Kaiser Permanente **Research**



THE CYCLE OF IMPROVEMENT





Contents

Message from the Senior Director	4
Research Highlights	
Maternal diabetes and risk for children	6
Social needs	10
Reducing heart disease	12
Opioid addiction	16
End-of-life care	20
Infectious disease and Valley fever	26
Accomplishments & Milestones	
Selected grants and contracts	32
Selected findings	34
Research program overview	38
Financial overview	39
Projects funded by the Regional Research Committee	40
Regional Research Committee	42
Investigators	
Overview of our investigators and scientific divisions	44
Division of Epidemiologic Research	45
Division of Behavioral Research	47
Division of Biostatistics Research	48
Division of Health Services Research & Implementation Science	49
Division of Clinical Trials Research	50
Affiliated researchers	52
Clinical trials principal investigators by specialty	54
Publications	58

Opposite: Wind turbines dot a field in California's Central Valley. Dusty wind, along with construction activities, are major contributors to the spread of the microscopic fungal spores that cause Valley fever, which is endemic in the Central Valley. Physician investigators in Bakersfield and the Antelope Valley are participating in a 5-year clinical trial of a drug to treat Valley fever. Learn more on page 26.

Message from the Senior Director



Discussion about learning health care systems—those which embed learning and quality improvement within care delivery—has intensified over the past few years. But what does one look like in a real-world setting? And where does research fit in? Here at Kaiser Permanente Southern California, our learning health care system promotes a continual cycle of improvement, powered by inquiry, investigation, and implementation with research as an embedded component.

The cycle of improvement begins with inquiry—asking a question. If a mother has elevated blood sugar during pregnancy, what are the health risks for her child? How might we identify patients who need help addressing social needs, from food and housing to social support? What strategies are effective in reducing opioid prescription?

Answers to these questions come through rigorous investigation, which fills in missing information and generates new evidence. Our scientists and physician researchers were involved in more than 1,400 active studies in 2018. Some of the ongoing investigations described in this report include:

- A follow up study on the Hyperglycemia and Adverse Pregnancy Outcomes, or HAPO, study (page 7)
- A project focused on improving care for elderly patients with depression (page 10)
- A study of the long-term effects of various combinations of anti-hypertensive medicines (page 13)
- An investigation into the effect of chronic prescription opioid use on mortality in patients ages 65 years and older (page 19)
- An analysis of survey results on how well next of kin understood their loved one's end-of-life wishes and how they felt Kaiser Permanente met them (page 22)
- A clinical trial of a new algorithm for diagnosing and testing Valley fever (page 27)

Findings can point to a better way to provide care or improve health. That's when the cycle moves toward implementation—applying results in the real world.

Implementation can take different forms, from updates to clinical guidelines to new partnerships in the community. Even after implementation, the cycle continues, opening new lines of inquiry and investigation.

I hope that the stories in our 2018 Annual Report provide a glimpse into the many ways our research program contributes to the cycle of continuous improvement at Kaiser Permanente. We have a wonderful group of talented and dedicated researchers and staff, both within the Department of Research & Evaluation and at medical centers around the Southern California region. I thank all of you for your contributions and for your continued support of our research program.

Steven J. Jacobsen, MD, PhD

Senior Director of Research



Maternal diabetes and risk for children:

How questions lead to answers that lead to more questions



ne way researchers at Kaiser Permanente work to make our next generation healthier is by studying children's environments *before* birth.

In 2018, several researchers looked at how mothers' blood sugar levels during pregnancy affected their children's risk for diabetes, overweight/obesity, and cognitive impairment. They looked at various conditions including the type of diabetes that develops in pregnancy, called gestational diabetes.

Kaiser Permanente Southern California researchers conducted studies that showed children born to women with type 1 diabetes are associated with about twice the risk of autism as those born to women who do not have any form of diabetes. Another study showed that children exposed to untreated gestational diabetes during pregnancy are more likely to be unable to properly absorb and use sugar for energy compared with children whose mothers did not have gestational diabetes.

The work was decades in the making. Each discovery was based on a question by a passionate and dedicated researcher that emerged after a previous discovery.

Physician began early investigation at Bellflower

Work at KPSC on glucose tolerance and big babies was first published in 1995. David Sacks, MD, an obstetrician at the Kaiser Permanente Bellflower Medical Center, knew from his reading and previous research that women with elevated blood sugar were more likely to give birth to larger babies. Children of women who have diabetes are at increased risk for a variety of complications at birth as well as later in life.

"But what I was curious about was whether the risk of having big babies changed with moms' increasing blood sugar values," he said.

He recruited more than 3,000 pregnant women who planned to give birth at the Bellflower Medical Center to determine the answer. The study followed the women who had elevated blood sugars but who did not reach the level of overt diabetes.



Dr. David Sacks tells Jenny Gutierrez how research into maternal diabetes began at Kaiser Permanente Southern California over 25 years ago.

"What we showed was that the relationship was continuous," said Dr. Sacks, who is now an associate investigator with the Department of Research & Evaluation. "There was a straight line that showed that the higher the blood sugar, the higher the chance of having an overly large baby."

Joining with others to investigate the question

During this early work Dr. Sacks learned that a consortium of 15 hospitals and research centers was also studying elevated blood sugars in pregnant women, although it was looking at additional outcomes. That group invited him to join them in the Hyperglycemia and Adverse Pregnancy Outcomes, or HAPO, study, as field center principal investigator at Bellflower.

The first large-scale study published by HAPO in 2008 determined that in pregnant women, levels of maternal blood sugar lower than those which defined overt diabetes are associated with a number of negative outcomes for offspring, including increased birth weight and hormone levels that are associated with fetal growth.

Opposite and page 5: At the West Los Angeles Medical Center, Dr. Michael Fassett shows patient Kneena Wolff the best way to use a blood glucose meter to test her blood sugar. Research shows keeping blood glucose under control during pregnancy is best for the baby.



Mayra Martinez, Dr. Anny Xiang, Ting Chow, and Janet Mora Márquez discuss ways to research the effect of the intrauterine environment on a child's cognitive development.

Implementation included new way to identify gestational diabetes

Because of their findings, the researchers developed a new lower criterion to identify gestational diabetes.

At the same time, R&E researcher Jean M. Lawrence, ScD, MPH, MSSA, published a paper in *Diabetes Care* showing that the prevalence of diabetes (type 1 and type 2) among pregnant women was increasing over time while the rate of gestational diabetes was remaining constant but high at around 7.5% of pregnancies. With so many children exposed to diabetes in pregnancy, learning more about the impact of these conditions became more pressing.

Investigations spurred more inquiries

The answers from the HAPO study led to more questions, and when a new study was initiated, Dr. Lawrence became the field center PI for the HAPO Follow-up Study. That study aimed to answer the question of what happened to the moms in the original HAPO study, as well as their children. More specifically, how did maternal glucose and maternal

body mass index influence a child's growth and a child's risk of prediabetes and diabetes? The study team began publishing results in 2018.

"In general, we found that outcomes 8 to 10 years after that pregnancy are along the same continuum as the ones we saw at the time of delivery," Dr. Lawrence said. "Children are more likely to have bad outcomes, such as insulin resistance, if their mom was in the higher end of the glucose distribution."

Inquiries into gestational diabetes

Anny Xiang, PhD, MS, director of R&E's Division of Biostatistics Research, began her career over 25 years ago at the University of Southern California. She was working to "understand the pathogenesis of gestational diabetes and diabetes in a cohort of Hispanic women."

She worked on research that:

- found that women with gestational diabetes are at high risk of developing diabetes after the pregnancy is over, and
- mapped the progression of gestational diabetes to type 2 diabetes.

Moving to Kaiser Permanente in 2010 opened the door for Dr. Xiang to address other questions she had about gestational diabetes, because of KPSC's large, diverse patient population.

Investigating racial/ethnic disparities in fetal growth

Dr. Xiang first focused on learning about racial and ethnic disparities in gestational diabetes.

- A 2011 study showed that black women with gestational diabetes had a much higher risk of developing diabetes after pregnancy.
- A 2015 study showed that children born to black women with gestational diabetes were more likely to be large for gestational age.

Those studies made her want to push further, for instance, "how does mom's gestational diabetes affect the brain of the fetus?"

"My interest in maternal and child health conditions is based upon the opportunity to identify people at risk and help them be healthier going forward."

- Jean M. Lawrence, ScD, MPH, MSSA



Dr. Michael Fassett examines patient Kneena Wolff as her partner, Abel Orozco, provides support. Researchers agree that for the health of the child, it's not only important to see a doctor during pregnancy, but also to see one before getting pregnant.

Inquiries progressed to cognitive functioning

In 2015, Dr. Xiang published a study in *JAMA* that showed that gestational diabetes diagnosed early was associated with autism risk in children. In 2018, she extended that work by including pregestational type 1 and type 2 diabetes and showed that both were also associated with risk of autism.

Also in 2018, she published work on attention deficit and hyperactivity disorder that showed that type 1, type 2, and gestational diabetes requiring medication during pregnancy were associated with a risk for attention deficit and hyperactivity disorder in children.

"A lot of disease tracks back to conditions during pregnancy," Dr. Xiang said. "We have now developed a large enough store of electronic health records covering many years at KPSC. With this, we can evaluate the potential effect of the intrauterine environment on a child's neurological development and other health outcomes."

Implementation as a takeaway: plan your pregnancy

Dr. Xiang notes that each piece of research seems to point to the importance of women seeing their doctors before pregnancy to make sure their babies have the best environment during pregnancy.

Dr. Lawrence and Dr. Sacks agreed.

"It's important to know whether or not you've got diabetes or prediabetes before you get pregnant," Dr. Sacks said. "Then, you and your doctor can do everything possible to make sure your baby has the healthiest start possible."

Social needs:

Building the capacity to help patients beyond medicine



here is a growing awareness in the health care community that treating a patient's medical symptoms may not be enough. Their social situation may be the true impediment to a cure.

But how does a doctor house the homeless veteran, feed the hungry child, or end loneliness for the aging widower?

Now, investigators at Kaiser Permanente Southern California are building the capacity to address these needs through research and partnerships.

"We can help many people decrease their need for health care if we address their social needs," said Adam Sharp, MD, MS, a researcher with the Department of Research & Evaluation.

Over the last few years, the role that social needs play in health care has slowly become more recognized in research and health care circles. Kaiser Permanente has been a leader in those efforts.

In 2019, Kaiser Permanente launched Thrive Local, a social health network to connect health care and social services providers to address social needs including housing, food, safety, and utilities for Kaiser Permanente members across the United States.

It is expected to be available to all Kaiser Permanente members by 2022.

The work was fueled by research, some of which was done at KPSC.

Inquiry leads to predictive model

Other efforts include using predictive modeling approaches to identify patients who might be at risk of having social needs and partnering with community organizations to address these needs, said Claudia Nau, PhD, a researcher with R&E.

"One of the very important things we can do to address the root cause of some social needs is to work with community-based agencies that are already providing services," Dr. Nau said.

Investigating partnerships to improve patients' lives

One project involves working to improve care for elderly patients with depression. KPSC researchers have partnered with 4 depression care managers and a community partner, Healthy African American Families (HAAF), to recruit 100 elderly Kaiser Permanente patients into the program.

"A lot of elderly patients struggle with loneliness and depression," Dr. Nau said. "We're finding that they also struggle with a lot of other things that hinder them from going out or living healthy."

Implementation may be as simple as checking batteries

Among the issues that HAAF community specialists addressed include:

- A woman with diabetes had trouble going grocery shopping and ordered salads from a fast food pizza delivery service to eat 'something healthy.' Specialists helped her sign up for a free meal delivery service for seniors.
- Another patient was worried about leaving her home because she wasn't sure the batteries on her portable oxygen tank were good. Specialists made sure her oxygen tank was working well.

Dr. Nau meets regularly with Kaiser Permanente depression care managers and the community specialists from HAAF to discuss cases.

"If we are to guide patients to optimal health, it's important to identify what their barriers are, and what's possible for them in their situation," she said. "Then we can be most effective in helping them live their best lives."

