DEPARTMENT OF **RESEARCH & EVALUATION**

2017 Annual Report

Kaiser Permanente
Research

Using real-world evidence

Transforming care for better health

KAISER PERMANENTE®

Contents

MESSAGE FROM THE SENIOR DIRECTOR

Dr. Steven Jacobsen

Randomized controlled trials have long been considered the gold standard in medical research. These studies help us learn about the efficacy of an intervention. That is to say: Can a new therapy work to successfully treat a health condition?

While important, randomized controlled studies have some potential limitations. Participation criteria often exclude people based on their age or health status. Trials have standardized protocols, while real-world clinical practice is much more varied. Many trials also lack ethnic and racial diversity.

Real-world evidence, on the other hand, helps us understand if a new treatment or approach works in real life. Information gleaned from routine clinical practice, for example, can shed light on the safety and effectiveness of treatments when they are used in patients who are older or who have underlying health conditions. Our vaccine research is a great example of this kind of real-world evidence (page 10).

Kaiser Permanente Southern California is an ideal setting for real-world studies. Our robust electronic health records system and our integrated care delivery allow researchers to track all care delivered to our large and diverse member population. We can also track outcomes of care. The Department of Research & Evaluation's skilled biostatisticians and programmers gather and analyze an abundance of these real-world data to help us answer real-world questions (page 20).

Being embedded within a large health care organization gives us great advantage. Our clinician partners point out questions that come right out of their own practice. And we can use tools within our system to propagate findings that have the potential to improve practice.

Researchers and clinicians work side by side to identify care gaps and develop and implement improvement strategies. Together, they have disseminated better practices for measuring pediatric blood pressure (page 12), inspired a new outreach program to improve pediatric lead screening (page 6), and developed decision-support tools (page 22).

Even randomized controlled trials take on a different aspect in our real-world setting, with our diverse member population. Our cancer clinical trials program is a great example (page 16).

I hope you enjoy reading the stories in our 2017 Annual Report. They give you a glimpse at our growing portfolio of real-world research. We are fortunate to have a talented and dedicated group of researchers and staff, as well as the support and insights of many clinical and operational partners. I thank them all for their many contributions to our research program.

Steven J. Jacobsen, MD, PhD

Senior Director of Research

Research Highlights

Lead levels in children

Making it easier for parents to get their kids screened

When Gloria Chi, PhD, MPH, arrived at the Department of Research & Evaluation for a 2-year assignment as an Epidemic Intelligence Service officer from the Centers for Disease Control and Prevention, she had a keen interest in researching how the environment affects our health.

Before the end of those 2 years, the newly minted PhD from the University of Washington would spark a change in the way Kaiser Permanente Southern California manages the testing for lead exposure—a major environmental hazard—in children.

"What started off as a very simple, straightforward question became a complex project addressing an important need," said Steven Jacobsen, MD, PhD, senior director of research for KPSC. "Dr. Chi was able to determine where the need for lead testing was the greatest, and that has provided insights we're using to reach out to parents of our pediatric members who are at greatest risk."

Dr. Gloria Chi meets with her mentors Dr. Jean Lawrence and Dr. Sara Tartof.

Dr. Chi brought CDC presence to R&E

In 2016, Dr. Chi became the first EIS officer assigned to KPSC's Department of Research & Evaluation, and the only one at that time at a nongovernmental agency.

EIS officers investigate public health threats in the United States and around the world. Most spend the 2-year training program at CDC headquarters in Atlanta while others are assigned to state and local health departments throughout the country or to other federal agencies.

Dr. Chi was interested in the intersection of public health and substantive real-world data. Her dissertation focused on the effects of air pollution on cardiovascular health.

The EIS position with R&E's Division of Epidemiologic Research was a perfect fit. Her primary supervisors and mentors were Jean M. Lawrence, ScD, MPH, MSSA, and Sara Tartof, PhD, MPH, both of whom had been EIS officers themselves.

When her assignment ended in May 2018, Dr. Chi had studied topics ranging from heart attack trends to diabetes surveillance to coccidioidomycosis antimicrobial treatment patterns. She investigated an outbreak of bacterial infections among ventilator-dependent patients at a non–Kaiser Permanente facility, the type of investigation that is typical for EIS officers. She also had written 5 manuscripts and given 8 presentations.

And she studied lead testing.

"Dr. Chi was able to determine where the need for lead testing was the greatest, and that has provided insights we're using to reach out to parents of our pediatric members who are at greatest risk."

— Steven Jacobsen, MD, PhD

Opposite: Francisco Meza, the son of Dr. Sara Tartof of the Department of Research & Evaluation, enjoys the pool on a warm day. To keep children healthy, the CDC recommends lead screening for children at 12 and 24 months of age.

Dr. Robert Riewerts at work in his office at Baldwin Park Medical Center.

Dr. Tim Ho and Royann Timmins, RN, discuss the new outreach program.

Lead exposure can harm children

"Coming to the EIS fellowship," Dr. Chi said, "I was wondering if I could do additional work in environmental epidemiology and explore what kinds of measurements we have of our KPSC members' exposures to environmental pollutants."

After a discussion with leadership, she pursued lead testing.

Today, at least 4 million U.S. households have children who are being exposed to high levels of lead, according to the CDC. For infants and young children, high blood lead levels can decrease their ability to learn, and even low levels of lead can be dangerous. In both young and old, lead can damage kidneys, blood, and the nervous system, and at very high levels can progress to coma, convulsions, or death.

Common sources of lead exposure for children include breathing contaminated dust and soils around older homes that contain lead-based paint or eating paint chips that contain lead.

Lead exposure often has no obvious symptoms, so it frequently goes unrecognized. Among KPSC members, it is generally caught only through blood tests, said Robert James Riewerts, MD, the regional chief of pediatrics for the Southern California Permanente Medical Group.

Lead exposure was in the news and on her mind

Dr. Chi said looking at lead levels in children makes sense right now because of increased awareness following news of elevated lead levels found in the water in Flint, Michigan. She also noted that there have been concerns in Southern California due to a now-closed battery recycling plant in Vernon, 5 miles south of downtown Los Angeles.

The state of California requires all children covered by Medi-Cal (Medicaid) to be tested for lead, but the rate of testing statewide is low. Recent reports indicate that only 25% of children who receive their medical insurance coverage through Medi-Cal are routinely tested for lead exposure.

Dr. Chi, in collaboration with R&E biostatisticians Lie Chen, DrPH, MSPH, and Jeff Slezak, MS, dug into the data available at KPSC with 3 objectives: to determine the trends of

elevated blood lead levels from 2008 to 2015; to determine the associations between sociodemographic characteristics and lead testing and elevated blood lead levels; and to identify where geographic clusters of elevated blood lead levels among children might exist.

She found that:

- Children covered by Medi-Cal were more likely to receive blood lead tests than children who received their KPSC insurance through other sources.
- Children living in neighborhoods with older homes and greater socioeconomic disadvantage had higher rates of testing than children living in newer and more affluent neighborhoods.
- The proportion of children tested that had high elevated blood lead levels is decreasing.
- There were "hot spots" of higher lead levels in areas of Los Angeles and San Diego counties.

Dr. Chi also found that children living in poorer neighborhoods with older homes had risks of elevated blood lead levels that were more than twice as high as children without either of these risk factors.

Overcoming barriers to lead testing

Dr. Jacobsen recognized that the results could be translated directly into practice, and connected Dr. Chi with clinical and operational leadership at KPSC. They saw her work would enable them to create new tools to improve health.

"Her findings show there's no question that parts of our population in Southern California are more likely to be at risk for lead poisoning than others, and therefore would benefit from being tested," said Dr. Riewerts.

Currently, physicians and nurses receive alerts on the Kaiser Permanente HealthConnect® system when a patient is due for lead testing. But there are often barriers to getting the test, which requires a blood draw, said Tim Ho, MD, MPH, the regional assistant medical director, Quality and Complete Care for SCPMG.

Often when parents bring their children into the medical clinic it is because they are sick, he said.

"So, a physician may recommend that the child get tested for lead during that office visit. But the parent often wants to wait until the child is well, and then gets busy and forgets to return," Dr. Ho explained.

To address the situation, physicians ordered blood tests for children who were on Medi-Cal but had not yet been tested. Then, in summer 2018, letters began to go out to parents of those children explaining the reason for the test. So now, all parents have to do is bring their child to a Kaiser Permanente laboratory.

"We wanted to remove as many barriers as possible," Dr. Ho said.

That outreach campaign began in June 2018.

Dr. Chi provided a great example of collaboration

"Gloria was a trailblazer," Dr. Tartof said. "Her dedication, experience analyzing medical record data, and the presentation of her findings at the EIS conference and elsewhere demonstrated to the CDC that KPSC is an excellent site for an EIS officer."

The success resulted in a second match between an incoming EIS officer and KPSC. The CDC assigned R&E a new EIS officer, Lisa Oakley, PhD, MPH, who will be with us from August 2018 to June 2020.

Once a doctor signs an order for a blood test for a child, Complete Care sends a letter to his or her parent.

Vaccine effectiveness

Informing decision-makers with real-world evidence

Dr. Katia Bruxvoort, Dr. Hung Fu Tseng, and Lina Sy take a break outside of the offices in Pasadena.

Real-world evidence could be a critical component in creating federal policies and regulations about vaccines, but it hasn't always been considered. Scientists at Kaiser Permanente Southern California's Department of Research & Evaluation provide an example that shows the important role of real-world evidence in regulatory decision-making.

Real-world evidence is information obtained from real-life clinical settings. It provides insight into the potential risks and benefits of medical treatments. One way R&E researchers collect real-world evidence is through the electronic health records of our large and diverse patient population.

In this study, researchers examined the effectiveness of giving the live shingles vaccine at the same time as the pneumonia vaccine. Their aim was not only to confirm previous research, but also to show the importance of real-world evidence in light of legislation that requires the U.S. Food and Drug Administration to consider real-world evidence to support regulatory decision-making.

We asked the study authors Katia Bruxvoort, PhD, MPH; Lina S. Sy, MPH; Yi Luo, PhD, MS; and senior author Hung Fu Tseng, PhD, MPH, about the research they conducted, its findings and implications.

Why is this topic of real-world evidence for regulatory decision-making important now?

Evidence generated from randomized controlled trials has always been the gold standard when vaccines and drugs are being considered for licensure. The results of these trials are usually included in the product label.

Recently, there has been a greater interest in trying to use non–clinical trial data, such as real-world evidence, to expand or revise the label for new indications, new populations, new dosing modifications, potential drug interactions, or new safety concerns. Some drivers come from the fact that more and better real-world data are being collected from a variety of sources, including electronic health records.

