

# Illuminating the path through the pandemic









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## Message from the Senior Director



My role as interim senior director began in January 2021, so I first want to acknowledge the leadership of former senior director, Dr. Steve Jacobsen, who led the growth of the research program at Kaiser Permanente Southern California into what it is today. He expanded the program, recruited a deep bench of scientific talent, and cultivated the capabilities necessary to conduct research that would have a real-world impact. Because of that strong foundation, our research program was well positioned to illuminate the path through the pandemic.

In the first months of the pandemic, scientists, clinicians, and staff leapt in to initiate research on the novel coronavirus. At the outset, the global medical community didn't understand who was most at risk from the disease. We had no approved treatments, much less a vaccine. We lacked evidence to guide clinical decision-making.

Within a matter of months, that began to change. Kaiser Permanente Southern California enrolled hundreds of patients in the clinical trial for remdesivir, which became the first authorized treatment for COVID-19. We began to introduce clinical decision tools based on our research into Kaiser Permanente HealthConnect®.

Our researchers contributed practical insights to decision makers both within and outside of Kaiser Permanente. Our Epidemic Intelligence Service officers helped shape Kaiser Permanente's COVID-19 strategies. Risk prediction models, including those developed with artificial intelligence and machine learning techniques, helped inform care decisions for patients with COVID or COVID-like symptoms. Research on mask adherence helped inform local public health departments. And our research on the risks of obesity made national headlines.

By late summer, our team was enrolling participants in the clinical trial for the Pfizer-BioNTech COVID-19 vaccine. In December, the first dose administered outside of a clinical trial in California was given at the Kaiser Permanente Los Angeles Medical Center, the site of our trial. It was a proud moment for all of us.

While much of the focus in 2020 was on the pandemic, vital research continued on many other fronts. Important clinical trials, including those for treatment of stroke, cancer, cardiovascular conditions, and 2 dozen other important therapeutic areas. Our researchers were awarded new grants to study on topics spanning cancer survivorship, adverse childhood events, air pollution, sugary beverage taxes, park prescriptions, tuberculosis screening, diabetes, vaccine safety, and more. Authors from our region published more than 475 original research papers.

Our researchers, clinical partners, and staff did all of this while juggling the many personal and professional challenges that came with living through what I hope is a once-in-a-lifetime pandemic. My thanks go out to all of you for rising to the challenge. It has been a true privilege to work side by side with you during this historic time.

A handwritten signature in black ink, reading "Ben Broder". The signature is fluid and cursive.

**Benjamin Broder, MD, PhD**

Interim Senior Director of Research

*To learn more about research currently underway, including COVID-19 projects, please visit our website ([kp.org/research](https://kp.org/research)), subscribe to our IMPACT newsletter, or follow us on Twitter (@KPSCalResearch).*



# RESEARCH HIGHLIGHTS







Dr. Sara Tartof in her office at the Department of Research & Evaluation in Pasadena, California

## Researchers and physicians quickly galvanize to determine who is most at risk from COVID-19

As the COVID-19 pandemic emerged, swelled, and consumed Southern California, researchers and physicians at Kaiser Permanente Southern California quickly mobilized to determine who was at the most risk and how to better protect them. Their work made headlines in major publications such as *The New York Times* and helped clinicians determine who needed the most focus at a time when resources were limited.

One of the first studies from the Department of Research & Evaluation to garner national attention was led by epidemiologist Sara Tartof, PhD, MPH. Published in *Annals of Internal Medicine*, the research showed that obesity was associated with a substantially increased risk of death from COVID-19. However, the risk of death from COVID-19 associated with obesity was not uniform,

but instead disproportionately affected men and people under 60 years of age.

Researchers looked at the electronic health records of nearly 7,000 Kaiser Permanente Southern California members who tested positive for COVID-19 between February 13 and May 2, 2020. Patients with severe obesity had nearly 3 times the risk of death and those with extreme obesity had over 4 times the risk of death from COVID-19 compared to those of normal weight. (A body mass index, or BMI, of 30 to 39 is considered obese, 40 to 44 is severely obese, and 45 or higher is extremely obese.)

The study also found a difference between the risk of obesity in gender: Men with severe or extreme obesity had a very high risk of death, while



*The study also found a difference between the risk of obesity in gender: Men with severe or extreme obesity had a very high risk of death, while women had no increased risk of death associated with obesity.*

women had no increased risk of death associated with obesity. Also, people of Black or Latinx race/ethnicity did not have an increased risk of death from COVID-19 based on their race/ethnicity alone.

Sameer B. Murali, MD, an internal medicine physician at the Kaiser Permanente Fontana Medical Center and senior author on this study, noted that the data showed that the mortality risk of severe obesity eclipsed 11 out of 12 other medical conditions that were included in their research model.