Early inquiry aimed to understand who would benefit

Dr. Sharp, who is also an emergency physician at the Kaiser Permanente Los Angeles Medical Center, looked at the issue of social needs beginning in 2015.

First, he collaborated on a pilot project with a nonprofit organization to assess patients' social needs and guide them to community resources. The project aimed to understand who would benefit from social needs assessments and assistance, and how that would affect their utilization of health care services.

Results were presented at the Kaiser Permanente 2018 National Quality Conference and are expected to be published in 2019.

"It didn't affect health care utilization among patients overall. But in subgroups of patients that were disadvantaged, there was significant benefit," Dr. Sharp said.

Opposite: Dr. Claudia Nau (second from left) meets regularly with Healthy African American Families staff to help improve care for elderly patients with depression. Outside their office in Los Angeles, she discusses the program and research with HAAF's Andrea Jones, finance; Felica Jones, CEO; and home visit specialists Anthony Brown and Ericka Wright.



Anthony Brown counsels client Loretta Darden on exercise options near her Los Angeles home.

Investigation reveals physicians want to support patients' social needs

Next, Dr. Sharp assessed the level of support from Permanente physicians and nurses, pharmacists, and administrators in KPSC to address socials needs.

That research, expected to be published in 2019, showed that:

- the overwhelming majority of health care professionals support social needs screening, but
- only a minority are confident in their ability to address social needs.

The findings were key to fueling and informing the Thrive Local work, Dr. Sharp said.

"This work has changed the question from 'Should we screen and address social needs?' to 'How should we be screening and addressing these needs?," Dr. Sharp said. "And now we are taking steps toward tangible changes."

Implementation includes a standardized assessment

The changes include adding a standardized assessment of social needs on electronic health records that physicians can use to screen patients.

Dr. Sharp also is a member of the SONNET (Social Needs Network for Evaluation and Translation) steering committee. This Kaiser Permanente national group is working to find ways to address the social, economic, and behavioral needs of members, and is assisting with the evaluation of Thrive Local.

Dr. Nau said this is an exciting time for researchers in her field. "There's a shift now in the thinking of the medical community that not only does care matter environment matters," she said. "Through research we now have the evidence base to back that up."

Social needs 11

Reducing heart disease:

Researchers investigate blood pressure at home and abroad



educing heart disease has long been a focus for Kaiser Permanente Southern California's Department of Research & Evaluation.
And as a learning health care organization, clinicians are often able to quickly incorporate results of the studies into practice.

Because high blood pressure is a major risk factor for heart disease and stroke, research conducted in 2018 delved into several aspects of blood pressure. One study considered how low is too low for blood pressure, another how variability in blood pressure can affect falls, and yet another how to decrease disparities in blood pressure treatment adherence rates between white and black patients.

Also in 2018, Kaiser Permanente began using data from its comprehensive electronic health record system for global benefit through an international program called Resolve to Save Lives.

"They came to us to see if we could provide some real-world evidence on the long-term effects of various combinations of antihypertensive medication to help find the best combinations for patients in countries with few resources and little chance for regular follow-up labs," said Kristi Reynolds, PhD, MPH, director of R&E's Division of Epidemiologic Research. "This is an exciting opportunity to provide real-world evidence that will guide international guidelines aimed at saving lives around the globe."

Hypertension becoming a global concern

The work is coming full circle for Dr. Reynolds. She began graduate school at the Tulane University School of Public Health and Tropical Medicine with a focus on infectious diseases. However, she completed



At the West Los Angeles Medical Center, Dr. Jeffrey Brettler discusses finding the right antihypertensive regimens for patients in low-income countries with Tiffany Luong.

her doctoral studies in cardiovascular disease after realizing that cardiovascular disease may be more important in the long term. She feels now she made the right choice.

"While there's still a lot of effort looking at infectious diseases in underdeveloped countries, people are living longer, their diets have changed, and they aren't getting as much exercise," Dr. Reynolds said. "So we are seeing that high blood pressure has become a big challenge globally."

Resolve to Save Lives is an initiative of the global public health organization Vital Strategies, which helps governments and communities prevent deaths

"Resolve to Save Lives came to us to see if we could provide some real-world evidence on the long-term effects of various combinations of antihypertensive medication in order to find the best combinations for patients in countries with few resources and little chance for regular follow-up labs."

Kristi Reynolds, PhD, MPH

Opposite: At the Los Angeles Medical Center, Dr. John Sim shows patient Eduardo Escobedo how the 24-hour ambulatory blood pressure monitoring device can help determine a patient's true blood pressure. Using this device on patients, current research will test whether a larger "white coat" effect is associated with a higher risk of falls among older adults with treated hypertension.

Reducing heart disease 13



Dr. Kristi Reynolds and Teresa Harrison discuss research efforts at Kaiser Permanente aimed at helping people with hypertension locally and across the globe.

from cardiovascular disease and epidemics, with a focus on low- and middle-income countries. Marc G. Jaffe, MD, who was the clinical leader of Kaiser Permanente's National Integrated Cardiovascular Health Guidelines Team, is now the senior vice president of Resolve's Cardiovascular Health initiative.

Dr. Jaffe was familiar with the work that had been done by Dr. Reynolds and Jeffrey William Brettler, MD, the regional hypertension physician lead for the Southern California Permanente Medical Group. Dr. Jaffe asked them to help in the project.

Implementation of results could save lives globally

"KPSC has great records on patients' experiences with high blood pressure medications and combinations of medications, and we have actually published on their long-term outcomes," said Dr. Brettler. "When you go into under-resourced developing countries, you want to use the most efficient regimens you can get. Through our research, we can discover what those regimens should be."

Dr. Brettler noted that from a global perspective, by developing simple regimens to control hypertension "you can potentially affect more lives than almost any other intervention."

Physician investigates how low is too low for blood pressure

Closer to home, John J. Sim, MD, a nephrologist with the Kaiser Permanente Los Angeles Medical Center, had noticed something in his practice as efforts to lower patients' blood pressure increased. Older patients with very low blood pressure were feeling poorly and falling more often.

He pursued research that was published in the *American Journal of Preventive Medicine* in 2018. The study found if patients taking prescribed hypertension medications have episodically low blood pressures—systolic blood pressure under 110mmHg—they were twice as likely to experience a fall or to faint as patients whose treated blood pressure remained at 110mmHg or above.

Blood pressure findings implemented into hypertension guidelines

"Our study looked at what happens in a realworld clinical environment with very successful hypertension control rates where people are treating to a goal of less than 140 and often less than 130," Dr. Sim said.

The results were incorporated into the KPSC hypertension guidelines for physicians. It also informed work being led by Dr. Reynolds, who is looking at the variability of patients' blood pressure over 24-hour periods.

Treating hypertension can be a balancing act

Hypertension affects nearly two-thirds of adults ages 60 years and older in the United States. But falls are the leading cause of injury-related hospitalization and death among older U.S. adults, so clinicians often must weigh the cardiovascular benefits of increasing hypertension medication against the potential risk for falls, Dr. Reynolds said.

Blood pressure readings taken in the clinic may be higher than average for some patients due to what's called "white coat" effect, or stress at being at the doctor's office. Also, readings naturally fluctuate throughout the day, especially among older adults treated for hypertension.

The idea of 24-hour blood pressure monitoring to determine a person's true blood pressure has become common in Europe. But it's not practical for the 860,000 or so KPSC members with hypertension.

Inquiry based on previous hypotension findings

"So, we started to think, who are the patients who could really benefit?" Dr. Reynolds said. "Dr. Sim and I had a couple of conversations about the potential for overtreating older adults. There's anecdotal evidence that the "white coat" effect may be larger in older adults—and that's where we came up with the study idea."

Their research will test whether a larger "white coat" effect is associated with a higher risk of falls among older adults with treated hypertension, or whether people whose blood pressure drops substantially after a meal are more likely to have falls. The study is funded by the National Heart, Lung, and Blood Institute of the National Institutes of Health.

"Ultimately, we hope the study will help physicians determine when it's safe to increase patients' antihypertensive medication."

- Kristi Reynolds, PhD, MPH

In early 2019, the researchers started fitting patients with the 24-hour blood pressure monitors. They will continue to monitor the patients for a year to determine the results. They plan to enroll 1,250 patients over the 4-year study period.

"Ultimately, we hope the study will help physicians determine when it's safe to increase patients' antihypertensive medication," Dr. Reynolds said.

Reducing racial disparities in blood pressure control

In another study, Dr. Reynolds examined the racial disparities in hypertension control. Hypertension control at KPSC increased from 54% in 2004 to 86% in 2012. Like elsewhere in the country, however, control rates were lowest in black patients. In 2010, KPSC started measures to reduce those disparities. They included staff education, walk-in blood pressure clinics, a more stringent approach to medication adherence, and monthly reporting on hypertension racial disparity throughout the region.

The study, not yet published in 2018, followed patients from 2008 to 2016. It showed that hypertension control increased across all racial/ethnic groups and blacks experienced the largest improvement in hypertension control.

Helping people with hypertension live their best lives

Overall, the Department of Research & Evaluation is investigating blood pressure both near and far to help people live their best lives wherever they call home.

"It's important to study blood pressure because it's a major risk factor for stroke and heart disease. High blood pressure is extremely prevalent in the United States and is becoming more prevalent across the globe," Dr. Reynolds said. "Yet it is a disease that can be treated and controlled."

Reducing heart disease 15

Opioid addiction:

How researchers and physicians have worked to stem the crisis



s lead physician for Kaiser Permanente Southern California's Controlled Substance Task Force, Steven Steinberg, MD, has long led the charge to find ways to safely treat pain without addiction, including reducing the use of brand-name opioids, which decreased the incentive for patients to illegally sell their prescriptions.

Dr. Steinberg, who is also the regional chief of Family Medicine, is currently working with Rulin Hechter, MD, PhD, of the Department of Research & Evaluation on several studies aimed at reducing opioid addiction and overdoses, something he personally understands well.

In 2018, Dr. Steinberg fell 9 feet from his attic onto the concrete floor of his garage. He suffered multiple injuries including a skull fracture. He was in the intensive care unit for 2½ days.

He was given one of the opioids prescribed to patients with severe pain. Two weeks later he was at home and stopped taking the powerful narcotic. Lying on his couch at home, his body was racked with chills and sweat. He was hit with waves of nausea. He was experiencing withdrawal.

"You have the person who's usually in charge of controlled substances having to go through drug withdrawal himself," he said, "And what it illustrated for me was, that these drugs are really, really addictive, even when appropriately prescribed."

KPSC's inquiry into opioid addiction began a decade ago

In 2009, physicians looked at the medications being prescribed for Kaiser Permanente members in Southern California. They were surprised to find that opioid painkillers and highly addictive narcotics were prescribed more often than medications for diabetes or hypertension.

Physicians responded by launching a comprehensive initiative to transform the way chronic pain was



At the Panorama City Medical Center, Dr. Rulin Hechter and Dr. Steven Steinberg discuss several of their ongoing studies aimed at reducing opioid overdose deaths.

viewed and treated at KPSC. They conducted a study that described in detail the program to reduce dangerous and inappropriate opioid usage and to measure its effectiveness, said Michael Kanter, MD, medical director of Quality and Clinical Analysis for the Southern California Permanente Medical Group. (In 2019, Dr. Kanter became chair and professor for the Department of Clinical Sciences, Kaiser Permanente School of Medicine.) The study showed that between 2010 and 2015, there was a 30% reduction in prescribing opioids in high doses and a 95% reduction in prescribing of brand-name opioid-acetaminophen products.

"We are prescribing much fewer opioids," said Dr. Kanter, who is also executive vice president and chief quality officer for The Permanente Federation. "The study showed us to be a leader in opioid reduction, but there is still much we need to know."

"We are working to provide evidence to support policy change and identify the best strategies to tackle this epidemic."

- Rulin Hechter, MD, PhD

Opposite: One reason Kaiser Permanente researchers have an advantage in opioid research is their partnership with front-line clinicians. Before he got involved in research, Dr. Craig Chang (right) created a dashboard to closely track opioid prescription and dispensing doses. Here he reviews some important statistics with Anthony Aguino at the Panorama City Medical Center.