Most important, recent legislation in the 21st Century Cures Act and the 6th Prescription Drug User Fee Act (PDUFA VI) calls for the FDA to utilize real-world data and to evaluate the use of real-world evidence in informing regulatory decisions.

What are some potential benefits for regulatory decision-making?

Real-world evidence from carefully designed and analyzed studies can fill in the evidence gaps that are not typically addressed with traditional randomized controlled trials. For example, real-world evidence can reflect the actual use of products in patients with multiple illnesses or rare diseases, who are often not included in clinical trials. It also can be used to evaluate long-term outcomes, which are often not assessed in clinical trials of modest duration. Real-world evidence may significantly reduce the time and cost of developing evidence for regulatory decisions.

Can you give us some background about your study?

A previous randomized controlled trial looked at people who received the shingles (live zoster) vaccine and the pneumonia (pneumococcal polysaccharide) vaccine at the same time and compared them to people receiving the vaccines 4 weeks apart. That study found patients who received the vaccines at the same time had lower levels of antibodies against the virus that causes shingles. Based on that, the FDA required changes to the vaccine labels to state that these vaccines should be given at least 4 weeks apart. However, studies have shown that antibodies are not a good marker of vaccine protection against shingles.

Can you give us some details about your study?

We conducted a study using almost 10 years of electronic health records from over 35,000 KPSC members who received the live shingles vaccine, and followed them electronically to see if they developed shingles. We found there was no difference in the risk of shingles between people who received the live shingles vaccine and pneumonia vaccine at the same time and those who received the vaccines at least a month apart.

Why does it matter whether people get the shots at the same time?

If we tell people to get their shots a month apart, fewer might get the vaccine because some may not return for the other shot. Allowing people to get both shots at the same time removes barriers for patients and helps to improve the vaccination rate.

Why is this study a test case for regulatory decision-making?

Historically, the FDA relied on randomized controlled trial data for regulatory decision-making. This research is part of changing that paradigm. Using real-world evidence gives regulators a better idea of how vaccines will be used in actual clinical practice, rather than an ideal randomized controlled trial setting. This research, published in the *American Journal of Epidemiology* in early 2018, highlights how these findings from our integrated system can potentially be used to revise product labels and remove barriers to concomitant vaccination.

How can real-world evidence continue to shape regulatory decision-making for vaccines?

Real-world evidence will be even more critical in the evaluation of the safety and effectiveness of the new shingles vaccine (zoster vaccine recombinant, adjuvanated, or Shingrix). Randomized controlled trials show the new vaccine to be safe and effective, but limited data are available about its long-term outcomes, effects on high-risk populations, and potential interactions with other vaccines. The new vaccine is being used in the elderly, so it will be critical to monitor its safety and the effect of giving it at the same time as other vaccines. It also will be important to monitor compliance with the 2-dose schedule. We plan to study both the safety and the effectiveness of the new vaccine to address these evidence gaps.

The knowledge gained from the research conducted within Kaiser Permanente's integrated health care system can inform not just the care we give to our members, but can also shape national regulations and policies around immunization practices.

A patient receives a shingles vaccine at Los Angeles Medical Center.

Hypertension in children

Asking questions that improve real-world care for kids

Remarkable research findings are often the result of exceptional questions.

At Kaiser Permanente Southern California, those questions that improve practice can come from just about anywhere, including leadership, clinicians, and researchers.

Sometimes they even come from the inability to answer an initial question.

Five years ago, Corinna Koebnick, PhD, MSc, a research scientist with the Department of Research & Evaluation, wanted to research children's repeated blood pressure readings within Kaiser Permanente. But she couldn't. The data for repeated blood pressures weren't available.

She didn't stop there. She asked, "Why?"

"The most recent recommendations were that clinicians should determine a child's blood pressure by averaging 2 or more repeated blood pressure readings," Dr. Koebnick said. "But I couldn't do that when I looked at the real-world data. Most of the time the blood pressure reading wasn't repeated in the medical record."

Dr. Corinna Koebnick and her physician collaborator Dr. Beatriz Kuizon work to make sure that hypertension isn't missed in pediatric patients.

Researchers work with clinicians to find answers

During her search to discover why so few high blood pressures were repeated, Dr. Koebnick met with Robert James Riewerts, MD, the regional chief of pediatrics for the Southern California Permanente Medical Group, and Beatriz Kuizon, MD, a pediatric nephrologist who had initiated some efforts to add a reminder to nurses and clinicians to repeat elevated blood pressure readings. Together they worked on educating physicians.

Then, they drafted 2 new studies to assess the success of their efforts. The studies showed that the rate of taking second or third blood pressure readings among children at KPSC improved by over 40%. The first of 2 papers published in 2017.

They are now working to take this to the next step—to make sure every child with an initial high blood pressure reading is re-checked.

Hypertension is rare—but can be serious—for children

High blood pressure can progress to sustained hypertension and lead to stiff arteries, even at an early age. Hypertension is a chronic condition (mainly affecting adults) in which elevated blood pressure forces the heart to work harder than normal to circulate blood throughout the body. It is a major contributing risk factor for heart failure, heart attack, stroke, and chronic kidney disease and accounts for an estimated 18% of cardiovascular deaths in the United States.

Opposite: Marisa Ortiz walks with her sons Jacob Nunez (left) and Justin Nishimoto (right) after a visit to their pediatrician at the Baldwin Park Medical Center, where both boys had their blood pressure checked. Research shows it is important for clinicians to re-check a child's blood pressure reading if it appears high the first time to catch cases of childhood hypertension.

A nurse takes blood pressure readings of pediatric patients at Baldwin Park Medical Center.

Dr. Koebnick's research showed that 2.3% of youth ages 3 to 17 years at KPSC had sustained high blood pressure over time. Children with elevated blood pressure are 2 to 3 times more likely to develop hypertension as adults.

But children's blood pressure can be variable, and being nervous at the doctor's office sometimes can cause them to have elevated blood pressure readings even when they aren't hypertensive.

Pediatricians see increases in hypertension

Dr. Kuizon has been seeing increasing numbers of children with hypertension in her practice at the Los Angeles Medical Center.

"Children with hypertension are usually asymptomatic but may already have target organ damage," she said, "and they're more likely to develop hypertension in adulthood. So early identification and intervention may reduce long-term consequences from hypertension."

But often, because false readings are so prevalent and high blood pressure among children is so rare, actual cases of hypertension weren't being caught.

Building a case for re-checking blood pressure

The first study that Dr. Koebnick led showed that nearly one-quarter of children and teens who had their blood pressure screened at a primary care appointment had a reading in the hypertensive range, but less than half of those high readings could be confirmed when the blood pressure was repeated.

Dr. Koebnick gave presentations to physician groups to increase awareness about the need for follow-up when blood pressure is still high after being repeated. Dr. Kuizon championed her work and spread the word beyond those meetings.

In 2015, a best practice alert was added to the Kaiser Permanente HealthConnect electronic health record system to remind clinicians and office staff to take that second, and maybe third, reading when a child's blood pressure is high.

Best practice alerts change practice

A second study looked at whether the alert changed practice. It did. After implementation of the alert, the odds of repeating a blood pressure test were significantly higher in all areas of KPSC.

The study also showed that children with obesity have higher odds of having their blood pressure tests repeated than children who are not obese. Younger children are less likely to have blood pressure tests repeated than older children.

Dr. Riewerts noted, "We were concerned that we weren't appropriately picking up children who truly had hypertension, but that can be like looking for a needle in a haystack. This helped us find those needles."

In the end, real-world data showed the gap between the guidelines and day-to-day practice, and children with high blood pressure will be more quickly identified in the future.

"It was really, really great work," Dr. Riewerts said.

Untying the knot of weight, poverty, and race in hypertension

Dr. Claudia Nau and Dr. Deborah Rohm Young

Real-world evidence, such as that at Kaiser Permanente Southern California, can give insight into real-world issues. For example, how does a person's race or ethnicity affect their chance of developing hypertension if where they live and what they weigh aren't factors?

"We know that higher rates of hypertension are associated with lower economic status, obesity, and some races/ethnicities," said Deborah Rohm Young, PhD, MBA, director of the Division of Behavioral Research for the Department of Research & Evaluation. "And so, it made us think, maybe this association is really not related to race—maybe it's a factor of either obesity status or poorer socioeconomic status."

Dr. Young led the team that analyzed the electronic health records of 4,060,585 overweight or obese adults from the Patient Outcomes Research to Advance Learning network. PORTAL includes Kaiser Permanente in Southern California, Northern California, Colorado, the District of Columbia, Georgia, Hawaii, Maryland, Oregon, Virginia, and Washington, as well as HealthPartners in Minnesota and Wisconsin, and Denver Health in Colorado.

From this sample of geographically, ethnically, and economically diverse patients, the researchers found that people who are African-American, American Indian/native Alaskan, Asian, or native Hawaiian and other Pacific Islanders have a significantly greater chance of developing hypertension than people who are white or Hispanic—even if they are in the same weight category or live in neighborhoods with similar education levels. The study was published in 2017 in *The Journal of Clinical Hypertension*.

Claudia Nau, PhD, an R&E research scientist and one of the co-authors of the study, focuses on the social determinants of health and prevention of obesity and chronic disease. She noted that "race, socioeconomic status, and obesity are closely intertwined. Better understanding of the interplay of these factors can help target and tailor interventions."

Hypertension is one of the risk factors for cardiovascular disease and stroke that many people can change by losing weight, eating better, exercising more, and taking medication.

"Your weight status and where you live are key factors for developing hypertension," Dr. Young said. "But there are other factors within race and ethnicity that also increase your risk."

Cancer clinical trials

Translating real-world experience into new models of patient care

Kaiser Permanente Southern California clinical trials investigators are involved in more than 400 clinical trials. They're focused on finding the most effective therapies with the fewest side effects. Patients who participate in clinical trials help us determine if new and novel treatments are better than current practice.

Han Koh, MD, is the director of the Cancer Clinical Trials Access Program and works with cancer clinical trial investigators across KPSC. The program currently has 41 active trials, 17 of which were added in 2017. We asked Dr. Koh to explain the importance of real-world evidence collected through clinical trials at KPSC and its benefits to patients.

Dr. Farah Brasfield and Dr. Richard Green exchange ideas at a Cancer Clinical Trials Access Program meeting.

Tell us about cancer clinical trial research at KPSC.

When we talk about research, we often talk about basic research, like looking at the cell cultures of animals. Clinical trials are different. We're working with an actual human being who is being treated with chemotherapy or other cancer treatment and documenting their outcomes.

