

2017 Director's Letter

Transforming Health Care Research Through the Decades



More than 70 years ago, [Morris F. Collen, MD](#), the founder of the Kaiser Permanente Division of Research, published his first peer-reviewed article. It was 1946 and he looked at aspirin's analgesic effects on pain. I think if Dr. Collen were still with us, he'd be gratified at how far Kaiser Permanente research has come. As we look back on 2017 in this year's Annual Report it's worth noting what has—and hasn't—changed in what we do.

Morrie was instrumental in developing the first [Automated Multiphasic Examinations](#) for Kaiser Permanente. In the 1960s when the screening tests first began, we used punch cards and mainframe computers to record patient health data.

Recognizing the importance of those first multiphasic exams, the Smithsonian's National Museum of American History this past year [took ownership](#) of some of those early punch cards to help share an important part of our country's health care history.

Ted Van Brunt, an early director of DOR and supervisor of the multiphasic exams, [passed away](#) in 2017 and unfortunately never had a chance to see that momentous hand-over take place.

In the decades since the multiphasic exams were started, we've advanced to where we are now with bioinformatics, biobanks, and genomics — vast amounts of data to be parsed and understood, nearly at the blink of an eye.

And change doesn't just come in the form of technology. We're also pioneering a new way to leverage Kaiser Permanente research to help clinicians care for our members.

This year we launched the [Physician Researcher Program](#): six clinicians given an opportunity, thanks to support from The Permanente Medical Group, to spend a portion of their time focusing on research. With the help of DOR researchers and staff, these inaugural physician researchers are devoting 20 to 40 percent of their time to research projects that are designed to systematically evaluate clinical care. They are expected to implement what they've found across Kaiser Permanente Northern California.

Part of our job is to adapt and look into the future: Where do we see ourselves when it comes to having a role for our members, physicians, and hospitals?

And regardless of what we see in our crystal ball, what hasn't changed is our goal: to do research that helps Kaiser Permanente become even better at delivering care, and society to understand and foster health.

We'll continue to build on Dr. Collen's vision in clinical informatics, and while it may not be looking at aspirin anymore, what we do next will be even more important.

Warm regards,

A handwritten signature in dark blue ink that reads "Tracy Lieu". The signature is fluid and cursive, with the first name "Tracy" and last name "Lieu" clearly distinguishable.

Tracy A. Lieu, MD, MPH
Director, Division of Research

2017 Research Highlights



Behavioral Health and Aging

Dementia Risk Factors: High blood pressure in mid-adulthood is linked to dementia risk in women, but not in men, according to research published in *Neurology* by Rachel Whitmer, PhD, Paola Gilsanz, ScD, and colleagues. At a July Alzheimer's conference, Whitmer and Gilsanz presented additional research showing that early life adversity and birthplace contribute to racial disparities in dementia rates that persist even among the oldest of the elderly. Another study in *JAMA Neurology* linked being born in the United States. "Stroke Belt" with increased dementia risk in people who eventually lived elsewhere.

[Read more](#)

Marijuana Use During Pregnancy: Data on marijuana use during pregnancy is limited, hampering efforts to identify potential risks. Kelly C. Young-Wolff, PhD, MPH, Nancy Goler, MD, and colleagues addressed this gap using data from almost 300,000 pregnant women treated at Kaiser Permanente Northern California. As reported in the *Journal of the American Medical Association*, they found that maternal prenatal marijuana use increased from 4 to 7 percent from 2009 to 2016. Now that marijuana can be bought legally in California, "it will be important to monitor whether prenatal marijuana use escalates further," Young-Wolff said.

[Read more](#)

Genetics and Glaucoma: Analysis of DNA from nearly 70,000 Kaiser Permanente Northern California patients uncovered 47 specific positions, or loci, in the genome that are associated with variations in pressure inside the eye. The findings, which could help clarify how elevated eye pressure leads to glaucoma, were published in *Nature Communications* by Eric Jorgenson, PhD, Hélène Choquet, PhD, and colleagues. "Knowing which genes are involved, and how, could suggest new avenues for development of novel treatments," said co-author Ronald Melles, MD.