Opioid addiction 17



At the Panorama City Medical Center, Dr. Rulin Hechter and Dr. Steven Steinberg discuss how they expect the results of their ongoing studies will help inform safer clinical practice, policies, and guidelines.

Multiple investigations are aimed at reducing opioid addiction and death

Research is integral to KPSC's robust program focused on reducing opioid prescriptions and overdoses. Scientists in 2 of R&E's scientific divisions are separately pursuing active studies with multiple partners.

"We are working to provide evidence to support policy change and identify the best strategies to tackle this epidemic," said Dr. Hechter, a researcher in the Division of Epidemiologic Research. "That includes improving the quality of patient care and increasing patient safety when we prescribe opiates and looking for alternative ways to tackle chronic pain."

Adam Sharp, MD, MS, a researcher in the Division of Health Services Research & Implementation Science, has collaborated with Patrick Van Winkle, MD, and Ali Ghobadi, MD, of Kaiser Permanente Orange County to focus on opioid prescribing in the emergency department.

Research boosts clinician confidence to reduce opioids

Dr. Sharp, who is also an emergency physician at the Kaiser Permanente Los Angeles Medical Center, recently published studies in 2018 that:

- Showed that reducing opioids for chronic pain did not affect patients' satisfaction with care
- Showed that having a standard emergency department opioid policy decreased likely unwarranted opioid prescriptions
 - Dr. Adam Sharp Identified adolescents and young adults at higher risk of being prescribed opioids, which could help inform future



interventions to prevent addiction

"Steve Steinberg has been leading the fight against opioid addiction for a long time and they've done a lot of things to work on these issues," Dr. Sharp said. "The research that we have been doing has helped to inform those efforts and to evaluate the impact."

Physicians partner with research to find answers

One reason Kaiser Permanente researchers have an advantage in opioid research is their partnership with front-line clinicians. Before he got involved in research with Dr. Steinberg and Dr. Hechter, Craig Chang, MD, physician in charge of pain management for Kaiser Permanente Panorama City, created a dashboard to closely track opioid prescription and dispensing doses.

Pain management is challenging, he explained. And finding better ways to track how much opioid medication patients were getting became increasingly important over the past decade.

"For a select number of patients, opioids have a very critical role in managing chronic pain," he said. "And some of these patients have opioid tolerance that requires higher than usual doses. The major challenge is balancing that need to be compassionate with considering the underlying safety issues that come with the therapy."

The study team harnessed Dr. Chang's algorithm to calculate a near real-time daily dosage—and his experience as a pain management specialist—to further their investigations, Dr. Hechter said.

Researchers study many different aspects of opioid use and addiction

Dr. Hechter is actively working on 3 projects with Dr. Steinberg, Dr. Chang, and other physicians to evaluate:

- The effects of prescription opioid use while also using tranquilizers or gabapentin, which is used to control seizures or nerve pain, on risk of overdose
- The effects of decreasing and discontinuing opioids on risk of overdose among chronic opioid users who are at high dose and whether certain dose-decreasing strategies, e.g., how fast the dosage is decreased, are safer
- The effect of chronic prescription opioid use on mortality in patients age 65 years and older



Dr. Craig Chang hands Anthony Aquino a vial of medicine at the Panorama City Medical Center.

Dr. Hechter is also principal investigator and site PI on several opioid studies being done across multiple Kaiser Permanente regions and other health care organizations.

Implementation of results could change opioid tapering strategies

"We anticipate the results from those studies will provide us a better picture of opioid misuse and its impact on patient health outcomes in our region. It will also inform safer clinical practice, policies, and guidelines regarding prescribing opioids and strategies for tapering," Dr. Hechter said.

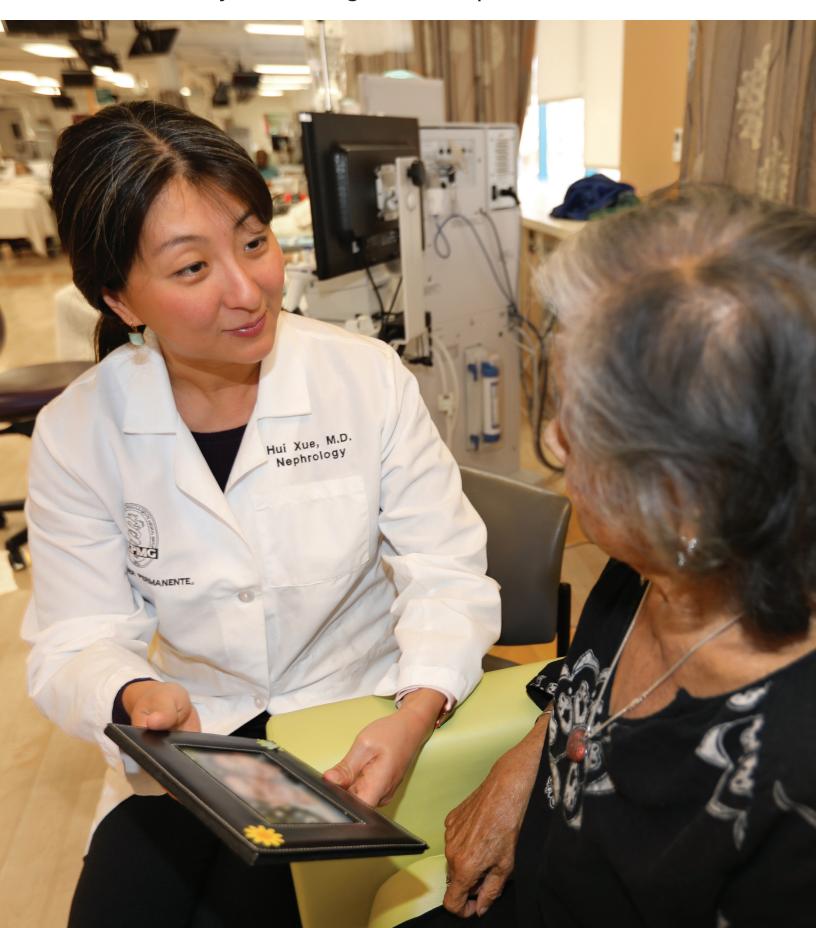
Dr. Kanter said the work being done by Dr. Sharp has removed barriers for physicians trying to reduce opioid prescriptions. The other studies also have the potential to change practice.

"We're way ahead of the rest of the country with our holistic integrated approach to opioid prescribing," he said, "But our next steps will be determined by the results of the research that is being done now."

Opioid addiction 19

End-of-life care:

Research is key to believing the best is possible



he care patients receive at the end of their lives is often driven by anecdote.

For patients, the experience may be rooted in what they see in the media. For physicians, their decisions may be influenced by a lack of comprehensive training and limited personal and professional experiences with death.

"To improve the care experience at the end of life, we must believe that a good outcome is possible," said Susan Wang, MD, medical director of Life Care Planning for Kaiser Permanente Southern California.

"Research is the key," she continued. "The goal of medicine is to prevent, address, and alleviate suffering. But if we don't know better, we may accept that a low standard of care is 'inevitable.' For us to have a meaningful impact, we need more research to better understand which treatments, decisions, and services best meet the needs of our sickest patients."

Research takes many approaches to end-of-life care

At the KPSC Department of Research & Evaluation, a number of researchers are working to make life transitions better for patients and their families including:

- David Glass, PhD, who has been working to determine if KPSC is giving patients the care they want at the end of life, and how to improve that care
- Huong Q. Nguyen, PhD, RN, who is starting work on increasing the efficiency, access, and care experience for home-based palliative care, including the integration of physician video visits
- Chun Chao, PhD, MS, who is researching the quality of end-of-life care for adolescents and young adults



Dr. David Glass has been working to determine if KPSC is meeting patients' needs as they approach the end of their lives.

 Hui Xue, MD, MMSc, a clinician investigator, who is researching how dialysis affects quality of life and longevity for elderly patients with chronic kidney disease

Care for seriously ill patients can encompass both palliative and hospice care. Palliative care, which can be provided in the clinic, hospital, and in patients' homes, is focused on providing relief from the symptoms and stress of a serious illness. It can be provided along with curative treatment. Hospice care is a benefit provided to people with limited life expectancy who are not pursuing curative treatment, to optimize their quality of life.

"Ultimately, the biggest question people want to know is how long are they are going to live and how they are going to spend those days."

- Hui Xue, MD, MMSc

Opposite: When Dr. Hui Xue realized that little was known about elderly patients and their prognosis on dialysis, she began researching the subject and made some intriguing discoveries. Here she shares a moment with patient Charlene Patino in the dialysis unit at the Los Angeles Medical Center.

End-of-life care 21



Dr. Susan Wang and nurse Kristin Olomu visit with 91-year-old patient Faye Crawford in her Los Angeles home.

Inquiry: Are patients' end-of-life care wishes being carried out?

Dr. Wang recalls embarking on a study with Dr. Glass in 2015 to determine if patients' end-of-life care wishes were being carried out at KPSC. Those wishes include a patient and family deciding they no longer want life-sustaining measures, such as CPR, artificial feeding, or mechanical ventilation, to keep the patient alive.

"I see the mismatch between preference and treatment as very serious," she said. "But the culture of medicine is always to err on the side of survival, so, if a physician wasn't sure about a patient's wishes, they would always try to revive the patient even if that was not what the patient may have wanted."

Dr. Wang; Dr. Glass; Michael Kanter, MD, thenmedical director of Quality and Clinical Analysis for the Southern California Permanente Medical Group; and others conducted the study to determine how well KPSC is meeting the end-of-life wishes of members by honoring their values and expectations.

The project started with focus groups with the next of kin of Kaiser Permanente members who had passed away. Previous research had suggested that next of kin didn't necessarily know what their loved one wanted before they died.

"But, these next of kin were adamant, no matter how we asked it, that they did have discussions with their loved one, they did know their loved one's wishes, and they did know how well we had done in meeting them," Dr. Glass said.

The researchers knew they could learn even more with a quantitative study. The team surveyed next of kin of 715 Southern California members ages 65 years or older who died in April and May 2017. The analysis and writing were completed in 2018 and the



At the West Los Angeles Medical Center, Dr. Susan Wang, Dr. Jason Ngo, and Dr. Andre Cipta discuss the importance of meeting patients' end-of-life wishes.

project will be presented at the Kaiser Permanente Quality Conference in June 2019.

Researchers found that nearly 85% of the patients had talked with their loved ones about their preferences. An equal proportion had filled out an advanced directive to document their wishes concerning medical treatments at the end of life. About 65% had spoken with a physician or staff about their end-of-life treatment preferences.

Almost 90% of the patients' loved ones agreed or strongly agreed that Kaiser Permanente gave "care and treatment over the last year of my loved one's life that met my loved one's wishes." The study also found that the cost of care at end of life did not necessarily equate to satisfaction with care at the end of life.

The investigators said the 2 factors that provided the best opportunities to better fulfill patient wishes were to better accommodate members' wishes to die at home and to hold more end-of-life discussions.

Investigation to implementation: Achieving better connections in palliative care

When one of her studies found that palliative care services for patients going home from the hospital were limited and not always reliable, Dr. Nguyen obtained \$14 million in funding from the Patient-Centered Outcomes Research Institute in 2018 to test a more efficient model of home-based palliative care that integrates video consultations with physicians.

Dr. Nguyen's research into end-of-life care, which she prefers to call simply part of a patient's journey, compares a standard home-based palliative care model that includes routine home visits by nurses and physicians with a tech-supported model that includes video consultation with the physician.

"With the tech-supported approach, the nurse is in the patient's home and facilitates a video conference, so the physician can talk with the patient and the family in a synchronous way." Dr. Nguyen said. "We

End-of-life care 23



Nurse Kristin Olomu facilitates a teleconference between patient Faye Crawford and Dr. Susan Wang from the comfort of Crawford's Los Angeles home.

"With the tech-supported approach, the nurse is in the patient's home and facilitates a video conference, so the physician can talk with the patient and the family in a synchronous way."

- Huong Q. Nguyen, PhD, RN

believe that the nurse and physician addressing the patient's and the family's concerns together will build the patient's and family's trust in the care team."