"This observation goes beyond merely improving our understanding of COVID-19," Dr. Murali said. "It clearly demonstrates that obesity is just as dangerous a disease condition as heart disease, kidney failure, COPD, diabetes, and others, and like COVID-19, it requires a more comprehensive response from all sectors of our society."

### **People on dialysis have higher risk from COVID-19**

Physicians and researchers knew that patients with end-stage kidney disease on dialysis might be at higher risk of poor outcomes from COVID-19. However, there was some hope that they might avoid the cytokine storm—the body's immune response to COVID-19 that can have devastating effects—because of their immunocompromised condition.

The study, published in *Kidney Medicine*, found that these patients had 18 times higher risk of hospitalization and death from COVID-19 than people who do not have end-stage kidney disease. The lead researcher on the study was John J. Sim, MD, who is a clinician researcher with



the Department of Research & Evaluation, and a nephrologist with the Kaiser Permanente Los Angeles Medical Center.

"This study raises awareness and stresses the deadly consequences for people on dialysis," Dr. Sim said. "It also made clear the need for these patients to be even more careful about taking COVID precautions."

Among 7,533 patients with end-stage kidney disease, 133 (16 peritoneal and 117 hemodialysis) patients were diagnosed with COVID-19 between March 1 and June 30, 2020. Researchers found that patients with end-stage kidney disease who contracted COVID-19 had a much higher mortality rate than other Kaiser Permanente Southern California members with COVID-19 (23% vs. 1.3%). There appeared to be no differences in mortality by race/ethnicity and socioeconomic status.

The study prompted discussion about prioritizing COVID-19 vaccinations for patients with end-stage kidney disease. The American Society of Nephrology subcommittee on COVID cited the work when they recommended that vaccinations for patients with end-stage kidney disease be a priority.





Dr. John J. Sim at the dialysis unit at the Los Angeles Medical Center

Dr. Sim added, “more importantly, this study was the platform that launched subsequent studies by physicians.” One evaluated the high mortality rates (68%) in COVID-19 patients who went into the hospital with healthy kidneys but needed dialysis as a result of COVID-related kidney injury. That research helped physicians to have better shared decision-making conversations with patients and their families during the pandemic surge. Another study began evaluating the safety and efficacy of remdesivir use for patients with end-stage kidney disease because they had often been excluded from early COVID-19 clinical trials.

### **Pneumonia vaccine may affect course of COVID-19**

Early in the pandemic, before COVID-19 vaccines were available, several researchers began to examine whether the pneumococcal conjugate vaccine PCV13 could affect the course of

COVID-19 among adults 65 and older. The study, published in *The Journal of Infectious Diseases*, found PCV13 vaccination affected both the diagnosis and the outcomes of COVID-19.

Patients who received the PCV13 experienced 35% lower risk of COVID-19 diagnosis, had a 32% lower incidence of COVID-19 hospitalization, and had a 32% lower incidence of COVID-19 death, than those who did not receive the vaccine.

The patients who received PCV13 received some protection against COVID-19, while those who received PPSV23, another pneumococcal vaccine, did not. PCV13 prevents acquisition of certain pneumococcal strains. In contrast, PPSV23 prevents severe pneumococcal disease, but does not prevent infection.

“The study provided important evidence that bacterial-viral interactions may play out in ways that shape the course of COVID-19,” said Dr.



*“The study provided important evidence that bacterial-viral interactions may play out in ways that shape the course of COVID-19.”*

– Sara Tartof, PhD, MPH

Tartof, the senior author. “At the time we were doing this research there weren’t any really good COVID-19 treatments or safety options. PCV13 was something safe and available that we were able to show was preventative.”

### **Mortality risk factors for patients under 50**

Ahmed Dehal, MD, MPH, a surgical oncologist at the Kaiser Permanente Panorama City Medical Center, noticed that while older patients had a higher risk of dying from COVID-19, the disease could also be deadly for younger people. He decided to determine who among young people would be most at risk.

In an initial investigation, Dr. Dehal and his colleagues examined KPSC member data from the first few months of the pandemic. They found that COVID-19 patients under age 50 had a significantly higher risk of dying from the disease if they were of nonwhite racial or ethnic backgrounds, had obesity, and had underlying illnesses, such as diabetes.

“When it comes to younger patients, you have to dig a little deeper to see who is at risk,” Dr. Dehal said. “We identified this high-risk subgroup that should be considered in future planning for resource allocation, such as vaccine distribution.”

The team continued to analyze data from additional patients before publishing the results. “Our integrated system with its huge number of patients gives us the opportunity to conduct a strong analysis with follow-up over time,” Dr. Dehal said.