[Read more](#)

Cognitive Health in the Oldest-Old: The oldest-old – people aged 90 and older – are the fastest-growing segment of the elderly population in the United States. The National Institute on Aging has awarded the Division of Research a six-year grant to investigate cognitive health in this population. Led by senior research scientist Rachel Whitmer, PhD, the study aims to determine if in the oldest-old there are ethnoracial differences in the incidence of mild cognitive impairment and dementia, to quantify mid- and late-life risk and protective factors for these conditions, and to understand the burden of cerebral and brain pathologies in this group.

[Read more](#)

Cognitive Health in the Oldest-Old: The oldest-old – people aged 90 and older – are the fastest-growing segment of the elderly population in the United States. The National Institute on Aging has awarded the Division of Research a six-year grant to investigate cognitive health in this population. Led by senior research scientist [Rachel Whitmer, PhD](#), the study aims to determine if in the oldest-old there are ethnoracial differences in the incidence of mild cognitive impairment and dementia, to quantify mid- and late-life risk and protective factors for these conditions, and to understand the burden of cerebral and brain pathologies in this group.

[Read more](#)

Interventions for Alcohol Use, Depression: Short counseling sessions, or “brief interventions,” for unhealthy alcohol use may also help improve blood pressure control in patients with hypertension. Senior author [Stacy Sterling, DrPH, MSW, MPH](#), and Division of Research colleagues published the findings in the *Journal of Substance Abuse Treatment*. Funded by the National Institute of Alcohol Abuse and Alcoholism, Sterling is currently leading [research](#) into the effects of system-wide implementation of screening, brief intervention, and referral to treatment (SBIRT) for alcohol use among adults within Kaiser Permanente Northern California. Sterling is also lead author of a *Journal of Adolescent Health* study showing that referral to behavioral clinicians trained in delivering SBIRT for substance use could benefit adolescents with depression symptoms.

[Read more](#)



Biostatistics Core

Large data set reveals waning effectiveness of shingles vaccine: A [study](#) published in the *American Journal of Epidemiology* by biostatistician [Bruce H. Fireman, MA](#), and colleagues (including posthumous author [Roger Paul Baxter, MD, FACP](#)) analyzed data from nearly 400,000 adults in Kaiser Permanente Northern California who received the live attenuated zoster vaccine between 2007 and 2014. They found that the vaccine was about 68 percent effective initially against shingles, but its effectiveness waned over time. Kaiser Permanente’s large population of members receiving the vaccine at age 65 and older, electronic records for a long follow-up period, and innovative statistical methods yielded precise estimates of the trajectory of waning vaccine effectiveness for 8 years after vaccination.

[Read More](#)

Research Consultations: Under the direction of [Mary Anne Armstrong, MA](#), in 2017 the [Biostatistical Consulting Unit](#) provided support for 166 resident and fellow research projects, 27 miscellaneous funded projects, and 14 miscellaneous unfunded consultations (via funding from the [Clinical Trials Program](#)); and helped clinical partners develop 62 Community Benefit grant proposals. The unit also provided intensive consultations on 24 Community Benefit projects that were funded in 2017. Throughout the year, unit staff contributed to 27 publications and 42 conference presentations for their clients.

[Read More](#)

Statisticians Join Core: Two statisticians have joined the Biostatistics Core. [Catherine Lee, PhD](#), received a PhD in mathematics from University of California, Los Angeles, and a PhD in biostatistics from Harvard University. Lee's current research includes the development of methods for joint risk prediction using semi-competing risks data. [Stacey E. Alexeeff, PhD](#), earned her MSc in Statistics at Carnegie Mellon University and her PhD in biostatistics from Harvard University. Alexeeff's projects include studies of genetic and environmental risk factors for disease, intervention studies, and diagnostic prediction modeling.

[Read More](#)



Cancer

Colonoscopy Urgency: If a fecal immunochemical test (FIT) detects a small amount of blood in a patient's stool, they receive a colonoscopy to find and possibly remove any cancerous or pre-cancerous polyps. A large study led by [Douglas A. Corley, MD, PhD](#), and [Theodore R. Levin, MD](#), found that the risk of colorectal cancer increased significantly when colonoscopy was delayed by more than nine months following a positive fecal screening test. The findings appear in the [Journal of the American Medical Association](#).