To determine whether video visits could be similarly effective for patients as the standard model, about 100 registered nurses were randomized to the 2 models so that approximately half of the patient-caregiver pairs are in each model.

Researchers will continue to recruit patients and their caregivers over the next 2 years.

"Video visits are not appropriate for all encounters, but we hope to better understand under what circumstances video visits are effective for patients and their caregivers," she said.

Investigating end-of-life care for adolescents and young adults

As KPSC researchers look for ways to make life transitions better for all patients, some researchers are looking at very specific patient populations. Dr. Chao is studying those who are ages 12 to 39 years.

She conducted a pilot study of the more than 600 young people with cancer at KPSC who died between 2001 and 2010 and found that more than two-thirds received medically intensive end-of-life care. The findings led to Dr. Chao obtaining a grant in 2018 from the National Cancer Institute to expand the study to end-of-life care for 2,500 young people in 3 different health systems.

"Young people's end-of-life care has been very understudied," Dr. Chao said. "And, it is a very different thing for someone to face death when they are 20 versus 70. Many of the young people have not had a chance to realize their life goals and some are still trying to complete their education. It can be devastating for the patient and the caregiver."

Her previous work found that in their final month of life, young people were receiving chemotherapy and being put into intensive care more often than older adults.

"Is it because the patient really wanted it or does the doctor feel obligated to do those things? We don't know," she said. "But we believe that, by understanding the end-of-life care preferences of younger patients and their caregivers, we can improve the way care is provided for this group."

"We believe that, by understanding the end-of-life care preferences of younger patients and their caregivers, we can improve the way care is provided for this group."

-Chun Chao, PhD, MS

Inquiry: What's best for aging patients with chronic kidney disease?

Dr. Xue, a nephrologist at the Kaiser Permanente San Diego Medical Center and a clinician investigator with R&E, is studying patients at the other end of the age scale, those who are 75 years of age and older, specifically those in the final stages of chronic kidney disease.

She targeted this group because as a physician she saw a gap in knowledge that only someone working at a place like Kaiser Permanente—with its integrated health care system and large diverse patient population—could answer.

"So, I'm looking at these people who are very near their life expectancy for individuals in America, right before they're about to go on dialysis," Dr. Xue said. "Are they going to live longer if they go on dialysis versus if they don't go on dialysis and die from natural kidney function decline? And most importantly, what is the effect on their quality of life?"

The study of about 2,000 patients, with quality of life considered, found they gained about 7 months by being on dialysis.

"The group on dialysis had twice as many emergency department visits and twice as many hospital stays," Dr. Xue said. "Overall, it seemed like they had a harder life."

Implementation: Sharing findings with other nephrologists

In 2018, the research was shared at a meeting with all the nephrologists in Kaiser Permanente Southern California, so they can all be better counselors for



Nancy Cannizzaro and Dr. Chun Chao discuss a study about end-of-life care.

their older patients with chronic kidney disease. It will be submitted for publication in 2019.

Dr. Xue said that whenever she discusses end of life with patients she urges them to "not get lost in the trees. To take a step back and look at the forest." Focusing on every single small decision, each drug, each procedure, each small adjustment can be overwhelming for the patients and their caregivers.

"And it does not bring joy," Dr. Xue said.

Research can give patients a broader view of their potential and possibilities at the end of life, provide a more holistic view of what is ahead, and inform the larger decisions.

"Ultimately, the biggest questions people have are how long are they going to live," she said, "and how are they going to spend those days?"

End-of-life care 25

Focusing on infectious disease:

Clinical trials and epidemiologic research into Valley fever



ver the years, the Department of Research & Evaluation's Division of Clinical Trials Research has tackled some of the most serious infectious diseases facing Americans. In the 1980s, researchers conducted trials to help patients with HIV/AIDS to survive. In 2011, clinical trials began focusing on hepatitis C.

Recently, clinical trials and R&E epidemiologists targeted a deadly regional disease: Valley fever. Also known as coccidioidomycosis, Valley fever is a respiratory disease caused by inhaling microscopic fungal spores that live in dry desert soil in the southwestern United States.

Most people who breathe in the spores don't get ill, but others can develop fever, chest pain, and coughing, which look like flu or pneumonia. In some cases, the spores spread into the bloodstream, leading to very serious health issues including death.

High number of Valley fever cases prompt inquiry

The number of reported Valley fever cases in California was 5,372 in 2016, a record level and a jump of 71% from the previous year, according to the state's Department of Public Health. In northern Los Angeles County's Antelope Valley, Valley fever cases increased 258% from 2001 to 2016, when nearly 600 cases were reported.

Physicians in Kern County and Antelope Valley said numbers seem to have increased since then.

Investigation required expansion of clinical trials

To develop a clinical trial program focused on determining the best time to treat patients for Valley fever with antifungal treatments, the division implemented clinical trials in endemic areas that had never conducted clinical trials before—the Antelope Valley and Bakersfield in Kern County, California.

"Despite Kaiser Permanente being a very large entity, we can quickly accommodate research needs where



More than 5,300 cases of Valley fever were reported in California in 2016. Here, Dr. Sara Tartof points to areas most affected in Southern California.

they exist," said William Towner, MD, director of the Division of Clinical Trials Research. "The only place we could study Valley fever is in Kern County or Antelope Valley, because that's where the patients are. So, when the opportunity arose for a Valley fever research project, we adapted relatively quickly to establish a research program in these communities."

Epidemiological research adds to knowledge of Valley fever

Laying the groundwork for the Valley fever clinical trial, R&E researcher Sara Tartof, PhD, MPH, investigated the disease from an epidemiological perspective. Her first research article on the subject was published in *Emerging Infectious Diseases* in 2018.

The study looked at how many patients with community-acquired pneumonia were screened for Valley fever from 2001 to 2011. A second paper, not yet published in 2018, examined the sequence of events that Valley fever patients encounter as they make their way through the health care system.

Opposite: Dr. Jonathan Truong, the assistant area medical director for infectious disease at Kaiser Permanente Antelope Valley, arrived in Lancaster in 2000 and quickly realized there was an issue with Valley fever. Through research, he's worked to understand why. And he was thrilled to help get a clinical trial study up and running to learn more about the disease that affects hundreds of people a year in the Antelope Valley.



Over the years, Dr. William Towner has conducted clinical trials for several infectious diseases including HIV/AIDS and hepatitis C. Recently, he and his team focused on a regional disease: Valley fever.

The research found that many patients were prescribed multiple rounds of antibiotics before getting a Valley fever diagnosis. It concluded that limited and delayed testing likely leads to underdiagnosis of the condition.

"Unlike pneumonia, cocci (Valley fever) is a fungal disease and antibiotic treatment doesn't work," Dr. Tartof said. "So, after multiple failed rounds, lots of imaging, and health care utilization with patients not getting better, they are finally tested for cocci."

Dr. Tartof's research and the clinical trials work share a joint aim to keep people healthier in the affected

areas by finding the most appropriate time to test for Valley fever and the best treatment for the disease. For instance, should antifungal treatments start before physicians are even sure the patient has Valley fever?

History of clinical trials in infectious disease

The history of infectious disease clinical trials at Kaiser Permanente Southern California began with HIV/AIDS clinical trials starting in the 1980s. At that time, physicians spent their own after-hours time working to find the best treatment for HIV/AIDS.

"Without the willingness and enthusiasm of the administration at Kaiser Permanente's facilities in Bakersfield and Antelope Valley, it would have been impossible to get these clinical trials up and running."

- William Towner, MD

In 2002, Dr. Towner and Hai Linh Kerrigan, PharmD, developed the infrastructure to support physicians conducting these clinical trials. This provided more consistent care for patients and more support for physicians by taking care of the administrative research requirements and regulations.

The program tested new HIV/AIDS drugs and drug regimens that were on the path to FDA approval. With access to new drugs, some of which turned out to be effective, many patients survived who may have otherwise died, Dr. Towner said.

Dr. Kerrigan said that "the clinical trials work we are doing in the area of infectious disease really started with HIV, and as soon as that disease started stabilizing, we examined the drug pipeline to see what other needs existed."

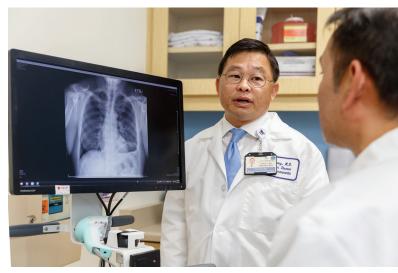
Clinical trials in hepatitis C became their next big push

"New novel therapies were coming out that had the potential to significantly improve treatment for hep C, so we had to get our hands on them in the hopes it would help our patients," Dr. Kerrigan said.

Like with HIV/AIDS, the clinical trials allowed patients with hepatitis C to get new medications with higher cure rates sooner. Also, the trials provided these new expensive drugs to patients at no cost.



Scientifically known as coccidioidomycosis, Valley fever is a respiratory disease caused by inhaling microscopic fungal spores that live in dry desert soil in the southwestern United States.



Valley fever symptoms often mimic pneumonia. Here, Dr. Jonathan Truong discusses a lung X-ray with colleague Dennis Edora at the Antelope Valley Medical Offices.

Kaiser Permanente asked to conduct clinical trials

The issue of Valley fever came to Kaiser Permanente Southern California after U.S. Rep. Kevin McCarthy, whose district includes Bakersfield and much of the Antelope Valley, secured \$5 million in federal funding to launch a 5-year clinical trial of a drug to treat Valley fever. Initial efforts to enroll patients were poor. The National Institutes of Health asked Kaiser Permanente to join.

But the timeline to get the program going was much quicker than with HIV/AIDS or hepatitis C, Dr. Towner said.

"Without the willingness and enthusiasm of the administration at Kaiser Permanente's facilities in Bakersfield and Antelope Valley, it would have been impossible to get these clinical trials up and running," Dr. Towner said.

Physicians power clinical trials with commitment

Jonathan Truong, MD, has been chief of infectious disease at Kaiser Permanente Antelope Valley since 2000. He has also served as assistant medical director for medical subspecialty services since 2010.

"When I came out here, I said, 'this place has totally too much cocci," he said. He began to work to understand why.



Dr. Jonathan Truong looks at fungal spores that cause Valley fever under a microscope at the Antelope Valley Medical Offices.



In Bakersfield, Kelly Rappaport and Dr. Aung Htoo discuss the recent cases of Valley fever they have seen. Physicians in the area say the numbers seem to have been rising the past few years.

Dr. Truong published research on meningitis caused by the Valley fever pathogen *Coccidioides immitis* in 2010 and has been a co-author on Dr. Tartof's Valley fever studies. After becoming a physician lead on the trial, he recruited other physicians to work on the project as well.

As patients come in to the emergency department or urgent care or for general appointments with pneumonia-like symptoms, the physicians ask them if they would like to be part of the study. If they agree, physicians follow them for 2 years and learn what percentage of them are ultimately diagnosed with Valley fever, how well they respond to antifungal treatments, and in what percentage did the fungal infection spread to the brain and other parts of the body.

"Together, we committed ourselves and changed our work flow to make sure the study would be successful at Kaiser Permanente," Dr. Truong said. "And we aggressively worked hard to enroll patients into the study and to manage them because we felt it was an important study."

Implementation: Clinical trials expected to lead to new protocols

One of the first physicians that joined Dr. Truong in the study was Aung Kyaw Htoo, MD, in Bakersfield.

"Right now, Valley fever is affecting a lot of people in this area, and all the doctors are treating it based on their own experience and intuition," Dr. Htoo said. "There is no proper set protocol. And we want a proper protocol for how to treat patients, how to do the proper follow-up, how to determine the indicators for the disease process. That's what we are trying to achieve with the new study."

Dr. Towner is pleased that the infectious disease work done by clinical trials has progressed to the point it can specifically target the health of KPSC members.

"It is truly satisfying to be able to make a difference like this for our members and the community," Dr. Towner said.



Accomplishments & Milestones

Selected grants and contracts

Our scientists and clinician researchers lead studies that have potential to change practice well beyond the walls of our organization. Many studies receive external funding from federal agencies and non-governmental organizations. Below is a small sample of newly funded projects that will address important public health questions.