Unlike research hospitals, Kaiser Permanente conducts clinical trials in a community setting. The population of clinical trials at research hospitals typically reflects people who are referred to those trials, which may not represent the broader population. Our setting is more representative of the community.

Why are clinical trials important?

The U.S. Food and Drug Administration won't approve any treatment unless we can show them that the new treatment works better and has fewer side effects than the previous treatment. So, a clinical trial is the last step before a new treatment becomes available to the public.

For someone with an advanced stage of cancer, having access to state-of-the-art treatment that may ultimately prove effective is a great benefit.

How do KPSC clinical trials help improve treatment?

We've got a large and diverse patient population to draw upon for our clinical trials. In 2017, KPSC was recognized as a top U.S. recruiter in a half-dozen clinical trials of treatments for illnesses including cancers of the lung, breast, and prostate.

Also, we work with cooperative groups such as the Southwest Oncology Group, which includes hundreds of medical center sites, to pool our study results and draw conclusions. This allows us to include many more patients and to see results of clinical trials sooner. As one of the largest health care organizations in the country, we make a significant contribution to those efforts.

The results from these clinical trials are translated directly into new models of patient treatment.

Opposite: Dr. Han Koh, who leads the Cancer Clinical Trials Access Program, discusses the wide range of clinical trials conducted at Kaiser Permanente Southern California with a colleague in his office at Downey Medical Center.

At Riverside Medical Center, Dr. Helen Moon demonstrates how to prepare an oncologic viral therapy.

Dr. Devansu Tewari listens intently to Dr. Ricardo Spielberger.

Can you give us an example?

The standard treatment following colon cancer surgery used to be 6 months of chemotherapy. We worked to help determine whether 3 months of chemotherapy could avoid some of the side effects and improve quality of life better than 6 months of chemotherapy. The results were recently published, and it turns out that 3 months is equally effective. Because of that work, the standard treatment duration for chemotherapy after colon cancer surgery has been changed to 3 months. That benefit can be translated to colon cancer patients across the United States and around the world.

Can you tell us about precision medicine and clinical trials?

Precision medicine trials look at what therapies to use for a specific mutation that may be driving a patient's cancer. Through genomic sequencing—a method of determining the genetic makeup of cancer cells—we can often determine if a patient's tumor has one or more mutations that we can treat with targeted therapies.

It is a major shift in the way we treat cancer.

In the old days, regardless of the type of cancer, we gave the same combination of chemo or chemo/radiation to everybody. But we are smarter now.

We can sometimes use gene sequencing that can highlight gene changes that may be causing disease. Then we can classify cancer into different types and customize the best treatment for some subgroups of cancer. When we can use a specific treatment for a cancer, we can often increase the effectiveness and minimize the side effects.

Also, precision medicine can address a host of personal characteristics in additional to gene mutations, such as social situation and family history.

What are some current precision medicine clinical trials at KPSC?

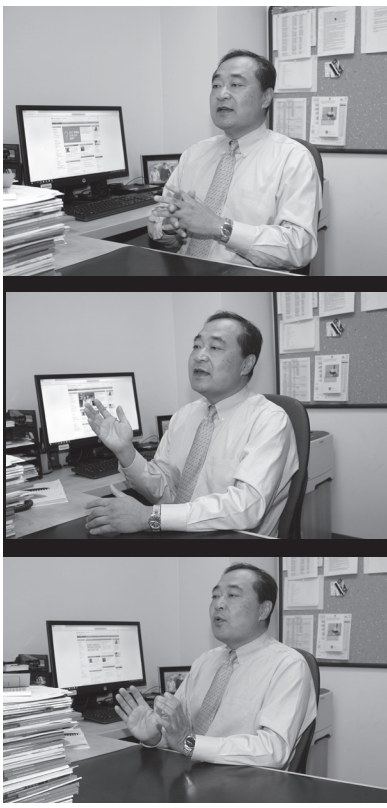
Two of the clinical trials we are currently working on are the ALCHEMIST and MATCH clinical trials, which are both precision medicine trials.

ALCHEMIST is a group of randomized clinical trials for patients with early-stage non-small cell lung cancer whose tumors have been surgically removed. The trials test to see if adding targeted therapy based on the patients' tumor genetics will help prevent the cancer from returning.

The MATCH trials are for patients with advanced solid tumors, lymphomas, or myeloma or other cancers where there is no standard treatment. They are aimed at determining whether treating cancer based on specific genetic changes is effective.

"In the old days, regardless of the type of cancer, we gave the same combination of chemo or chemo/radiation to everybody. But we are smarter now."

— Han Koh, MD



Dr. Han Koh discusses the importance of clinical trials in a real-world environment.

What are you finding with these targeted treatments?

There is a tremendous amount of potential, and a few agents are already approved. Potentially 100 times more treatments will become available on the market within the next 5 to 6 years.

These clinical trials are very exciting. But they're also very humbling because we learn ways cancer cells can fool us. Sometimes the target therapy we think is going to work turns out not to be effective. Cancer cells can develop ways to circumvent our targeted therapy, developing other pathways where the cancer cells can continue to grow rapidly.

Eventually we hope to use all this knowledge to develop truly effective treatments for each subtype of cancer.

What is the next frontier for fighting cancer?

We are currently doing research in immunotherapy, which can help the immune system attack the cancer directly or stimulate the immune system in a more general way to fight the cancer.

The way I explain it to patients is that we are teaching the cancer patient's own immune system to recognize the cancer cells and then destroy them.

Immunotherapy has the potential to have fewer side effects and work better than chemotherapy in some cancers. The challenge is that we haven't identified a way to find out whose cancer is going to respond to immunotherapy better than the others. So those are the areas in which we are doing active research.

What is the future of KPSC clinical trials?

Chemotherapy, radiation therapy, or a combination of both have been the traditional ways of attacking cancer. In the last 10 or 15 years, we became interested in precision therapy and harnessing our knowledge of genes to fight cancer. In the past 5 years or so, a new way—immunotherapy—has developed.

The future is probably a combination of all of those. And clinical trials will be an essential tool in determining the right combination for patients at Kaiser Permanente and others with cancer throughout the country and world.

Biostatisticians at R&E

Using numbers to create connections between research and practice

Dr. Jiaxiao Shi and Dr. Bechien Wu discuss scientific posters at Los Angeles Medical Center's Research Days.

Dr. Heidi Fischer teaches other biostatisticians and programmers how to use a statistical methodology.

Growing up in Ventura, California, Heidi Fischer, PhD, MS, was always good at numbers. But, the self-proclaimed "math nerd" had no idea that would translate into a job she found meaningful.

It wasn't until she was out of college and working in economics that she heard about biostatisticians who used their mathematical expertise to improve people's health. She left the world of GDP trends for Kaiser Permanente Southern California's Department of Research & Evaluation.

In 2017, Dr. Fischer applied a novel statistical model to determine how bariatric surgery influences the relationship between weight and other health measures, such as kidney function, blood pressure, and diabetes.

"I'm not just looking at numbers," said Dr. Fischer. "I can actually connect these numbers to real-world clinical practice, and that is cool."

The desire to find solutions fuels biostatics team

The challenge of turning real-world evidence into real-world health solutions fuels R&E's biostatistics team of 26 programmers, 24 biostatisticians, 9 database developers, and 3 natural language processing specialists (staff counts are as of December 2017).

Each project begins with discussion of a medical or care issue with R&E researchers or medical center clinicians. The biostatisticians then help design studies to address the pressing questions, collect the available data and clean them to remove inaccurate information, and then analyze the data. Last, they interpret that data.

"Each step is important to create accurate, interpretable, and meaningful information," said Anny Xiang, PhD, MS, director of R&E's Division of Biostatistics Research. "And through all this, of course, we collaborate with our scientific partners."

Overcoming the issues of real-world data

R&E biostatisticians don't have the luxury of working with the simple data of traditional academic research, where research participants are recruited or assigned to an experimental group or a control group with a strict control of treatment options and data collection.

R&E biostatisticians need to work on data collected from populations in a real-world situation. In the clinical trial setting, patients are assigned to different treatment groups and the treatments are delivered in a tightly controlled environment. By contrast, in the real world, a patient and physician together choose the treatment they believe might have the best outcome.

Biostatisticians must find mathematical ways to reduce the chances of bias. Also, they work with data entered by hundreds of different people across the region and from multiple sources, which can result in missing data and miscoding, which can be another challenge.

"We specialize in working with large and real-world data that come from the electronic health records," Dr. Xiang said. "As a result, we create answers that address questions from a real-world perspective and are directly applicable to the general population."

Dr. Lei Qian and other biostatisticians at R&E work together to turn real-world evidence into real-world health solutions.

Steven Jacobsen, MD, PhD, senior director of research for KPSC, noted that R&E's biostatisticians excel at continually finding new and better statistical models and algorithms to work with the real-world data.

"Whether it's taking methods used in different disciplines and applying them in our setting, or keeping tabs on the newest methodologic research, they figure out ultimately what works and what doesn't. Then, we can help clinicians make decisions about best treatments," he said.

Physicians work directly with biostatisticians

Bechien Wu, MD, MPH, is chair of the Regional Research Committee, which provides funding to clinical investigators for their projects. He is also one of the investigators who has worked directly with biostatisticians. He and other clinicians develop research questions based on the needs they see within their own practices.

"I bring my medical background and knowledge and the biostatisticians bring their knowledge of data analysis and data structure. Together we can formulate a rigorous scientific study that benefits our patients, the organization, and the scientific community in general," Dr. Wu said.

One of Dr. Wu's studies that emerged was about the management of pancreatic cysts. The collaborators found that it doesn't make sense to aggressively monitor these cysts in patients who are dealing with multiple illnesses. The study prompted a new clinical guideline a few years ago, which was updated in 2017.

Jiaxiao Shi, PhD, who leads the 10-member team that works with medical center investigators, called the collaborations a "true partnership."

Biostatisticians consider complex possibilities

Dr. Fischer, the former economist, works primarily with researchers within R&E. In 2017, she was awarded funding for a new project by the Division of Biostatistics Research. She created a multivariable model to look at how bariatric surgery affected kidney function over time. The model is often used in statistics work but not often in health care, and it hadn't been previously applied to data at R&E.

The model allowed her to see new possibilities based on the real-world data collected.

"We have records for people before and after surgeries, so if we have a question, we can actually answer it here," she said. "There are so many possibilities and ways to look at things. It's incredibly exciting to me as a biostatistician to have all these options."

Decision-support tools

Creating tools to reduce risk and improve care

Ten or 20 years ago, when physicians had a question about a condition, they might have pulled a dusty textbook off the shelf and searched the index. Or grabbed the informational index cards from the pocket of their white doctors' coats. That's what Ben Broder, MD, PhD, now regional assistant medical director of Quality and Clinical Analysis, did in the early 2000s before Kaiser Permanente Southern California had electronic health records in Kaiser Permanente HealthConnect.