[Read More](#)

Breast Cancer Survivorship: Women with more vitamin D in their blood after a breast cancer diagnosis had significantly better long-term outcomes, according to a [JAMA Oncology](#) study that used data from [Pathways](#), an ongoing project led by [Lawrence H. Kushi, ScD](#). A second study led by [Candyce H. Kroenke, ScD, MPH](#), and published in [Cancer](#) showed that invasive breast cancer patients with more social ties had lower risks of recurrence and mortality, providing support for the [peer navigation program](#) at the Kaiser Permanente Oakland Breast Care Center.

[Read More](#)

Understanding Disparities: Urban American-Indian and Alaskan Native patients had lower survival rates than non-Hispanic white patients following a diagnosis of invasive prostate or breast cancer, according to research performed by [Laurel A. Habel, PhD](#), and colleagues. The study, published in *Cancer Research*, helps fill a gap in understanding of the cancer experience for American-Indian and Alaskan Native patients living in urban settings.

[Read More](#)

New Bladder Cancer Study: The [Be-Well Study](#), the largest and most comprehensive study of bladder cancer survivorship, was launched in 2017. By gathering information about diet and lifestyle, [Marilyn L. Kwan, PhD](#), [Lawrence H. Kushi, ScD](#), and colleagues at Kaiser Permanente Southern California and at Roswell Park Cancer Institute in Buffalo, N.Y., aim to find out whether lifestyle choices have any effect on disease recurrence and health after bladder cancer diagnosis.

[Read More](#)

Treating HER2-Low Breast Cancer: Adding trastuzumab (Herceptin) to standard adjuvant chemotherapy can improve outcomes for HER2-positive breast cancer patients. However, in a randomized, phase III [clinical trial](#), this treatment did not improve invasive disease-free survival for patients with early-stage breast cancer who have low HER2 protein levels or few HER2 gene copies. [Louis Fehrenbacher, MD](#), presented these findings at the 2017 [San Antonio Breast Cancer Symposium](#).

[Read More](#)

Molecular Testing for Prostate Cancer: A patient's Genomic Prostate Score relies on molecular testing of 17 genes and can help determine how aggressively his cancer should be treated. New research conducted by [Stephen K. Van Den Eeden, PhD](#), [Joseph Presti, MD](#), and colleagues showed that the Genomic Prostate Score can strongly predict long-term risks of metastasis and death after radical prostatectomy in men with low- and intermediate-risk prostate cancer. The findings, published in *European Urology*, support the use of the score when deciding on a patient's best course of treatment.

[Read More](#)



Cardiovascular and Metabolic Conditions

Stroke Risk in Atrial Fibrillation: Clinical trials show that the drugs warfarin and dabigatran can reduce the risk of ischemic stroke in people with atrial fibrillation. A new study led by [Alan Go, MD](#), director of the [Clinical Trials Program](#) within the Kaiser Permanente Division of Research, has now found that outcomes for typical patients with atrial fibrillation who receive these medications are consistent with clinical trial results, as reported in *Annals of Internal Medicine*. [Read More](#)

Outstanding Work on Heart Disease: Senior research scientist [Stephen Sidney, MD, MPH](#), was honored at the annual meeting of the [National Forum for Heart Disease and Stroke Prevention](#) for his “exceptional contributions” and his work on understanding national trends in cardiovascular disease. At the event, Sidney presented his new [National Forum report](#), which draws attention to a [recent slowing](#) of the rate of decline in deaths from heart disease and stroke in the United States. [Read More](#)

Heart Failure Deaths Rising in United States: A long-term, nationwide decline in deaths from heart disease reversed in 2015, but death rates for different heart disease subgroups followed different trends, according to research published in *BMC Cardiovascular Disorders* by [Stephen Sidney, MD, MPH](#), [Jamal S. Rana, MD](#), [Alan Go, MD](#), and colleagues. Ischemic heart disease mortality continued to drop from 2011 to 2015, but deaths from heart failure and all other heart diseases rose. The authors called for “urgent attention” to address these trends. [Read More](#)

Public Health Education Partnership: Residents at Kaiser Permanente Oakland Medical Center can enhance their medical training with formal public health education through an innovative collaboration with the [University of California Berkeley School of Public Health](#). A paper and video published in *Advances in Medical Education and Practice* by [Joan C Lo, MD](#), and colleagues showed how the [combined residency–Masters in Public Health](#) program successfully trains future physician leaders in public health. [Read More](#)

Record-Breaking Stroke Drug Delivery: Kaiser Permanente hospitals in Northern California are delivering the clot-busting medication alteplase to new stroke patients more than twice as fast as the national average, thanks to regionwide adoption of an integrated telemedicine program. “Door to needle times” average just 34 minutes at all 21 Northern California hospitals, as reported by leader author [Mai Nguyen-Huynh, MD, MAS](#), senior author [Alexander Flint, MD](#), and colleagues in the journal *Stroke*.