Ambulatory blood pressure and falls

Principal investigator: Kristi Reynolds, PhD, MPH Funder: National Heart, Lung, and Blood Institute KPSC co-investigators: Joel Handler, MD; John Sim, MD

Two-thirds of adults in the United States ages 60 years and older have hypertension. Although treatment with antihypertensive medication has known benefits for reducing cardiovascular disease, accumulating data suggest that intensification of

treatment may increase the risk for falls in this population. Clinically measured blood pressure is commonly used to make decisions regarding antihypertensive medication intensification, but



blood pressure outside the clinic setting is often lower and can fluctuate widely throughout the day. In this study, researchers will evaluate the usefulness of ambulatory blood pressure monitoring to identify older patients who may be at increased risk for falls if blood pressure treatment is intensified. The study investigators will enroll more than 1,000 Kaiser Permanente Southern California members ages 65 years and older who have hypertension and are taking antihypertensive medication. The study is designed to answer whether a larger white-coat effect and blood pressure variability over 24 hours and, secondarily, whether a drop in blood pressure after a meal are associated with an increased risk for falls among older treated adults. These findings may help physicians better evaluate individual risks and benefits to older adults when considering intensification of blood pressure treatment. The findings may also help identify patients who could benefit from evidence-based strategies to prevent falls.

Engaging patients in mental health research

Principal investigator: Karen Coleman, PhD, MS Funder: Patient-Centered Outcomes Research Institute

The goal of the Mental Health Research Network is to apply the learning health system model to 13 health systems that serve approximately 12.5 million patients (17% of whom have a mental health condition) across 15 states. This



goal may not be adequately met, however, without the robust engagement of patients, their caregivers and families, and the communities and advocacy groups who represent them. In this project, the study investigators will develop an infrastructure to engage patients at both national and local health system levels. At the national level, the project team will add patient, caregiver, and family stakeholders and representatives from the community and advocacy groups who serve them to the national MHRN executive leadership team. At the local level, a second goal is to adapt the Henry Ford Health System's model of patient-engaged research for use within KPSC. Funding will be used to recruit team members to the KPSC Mental Health Research Implementation Team to represent patients, their caregivers and family members, providers, health system leaders, and researchers from the local KPSC health system. Creating a shared agenda between local and national leaders and patients, caregivers, and advocacy groups may improve the diagnosis, treatment, and monitoring of all patients with mental health conditions.

Embedded research conference

Principal investigators: Brian Mittman, PhD; Michael Gould, MD, MS

Funders: Agency for Healthcare Research & Quality and Patient-Centered Outcomes Research Institute

Research can contribute to improving the quality and outcomes of health care. For this to happen at a pace that truly influences daily clinical practice, however, new forms of collaboration are needed between researchers, providers, and clinical leaders. Partnership or "embedded" research approaches that form collaborations between researchers and health system leaders are a promising strategy for enhancing the relevance, timeliness, and appropriate use of research in health system decision making. With the funding provided for this project,

researchers from the
Department of Research
& Evaluation organized
the conference
"Accelerating the
Development of
Learning Healthcare
Systems Through
Embedded Research:
Expert Meeting," held



February 19 to 21, 2019. During the conference, small groups met to identify the types of models available for embedded research and the questions, study designs, and methods that best balance practice and science. The planned outcome is to generate specific recommendations and guidance for establishing and managing a partnership research program. Findings will be disseminated through a posted report, a summary journal article, conference presentations, and webinars. The conference and post-meeting activities will contribute to more successful implementation of research findings by creating a road map for growing and improving embedded research programs.

Depression and prostate cancer

Principal investigator: Reina Haque, PhD, MPH **Funder:** National Cancer Institute

KPSC co-investigators: Steven Jacobsen, MD, PhD; Jeff Slezak, MS; Stephanie Reading, PhD, MPH

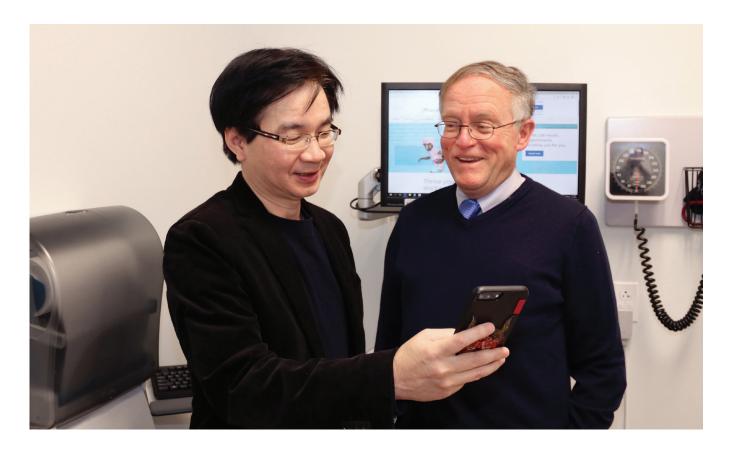
Prostate cancer is the most common cancer in men worldwide. In the United States, about 1 in 9 men will receive a diagnosis of prostate cancer in their lifetime. Most deaths from prostate cancer occur in men with advanced-



stage disease, but the risk factors for disease progression are not well understood. Depression may be one such risk factor. Depression is highly prevalent in men with early-stage prostate cancer and may share some of the biological mechanisms proposed for prostate cancer progression. In this study, researchers will examine whether men diagnosed with depression and early-stage prostate cancer are at increased risk for biochemical progression or development of advanced-stage disease. Using electronic health record data of nearly 36,000 male KPSC members diagnosed with earlystage prostate cancer between 2000 and 2014, researchers will study the links between a diagnosis of depression and prostate cancer biochemical progression, and if depression treatments (antidepressants or psychotherapy) modify this association. Other factors researchers will study include the patients' sociodemographic variables, overall health history, and tumor characteristics. In addition to providing insight into the risk factors for prostate cancer progression, these findings may help to identify men who could benefit from depression screening and shed light on potential disparities in the burden of depression.

Selected findings

In 2018, Kaiser Permanente Southern California scientists and clinician researchers made important findings in a variety of research areas. The following is a small sample of some of these discoveries.



Respiratory syncytial virus infection in hospitalized older adults tied to increased morbidity and mortality

The seriousness of infection with respiratory syncytial virus (RSV) in older adults may be under recognized by physicians. Researchers compared the consequences of infection with RSV (645 adults) or influenza (1,878 adults) in older adults hospitalized at Kaiser Permanente Southern California hospitals. Patients who tested positive for RSV or influenza were identified from electronic health records. In the short term, RSV infection was associated with greater odds of a length of stay longer than 7 days, admission to the intensive care unit, pneumonia, and worsening of conditions like chronic obstructive pulmonary disease. In the long term, RSV infection was associated with greater mortality within 1 year.

Ackerson B et al. Clin Infect Dis. 2018 Nov 19.

Bisphosphonate drug holiday and fracture risk

Atypical femoral fractures are a rare adverse effect of bisphosphonate use. A drug holiday-a planned period of time during which a patient stops taking a medication-may be a viable strategy to reduce the risk for these events if the risk of osteoporosis-related fractures does not increase. Researchers studied 39,502 women ages 45 years and older who had taken bisphosphonates continuously for 3 years. Participants who stopped taking bisphosphonates for 12 months (drug holiday group) were compared with participants who continued to use bisphosphonates regularly (at least 50% adherence) and those who continued to use bisphosphonates intermittently (<50% adherence). Compared with ongoing bisphosphonate users, the drug holiday group did not appear to be at greater risk for osteoporosisrelated fracture.

Adams AL et al. J Bone Miner Res. 2018 Jul;33(7):1252-1259.

Tdap vaccination not associated with increased risk for autism spectrum disorder

In this retrospective cohort study of 81,993 children born from 2011 to 2014, researchers reported that prenatal tetanus, diphtheria, acellular pertussis vaccination was not associated with an increased risk for autism spectrum disorder in offspring, an outcome of significant public interest. Information on vaccinations and ASD diagnosis (International Classification of Diseases, Ninth and Tenth Revision, codes) was obtained from electronic health records. The incidence rate of ASD was 3.78 per 1,000 person-years in the Tdap-exposed group and 4.05 per 1,000 person-years in the unexposed group (hazard ratio: 0.98, 95% confidence interval: 0.88–1.09; adjusted HR: 0.85, 95% CI: 0.77–0.95).

Becerra-Culqui et al. Pediatrics. 2018;142(3): e20180120.

Novel febrile neutropenia risk factors in chemotherapy-treated patients

Patients' clinical conditions may affect their risk of developing chemotherapy-induced febrile neutropenia (FN), a dangerously low white blood cell count accompanied by fever and other signs of infection. Using data from electronic health records, researchers assessed risk factors for FN in 15,971 patients diagnosed with non-Hodgkin's lymphoma or breast, lung, colorectal, ovarian, or gastric cancer and treated with myelosuppressive chemotherapy, which kills cancer cells as well as normal cells in bone marrow. Of the patients studied, 4.3% developed FN in the first chemotherapy cycle. The researchers found that corticosteroid use was significantly associated with increased risk for FN. Selected conditions of the skin and mucous membrane (that might affect barrier integrity) and intravenous antibiotic use were marginally associated with increased risk for FN. Clinicians should consider these patient characteristics when making treatment decisions.

Family L et al. J Natl Compr Canc Netw. 2018 Oct; 16(10):1201-1208.



Trends in statin use before and after publication of the 2013 ACC/AHA guidelines

More than 2 million people were included in this study of trends in statin use before and after introduction of the 2013 American College of Cardiology/American Heart Association guidelines. Using electronic health record data from 2009 to 2015, researchers categorized KPSC members into 4 mutually exclusive statin benefit groups: those with atherosclerotic cardiovascular disease (ASCVD), high cholesterol, diabetes (ages 40 to 75 years), or 10-year ASCVD risk of 7.5% or more. Statin use increased for patients with 10-year ASCVD risk of 7.5% or more. High-intensity statin use also increased 142% and 54% for patients with high cholesterol and ASCVD, respectively. Room for improvement remains, however. About 135,000 eligible patients were not receiving statins in 2015.

Harrison TN et al. Cardiovasc Drugs Ther. 2018 Aug;32(4):397-404.



Developing innovative models of care for cancer survivors

Formative evaluation is critical before implementing new processes. Researchers used the Consolidated Framework for Implementation Research to assess the acceptability and feasibility of a model of cancer survivorship care delivered by primary care providers. The identified stakeholders within KPSC included oncologists, operational leaders, and patients. Oncologists and operational leaders felt the model provided solutions to issues of capacity and efficiency with the potential to improve quality, but some perceived negative consequences like "[loss of] the joy of medicine." Patients were less enthusiastic, but had suggestions for facilitating implementation. Keys to successful implementation include training and support of engaged PCPs and early introduction of a patient transition plan.

Hahn EE et al. Support Care Cancer. 2018 Aug 24.

Breast cancer outcomes in a racially and ethnically diverse cohort

Researchers followed 6,154 breast cancer survivors to examine how subsequent breast cancer outcomes (recurrence, metastases, death due to breast cancer) varied by race/ethnicity and biological subtype. With control for race/ethnicity, compared with women with luminal A tumors (reference), women with luminal B, HER2-enriched, and triple-negative tumors had higher risks for developing subsequent breast cancer. Higher stage, larger tumor size, positive lymph nodes, and no adjuvant endocrine or chemotherapy were associated with increased risk, rather than race/ethnicity. In this diverse cohort of women (62.4% non-Hispanic white, 13.2% Hispanic, 14.9% African American, and 9.5% Asian), disparities according to race/ethnicity disappeared in the multivariable analyses.

Hague R. Ethn Dis. 2018 Oct 18;28(4):565-574.

Inquiry. Investigation. Implementation.



CT use in the emergency department after implementation of the Canadian CT Head Rule

About 1 in 3 computed tomography scans performed for head injury may be avoidable. In this multicomponent intervention, researchers introduced a decision support tool for determining CT use. The study included 43,053 adult trauma patients seen in 13 KPSC emergency departments from January 2014 to December 2015. The intervention included clinical leadership endorsement of the Canadian CT Head Rule (CCHR), physician education, and a clinical decision support tool that prompted ED physicians to avoid CT imaging on the basis of the CCHR recommendations. After implementation of the intervention, 12 of 13 EDs reduced head CT use. The overall percentage reduction in CT use was 5.3%.