Today, physicians have electronic health records and electronic alerts and assessment tools to help them find the answers they are looking for—much more quickly and efficiently. They also can determine a patient's risk of developing a health condition with these new tools.

Dr. Ben Broder has been part of the evolution of physician decision-support tools from index cards to electronic assessments embedded in patient records.

Decision-support tools make complex calculations

"Decision-support tools on the computer allow us to do much more complicated calculations to determine risk for heart disease and cardiovascular disease," Dr. Broder said. "It's not new; it's just a different way of managing it. And you probably could never have enough index cards to stuff in your pocket now."

These tools are often created collaboratively by researchers and physicians who discover the need in real-world practice, find the answers using real-world data, and then create simple-to-use models to prompt the best care possible for real-world patients.

Decision-support tools can be simple

"At its simplest, a decision-support tool flashes a reminder in the patient's electronic health record about drug allergies or the need for a test," said Michael K. Gould, MD, MS, the director of the Division of Health Services Research & Implementation Science for the Department of Research & Evaluation.

More complex decision-support tools help physicians predict patient outcomes and give them information on how to reduce risk, Dr. Gould said.

It takes time to develop decision support

Dr. Gould has been working on a decision-support tool to prevent venous thrombo-embolism for about 4 years. VTE is a blood clot that starts in a vein, often in the deep veins of the leg. If the thrombus breaks off it can flow into the lungs, which can be fatal.

Physicians try to prevent clots with blood-thinning medications, compression stockings, and devices placed around the legs that intermittently fill with air to compress the legs.

The model extracts information from the patient's electronic health record and asks the physician a few simple questions to then predict the risk that the patient will develop a VTE while in the hospital or shortly after discharge.

Opposite: Dr. Luis Moreta-Sainz and Dr. Michael Gould collaborate to create decision-support tools that help physicians determine which treatments are the most likely to help patients.

Dr. Adam Sharp applies research to solve problems in real-world emergency medicine. He practices at Los Angeles Medical Center.

Decision-support tools often begin with research

Dr. Gould began with a study that looked at VTE risk factors, patients' preventive care, and who developed blood clots. Then, he assembled a cohort of 250,000 patients who were admitted to a KPSC hospital between 2010 and 2014.

"We found that a quarter of the VTEs occurred during the hospital stay, and half of them within a month of discharge. The rest occurred 1 to 3 months after discharge," he said.

Armed with this information, Dr. Gould developed the model in conjunction with a regional quality group and a collaborative of clinicians from each of KPSC's 15 medical centers. The work was directed by a regional steering committee.

Clinicians are becoming more comfortable using risk models

"I think people are increasingly more comfortable using quantitative risk models to help make these decisions," Dr. Gould said. "And with electronic health records, we have the ability to provide information at the point of care to allow physicians and patients to make better decisions."

One of the biggest challenges can be to convince busy physicians to use the tools once they are created.

"We want to create tools so the busy clinician doesn't have to leave their workspace, go to an external website, or do any additional work such as checking boxes or providing information," Dr. Gould said.

Testing is key to successful implementation

Akshay Manek, MD, chief of hospital medicine at the Panorama City Medical Center, is one of several people who helps to avoid those pitfalls by testing the tools before they go into routine use.

"In the first iteration of this model, I had to put the patient's information in a second time and that's a no-no," he said, "so it went back."

The next step was to use it during a patient workup. The model popped out a risk score with recommendations for care.

"You see the score and it does influence you," Dr. Manek said. "If you don't have something warning you, 'this is a high-risk patient,' you may decide not to add the prophylactic medicine. But if an alert is telling you the patient is at high risk, you know to be concerned."

The tool is now available to clinicians throughout the Southern California Region.

Tools prove valuable in the emergency department

Adam L. Sharp, MD, MS, an emergency medicine physician and researcher, has introduced tools to reduce antibiotic prescribing for sinusitis and to reduce unnecessary head CT scanning for patients with minor trauma.

In 2014, Dr. Sharp began working on a decision-support tool to determine which patients who came to the emergency department with chest pain—and who had not had a heart attack—should be admitted to the hospital and which could go home.

"I had been to many hospitals and found it's addressed in such a subjective way by each physician that I realized we should use a more evidence-based standard, at least as our default," Dr. Sharp said, noting, "there are always exceptions to any clinical decision rule."

Dr. Akshay Manek, who practices at Panorama City Medical Center, tests the decision-support tools to work out issues before they go into routine use by physicians.

After getting agreement with the emergency medicine chiefs, Dr. Sharp researched the literature and found several different standards. He chose a pre-existing tool called HEART that was developed in the Netherlands and validated in Europe because it rated patients on a simple 1-to-10 scale. HEART is an acronym for history, EKG, age, risk factors (such as weight, smoking, family history), and initial troponin, which is an indicator of heart muscle damage.

In spring 2016, HEART was launched in KP HealthConnect to help direct physician management of chest pain.

Decision-support tool assesses risk

With these tools, physicians quickly get information on whether the patient had low, moderate, or high risk of a heart attack, and see recommendations based on the risk.

"For example, if a patient is low risk, there's no reason to necessarily be hospitalized or observed in the hospital," Dr. Sharp said. "The patient would follow up with their primary care doctor."

Patients in the high-risk group would be the ones most likely to benefit from hospitalization and cardiology consultation, he added.

In the first year of implementation, the number of low-risk patients with chest pain being admitted or stress tested dropped from 12% to 5%.

Some tools aimed at patients

Sometimes tools are created for patients, not physicians. One example is when the team who developed the KPSC online patient portal, Online Personal Action Plan, created an order button for colorectal cancer screening kits. If patients pressed the button, they received a kit they could do at home. Those who didn't push the button still received the kit as part of the regional mail-based strategy.

Wahid Wakach and Dr. Erin Hahn collaborate on a new online patient tool.

The team asked R&E research scientist Erin Hahn, PhD, MPH, to determine whether pressing the button made a difference in the colon cancer screening completion rates.

"The team members are innovators," Dr. Hahn said. "I thought it was a cool idea. Would people be more likely to complete the test if they ordered it, like a buying a product online, than if they passively received it at home?"

Pushing a button increased completion rates

"When we looked at the very raw data, people who pushed the button completed their kit faster. And they had a much higher completion rate," she said. "Around 30% or 40% typically complete the test sent passively, versus 80% of those who pushed the button.

Dr. Hahn did deeper analysis to determine whether pushing the button compelled people to complete their screening or if those people were just more likely to complete the test anyway. She found that introducing the button resulted in several thousand members completing a kit who had not completed it the year before.

She is looking forward to broadening the idea to ask whether this type of commitment could make a difference in other areas such as overdue lab orders and mammograms.

Key to success: fulfilling an unmet need

Dr. Gould said that the most important factor in the success of decision-support tools, whether it be for the clinician or the patient, is whether it fills an unmet need in the real world of health care.

"It takes a lot of work and effort to develop these tools," he said. "But it is worth pursuing if we can have a positive impact on practice and patients."

Accomplishments & Milestones

Selected grants and contracts

Our scientists and clinician researchers lead studies that have the potential to change practice well beyond the walls of our organization. Many studies receive external funding from federal agencies and nongovernmental organizations. The following is a small sample of projects funded in 2017 that will address important public health questions.

SB27 and antimicrobial resistance

Antimicrobial resistance is an increasingly serious threat to public health. It greatly increases the risk of infection with organ transplantation, chemotherapy, diabetes management, and major surgery and increases the cost of health care. Overuse of antibiotics is a known contributor to antimicrobial resistance.

About 70% of antibiotics sold in the United States are for use in livestock. To address antimicrobial resistance and ensure judicious use of antibiotics, California Senate Bill 27 (SB27; effective January 1, 2018) bans all nontherapeutic uses of antimicrobials in livestock and requires a veterinarian's prescription for therapeutic indications.

What will we do?

In this study, Kaiser Permanente Southern California researchers will examine the real-world implications of SB27 on human health. Using whole-genome sequencing and expansive electronic health record data, the researchers will examine changes in the antimicrobial resistance of *Escherichia coli* isolated from retail chicken meat and from human cases of urinary tract infection before and after implementation of SB27.

E. coli is an ideal pathogen for evaluating changes in antimicrobial resistance because the resistance profiles of *E. coli* circulating in livestock and humans overlap, and extraintestinal pathogenic *E. coli* is a leading cause of human urinary tract infection.

What difference will this study make?

These findings will add to the evidence base connecting food systems and urinary tract infection. SB27 provides an excellent opportunity for a natural experiment to study whether an upstream, first-of-its-kind statewide policy to reduce antibiotic use in livestock has a downstream, beneficial impact on human health.

Principal investigator: Sara Tartof, PhD, MPH

Funder: National Institute of Allergy and Infectious Diseases

Antimicrobial stewardship programs

Up to 50% of antibiotics prescribed in U.S. acute care hospitals are either unnecessary or inappropriate. Overprescribing and misprescribing contribute to the growing challenges posed by antibiotic-resistant bacteria. The Centers for Disease Control and Prevention estimates that at least 2 million illnesses and 23,000 deaths are caused by antibiotic-resistant bacteria each year.

Antibiotic stewardship programs, which consist of coordinated interventions to reduce unnecessary use of antimicrobials in inpatient settings, are underway to preserve the effectiveness of the antibiotics that we do have. However, comprehensive studies to assess whether these programs are effective are limited.

What will we do?

KPSC was one of the first organizations to implement a standardized, regional inpatient antibiotic stewardship program in several hospitals. The program was introduced at various times across hospitals in the region.

This study will harness KPSC's ideal triad of sufficient infrastructure, time, and data to evaluate changes in the consumption of drugs targeted by antibiotic stewardship programs.

Researchers will also study changes in inpatient infection rates with clinically important drug-resistant organisms. To learn more about how and why these changes occur, researchers will analyze the rate of change of infection rates and covariates such as program staffing and other hospital-level characteristics.

What difference will this study make?

The recent federal recommendations for antibiotic stewardship programs herald a large expansion of such programs worldwide. This timely study will provide an evidence base to support or refute these recommendations.

Principal investigator: Sara Tartof, PhD, MPH

Funder: NIAID

KPSC co-investigators: Kalvin Yu, MD; Gunter Rieg, MD; Frances Wong, PharmD, MEd, MPH, BCPS

Dr. Sara Tartof, Dr. Jean Lawrence, and Dr. Gloria Chi

Antibiotics and body weight in children

Between 40% and 80% of children with excess weight or obesity will become adults with excess weight or obesity. Antibiotic use may disrupt the microbial composition of the gut, and findings from animal studies have suggested that disruption of the microbiome is associated with obesity.