[Read More](#)

World’s Highest-Impact Researchers: Cardiovascular research scientist [Alan Go, MD](#), and Kaiser Permanente Northern California oncologist [Louis Fehrenbacher, MD](#), are among the less than 400 people in the world named as [Highly Cited Researchers](#) in clinical medicine for 2017 by Clarivate Analytics. The annual list recognizes investigators whose research ranks in the top 1 percent most cited works in their field, indicating exceptional scientific impact. “This is a remarkable achievement,” said Philip Madvig, MD, associate executive director of [The Permanente Medical Group](#).

[Read More](#)



Healthcare Policy and Delivery

Disparities in Cancer Care: [Devon Check, PhD](#), a second-year [Delivery Science Fellow](#), led an analysis of data from the [Pathways](#) study, finding that cancer patients who were racial/ethnic minorities were more likely than white patients to report a high burden of side effects during treatment. Check reported these findings at the [2017 Palliative and Supportive Care in Oncology Symposium](#) in San Diego, Calif., supported by a [Merit Award](#) from the Conquer Cancer Foundation of the American Society of Clinical Oncology (ASCO).

[Read More](#)

Patient Portal Helps Families: Kaiser Permanente offers its members an online [patient portal](#) that allows them to access health care information and engage with clinicians. A new survey study — designed with the direct assistance of Kaiser Permanente members — found that more than a quarter (27.5 percent) of 1,392 members with chronic conditions who were registered to use [kp.org](#) also used it to help a family member. Research scientist [Mary E. Reed, DrPH](#), and colleagues published their findings in *JAMA Internal Medicine*.

[Read More](#)

Low Blood Sugar Emergencies: A multi-institutional team led by senior research scientist [Andrew J Karter, PhD](#), used machine learning techniques to develop and validate [a practical tool](#) for identifying diabetes patients who are at the highest risk for ending up in an emergency department or hospital due to very low blood sugar. The team, supported by funding from the U.S. Food and Drug Administration, reported the success of their innovative tool in [JAMA Internal Medicine](#). The paper received the Division of Research's Gary D. Friedman Outstanding Paper Award for 2017.

[Read More](#)

Improving Surgical Outcomes: A comprehensive Enhanced Recovery After Surgery program implemented at Kaiser Permanente's 20 Northern California medical centers involved nearly 9,000 surgical patients and resulted in a [one-third relative reduction](#) in postoperative complication rates and a 21 percent reduction in opioid prescribing rates, according to a study published in [JAMA Surgery](#). The program aims "to reduce the stress of surgery, reduce complications, and maximize the potential for recovery," said study leader [Vincent Liu, MD](#).

[Read More](#)

Weight Coaching by Telephone: Kaiser Permanente offers voluntary wellness coaching by phone to all its members nationwide for no additional fee. A new study led by [Julie A. Schmittiel, PhD](#), and published in the journal [Obesity](#) found that members who voluntarily participated in individual wellness coaching by telephone for weight management lost [an average of 10 pounds](#) each and changed their weight trajectories from upward to downward.

[Read More](#)

2017-18 Member Health Survey Underway: The confidential Kaiser Permanente Member Health Survey is conducted every three years by [Nancy Gordon, ScD](#), since 1993. All [results](#) for the 2014-15 Member Health Survey cycle are now available, and results of a small survey of Spanish-speaking members was posted in early 2018. Data collection for the 2017 Member Health Survey will be completed in early 2018 and results will be available in 2019.