Dr. Ahmed Dehal outside his office at the Panorama City Medical Center

### **Rapid research on antihypertensive medications**

In the pandemic’s early days, urgent concerns arose that certain types of medications to treat high blood pressure might increase COVID-19 risk or worsen outcomes. Jaejin An, PhD, a research scientist in the R&E’s Division of Epidemiologic Research, leapt into action and obtained funding from the American Heart Association to quickly address these questions.

Her team’s analysis of 824,650 KPSC members with high blood pressure showed that there was no association between risk of COVID-19 infection and use of antihypertensive medications—specifically, angiotensin-converting enzyme (ACE)



inhibitors and angiotensin II receptor blockers (ARBs). These findings appeared in the *Journal of the American Heart Association*.

“It was a huge relief to find that people with high blood pressure can, and should, continue to take the medications they’ve been prescribed,” Dr. An said. “It’s thanks to our tireless team and amazing clinicians that we could confirm this so quickly.”

Now she and her colleagues are examining whether antihypertensive medications are associated with better or worse COVID-19 outcomes, such as mortality, ICU admission, or use of mechanical ventilators.

## Racial and ethnic inequities in COVID-19 outcomes

Claudia Nau, PhD, a research scientist in R&E’s Division of Behavioral Research, led an analysis of health records from nearly 300,000 KPSC members who received a COVID-19 test or diagnosis.

The investigation showed that people of color—in particular, Asian and Pacific Islander patients—were more likely to be diagnosed with COVID-19 and were at higher risk of hospitalization or intensive-level care than people who were white. These disparities persisted even after accounting for underlying health conditions, such as diabetes, that are commonly blamed for health inequities.



Temperature check taken at the Chino Grand Medical Offices in Chino, California



*"We hope to find a factor that signals the doctors to intervene and potentially reduce hospitalization in stressed health care systems."*

– Cheng-Wei "Charlie" Huang, MD

"Our findings suggest there are key factors related to exposure and vulnerability for these patients that have nothing to do with preexisting conditions," Dr. Nau said. "We need to think beyond comorbidities in order to address the pandemic equitably."

This work was conducted with funding from Genentech. The study was published in the *Annals of Internal Medicine*.

Now, she and her team, which includes Dr. Sara Tartof, are investigating social determinants of health that could be contributing to COVID-19 disparities, such as being an essential worker or living in a crowded, multi-generational household. The researchers will be using neighborhood-level data for the project that will allow them to determine a person's likelihood of being an essential worker then living in a crowded household, Dr. Nau explained.

"Virtually every disease shows racial and ethnic disparities, but they are just so much more visible during a pandemic," Dr. Nau said. "KPSC's diverse membership enables us to explore these disparities in greater depth than most studies can."

### Understanding hospital readmissions

After being hospitalized for COVID-19, some patients are later readmitted. Understanding the likelihood of readmission and who is most at risk could inform efforts to reduce readmission and keep hospital beds open.

A study supported by the Department of Research & Evaluation's Care Improvement Research Team showed that 7.6% of KPSC members who were hospitalized for COVID-19 were later readmitted, usually for respiratory issues. In line with



Dr. Cheng-Wei "Charlie" Huang checks his phone in a hallway of the Los Angeles Medical Center

expectations, patients who were older, frailer, and had more chronic health conditions were more likely to be readmitted.

The analysis also found that readmission tended to occur within days of discharge from the initial hospital stay, rather than weeks. "Given what we know about the typical timeline of a COVID-19 infection, our data suggest that most people are readmitted when their initial disease worsens," said Cheng-Wei "Charlie" Huang, MD, a hospitalist from the Kaiser Permanente Los Angeles Medical Center, who led the research.

The study was published in the journal *Infectious Diseases*. Authors included Huong Q. Nguyen, PhD, RN, interim director of R&E's Division of Health Services Research & Implementation Science.

Dr. Huang continues to explore COVID-19 readmissions with the goal of identifying potential strategies for prevention. He said: "We hope to find a factor that signals the doctors to intervene and potentially reduce hospitalization in stressed health care systems."





Dr. Hai Linh Kerrigan and Dr. William Towner at the Los Angeles Medical Center, site of several pivotal COVID-19 clinical trials during the pandemic

## Clinical trials bring hope during global pandemic

On a Saturday morning in mid-March 2020, William Towner, MD, FACP, FIDSA, and Hai Linh Kerrigan, PharmD, the leaders of Kaiser Permanente Southern California's clinical trials program in the Department of Research & Evaluation, huddled on a conference call discussing the feasibility of getting a trial launched quickly for an investigational drug called remdesivir, then considered a promising candidate for treatment of COVID-19.