Sharp AL et al. Ann Emerg Med. 2018 Jan;71(1):54-63.e2.

Associations of overweight/obesity and socioeconomic status with hypertension prevalence across racial and ethnic groups

Researchers examined whether racial/ethnic disparities in the prevalence of diagnosed hypertension are partially explained by racial/ ethnic differences in weight and neighborhood socioeconomic status. Data were extracted from electronic health records for 4,060,585 adults with overweight or obesity across 10 health care systems from the Patient Outcomes Research to Advance Learning network. Some racial/ethnic groups had a greater chance of developing hypertension regardless of their weight or where they lived. Odds ratios for hypertension prevalence were greater for blacks, American Indians and Alaskan Natives, Asians, and Native Hawaiians and other Pacific Islanders compared with whites and lower for Hispanics in similar weight categories and neighborhood education levels.

Young DR et al. J Clin Hypertens (Greenwich). 2018 Mar;20(3):532-540.

For a full list of 2018 publications, please see the bibliography starting on page 58.

Research program overview

Investigators & Staff

65+



INVESTIGATORS

Includes 30 full-time staff scientists plus clinical trials program leaders and affiliated researchers (retired and active physicians), and trainees (post-doctoral research fellows and Epidemic Intelligence Service officers).

Hundreds of physicians participate in research as collaborators and clinical trials investigators.

275+

RESEARCH STAFF

Includes research project managers and research associates, clinical trials support staff, programmers, biostatisticians, and clinical informatics personnel.

80+

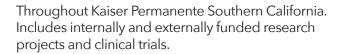
SUPPORT STAFF

Includes division administration, business office, operations, research IT, and communications staff.

Projects & Publications







400

ORIGINAL RESEARCH PAPERS PUBLISHED

In medical and scientific journals. Excludes case reports, editorials, and letters.

Southern California Research Environment



FACILITIES

15 medical centers

231 medical offices

LAB & PHARMACY SERVICES

31.8 million outpatient prescriptions filled47 million lab tests processed

PHYSICIANS & STAFF

7,400+ physicians

26,000+ nurses

75,000+ employees

SEX

51% Female **49%** Male

M.

Southern California Member Population

AGES

RACE/ETHNICITY

20 years and younger **25%**21 to 39 years **27%**

43% Hispanic or Latino **35%** White

40 to 64 years **33%**65+ years **15%**

12% Asian or Pacific Islander

9% Black or African American

1% Other races

MEMBERSHIP RETENTION RATES

88% remain with Kaiser Permanente more than 1 year

78% remain with Kaiser Permanente after 3 years

71% remain with Kaiser Permanente after 5 years

Financial overview

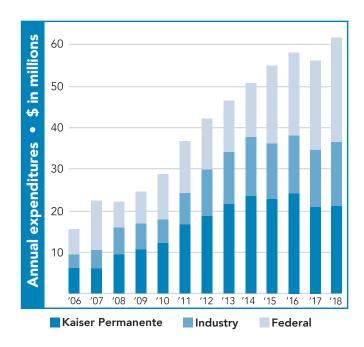
Funding for research at Kaiser Permanente Southern California has increased in the past decade to support a growing portfolio of innovative and clinically relevant research.

Total research expenditures

\$62.4 million in 2018

Federal grants: \$24.7 million Industry contracts: \$16.1 million

Kaiser Permanente provided the remaining funds. Internal funding sources included the Kaiser Permanente Community Benefit program, the Southern California Permanente Medical Group, the Sidney R. Garfield Memorial Fund, and the Center for Effectiveness & Safety Research.



2018 grants and awards

New grants and contracts awarded in 2018 will fund research at KPSC over a period of years.



2018 grant submissions

(new grants only, excludes clinical trials)

Grants submitted 144 Grants awarded 107

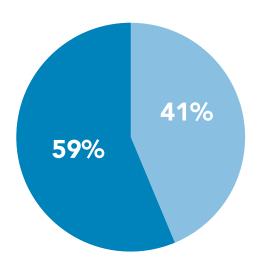


New grants and contracts (all years)

Direct costs \$13.1 million Indirect costs \$7.0 million **Total \$20.1 million**

Continued grants and contracts (all years)

Direct costs \$21.6 million Indirect costs \$8.8 million **Total** \$30.4 million



In 2018, Kaiser Permanente Southern California was the lead, or prime, institution for 59% of all the grants and contracts submitted, and was the subcontractor institution for the remaining 41%.

Projects funded by the Regional Research Committee

The Regional Research Committee awards funds from Kaiser Permanente's Direct to Community Benefit Investment fund for research projects led by clinicians and other health care professionals in Kaiser Permanente Southern California.

These projects address real-world clinical questions and have the potential to point to smarter ways to prevent and treat common health conditions. In 2018, the committee awarded funds to the following studies.

Emergency Medicine

Association of fascia iliaca block on decreasing opiate use for patients with hip fractures using a multidisciplinary management pathway.

Principal investigator: Kenneth Perry, MD, San Diego

Comparative analysis of drug adverse events between Warfarin and Dabigatran in the treatment of venous thromboembolism.

Principal investigator: Michael Young, DO, FACMT, FACEP, San Diego

Family Medicine

Associations between self-compassion and burnout among first-year residents in KPSC residency programs.

Principal investigator: Stephanie Chu, MD, Los Angeles



Surveillance of pancreatic cystic lesions beyond 5 years: Rates of malignancy, high-risk stigmata, and worrisome features.

Principal investigator: Brian Lim, MD, MS, MAS, San Diego

Assessment of a novel care pathway for Nonalcoholic Fatty Liver Disease (NAFLD).

Principal investigator: Heather Patton, MD, San Diego

Internal Medicine

Effects of bisphosphonates on fracture incidence in young adults.

Principal investigator: Manita Choudhary, MD, San Bernardino

Effect of CURB65 on outcomes and utilization of patients presenting to the emergency room with pneumonia.

Principal investigator: Daniel Kim, MD, MSCR, West Los Angeles

Reducing hospital-acquired pressure injuries by identifying high-risk patients using a new risk scoring system.

Principal investigator: David C. Shieh, MD, Orange County

Neurology

Adherence to mail-order medications and cardiovascular outcomes.

Principal investigator: William Neil, MD, San Diego

Inquiry. Investigation. Implementation.



Ob-Gyn

Long-term outcomes after placement of mid-urethral slings in patients with stress urinary incontinence.

Principal investigator: Alexander Berger, MD, MPH, San Diego

Etonogestrel Implant Mental Health Initiative.

Principal investigator: Ellen Lorange, DO, MPH, Los Angeles

Orthopedics

Opioid utilization beyond 90 days after primary total knee and total hip replacement: prospective evaluation of risk factors and psychological profile for extended use.

Principal investigator: Dhiren Sheth, MD, Orange County

Pharmacy

Eradication of hepatitis C virus: how does this effect glycemic control in type 2 diabetes?

Principal investigator: John Sie, PharmD, Downey

Psychiatry

Impact of length of stay on inpatient psychiatric readmissions within 30 days in patients with a primary substance-related disorder.

Principal investigator: Hilary Bennett, MD, San Bernardino

Regional Research Committee

Bechien U. Wu, MD, MPH

Chair, Regional Research Committee

Antelope Valley

Jonathan Truong, MD, Area Research Chair

Baldwin Park

Gregory B. Maletis, MD, Area Research Chair Gaurav Khanna, MD, Vice Area Research Chair

Downey

Eugene A. Chu, MD, Area Research Chair Rajeev Attam, MD, Vice Area Research Chair

Fontana/San Bernardino

Robert E. Sallis, MD, Area Research Chair Steve S. Lee, DO, Vice Area Research Chair

Los Angeles

John J. Sim, MD, Area Research Chair Gary W. Chien, MD, Vice Area Research Chair

Orange County

Patrick J. Van Winkle, MD, Area Research Chair Emily L. Whitcomb, MD, Vice Area Research Chair

Panorama City

Shireen Fatemi, MD, Area Research Chair

Riverside/Palm Springs

Rachid A. Elkoustaf, MD, Area Research Chair Vivienne S. Hau, MD, Vice Area Research Chair

San Diego

Shawn A. Menefee, MD, Area Research Chair Clifford J. Swap, MD, Vice Area Research Chair

South Bay

Bradley K. Ackerson, MD, Area Research Chair William W. Crawford, MD, Vice Area Research Chair

West Los Angeles/Kern County

Michael J. Fassett, MD, Area Research Chair Daniel T. Lang, MD, Vice Area Research Chair

Woodland Hills

Lester D. Thompson, MD, Area Research Chair Armen Aboulian, MD, Vice Area Research Chair

Department of Research & Evaluation

Stephanie Tovar, MS, Regional Research Committee Operations



Overview of our investigators and scientific divisions



"Our investigators come from many fields and partner with clinical collaborators from dozens of specialties and sub-specialties.

Through these partnerships, we've built a research program that makes a difference in real-world health care."

- Steven J. Jacobsen, MD, PhD | Senior Director of Research

Dr. Jacobsen is an epidemiologist with research interests in:

- Vaccine safety and effectiveness
- Chronic kidney disease
- Men's urologic health
- General chronic disease epidemiology

Our research program includes 5 scientific divisions as well as affiliated researchers (see page 52).

Epidemiologic Research (page 45)

Our epidemiologists apply rigorous research methods to address important health questions that have the potential to change clinical practice and health care delivery. The division's research portfolio spans the care continuum, from etiology and prevention to survivorship and quality of life. Current research areas include cancer, cardiovascular disease, diabetes, infectious disease, molecular epidemiology, orthopedics and bone health, perinatal health, pharmacoepidemiology, and vaccines.

Behavioral Research (page 47)

Our behavioral scientists focus on research that has the potential to reduce disease risk by identifying modifiable risk factors and encouraging health-promoting behaviors. Investigators have expertise in the following areas: adverse childhood experiences, cancer, chronic disease prevention and screening, diet and nutrition, mental health, obesity, physical activity, sedentary behavior, social determinants of health, and weight loss surgery and interventions.

Biostatistics Research (page 48)

Our collaborative biostatistician research scientists work closely with investigators in other scientific divisions, as well as physician researchers at medical centers across Kaiser Permanente Southern California. They provide expertise and guidance on study design, power and sample size calculations, data management, data analysis and interpretation, and statistical methodology.

Health Services Research & Implementation Science (page 49)

Investigators with the Division of Health Services Research & Implementation Science study how care is delivered, identify opportunities for care improvement, and implement new approaches for organizing and delivering health services. The division is home to the Care Improvement Research Team, which works closely with clinical and operational partners to identify, prioritize, and solve problems related to quality and affordability.

Clinical Trials Research (page 50)

The Division of Clinical Trials Research advances medical innovation by supporting evaluation of new drugs, therapies, and devices to prevent and treat health problems. Our physician investigators work with cooperative groups and industry sponsors to conduct clinical trials for investigational drugs, biologics, and devices. In addition, the division develops pragmatic trials that help answer questions about care delivery. See our clinical trials principal investigators by specialty on page 54.