[Read More](#)

Dropping Caps on Drug Coverage: [Alyce Adams, PhD](#), and colleagues investigated changes in non-cancer medication use among dual Medicare/Medicaid patients with cancer, after the 2006 Medicare Modernization Act shifted their prescription coverage to Medicare Part D plans that do not cap drug coverage. Dropping drug coverage caps was associated with increased medication use and reduced racial gaps in medication use. The findings appeared in [Value in Health](#), the official journal of the International Society for Pharmacoeconomics and Outcomes Research.

[Read More](#)



Infectious Diseases

Whooping Cough Protection: Among infants whose mothers received the Tdap pertussis booster vaccine during pregnancy, the risk of contracting pertussis, or whooping cough, decreased by about [91 percent](#) during the first two months of life — the critical period before they can receive [their first](#) childhood pertussis vaccine. Reported in [Pediatrics](#), these findings from the [Kaiser Permanente Vaccine Study Center](#) “demonstrate that maternal Tdap administered during pregnancy provides the best protection against pertussis,” said senior author [Nicola P. Klein, MD, PhD](#). The paper received the Division of Research’s Gary D. Friedman Outstanding Paper Award for 2017.

[Read more](#)

Vaccination During Pregnancy: Postdoctoral researcher [Ousseny Zerbo, PhD](#), was lead author on two studies that found no association between influenza vaccination during pregnancy and increased risk of autism spectrum disorder in children, nor with birth outcomes such as preterm birth, need for mechanical ventilation, and low birth weight. The authors do not recommend any policy or practice changes, but noted that the findings suggest a need for more research. The autism findings appeared in [JAMA Pediatrics](#) and the birth outcome results in [Vaccine](#).

[Read More](#)

HIV and Alcohol Use: With support from the National Institute on Alcohol Abuse and Alcoholism, Kaiser Permanente and the University of Bristol [are joining](#) the Veterans Healthcare System to participate in COMpAAAS: the Consortium to improve Outcomes in HIV/Aids, Alcohol, Aging & multi-Substance. The partnership will enable evaluation of the risk of alcohol and tobacco exposure on mortality, hospitalizations, comorbidities, and physiologic frailty for people living with HIV. Division of Research scientist [Michael J. Silverberg, PhD, MPH](#), and psychologist [Derek Satre, PhD](#), are co-principal investigators on the project.

[Read More](#)



Women's and Children's Health

Fewer Antibiotics for Newborns: A study published in [JAMA Pediatrics](#), led by research scientist [Michael Kuzniewicz, MD, MPH](#), showed that the development and implementation of a neonatal sepsis risk calculator safely reduced antibiotic use by nearly 50 percent in newborns in Kaiser Permanente's Northern California region. "By dramatically reducing the use of antibiotics, the risk calculator allows mothers and babies to stay together in the days after birth," said co-author [Allen Fischer, MD](#), director of neonatology for Kaiser Permanente Northern California. The study demonstrates how [predictive analytics](#) can aid in the development of tools that lead to direct improvements in patient care. The paper received the Division of Research's Gary D. Friedman Outstanding Paper Award for 2017.

[Read More](#)

Minimally Invasive Hysterectomy: The rate of minimally invasive surgery for routine hysterectomy increased from 40 percent to 93 percent in Kaiser Permanente's Northern California region between 2008 and 2015, with significantly reduced post-operative complications and hospital stays, according to a study published in [Obstetrics & Gynecology](#) by senior author [Tina Raine-Bennett, MD, MPH](#), research director of the Kaiser Permanente Women's Health Institute, and lead author [Eve Zaritsky, MD](#). "Women who have hysterectomies with minimally invasive surgery have shorter recoveries, less pain, and smaller scars," Zaritsky said.

[Read More](#)

Environmental Influences on Child Health: The Division of Research has launched a new 7-year, \$24 million study, funded by the National Institutes of Health, on how exposures to environmental chemicals during pregnancy may influence the risk of obesity and neurodevelopmental disorders in children. Division of Research associate director [Assiamira Ferrara, MD, PhD](#), is principal investigator, along with co-principal investigator [Lisa A. Croen, PhD](#), director of the [Autism Research Program](#). The study is part of NIH's \$144 million [Environmental Influences on Child Health Outcomes](#) (ECHO) program, which is investigating how exposure to a range of environmental factors from conception through early childhood influences the health of children and adolescents.