Exposure to antibiotics starts in utero. Antibiotics account for 80% of the medications prescribed during pregnancy. Antibiotic use during pregnancy alters the vaginal microbiome before birth and alters the early microbial colonization of the newborn.

This disruption in the child's gut microbiome may reverse after the exposure to antibiotics ends, or it may result in long-lasting effects such as increased body weight. The evidence is inconsistent, and previous studies of the association between prenatal exposure to antibiotics and body weight in children were limited.

What will we do?

Using the KPSC electronic health records for more than 195,000 children, investigators will study the association between prenatal exposure to antibiotics and body weight in children.

With the highly detailed clinical records in the electronic health record system, the investigators will be able to address the limitations of previous studies by identifying potential mediators, such as low birth weight, and potential confounders, such as maternal health conditions, that previous studies could not.

The study will also examine how breastfeeding modifies the association between prenatal exposure to antibiotics and growth, a confounder that was not addressed previously.

What difference will this study make?

We will learn more about the risks associated with antibiotic use during pregnancy. Knowing more about the mediators that influence risk, like low birth weight, delivery mode, and childhood infections, can inform evidence-based clinical guidelines.

Principal investigator: Corinna Koebnick, PhD, MSc

Funder: CDC

KPSC co-investigators: Darios Getahun, MD, PhD, MPH; Sara Tartof, PhD, MPH; Margo Sidell, ScD, MSPH; Anny Xiang, PhD, MS

Dr. Katia Bruxvoort and Dr. Hung Fu Tseng

Screening mammography decisions

Conflicting guidelines about screening mammography for women ages 40 to 49 years at low-to-average risk for breast cancer have led to confusion among both women and their clinicians about screening. Also of concern, a recent national survey found that fewer than 50% of women discussed initiating or continuing screening mammography with their physician.

Decision aids could provide critical information about screening mammography to women in this age group, especially those at low-to-average risk.

Breast Screening Decisions is a web-based decision aid that was created to help women decide when to start and how often to have routine screening mammograms. When it was used at an academic medical center, Breast Screening Decisions supported informed decision-making and facilitated discussion between women and their clinicians.

What will we do?

This project aims to evaluate the effectiveness of Breast Screening Decisions in a community health care setting. Researchers will use data from KPSC's comprehensive electronic health records to invite a sample of women ages 40 to 49 years who have low-to-average risk for breast cancer to participate in the study. Given the results in the academic medical center setting, the researchers anticipate that use of the decision aid will improve informed decision-making and knowledge about breast cancer screening among the women studied.

What difference will this study make?

This study provides an opportunity to determine the real-world effectiveness and feasibility of broad implementation of the Breast Screening Decisions aid. Expanding the use of decision aids can support more women in making informed, individualized decisions about screening mammography.

Principal investigator: Erin E. Hahn, PhD, MPH

Funder: National Cancer Oncology Research Program/ National Institutes of Health

KPSC co-investigators: Steven L. Farr, MD; Yung-Mee Park, MD; Corrina H. Wood, MD; Michael K. Gould, MD, MS

Access to home-based palliative care

Palliative care services are needed at many stages to alleviate suffering and improve quality of life for patients and family caregivers. When patients have symptoms or physical limitations that make clinic-based models of palliative care unsuitable, home-based palliative care (HBPC) may be the best option.

Evidence from research findings is needed to determine how to best refine these services to meet the rapidly growing demand for them, while preserving effectiveness and affordability.

What will we do?

Kaiser Permanente has nearly 10 years of experience providing HBPC. In this comparative effectiveness study, researchers will study 2 models of care.

In one model (Usual HBPC), members of the interdisciplinary palliative care team will continue to make routine home visits at the start of care. This includes physicians, who will complete their visit within 14 days of the nurse's initial visit. In another, potentially more efficient, technology-facilitated model (Enhanced HBPC), physicians will participate simultaneously via video to discuss and review the care plan with the patient, caregiver, and nurse during the start of home care visits.

The project team hypothesizes that the Enhanced HBPC model that provides timely remote access to the physician will be as effective as the Usual HBPC model in improving the outcomes that matter most to patients and caregivers.

What difference will this study make?

This study addresses one of the persistent barriers to expanded HBPC: insufficient numbers of specialty palliative care–trained physicians. If successful, the technology-facilitated model can allow for expansion of affordable care to the growing number of older patients and their caregivers who are in desperate need of palliative services in their homes.

Principal investigator: Huong Q. Nguyen, PhD, RN

Funder: Patient-Centered Outcomes Research Institute

KPSC co-investigators: Susan E. Wang, MD; Brian S. Mittman, PhD; Ernest Shen, PhD

Vaccine Safety Datalink

The Vaccine Safety Datalink is a collaborative project begun in 1990 between the Immunization Safety Office of the CDC and 8 health care organizations. KPSC has fully participated as a study site for the past 10 years.

Vaccines are generally regarded as safe and effective. However, serious adverse events after immunization can occur. The data collected through the VSD allow researchers to study adverse events after immunization.

What will we do?

Through the funding provided by this renewal, KPSC will continue to collaborate with investigators from the CDC and other health care organizations to monitor and carry out studies of adverse events after immunization.

Activities will include monitoring and evaluating the safety of newly licensed vaccines, evaluating the safety of new recommendations for existing vaccines, assessing vaccine safety in high-risk populations, evaluating methodologies for vaccine safety assessment, and responding to vaccine safety concerns through ad-hoc analyses and studies.

KPSC recently led a pilot study of natural language processing in the VSD. This novel use of NLP could improve the efficiency and consistency of extracting information from clinical notes.

What difference will this study make?

This most recent award extends funding for the VSD partnership through 2022. The vaccines and events studied in the upcoming years will be driven by public concern, new recommendations, and new products. The daily work put into strengthening the VSD infrastructure allows investigators to react quickly to these drivers of vaccine safety research.

Principal investigator: Steven J. Jacobsen, MD, PhD

Funder: CDC

KPSC co-investigators: Hung Fu Tseng, PhD, MPH; Darios Getahun, MD, PhD, MPH; Rulin Hechter, MD, PhD; Sara Tartof, PhD, MPH; Lei Qian, PhD; Bruno Lewin, MD; Chengyi Zheng, PhD, MS

Selected findings

Dr. Jiaxiao Shi, Dr. Reina Haque, Joanie Chung, and Chantal Avila

In 2017, 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.

Research documents Kaiser Permanente's successful approach to safer opioid prescribing

Kaiser Permanente Southern California launched a comprehensive initiative to transform the way that chronic pain is viewed and treated in our system. It included addressing the use of opioid painkillers. Clinical data demonstrated that chronic pain was not effectively managed with high-dose opioids and that these drugs had significant risks associated with them. Research published in 2017 describes the elements of KPSC's intervention, outlines the implementation process, reports on short- and intermediate-term outcomes, and discusses how this initiative could be adopted by other health care systems.

Dr. Michael Kanter

The various efforts to reduce opioid prescribing included prescribing and dispensing policies, monitoring and follow-up processes, and clinical coordination with electronic health records. Reductions were observed in all the tracked outcomes, including a 30% reduction in prescribing opioids in high doses.

Losby JL et al. J Eval Clin Pract. 2017 Dec;23(6): 1173-1179.

Testosterone replacement therapy associated with lowered risk of heart attacks

Researchers found that men who used testosterone replacement therapy to treat symptoms of androgen deficiency had a 33% lower risk of cardiovascular events such as heart attacks and stroke compared to those who did not receive any hormone therapy. The study evaluated 44,335 male patients at Kaiser Permanente medical centers in Northern and Southern California who had been diagnosed with androgen deficiency between January 1, 1999, and December 31, 2010. Of these, 8,808 men were treated with testosterone replacement therapy,

while 35,527 were never dispensed testosterone. The men were followed for a median of 3.4 years and researchers found that of the men who never received testosterone, 10.2% had a heart attack or stroke during the study period. Of those men who received testosterone replacement therapy, 8.2% had a heart attack or stroke during the study period.

Cheetham TC et al. JAMA Intern Med. 2017;177(4):491-499.

People with COPD who have social support are more active

People with chronic obstructive pulmonary disease are more likely to be active and to participate in pulmonary rehabilitation if they live with others and have a caregiver. Participants in the study were recruited from 2 Veterans Health Administration hospitals and 2 academic medical centers and had moderate-to-severe COPD. They had an average age of 68 years. Researchers found that participants who lived with others took 903 more steps each day. Those who had a spouse or partner caregiver were 11 times more likely to participate in pulmonary rehabilitation.

Chen Z et al. Ann Am Thorac Soc. 2017;14(9): 1419-1427.

Androgen deprivation and early-stage prostate cancer

Men with localized prostate cancer who received androgen deprivation therapy were at higher risk of heart failure than men who did not receive this therapy. Researchers followed a cohort of 7,637 men diagnosed with localized prostate cancer between 1998 and 2008 who were initially under active surveillance. Nearly 30% were treated with androgen deprivation therapy. Researchers followed them for up to 12 years after diagnosis. Among the key findings from this research: For men with localized prostate cancer, androgen deprivation therapy was associated with an 81% increased risk of heart failure in men without pre-existing cardiovascular disease.

Haque R et al. Br J Cancer. 2017;117(8):1233-1240.

Reducing antibiotic prescriptions through physician education and intervention

Physicians at KPSC reduced the odds of prescribing an antibiotic for sinusitis by 22% using computer alerts to inform doctors when antibiotics may not be the best course of treatment. During an 8-month period (September 2014 through April 2015), the researchers studied nearly 22,000 initial acute sinusitis encounters by adults at primary and urgent care offices. The intervention also was associated with a substantial decrease in acute sinusitis diagnoses.

Sharp AL. Am J Manag Care. 2017;23(11):e360-e365.

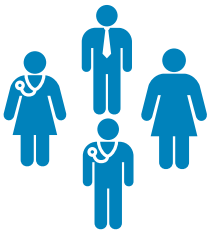
For a full list of 2017 publications, please see the bibliography starting on page 54.

Dr. Adam Sharp

Research program overview

Department of Research & Evaluation

The Department of Research & Evaluation focuses on conducting research with real-world implications and translating findings into practice. This helps Kaiser Permanente determine how to provide better care for our members and communities, as well as bridge the gap between research and practice.