Division of Epidemiologic Research

Research scientists



Kristi Reynolds, PhD, MPH
Director

- Cardiovascular risk factors, treatment, and outcomes
- Chronic disease epidemiology
- Pharmacoepidemiology
- Quality of care



Annette L. Adams, PhD, MPH

- Osteoporosis
- Bone health
- Injury epidemiology



Jaejin An, PhD

- Pharmacoepidemiology and comparative effectiveness research
- Medication adherence
- Cardiovascular risk factors, treatment, and outcomes



Chun Chao, PhD, MS

- HPV vaccine and cervical cancer prevention and screening
- Adolescent and young adult cancer and survivorship
- Etiology and prognosis of lymphoid malignancies
- Chemotherapy toxicity



Kim N. Danforth, ScD, MPH

- Cancer epidemiology and prevention
- Cancer care quality and survivorship
- Ambulatory care safety and quality
- Health services and implementation research



Darios Getahun, MD, PhD, MPH

- Women's and children's health
- Adverse pregnancy outcomes and health disparities
- Fetal origin of childhood diseases
- Risk for childhood asthma and neurodevelopmental diseases



Reina Haque, PhD, MPH

- Cancer epidemiology
- Cancer survivorship
- Pharmacoepidemiology



Rulin Hechter, MD, PhD

- HIV and infectious disease epidemiology and health services research
- Substance abuse treatment and patient engagement
- PrEP uptake and adherence
- Vaccine uptake, safety, and effectiveness



Jean M. Lawrence, ScD, MPH, MSSA

- Type 1 and type 2 diabetes in children and young adults
- Disparities in pregnancy complications and outcomes
- Perinatal mental health: diagnosis, treatment, and outcomes



Sara Yee Tartof, PhD, MPH

- Infectious diseases
- Antibiotic resistance
- Hospital infections

Division of Epidemiologic Research

continued



Hung Fu Tseng, PhD, MPH

- Vaccine safety and effectiveness
- Real-world evidence
- Infectious diseases





Gloria C. Chi*, PhD, MPH

- Chronic disease
- Environmental health
- Public health surveillance

* Dr. Chi left Kaiser Permanente in May 2018.

Post-doctoral research fellows



Tracy A. Becerra-Culqui, PhD, MPH, OTR/L

- Early childhood health
- Child mental health
- Exposures during pregnancy
- Vaccine safety in pregnant women and children



Lisa P. Oakley*, PhD, MPH

- Maternal and child health
- Infectious disease
- Social epidemiology
- Health equity
- * Dr. Oakley joined Kaiser Permanente in August 2018.



Katia Bruxvoort, PhD, MPH

- Infectious diseases
- Vaccine safety and effectiveness
- Antimicrobial resistance
- Medication adherence

Division of Behavioral Research



Deborah Rohm Young, PhD, MBA *Director*

- Physical activity interventions in community settings
- Primary prevention of overweight and obesity
- Racial and ethnic health disparities



Claudia Nau, PhD

- Social determinants and patient social needs
- Obesity and obesity-related diseases
- Stakeholder engagement
- Predictive modeling



Karen J. Coleman, PhD, MS

- Implementation research
- Mental health
- Health equity
- Weight loss surgery



Sonya Negriff, PhD

- Child maltreatment and early trauma
- Stress reactivity, HPA axis functioning
- Mental health and risk behaviors
- Timing of puberty



Corinna Koebnick, PhD, MSc

- Obesity and chronic disease epidemiology
- Health services research
- Primary care-based behavioral interventions
- Pediatric hypertension

Division of Biostatistics Research



Anny Hui Xiang, PhD

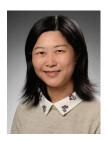
Director

- Biostatistics: design and analysis for clinical studies
- Diabetes, gestational diabetes, and obesity
- Pregnancy and women's and children's health
- Racial and ethnic disparities



Jiaxiao Shi, PhD

- Nonparametric methodology
- Study design and data analysis
- Pharmaceuticals and breast cancer risk
- Chronic kidney disease, hypertension, and cardiovascular risk



Lei Qian, PhD

- Statistical methods and study design
- Vaccine safety and effectiveness
- Cardiovascular risk factors, treatment, and outcomes



Margo A. Sidell, ScD, MSPH

- Biostatistics
- Behavioral health
- Preventive care
- Social determinants of health



Ernest Shen, PhD

- Biostatistics
- Structural equation modeling
- Robust statistics
- Health services research



Jeff Slezak, MS

- Predictive modeling
- Prostate cancer
- Vaccine safety
- Bladder cancer

Division of Health Services Research & Implementation Science



Michael K. Gould, MD, MS

Director

- Lung cancer screening, diagnosis, and staging
- Venous thromboembolism
- Comparative effectiveness and outcomes research
- Implementation science



Aniket A. Kawatkar, PhD, MS

- Health economics
- Patient preferences
- Comparative effectiveness



Stephen F. Derose*, MD, MSHS

- Sleep disorders and therapy
- Clinical epidemiology of chronic disease
- Health services research/ population health care
- * Dr. Derose left the department in February 2019.



Brian S. Mittman, PhD

- Implementation and improvement science
- Health care delivery science
- Complex interventions
- Learning health care systems



David Glass, PhD

- Global health
- End-of-life values and quality performance
- Primary care sustainability
- Episodes of care evaluation



Huong Q. Nguyen, PhD, RN

- Chronic disease self-management
- Care transitions
- Palliative care
- Implementation science



Erin E. Hahn, PhD, MPH

- Cancer care delivery research
- Cancer survivorship
- Dissemination and implementation science
- Delivery system science



Adam L. Sharp, MD, MS

- Health services research, implementation science
- Health system science, emergency medicine
- Social determinants of health

Division of Clinical Trials Research



William J. Towner, MD, FACP, FIDSA Regional Physician Director

- HIV clinical trials
- Delivery of HIV pre-exposure prophylaxis
- Infectious disease vaccine safety and effectiveness



Richard Green, MD

- Neuro-oncology
- Glioblastoma
- Central nervous system malignancies
- Primary CNS lymphoma
- Clinical trials



Gary Buchschacher Jr., MD, PhD

- Medical oncology
- Gastrointestinal cancers
- Prostate cancer
- Non-endocrine head and neck cancer
- Gene therapy



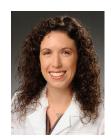
Nigel Gupta, MD

- Clinical cardiac electrophysiology
- Arrhythmia research and clinical trials
- Fellowship, teaching



Robert M. Cooper, MD

- Cancer clinical trials
- Cancer outcomes



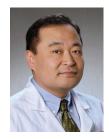
Kelley Hodgkiss-Harlow, MD

- Critical limb ischemia
- Carotid disease
- Vascular access



Lara Durna, MD

- Medical oncology
- Hematologic cancers
- Breast cancer



Han Koh, MD

- Lung cancer
- Benign hematology



Michael R. Girvigian, MD

- Benign and malignant tumors of the brain and spine
- Stereotactic radiotherapy procedures for precise targeting



Scott Lentz, MD

- Gynecologic oncology
- Hereditary cancer syndromes
- Surgical innovation



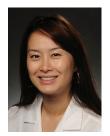
Shawn A. Menefee, MD

- Pelvic floor disorders
- Urinary incontinence
- Pelvic organ prolapse
- Urogynecologic surgery



Amandeep Sahota, MD

- Hepatitis B and C
- Fatty liver disease, nonalcoholic steatohepatitis (NASH)
- Liver transplant
- Biliary cholangitis



Helen Moon, MD

- Genitourinary cancers
- Prostate cancer
- Immunotherapy



Ricardo T. Spielberger, MD

- Hematopoietic cell transplantation
- Transplantation side effects
- Opportunistic infections



Jonathan A. Polikoff, MD

- Breast cancer
- General oncology
- General hematology



Devansu Tewari, MD, MBA

- Gynecologic oncology
- Health care economics, quality measurements
- Women's health cancer screening
- Surgical quality, timely access to cancer care

Affiliated researchers

Affiliated investigators



Somjot S. Brar, MD, MPH

- Cardiovascular disease and risk factors
- Medical devices and interventional procedures
- Clinical trials and meta-analysis



David A. Sacks, MD

- Diagnosis of gestational diabetes
- Diabetes during and after pregnancy
- Technology and diabetes in pregnancy



Donald S. Fong, MD, MPH

- Retinal diseases
- Diabetic retinopathy
- Macular degeneration
- Ocular safety of systemic medications



Michael Schatz, MD, MS

- Asthma and pregnancy
- Asthma patient-reported outcomes
- Asthma population management
- Asthma quality measures



Annette M. Langer-Gould, MD, PhD, MS

- Multiple sclerosis susceptibility and prognosis
- Comparative effectiveness of treatments for MS



Robert S. Zeiger, MD, PhD

- Asthma, chronic obstructive pulmonary disease, cough
- Immunotherapy outcomes research
- Asthma clinical trials





Sirichai Chayasirisobhon, MD

- Mechanism of refractory epilepsy
- Vagus nerve stimulation for epilepsy
- Clinical trials of new antiepileptic drugs



Adjunct investigators



Dennis Black, PhD

- Osteoporosis
- Fracture risk
- Clinical trials



R. James Dudl, MD

- Diabetes
- Cardiovascular disease prevention
- Glucose control



Paul Muntner, MD

- Hypertension
- Lipids
- Cardiovascular disease
- Renal disease
- Epidemiology methods



George F. Longstreth, MD

- Functional bowel disorders
- Diverticulitis



Lauren Wallner, PhD, MPH

- Delivery and quality of adult cancer care
- Multilevel interventions to improve cancer care
- Cancer health services research
- Survivorship care

Clinician investigators



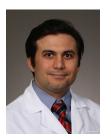
Raymond Chen, MD, DPhil

- Cardiac surgery
- Telemedicine
- Hospital readmissions



Navdeep Sangha, MD

- Vascular neurology
- Ischemic stroke and intracerebral hemorrhage
- Hospital systems of care



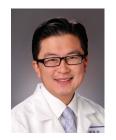
Bobeck S. Modjtahedi, MD

- Prediction analysis
- Population-based studies and care delivery
- Clinical outcomes analysis
- Telemedicine and e-health



John J. Sim, MD

- Hypertension and kidney diseases
- Resistant hypertension, glomerulonephropathies
- Patient safety
- Chronic kidney disease epidemiology and comparative outcomes



Casey K. Ng, MD

- Urology
- Hematuria
- Kidney stones
- Renal cysts
- Kidney cancer



Emily L. Whitcomb, MD, MAS

- Pelvic floor disorders
- Quality metric development in urogynecology



Chunyuan Qiu, MD, MS

- Anesthesiology
- Pain medicine
- Perioperative medicine



Bechien U. Wu, MD, MPH

- Pancreatology
- Gastrointestinal cancer



Joan J. Ryoo, MD, MSHS

- Radiation oncology
- Cancer care outcomes



Hui Xue, MD, MMSc

- Dialysis outcomes
- Chronic kidney disease
- Renal transplantation
- Bone mineral metabolism

Clinical trials principal investigators by specialty

Allergy

Michael Schatz, MD, San Diego Medical Center Robert Zeiger, MD, PhD, San Diego Medical Center

Cardiology

Vicken Aharonian, MD, Los Angeles Medical Center Somjot Brar, MD, MPH, Los Angeles Medical Center Jeffrey Cavendish, MD, San Diego Medical Center Lei Feng, MD, Los Angeles Medical Center Nigel Gupta, MD, Los Angeles Medical Center William Keen, MD, San Diego Medical Center Morris Salem, MD, Los Angeles Medical Center

Dermatology

Kim Chong, MD, Los Angeles Medical Center

Endocrinology

Patricia Wu, MD, San Diego Carmel Valley Medical Offices

Gastroenterology

Kevin Kao, MD, Downey Medical Center

Bechien Wu, MD, MPH, Los Angeles Medical Center

Hepatology

Anders Nyberg, MD, PhD, San Diego Medical Center Lisa Nyberg, MD, MPH, San Diego Garfield Specialty Care Center

Heather Patton, MD, San Diego Medical Center Amandeep Sahota, MD, Los Angeles Medical Center

Infectious Diseases

Jim Nomura, MD, Los Angeles Medical Center
William Towner, MD, Los Angeles Medical Center
Jonathan Truong, MD, Antelope Valley

Metabolic/Genetics

Divya Vats, MD, Los Angeles Medical Center

Nephrology

Victoria Kumar, MD, Los Angeles Medical Center

Neurology

Zahra Ajani, MD, Los Angeles Medical Center

Sirichai Chayasirisobhon, MD, Anaheim Kraemer Medical Offices

Annette Langer-Gould, MD, PhD, MS, Los Angeles Medical Center

William Neil, MD, San Diego Medical Center

Navdeep Sangha, MD, Los Angeles Medical Center

Inquiry. Investigation. Implementation.