[Read More](#)

Magnetic Fields and Miscarriage: A study of real-world exposure to non-ionizing radiation from magnetic fields, led by research scientist [De-Kun Li, MD, PhD](#), and published in [Scientific Reports](#), found that high exposure was associated with a significantly higher rate of miscarriage, providing new evidence regarding their potential health risks. Objective magnetic field measurements and pregnancy outcomes were obtained for 913 pregnant women; miscarriage occurred in 10.4 percent of the women with the lowest measured exposure level on a typical day, and in 24.2 percent of the women with the higher measured exposure levels, a nearly three times higher relative risk.

[Read More](#)

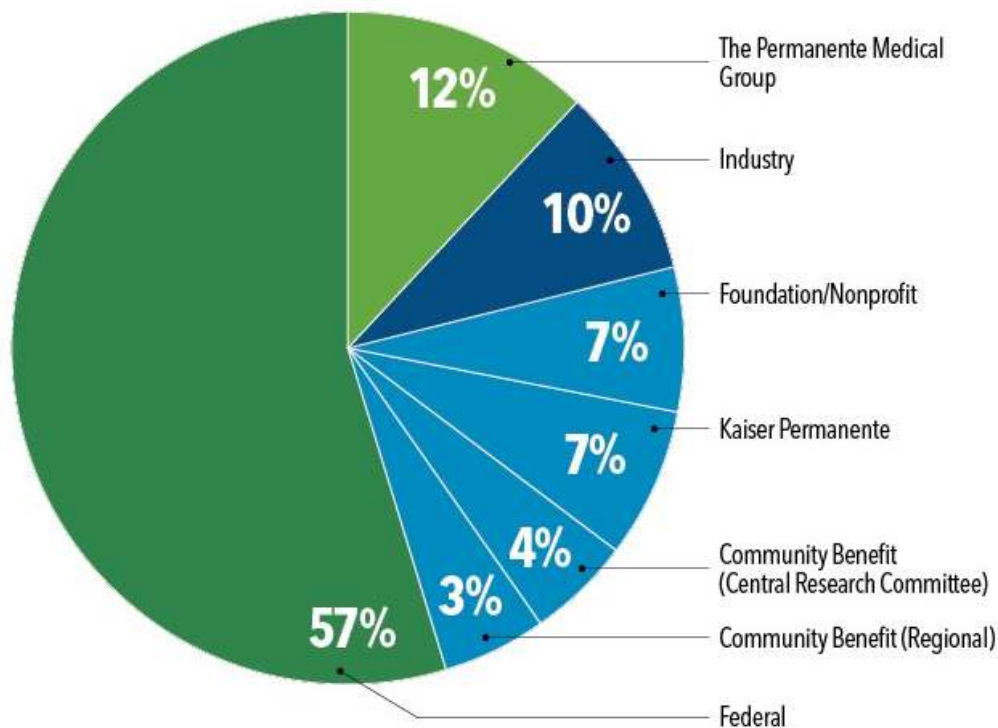
Best *Environmental Research* Paper: Lisa A. Croen, PhD, director of the [Autism Research Program](#), was a co-author of the [best paper of the year](#) (2016) in the journal *Environmental Research*. The paper, "[Presence of an epigenetic signature of prenatal cigarette smoke exposure in childhood](#)," by Ladd-Acosta et al., found that an epigenetic signature of prenatal exposure to cigarette smoke, originally discovered in other studies of cord blood at birth, is detectable in childhood blood samples at ages 3 to 5, providing evidence that prenatal exposure to tobacco smoke has lifelong health consequences.

[Read More](#)

2017 Financial Report

The Division of Research (DOR) is currently home to about 56 investigators and staff scientists, 13 research fellows, and nearly 600 employees. The DOR also has 35 adjunct investigators from within Kaiser Permanente and from other academic institutions. DOR scientists are involved in approximately 475 research studies. Since its founding in 1961, DOR researchers have published more than 4,000 peer-reviewed articles including more than 450 papers in 2017 alone.

Total expenditures: \$84 Million



Federal - 57 percent
The Permanente Medical Group - 12 percent
Industry - 10 percent
Foundation/Nonprofit - 7 percent
Kaiser Permanente - 7 percent
Community Benefit (Central Research Committee) - 4 percent
Community Benefit (Regional) - 3 percent