and public health settings. This was the first time that training has been held outside of a university setting.

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Chronic pancreatitis, diabetes, and pancreatic cancer: Kaiser Permanente is one of ten clinical sites participating in a National Institute of Diabetes and Digestive and Kidney Diseases/National Cancer Institute consortium that seeks to better understand relationships between chronic pancreatitis, diabetes and pancreatic cancer. The five-year study, led by Stephen K. Van Den Eeden, PhD, will develop algorithms to identify, recruit, and follow a cohort of 600 individuals with chronic pancreatitis and/or diabetes who are at high risk of developing pancreatic cancer, and conduct pilot genetic studies of chronic pancreatitis.

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Risk prediction model for lung cancer: Screening with low-dose computed tomography (LDCT) presents an opportunity to improve early detection and reduce mortality from lung cancer. However, the potential harms of LDCT screening, including frequent false-positive findings that lead to unnecessary procedures and repeated radiation exposure, have raised concerns. This five-year study, led by Lori Sakoda, PhD, and funded by the National Cancer Institute, seeks to evaluate whether the most predictive and clinically oriented risk model for lung cancer to date can be validated, extended, and applied to aid decision-making about LDCT screening.

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Social networks, breast cancer treatment, and survival: Research has shown that social networks — the web of social relationships that surround an individual — have a major role in breast cancer survival. The goal of this five-year study, funded by the National Cancer Institute and led by Candyce Kroenke, ScD, MPH, is to evaluate the influence of social networks on breast cancer treatment and survival, to better understand the potential for leveraging social relationships in breast cancer patients to improve outcomes. Results will be used to identify patients with compromised social networks and develop individual and system-level interventions to optimize treatment and improve prognosis.

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Adenoma detection rates and colorectal cancer: Douglas Corley, MD, PhD, led a team that evaluated the association between physician adenoma detection rate and colorectal cancer, the second leading cause of cancer death. In the team’s study published in the New England Journal of Medicine, patients of physicians with higher adenoma detection rates were at lower risk of developing future colorectal cancers. The work and his many other research accomplishments earned Dr. Corley The Permanente Medical Group’s prestigious Morris F. Collen Research Award.

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Cardiovascular and Metabolic Conditions

Heart attacks, bleeding after stent and mortality: In patients who received a stent to treat coronary artery blockage, those who experienced bleeding requiring hospitalization in the years after the procedure faced an increased risk of death that was similar to the risk faced by those who subsequently had heart attacks, according to a study of nearly 33,000 patients by Alan Go, MD and colleagues at the University of California, San Francisco.
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Breastfeeding, diabetes and gestational diabetes: The Study of Women, Infant Feeding and Type 2 Diabetes after GDM Pregnancy (SWIFT), led by Erica Gunderson, PhD, published its findings that women with gestational diabetes who exclusively or mostly breastfed for at least two months, and those who continued to breastfeed for several months, were half as likely to develop type 2 diabetes within two years after delivery.
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Thirty years of CARDIA: The Coronary Artery Risk Development in Young Adults Study (CARDIA) was highlighted in a San Francisco Chronicle feature story on the occasion of its 30th year. The CARDIA team, led by Stephen Sidney, MD, has followed a diverse cohort since the mid-1980s. CARDIA has had impressive scientific impact, with more than 600 papers, including many seminal studies of cardiac risk and related health care disparities.
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Death after hip fracture declines: In a study of more than 13,000 older women who experienced a hip fracture within Kaiser Permanente Northern California, Joan Lo, MD and colleagues found that the risk of complications and death after hip fracture is high but the risk of death during the 12 months has declined over time, particularly for Asian and Hispanic women.
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Ethnicity-based disparities in blood pressure control on Twitter: Kaiser Permanente Northern California, the Division of Research and the American Heart Association convened #HBPLeaderChat on Twitter during #strokemonth to focus on the particular challenges facing ethnic communities and African Americans in controlling hypertension. Mai N. Nguyen-Huynh, MD was among those identifying issues and answering questions in a robust Twitter discussion.
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Acute kidney injury and high blood pressure: In a study published in the Journal of the American Society of Nephrology, Alan Go, MD and colleagues at the University of California, San Francisco reported that hospitalized patients who experienced acute kidney injury were 22 percent more likely to develop high blood pressure during the two-year follow-up period after discharge than those who had not. The more severe the acute kidney injury, the greater the likelihood of developing high blood pressure.
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Health Care Delivery and Policy

Mail order pharmacy and health care disparities: A new study funded by the National Institute of Diabetes and Digestive and Kidney Diseases will test the effectiveness of strategies to encourage mail order pharmacy use in the Kaiser Permanente population and among groups at risk for disparities in health outcomes. Lead investigator Julie A. Schmitt, PhD, hopes to learn more about whether increased mail order use results in improved adherence to medication, as well as reduction of cardiovascular disease risk factors. Read More

Electronic health records, stroke, and emergency department care: The timely administration of a clot-dissolving treatment for emergency department patients with acute ischemic stroke nearly doubled following the introduction of new technology that enabled electronic order entry and offered care-decision support for physicians, according to a study by Dustin Ballard, MD, and David Vinson, MD, of the Kaiser Permanente CREST Network, published in the Annals of Emergency Medicine. Read More

Patients-doctor email and health care efficiency: A third of patients with chronic conditions who exchanged secure emails with their doctors said that these communications improved their overall health, according to a study by Mary E. Reed, DrPH, and colleagues published in The American Journal of Managed Care. Read More