Our team

Research scientists	30
Clinical trials principal investigators	70+
Affiliated investigators	19
Epidemic Intelligence Service officer	1
Post-doctoral research fellows	5
Support staff	300+

420+ scholarly publications in 2017
(excludes letters, editorials, and case reports)

Our top research areas

- Cancer
- Cardiovascular disease
- Diabetes
- Health services research & implementation science
- Obesity
- Vaccine safety & effectiveness

Kaiser Permanente Southern California

As an integrated health system—encompassing medical group, medical facilities, and health plan—Kaiser Permanente Southern California provides an ideal environment for population-based epidemiologic, clinical, and health services research.

Facilities and infrastructure

Our hospitals, medical offices, labs, and pharmacies are all linked by an information infrastructure that supports both clinical practice and business needs. Health information, especially from our vast electronic health records, can be leveraged for research that helps us answer questions about the care we deliver. It can also provide a means to support changes in practice based on what we learn through research.

Facilities

Medical centers	15
Medical offices	229

Physicians and employees

Physicians	7,270+
Nurses	24,700+
Employees	71,000+

Southern California membership (as of December 2017)

Members	4.5 million+
Ethnicities represented	260+
Languages spoken	150+

Nearly 90% stay with Kaiser Permanente after 1 year.
About 78% remain with Kaiser Permanente after 3 years.
Approximately 71% remain with Kaiser Permanente after 5 years.

Sex

Female	51%
Male	49%

Age

≤20 years	25%
21–39	27%
40–64	33%
65+	15%

Race

Hispanic or Latino	42%
White	36%
Asian/Pacific-Islander	12%
Black or African-American	9%
Other	1%

Funding 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.

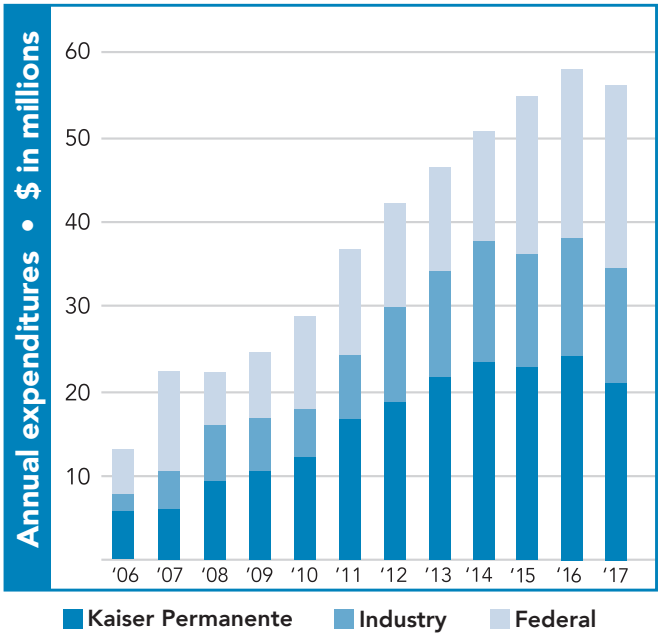
Total research expenditures

$55.7 million in 2017

Federal grants: $21.3 million

Industry contracts: $13.6 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.



2017 grants and awards

New grants and contracts awarded in 2017 will fund research at KPSC over a period of years.

2017 grant submissions

(new grants only, excludes clinical trials)

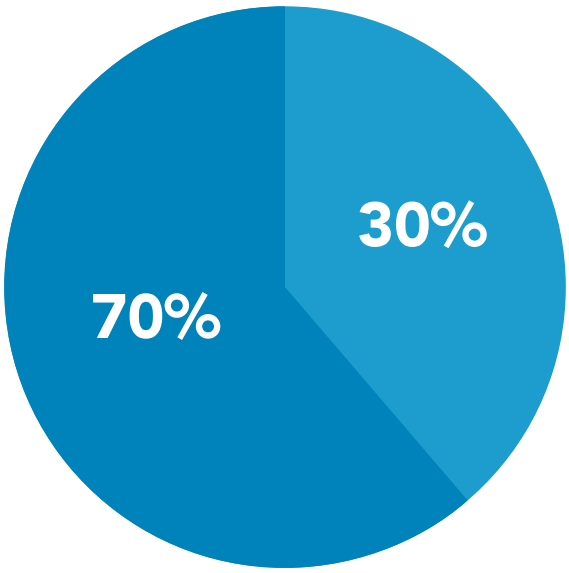
Grants submitted	157
Grants awarded	61

New grants and contracts (all years)

Direct costs	$19 million
Indirect costs	$10.5 million
Total	**$29.5 million**

Continued grants and contracts (all years)

Direct costs	$11.9 million
Indirect costs	$2.8 million
Total	**$14.7 million**



In 2017, Kaiser Permanente Southern California was the lead, or prime, institution for 70% of all the grants and contracts submitted, and was the subcontractor institution for the remaining 30%.

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 2017, the committee awarded funds to the following studies.

Cardiology

Prevalence and prognosis of heart failure with borderline ejection fraction.

Principal investigator: Ming Sum Lee, MD, Los Angeles

Dermatology

The risk of appendicitis, cholecystitis, or diverticulitis in patients with psoriasis.

Principal investigator: Jashin Wu, MD, Los Angeles

Diagnostic Radiology

Prediction of primary hepatic malignancy associated with liver cysts: a population-based retrospective cohort study.

Principal investigator: Christopher Molloy, MD, resident, Los Angeles

Family Medicine

Differences in health care utilization in the year prior to suicide death: a population-based, case-control study.

Principal investigator: Megan Chock, MD, resident, San Diego

Evaluation of the Healthy Balance Weight Management program: a weight management program within a large health care organization.

Principal investigator: Monique George, MD, Woodland Hills

Factors pertaining to statin treatment adherence during the first year of use: a retrospective study of a Southern California cohort.

Principal investigator: Bradley Richie, MD, Riverside

Does attending a culturally responsive hypertension education class have an impact on lowering blood pressure in African-American adults with benign essential hypertension?

Principal investigator: Christi Wiley, MD, Fontana

Gastroenterology

Irritable bowel syndrome and outpatient systemic antibiotic therapy: increased use and adverse effects.

Principal investigator: Carrie Wong, MD, San Diego

Geriatrics

Bleeding risk associated with anticoagulation in patients with atrial fibrillation at extremes of age.

Principal investigator: Thet Oo, MD, Fontana

Head and Neck Surgery

Salivary carcinomas: a clinical and pathological review.

Principal investigator: Gabriel Calzada, MD, San Diego

Internal Medicine

A randomized controlled trial of an automated telephone intervention to improve diabetic retinal screening rates.

Principal investigator: Michael Y. Chen, MD, Downey

Prevalence of pediatric myopia in Kaiser Permanente Southern California.

Principal investigator: Christos Theophanous, MD, resident, Los Angeles

Nephrology

Outcome of laparoscopic cholecystectomy in peritoneal dialysis patients.

Principal investigator: Scott Rasgon, MD, Los Angeles

An evaluation of iron deficiency anemia in the peritoneal dialysis population.

Principal investigator: Kevin Yu, MD, resident, Los Angeles

Ob-Gyn Oncology

Impact of opportunistic salpingectomy during hysterectomy and tubal sterilization in an integrated health care system.

Principal investigator: Jay P. Shah, MD, Orange County/Irvine

Ob-Gyn Urogynecology

Percutaneous tibial nerve stimulation: Is 8 weeks as effective as 12 weeks for treatment of overactive bladder?

Principal investigator: Gouri B. Diwadkar, MD, San Diego

Ophthalmology

Intraocular-pressure lowering drops and age-related macular degeneration.

Principal investigator: Bobeck S. Modjtahedi, MD, Baldwin Park

Pathology

Histologic classification and human papillomavirus correlation of oropharyngeal squamous cell carcinoma.

Principal investigator: Lester Thompson, MD, Woodland Hills

Dr. William Towner and Dr. John Sim

Pediatric Neonatology

Retrospective study of the existing Kaiser Permanente database to examine erythropoietin impact on bronchopulmonary dysplasia and neurodevelopment outcome in preterm infants with birth weight of 1,500 grams or less and born at 23 to 32 weeks gestation.

Principal investigator: Kim Chi T. Bui, MD, Los Angeles

Psychiatry

The metabolic effects of long-term prescription of atypical antipsychotics in young children: BMI, LDL and glucose.

Principal investigator: Kevin Guber, MD, resident, Fontana

Radiation Oncology

Cancer survivorship: (Re?)defining health maintenance goals during and after prostate cancer.

Principal investigator: Jung Julie Kang, MD, Los Angeles

Regional Research Committee chairs 2017

Somjot S. Brar, MD, MPH
Regional Research Committee Chair*

Antelope Valley
Jonathan T. Truong, MD, Area Research Chair

Baldwin Park
Gregory Maletis, MD, Area Research Chair

Downey
Eugene A. Chu, MD, Area Research Chair

Fontana/San Bernardino
Robert E. Sallis, MD, Area Research Chair

South Bay
Bradley K. Ackerson, MD, Area Research Chair

Los Angeles
John J. Sim, MD, Area Research Chair

Orange County
Patrick J. Van Winkle, MD, Area Research Chair

Panorama City/Valencia
Shireen Fatemi, MD, Area Research Chair

Riverside/Palm Springs
Brian S. Lim, MD, Area Research Chair

San Diego
Shawn A. Menefee, MD, Area Research Chair

West Los Angeles/Kern County
Michael J. Fassett, MD, Area Research Chair

Woodland Hills
Lester D. Thompson, MD, Area Research Chair

Department of Research & Evaluation
Stephanie Tovar, MS, Regional Research Committee Operations

**Bechien Wu, MD, MPH, succeeded Dr. Brar as chair at the beginning of 2018.*

Investigators

Department of Research & Evaluation scientific divisions

Steven J. Jacobsen, MD, PhD

Senior Director

- Men's urologic health
- Vaccine safety and effectiveness
- Renal diseases

The Department of Research & Evaluation includes 5 scientific divisions as well as affiliated investigators.

Division of Epidemiologic Research (page 41)

Our epidemiologists apply rigorous research methods to address questions that have the potential to change clinical practice and care delivery. Investigators have expertise in cancer, cardiovascular disease, diabetes, infectious disease, molecular epidemiology, neurology, orthopedics/injury, perinatal health, pharmaco-epidemiology, and vaccine safety and effectiveness.

Division of Behavioral Research (page 43)

Our behavioral scientists focus on research with the potential to reduce disease risk by encouraging health-promoting behaviors. Investigators have expertise in bariatric surgery, cancer, diet and nutrition, medication adherence, physical activity, and sedentary behavior. The division's portfolio includes qualitative and quantitative studies, as well as intervention studies.