Hematology Oncology

Gary Buchschacher, MD, Los Angeles Medical Center
Jian Chen, MD, San Diego Medical Center
Lara Durna, MD, San Diego Medical Center
Han Koh, MD, Downey Medical Center
Helen Moon, MD, Riverside Medical Center
Jonathan Polikoff, MD, San Diego Medical Center

Gynecologic Oncology

Scott Lentz, MD, Los Angeles Medical Center

Devansu Tewari, MD, MBA, Irvine Medical Center, Alton/Sand Canyon Medical Offices

Neuro-Oncology

Richard Green, MD, Los Angeles Medical Center

Radiation Oncology

Michael Girvigian, MD, Los Angeles Medical Center

Surgical Oncology

Vikram Attaluri, MD, Los Angeles Medical Center Anna Leung, MD, Los Angeles Medical Center Elisabeth McLemore, MD, Los Angeles Medical Center

Ophthalmology

Nicole Benitah, MD, West Los Angeles Medical Center

Vivienne S. Hau, MD, Riverside Medical Center

Orthopedics

Gregory Maletis, MD, Baldwin Park Medical Center Anshuman Singh, MD, San Diego Medical Center

Pediatric Oncology

Robert Cooper, MD, Los Angeles Medical Center

Pediatric Orthopedics

Jeffrey Kessler, MD, Los Angeles Medical Center Jennifer Weiss, MD, Los Angeles Medical Center

Pediatric Pulmonology

Muhammad Saeed, MD, Los Angeles Medical Center

Pediatric Surgery

Donald Shaul, MD, Los Angeles Medical Center

Clinical trials principal investigators by specialty

continued

Pulmonology

Aung Htoo, MD, Kern County

Kenneth Wei, MD, Los Angeles Medical Center

Rheumatology

Steve S. Lee, DO, Fontana Medical Center

Sleep Medicine

Dennis Hwang, MD, Fontana Medical Center

Urology

Polina Reyblat, MD, Los Angeles Medical Center

Christopher Tenggardjaja, MD, Los Angeles Medical Center

Eugene Rhee, MD, Otay Mesa Medical Offices

Urology/Reproductive/Gynecological Disorders

Emily Whitcomb, MD, Irvine Medical Center

John Nguyen, MD, Downey Medical Center

Shawn Menefee, MD, San Diego Pt. Loma Medical Offices

Jasmine Tan-Kim, MD, San Diego Pt. Loma Medical Offices

Keisha Dyer, MD, San Diego Pt. Loma Medical Offices

Karl Luber, MD, San Diego Medical Center

Vascular Surgery

Catherine Chang, MD, San Diego Medical Center

Linda Chun, MD, Los Angeles Medical Center

Kelley Hodgkiss-Harlow, MD, San Diego Medical Center

Elena Rakhlin, MD, San Diego Medical Center



Publications

2018 Publications

Scientists, clinicians, and other health professionals from Kaiser Permanente Southern California authored original research papers on a wide range of topics in 2018, from allergy and asthma to women's health. Kaiser Permanente Southern California authors are noted in **bold**.

Allergy and Asthma

Chipps BE, Bacharier LB, Farrar JR, Jackson DJ, Murphy KR, Phipatanakul W, Szefler SJ, Teague WG, **Zeiger RS.** The pediatric asthma yardstick: practical recommendations for a sustained step-up in asthma therapy for children with inadequately controlled asthma. *Ann Allergy Asthma Immunol.* 2018 Jun;120(6):559-579.e11.

Chipps BE, Haselkom T, Paknis B, Ortiz B, Bleecker ER, Kianifard F, Foreman AJ, Szefier SJ, **Zeiger RS**. Epidemiology and Natural History of Asthma: Outcomes and Treatment Regimens Study Group. More than a decade follow-up in patients with severe or difficult-to-treat asthma: the Epidemiology and Natural History of Asthma: Outcomes and Treatment Regimens (TENOR) II. *J Allergy Clin Immunol*. 2018 May; 141(5):1590-1597.e9.

Lang JE, Fitzpatrick AM, Mauger DT, Guilbert TW, Jackson DJ, Lemanske RF Jr., Martinez FD, Strunk RC, **Zeiger RS**, Phipatanakul W, Bacharier LB, Pongracic JA, Holguin F, Cabana MD, Covar RA, Raissy HH, Tang M, Szefler SJ; National Institutes of Health/National Heart, Lung and Blood Institute AsthmaNet. Overweight/obesity status in preschool children associates with worse asthma but robust improvement on inhaled corticosteroids. *J Allergy Clin Immunol.* 2018 Apr;141(4):1459-1467.e2.

Lee-Sarwar K, Hauser R, Calafat AM, Ye X, O'Connor GT, Sandel M, Bacharier LB, **Zeiger RS**, Laranjo N, Gold DR, Weiss ST, Litonjua AA, Savage JH. Prenatal and early-life triclosan and paraben exposure and allergic outcomes. *J Allergy Clin Immunol*. 2018 Jul;142(1):269-278.e15.

Lee-Sarwar K, Kelly RS, Lasky-Su J, Moody DB, Mola AR, Cheng TY, Comstock LE, **Zeiger RS**, O'Connor GT, Sandel MT, Bacharier LB, Beigelman A, Laranjo N, Gold DR, Bunyavanich S, Savage JH, Weiss ST, Brennan PJ, Litonjua AA. Intestinal microbial-derived sphingolipids are inversely associated with childhood food allergy. *J Allergy Clin Immunol*. 2018 Jul;142(1):335-338.e9.

Liu M, **Patel JP**, Huang E, Ong PY. History of eczema is associated with more severe hospital course in children hospitalized for asthma. *Ann Allergy Asthma Immunol*. 2018 Dec;121(6):735-736.

LoVerde D, Iweala OI, **Eginli A,** Krishnaswamy G. Anaphylaxis. *Chest.* 2018 Feb;153(2):528-543. PMCID: PMC6026262

Macy E, Vyles D. Who needs penicillin allergy testing? *Ann Allergy Asthma Immunol.* 2018 Nov;121(5): 523-529.

Mirzakhani H, Carey VJ, McElrath TF, Laranjo N, O'Connor G, Iverson RE, Lee-Parritz A, Strunk RC, Bacharier LB, Macones GA, **Zeiger RS, Schatz M,** Hollis BW, Litonjua AA, Weiss ST. The association of maternal asthma and early pregnancy vitamin D with risk of preeclampsia: an observation from Vitamin D Antenatal Asthma Reduction Trial (VDAART). *J Allergy Clin Immunol Pract*. 2018 Mar-Apr;6(2):600-608.e2.

Namazy JA, **Schatz M.** Management of asthma during pregnancy: optimizing outcomes and minimizing risk. *Semin Respir Crit Care Med.* 2018 Feb;39(1):29-35.

Savage JH, Lee-Sarwar KA, Sordillo J, Bunyavanich S, Zhou Y, O'Connor G, Sandel M, Bacharier LB, **Zeiger R,** Sodergren E, Weinstock GM, Gold DR, Weiss ST, Litonjua AA. A prospective microbiomewide association study of food sensitization and food allergy in early childhood. *Allergy*. 2018 Jan;73(1):145-152.

Bone Health and Orthopedics

Adams AL, Fischer H, Kopperdahl DL, Lee DC, Black DM, Bouxsein ML, Fatemi S, Khosla S, Orwoll ES, Siris ES, Keaveny TM. Osteoporosis and hip fracture risk from routine computed tomography scans: the Fracture, Osteoporosis, and CT Utilization Study (FOCUS). *J Bone Miner Res.* 2018 Jul;33(7): 1291-1301.

Bazarov I, **Kim J**, Richey JM, Dickinson JD, Hamilton GA. Minimally invasive plate osteosynthesis for treatment of ankle fractures in high-risk patients. *J Foot Ankle Surg*. 2018 May-Jun;57(3):494-500.

Bini SA, Darbinian JA, Brox WT, **Khatod M.** Risk factors for reaching the post-operative transfusion trigger in a community primary total knee arthroplasty population. *J Arthroplasty*. 2018 Mar;33(3):711-717.

Conaway WK, Hennrikus WL, **Ravanbakhsh S**, Winthrop Z, Mahajan J. Surgical treatment of displaced pediatric lateral condyle fractures of the humerus by the posterior approach. *J Pediatr Orthop B*. 2018 Mar;27(2):128-133.

Corrales R, Mediavilla I, Margalet E, Aramberri M, Murillo-González JA, **Matsuda D.** Endoscopic lesser trochanter resection with refixation of the iliopsoas tendon for treatment of ischiofemoral impingement. *Arthrosc Tech.* 2018 Apr;7(4):e321-e325. PMCID: PMC5981835

Daubs MD, **Brara HS**, Raaen LB, Chen PG, Anderson AT, Asch SM, Nuckols TK. How does sagittal imbalance affect the appropriateness of surgical indications and selection of procedure in the treatment of degenerative scoliosis? Findings from the RAND/UCLA Appropriate Use Criteria study. *Spine J.* 2018 May; 18(5):900-911.

Deon Kidd V, **De Claro AMO.** Preparing for autistic patients in orthopaedic surgery: tips for a successful health-care interaction. *J Bone Joint Surg Am.* 2018 Oct;100(20):e132.

Desai V, Chan PH, Prentice HA, Zohman GL, Diekmann GR, Maletis GB, Fasig BH, Diaz D, Chung E, Qiu C. Is anesthesia technique associated with a higher risk of mortality or complications within 90 days of surgery for geriatric patients with hip fractures? Clin Orthop Relat Res. 2018 Jun;476(6):1178-1188.

Dowsey MM, Choong PFM, **Paxton EW**, Spelman T, **Namba RS**, **Inacio MCS**. Body mass index is associated with all-cause mortality after THA and TKA. *Clin Orthop Relat Res*. 2018 Jun;476(6):1139-1148.

Gibbons MC, Fisch KM, Pichika R, Cheng T, Engler AJ, Schenk S, Lane JG, **Singh A**, Ward SR. Heterogeneous muscle gene expression patterns in patients with massive rotator cuff tears. *PLoS ONE*. 2018;13(1):e0190439. PMCID: PMC5749784

Kelly MP, Prentice HA, Wang W, Fasig BH, Sheth DS, Paxton EW. Reasons for ninety-day emergency visits and readmissions after elective total joint arthroplasty: results from a US integrated healthcare system. *J Arthroplasty*. 2018 Jul;33(7):2075-2081.

Khatod M. Kaiser Permanente: joint arthroplasty in an integrated capitated care delivery model. *J Arthroplasty*. 2018 Jun;33(6):1649-1651.

Mirzayan R, Acevedo DC, Sodl JF, Yian EH, Navarro RA, Anakwenze O, Singh A. Operative management of acute triceps tendon ruptures: review of 184 cases. *Am J Sports Med.* 2018 May;46(6):1451-1458.

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Additional photo captions

Cover images

Top: Dr. Susan Wang, Dr. Jason Ngo, and Dr. Andre Cipta

Bottom right: Dr. Kristi Reynolds, Teresa Harrison Bottom left: Dr. Michael Fassett, Kneena Wolff

Page 5: Dr. Michael Fassett, Kneena Wolff

Page 31: Eva Lustigova, Raul Calderon

Page 32

Left: Jonathan Arguello, Rossy Perez

Right: Dr. Karen Coleman

Page 33

Left: Dr. Brian Mittman

Right: Dr. Reina Haque, Chantal Avila, and Jeff Slezak

Page 34: Dr. Hung Fu Tseng, Dr. Bradley Ackerson

Page 36: Rong Wei, Teresa Harrison, and Dr. Deborah Ling Grant

Page 37: Felica Jones, Dr. Claudia Nau, and Ericka Wright

Page 40: Dennis Edora, Dr. Jonathan Truong

Page 41: Anthony Aquino, Dr. Craig Chang

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Vision

The Department of Research & Evaluation has an integral role in the success of Kaiser Permanente Southern California by conducting high-quality, innovative translational research that benefits the health of its members and the communities from which they come.

Mission

The mission of the Department of Research & Evaluation is to initiate and conduct high-quality, public-sector health services, epidemiologic, behavioral, and clinical research that has a demonstrable positive impact on the health and well-being of Kaiser Permanente Southern California members and the general population.

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