Delivery Science fellows: The delivery science fellowship program, initiated in 2013, aims to train postdoctoral fellows in research on identifying and implementing best practices for delivering care to diverse populations. Led by Richard Grant, MD, MPH, and Julie A. Schmitt, PhD, the program has attracted nationwide interest. Fellows who joined the Division of Research in 2014 and comprise the first delivery science fellowship graduating class include: Mark Lin, MD, and Yen S. Kim, MD. Fellows who joined the Division of Research in 2015 and will continue through June 2017 include: Cassandra Marshall, DrPH, MPH, and Cyrus K. Yamin, MD. Read More

Diabetes complications vary little by ethnicity: In one of the first studies of its kind, Andrew J. Karter, PhD, and colleagues found that the prevalence of geriatric conditions and diabetic complications among older, insured patients with diabetes did not vary significantly by ethnicity. The study was published in the Journal of Aging and Health. Read More
Funding for PORTAL, new national clinical research network: Led by Elizabeth McGlynn, PhD, and Tracy Lieu, MD, MPH, the Patient Outcomes Research to Advance learning (PORTAL) network has been approved for a three-year, $8.6 million funding award by the Patient-Centered Outcomes Research Institute (PCORI). As one of 34 health data networks that make up this national clinical research resource, PORTAL is studying the effectiveness of different approaches to diagnosis, treatment and management, in order to assist patients, their caregivers, and doctors in making better-informed decisions. Researchers hope to continue doing innovative work with patient groups in weight-related issues, as well as colorectal cancer and congenital heart disease.

Infectious Diseases and Vaccine Study Center

Safety of measles vaccines: A study of two measles-containing vaccines found that adverse outcomes were unlikely after either vaccine. The study, led by Nicola Klein, MD, PhD, included children who received measles-mumps-rubella-varicella (MMRV) or separately administered, same-day measles-mumps-rubella and varicella (MMR + V) vaccines. No new safety concerns were identified and most outcomes studied were uncommon after either vaccine.

Heart attack risk among people with HIV: Previously reported increased risk of heart attacks among HIV-positive individuals has been largely reversed in recent years in Kaiser Permanente’s California patients. A study by Daniel B. Klein, MD and Michael Silverberg, PhD found that the adjusted risk ratio for heart attacks among HIV-positive study participants went from an 80 percent increased risk in 1996 to no increased risk in 2010-2011.

PreP and HIV infections: In one of the first and largest published evaluations of the use of preexposure prophylaxis (PreP) to prevent HIV infection in a clinical practice setting, Julia L. Marcus, PhD, of the Division of Research, and physicians at Kaiser Permanente San Francisco Medical Center found no new HIV infections among patients during more than 2.5 years of observation. The data extends the understanding of the use of PreP to a “real-world,” routine health care setting.

Cancer risk for HIV-infected individuals: A large 14-year study offers a unique way of looking at the risk of cancer among HIV-positive individuals by accounting for the competing risk of death in the era of highly effective antiretroviral therapy. This approach provides estimates of the cumulative incidence of cancer by age 75 years, a measure that has not been reported previously in this population and may have clinical and public health utility since it approximates lifetime risk of cancer.
Women’s and Children’s Health

Undervaccination clusters in Northern California: In research led by Tracy A. Lieu, MD, MPH, investigators identified five statistically significant clusters of under-immunization among children who turned 36 months old during 2010-2012. The study, which appeared in *Pediatrics*, concluded that under-immunization and vaccine refusal cluster geographically and that spatial scan statistics may be a useful tool to identify locations with challenges to achieving high immunization rates.

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Gestational diabetes, weight loss, and exercise after baby: A diabetes prevention program administered within Kaiser Permanente Northern California was effective in helping women with a history of gestational diabetes reach weight loss goals and increase physical activity following the birth of their children. The study, led by Assiamira Ferrara, MD, PhD, was published in the journal *Diabetes Care*.

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New Autism Family Biobank: The Autism Research Program, under the leadership of Lisa Croen PhD, launched a new resource with the goal of collecting information from 5,000 trios — a child with an autism spectrum disorder and both biological parents. This information will be used in the future to look for the causes — as well as new treatments — for autism.

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Pregnancies spacing and autism risk: Second-born children who are conceived sooner than two years or later than six years after the arrival of their older sibling have a substantially increased risk of autism spectrum disorders, according to a new study led by Ousseny Zerbo, PhD and published in the journal *Pediatrics*.

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Social media and women’s health: In an insight extracted from examination of social media forums, Elizabeth Suh-Burgmann, MD, found an association between steroid injections and abnormal bleeding in postmenopausal women. The study was published in the *American Journal of Obstetrics and Gynecology*.

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Bladder cancer and common diabetes medication: The commonly prescribed diabetes medication called pioglitazone (Actos) was not associated with a clear increased risk of bladder cancer and several other cancers, according to a 10-year study published in *JAMA* conducted by Assiamira Ferrara, MD, PhD, and colleagues in the Division of Research, as well as the University of Pennsylvania and Rutgers University. Although there was no increased risk observed for most cancers, ever use of pioglitazone was associated with a 13 percent increased risk of prostate cancer and a 40 percent increased risk of pancreatic cancer.

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2015 Overview

The Division of Research (DOR) is currently home to 55 research scientists and staff scientists, with more than 550 employees. The DOR also works with 26 adjunct investigators from within Kaiser Permanente and from other academic institutions and has worked with more than 270 clinician collaborators from The Permanente Medical Group. DOR scientists are involved in more than 350 research studies. Since its founding in 1961, DOR researchers have published about 3,000 scientific papers, including more than 350 papers in 2015.

2015 Funding Sources Based on Expenditures

- $875 Million Total Annual Expenditures

- 50% Federal
- 13% Industry
- 14% Foundation/Nonprofit
- 10% The Permanente Medical Group
- 5% Community Benefit (Regional)
- 4% Community Benefit (Central Research Committee)
- 3% Community Benefit (National)
- 1% Kaiser Permanente(Other)