Division of Biostatistics Research (page 44)

Our biostatistics faculty collaborate closely with investigators in the other divisions, providing expertise and guidance on study design, power and sample size calculations, data management, data analysis and interpretation, and statistical methodology. Each division has at least one dedicated collaborative biostatistician research scientist who provides statistical guidance on its research studies.

Division of Health Services Research & Implementation Science (page 45)

Our health services researchers study how care is delivered, identify opportunities for improvement, and implement new approaches for 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.

Division of Clinical Trials Research (page 46)

Our physician investigators work with cooperative groups and industry sponsors to conduct clinical trials for investigational drugs, biologics, and devices. The division supports formal programs in oncology, infectious disease, cardiology, and hepatology as well as independent investigators (see page 50).

Affiliated researchers (page 48)

Our affiliated researchers include active and retired Southern California Permanente Medical Group physicians as well as adjunct investigators from other institutions. Our clinician investigators are part of a formal 2-year appointment for SCPMG physicians who want to incorporate research into their clinical careers.

Division of Epidemiologic Research

Research scientists

Kristi Reynolds, PhD, MPH

Director

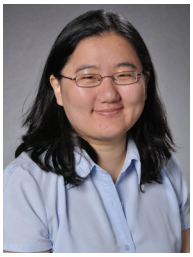
- Chronic disease epidemiology
- Cardiovascular outcomes
- Medication adherence

Annette L. Adams, PhD, MPH

- Screening, treatment, and outcomes of osteoporosis
- Pharmacologic influences on bone and fractures
- Fall and fracture risks

Chun Chao, PhD, MS

- Cervical cancer prevention and screening
- Lymphoid malignancies
- Outcomes in cancer survivors



Kim N. Danforth, ScD, MPH

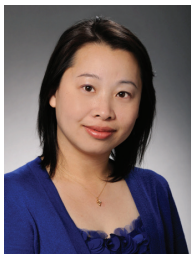
- Cancer epidemiology and prevention
- Cancer care quality and survivorship
- Health services research and ambulatory care

Darios Getahun, MD, PhD, MPH

- Population-based studies on maternal/child health care
- Genetic/environmental influences on health outcomes
- Fetal origin of childhood diseases

Reina Haque, PhD, MPH

- Cancer epidemiology, molecular markers of risk and survival
- Breast and prostate cancer survivorship
- Pharmacoepidemiology



Rulin C. Hechter, MD, PhD

- HIV and hepatitis C treatment and clinical outcomes
- Substance abuse treatment and integrated care
- Vaccine safety and effectiveness

Jean M. Lawrence, ScD, MPH, MSSA

- Diabetes in children and young adults
- Risk factors for adverse pregnancy outcomes
- Psychosocial and environmental determinants of health

Sara Tartof, PhD, MPH

- Antibiotic stewardship/resistance
- Vaccine safety and effectiveness
- Hospital-acquired infections

Hung Fu Tseng, PhD, MPH

- Vaccine safety and effectiveness
- Vaccine coverage and compliance
- Vaccine-preventable diseases

Continued on next page

Division of Epidemiologic Research | continued

Post-doctoral research fellows

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

- Childhood health and mental health
- Exposures during pregnancy
- Vaccine safety

Katia Bruxvoort, PhD, MPH

- Vaccine safety and effectiveness
- Medication adherence
- Antimicrobial resistance

Nirupa R. Ghai*, PhD, MPH

- Cancer epidemiology
- Health disparities
- Cancer prevention and screening

* Dr. Ghai left the department in February 2018.

Stephanie R. Reading*, PhD, MPH

- Cancer survivorship
- Mental health
- Cardiovascular epidemiology

* Dr. Reading left Kaiser Permanente in November 2017.

Epidemic Intelligence Service officer

Gloria C. Chi*, PhD, MPH

- Chronic disease
- Environmental health
- Public health surveillance

* Dr. Chi left Kaiser Permanente in May 2018.

Division of Behavioral Research

Research scientists

Deborah Rohm Young, PhD, MBA

Director

- Physical activity and cardiovascular risk factors
- Community-based physical activity/ obesity prevention
- Prevention to eliminate racial/ethnicity disparities

Corinna Koebnick, PhD, MSc

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

Karen J. Coleman, PhD, MS

- Health equity
- Mental health
- Bariatric surgery

Claudia Nau, PhD

- Social determinants of health
- Patient social needs
- Predictive modeling

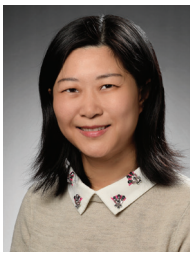
Division of Biostatistics Research

Research scientists

Anny Hui Xiang, PhD, MS

Director

- Diabetes and gestational diabetes and pregnancy
- Clinical trials: study design, monitoring, analysis
- Biostatistics: application and problem-solving

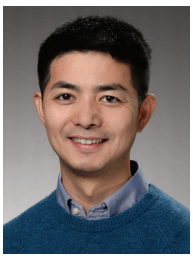


Lei Qian, PhD

- Vaccine safety and effectiveness
- Assessment of systematic intervention effects
- Statistical methods and study design

Ernest Shen, PhD

- Statistical methods/study design for health services research
- Structural equation modeling
- Bayesian statistics



Jiaxiao Shi, PhD

- Statistical methodology and study design
- Obstetrics-gynecology and breast cancer risk
- Chronic kidney disease, hypertension, and cardiovascular risk

Margo A. Sidell, ScD, MSPH

- Biostatistics
- Health behaviors
- Physical and social environmental factors

Jeff Slezak, MS

- Predictive modeling
- Bladder, prostate cancers
- Vaccine safety

Division of Health Services Research & Implementation Science

Research scientists

Michael K. Gould, MD, MS

Director

- Quality of care in thoracic oncology
- Implementation science
- Pragmatic trials and observational studies

Stephen F. Derose, MD, MSHS

- Sleep disorders and therapy
- Clinical epidemiology of chronic disease
- Health services research/population health care

David Glass, PhD

- Physician/patient decision making
- Patient decisions on sites of care
- End-of-life care

Erin E. Hahn, PhD, MPH

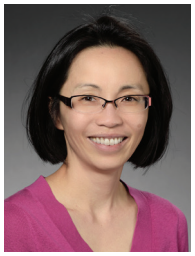
- Quality of cancer care
- Cancer survivorship
- Clinical practice guidelines/evidence-based practices

Aniket A. Kawatkar, PhD, MS

- Health economics
- Patient-reported outcomes
- Discrete choice experiments

Brian S. Mittman, PhD

- Implementation/improvement science
- Health systems science
- Patient-centered outcomes research



Huong Q. Nguyen, PhD, RN

- Care transitions
- Collaborative care for complex and advanced illnesses
- Physical activity monitoring and coaching

Adam L. Sharp, MD, MS

- Health system science/clinical decision support
- Health services/implementation research
- Social determinants of health

Post-doctoral research fellow

Shayna L. Henry*, PhD

- Chronic disease self-management
- Chronic kidney disease/end-stage renal disease
- Quality of health services

* Dr. Henry left the department in August 2017.

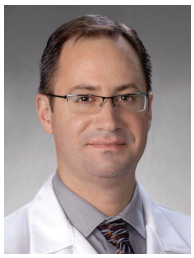
Division of Clinical Trials Research

Portfolio principal investigators

William J. Towner, MD, FACP, FIDSA

Regional Physician Director

- Infectious disease clinical trials
- HIV and hepatitis C
- Complex chronic disease management



Michael R. Girvigian, MD

- Radiation oncology
- Central nervous system tumors of the brain, spine
- Image-guided radiosurgery and stereotactic body radiotherapy

Gary Buchschacher Jr., MD

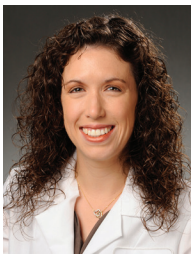
- Medical oncology
- Gastrointestinal cancers
- Genitourinary cancers

Richard Green, MD

- Neuro-oncology
- Glioblastoma
- Central nervous system malignancies

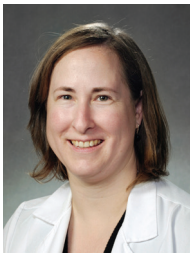
Robert M. Cooper, MD

- Pediatric, adolescent, and young adult cancers
- Treatment, survivorship, and end-of-life care
- Timeliness of cancer care delivery



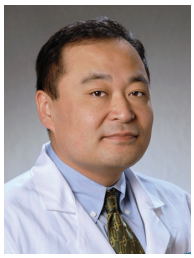
Kelley Hodgkiss-Harlow, MD

- Critical limb ischemia
- Carotid disease
- Vascular access



Lara Durna, MD

- Medical oncology
- Hematologic cancers
- Breast cancer



Han Koh, MD

- Medical oncology
- Lung cancers
- Cancer care research

Nigel Gupta, MD

- Cardiac implantable electronic devices
- Cardiac ablation
- Structural heart therapies

Scott Lentz, MD

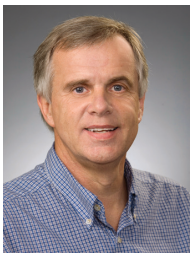
- Uterine sarcomas
- Ovarian carcinoma
- Hereditary influence on gynecologic cancers

Shawn A. Menefee, MD

- Pelvic floor disorders
- Urinary and fecal incontinence
- Pelvic organ prolapse

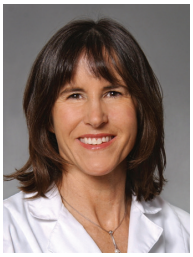
Helen Moon, MD

- Medical oncology
- Melanoma
- Renal cancers



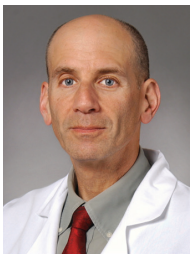
Anders Nyberg, MD, PhD

- Hepatitis B and C
- Fatty liver disease, nonalcoholic steatohepatitis (NASH)
- Gastrointestinal disorders



Lisa Nyberg, MD, MPH

- Hepatitis B and C
- Fatty liver disease, nonalcoholic steatohepatitis (NASH)
- Liver transplantation



Jonathan A. Polikoff, MD

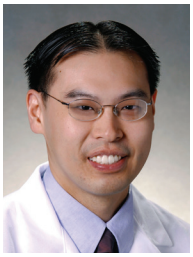
- Medical oncology
- Breast cancer
- Quality of life for cancer patients

Amandeep Sahota, MD

- Hepatitis B and C
- Fatty liver disease, nonalcoholic steatohepatitis (NASH)
- Liver transplantation

Ricardo T. Spielberger, MD

- Hematopoietic cell transplantation
- Transplantation side effects
- Opportunistic infections



Jashin J. Wu, MD

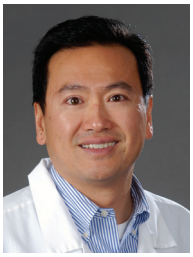
- Dermatology
- Psoriasis

Affiliated researchers

Affiliated investigators

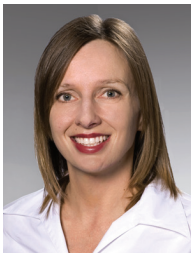
Somjot S. Brar, MD, MPH

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



Donald S. Fong, MD, MPH

- Myopia
- Diabetic retinopathy
- Glaucoma



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

- Multiple sclerosis
- Neuroepidemiology
- Prognosis of chronic diseases

Adam Schickedanz*, MD

- Impact of social needs on care utilization
- Evaluation of interventions addressing social determinants of health
- Perceptions of social needs interventions among clinicians

* Dr. Schickedanz left Kaiser Permanente in May 2018.

Adjunct investigator

Lauren Wallner, PhD, MPH

- Quality and delivery of cancer care
- Outcomes after cancer treatment
- Interventions to improve cancer care

Associate investigators

Sirichai Chayasirisobhon, MD

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

R. James Dudl, MD

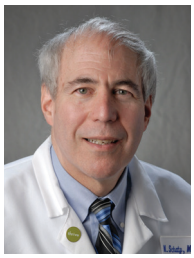
- Cardiovascular disease prevention
- Diabetes complication prevention
- Glucose control for patients with diabetes

George F. Longstreth, MD

- Irritable bowel syndrome
- Acute diverticulitis
- Gastrointestinal epidemiology

David A. Sacks, MD

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



Michael Schatz, MD, MS

- Asthma outcomes
- Asthma population management
- Asthma and pregnancy

Robert S. Zeiger, MD, PhD

- Prevention of asthma and allergic disorders
- Clinical trials of asthma treatments
- Outcomes research

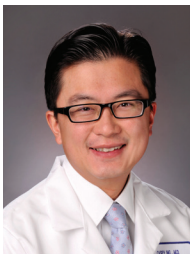
Clinician investigators

Raymond Chen, MD, DPhil

- Adult cardiac surgery and perioperative care
- Telemedicine and prevention of unnecessary readmissions
- Neural network detection of wound infection

Devansu Tewari, MD, MBA

- Gynecologic pre-invasive and invasive cancers
- Integrated health care systems and cancer delivery
- Quality metric developments in cancer therapy



Casey K. Ng, MD

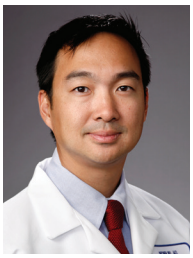
- Kidney stone prevention
- Evaluation of hematuria
- Natural history of renal cystic disease

Emily L. Whitcomb, MD, MAS

- Pelvic floor disorders
- Quality metric development in urogynecology

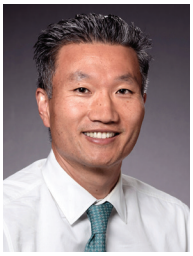
Navdeep Sangha, MD

- Ischemic stroke
- Stroke systems of care
- Telestroke



Bechien U. Wu, MD, MPH

- Acute, chronic pancreatitis
- Cystic neoplasms of the pancreas
- Gastric and pancreatic cancer



John Sim, MD

- Hypertension
- Glomerulonephropathies
- Cardiovascular outcomes in chronic kidney disease

Hui Xue, MD, MMSc

- Chronic renal disease progression
- Dialysis-related outcomes
- Kidney transplantation

Clinical trials principal investigators by specialty

Allergy

Michael Schatz, MD, MS, 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

Jashin Wu, MD, Los Angeles Medical Center

Endocrinology

Patricia Wu, MD, San Diego – Carmel Valley Medical Offices

Gastroenterology

Brian Lim, MD, Riverside 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

Jared Spotkov, MD, South Bay Medical Center

William Towner, MD, Los Angeles Medical Center

Metabolic

Anny Xiang, PhD, MS, Department of Research & Evaluation

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

Oncology, Adult

Vikram Attaluri, MD, Los Angeles Medical Center

Gary Buchschacher, MD, Los Angeles Medical Center

Jian Chen, MD, San Diego Medical Center

Louis DiFronzo, MD, Los Angeles Medical Center

Lara Durna, MD, San Diego Medical Center

Michael Girvigian, MD, Los Angeles Medical Center

Richard Green, MD, Los Angeles Medical Center

Han Koh, MD, Downey Medical Center

Scott Lentz, MD, Los Angeles Medical Center

Anna Leung, MD, Los Angeles Medical Center

Gregory Marrujo, MD, Riverside Medical Center

Elisabeth McLemore, MD, Los Angeles Medical Center

Helen Moon, MD, Riverside Medical Center

Jonathan Polikoff, MD, San Diego Medical Center

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

Marco Tomassi, MD, San Diego Medical Center

Ophthalmology

Nicole Benitah, MD, West Los Angeles Medical Center

Vivienne Hau, MD, Riverside Medical Center

Orthopedics

Gregory Maletis, MD, Baldwin Park Medical Center

Anshuman Singh, MD, San Diego Medical Center

Otorhinolaryngology

David Keschner, MD, Irvine Medical Center

Pediatric Infectious Disease

Evan Steinberg, MD, Los Angeles Medical Center

Pediatric Oncology

Robert Cooper, MD, Los Angeles Medical Center

Pediatric Ophthalmology

Ashish Mehta, MD, Anaheim 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

Pulmonology

Aung Htoo, MD, Kern County

Huong Nguyen, PhD, RN, Department of Research & Evaluation

Jonathan (Hien) Truong, MD, Antelope Valley

Reproductive/Gynecological Disorders

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

Karl Luber, MD, San Diego Medical Center

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

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

Rheumatology

Steve Lee, DO, Fontana Medical Center

Sleep Medicine

Aliya Ferouz-Colborn, MD, Fontana Medical Center

Surgery

Samir Johna, MD, Fontana Medical Center

Urology

Gary Chien, MD, Los Angeles Medical Center

Polina Reyblat, MD, Los Angeles Medical Center

Urology/Reproductive/Gynecological Disorders

Christopher Tenggardjaja, MD, Los Angeles 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

2017 Publications

Scientists, clinicians, and other health professionals from Kaiser Permanente Southern California authored scholarly publications on a wide range of topics in 2017, from allergy and asthma to women's health. Kaiser Permanente Southern California authors are noted in **bold.**

Allergy and Asthma

Chen M, **Land M**. Baked milk and baked egg oral immunotherapy. *Immunotherapy.* 2017 Nov;9(15):1201-1204.

Chen M, **Land M**. The current state of food allergy therapeutics. *Hum Vaccin Immunother.* 2017 Oct 3;13(10):2434-2442. PMCID: PMC5647972

Chipps BE, **Zeiger RS,** Luskin AT, Busse WW, Trzaskoma BL, Antonova EN, Pazwash H, Limb SL, Solari PG, Griffin NM, Casale TB. Baseline asthma burden, comorbidities, and biomarkers in omalizumab-treated patients in PROSPERO. *Ann Allergy Asthma Immunol.* 2017 Dec;119(6):524-532.e2.

Feuille E, Menon NR, **Huang F,** Greenhawt M, Nowak-Wegrzyn A. Knowledge of food protein-induced enterocolitis syndrome among general pediatricians. *Ann Allergy Asthma Immunol.* 2017 Sep;119(3):291-292.e3.

Macy E, Romano A, Khan D. Practical management of antibiotic hypersensitivity in 2017. *J Allergy Clin Immunol Pract.* 2017 May-Jun;5(3):577-586.

Pourang D, Batech M, Sheikh J, Samant S, Kaplan M. Anaphylaxis in a health maintenance organization: International Classification of Diseases coding and epinephrine auto-injector prescribing. *Ann Allergy Asthma Immunol.* 2017 Feb;118(2):186-190.e1.

Schatz M, Sicherer SH, **Zeiger RS**. The Journal of Allergy and Clinical Immunology: in practice - 2016 year in review. *J Allergy Clin Immunol Pract.* 2017 Mar-Apr;5(2):218-236.

Sordillo JE, Zhou Y, McGeachie MJ, Ziniti J, Lange N, Laranjo N, Savage JR, Carey V, O'Connor G, Sandel M, Strunk R, Bacharier L, **Zeiger R,** Weiss ST, Weinstock G, Gold DR, Litonjua AA. Factors influencing the infant gut microbiome at age 3-6 months: findings from the ethnically diverse Vitamin D Antenatal Asthma Reduction Trial (VDAART). *J Allergy Clin Immunol.* 2017 Feb;139(2):482-491.e14. PMCID: PMC5303123

Varshney R, Lee JT. Current trends in topical therapies for chronic rhinosinusitis: update and literature review. *Expert Opin Drug Deliv.* 2017 Feb;14(2):257-271.

Wolsk HM, Harshfield BJ, Laranjo N, Carey VJ, O'Connor G, Sandel M, Strunk RC, Bacharier LB, **Zeiger RS, Schatz M,** Hollis BW, Weiss ST, Litonjua AA. Vitamin D supplementation in pregnancy, prenatal 25(OH)D levels, race, and subsequent asthma or recurrent wheeze in offspring: secondary analyses from the Vitamin D Antenatal Asthma Reduction Trial. *J Allergy Clin Immunol.* 2017 Nov;140(5):1423-1429.e5.

Zeiger RS, Schatz M, Dalal AA, **Chen W, Sadikova E,** Suruki RY, **Kawatkar AA, Qian L**. Blood eosinophil count and outcomes in severe uncontrolled asthma: a prospective study. *J Allergy Clin Immunol Pract.* 2017 Jan-Feb;5(1):144-153.e8.

Zeiger RS, Schatz M, Li Q, Chen W, Khatry DB, Tran TN. Burden of chronic oral corticosteroid use by adults with persistent asthma. *J Allergy Clin Immunol Pract.* 2017 Jul-Aug;5(4):1050-1060.e9.

Bone Health and Orthopedics

Adams AL, Xue F, **Chantra JQ, Dell RM,** Ott SM, Silverman S, Giaconi JC, Critchlow C. Sensitivity and specificity of radiographic characteristics in atypical femoral fractures. *Osteoporos Int.* 2017 Jan;28(1): 413-417.

Anakwenze OA, Yehyawi T, Dillon MT, Paxton E, Navarro R, Singh A. Effect of age on outcomes of shoulder arthroplasty. *Perm J.* 2017;21:16-056. PMCID: PMC5499606

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