"We knew this would be a fast-moving disease with no FDA-approved treatment options available, which presented the perfect opportunity for clinical trials to help," said Dr. Towner, who is regional physician director of clinical trials. "We needed a treatment in late-stage development so we could get it to as many patients as we could. Remdesivir met all of our criteria."

Time was of the essence. The pandemic was closing in. Within days, officials would declare

it safer for Californians to stay home, as cases of COVID-19 began to climb in the state. No treatments were yet approved. The urgency was clear.

"Right after that conversation, we got on the phone to see if we could get a contract in place over the weekend," said Dr. Kerrigan, division research administrator for clinical trials.

### Launching a multisite trial in 8 days

Eight days after that initial phone call, the trial opened at 13 Kaiser Permanente medical centers in Southern California.

Everything happened quickly, but launching a large-scale trial at the start of a global pandemic was far from simple. It took a Herculean effort by the clinical trials team and an army of physicians, pharmacists, nurses, and research staff across the region.



*“There were so many things we did that we’ve never done before, from launching a central command center, to enrolling people 7 days a week at medical centers, to consenting patients electronically using specially configured iPads.”*

– Hai Linh Kerrigan, PharmD

More than 60 infectious disease specialists signed on as investigators. A group of ambulatory care pharmacists provided clinical monitoring for study participants, ensuring required labs were performed and checking for safety issues. And research staff from every division of the research department jumped in to help.

“There were so many things we did that we’ve never done before, from launching a central command center, to enrolling people 7 days a week at medical centers, to consenting patients electronically using specially configured iPads,” said Dr. Kerrigan.

A month and a half after the trial opened, the U.S. Food and Drug Administration (FDA) issued an emergency use authorization for remdesivir. By that time, KPSC had become one of the largest enrolling sites in the world, with 588 participants receiving remdesivir as a part of the clinical trial.

### Focusing on novel therapies

While having an approved treatment gave reason to celebrate, there was no time to rest. Trials for other potential treatments had kicked into high gear. Choosing which ones to participate in became the next challenge.

“We were getting about 4 or 5 different opportunities sent to us every week, but it was apparent we couldn’t possibly do all of the studies,” said Dr. Towner. “When there is a limited ability to do every study, we had to choose carefully.”

In consultation with physicians from multiple specialties as well as regional leaders, the clinical trials team weighed various options. They homed



Managerial Consultant Jennifer Charter, shown here with Clinical Trials Operations Manager Tiffany Castanon in the Healing Garden at the Los Angeles Medical Center, helped lead the data team during the remdesivir trial

in on novel therapies. Some of these included monoclonal antibodies, nitric oxide, and an oral treatment for COVID-19.

### Monoclonal antibodies

The need to develop new treatments rapidly as the pandemic spread quickly around the globe prompted members of the medical research community to explore clinical trials methods that could evolve as new treatments emerged.

In April 2020, the National Institutes of Health (NIH) announced a new public-private partnership, called ACTIV, which aimed to speed development of promising treatments and vaccines. One of the studies opened under this partnership was the ACTIV-2 Outpatient Monoclonal Antibodies and Other Therapies trial, which employed an adaptive trial platform when it launched a few months later in August.





Dr. Adam Schwartz in front of the Zion Medical Center in San Diego, being interviewed by reporters about trials for monoclonal antibodies

"Adaptive platforms are used when new drugs are being developed quickly, meaning there is a chance a better treatment will emerge during the life of the trial," said Adam Schwartz, MD, MS, who served as principal investigator for the ACTIV-2 trial at the Kaiser Permanente San Diego and Zion medical centers. "It allows the trial to stay within the same basic protocol, amending the appendix to add or subtract new agents as the trial goes along."

The ACTIV-2 trial was designed to test investigational agents, including monoclonal antibodies, in adults with mild-to-moderate COVID-19 symptoms. Monoclonal antibodies mimic the body's immune system's response but are produced in a lab.

Dr. Schwartz, who is chief of emergency medicine in San Diego, had previously served as principal investigator for another COVID-19 monoclonal antibody trial, the BLAZE-1 trial for bamlanivimab. During that trial, the study team screened almost 200 patients and enrolled 18 participants.

That experience helped lay the groundwork for the team to participate in the ACTIV-2 trial. Both the BLAZE-1 and ACTIV-2 trials required complex

logistics, including enrolling and consenting patients in the emergency department, managing rapid lab tests, administering intravenous drugs, and coordinating home follow-up.

"It took a lot of resources, especially nursing time, which was especially difficult during the pandemic in our very busy emergency departments," said Dr. Schwartz. "We couldn't have done it without a lot of support, both from the Department of Research & Evaluation crew and our local leadership."

The ACTIV-2 trial remained open at both San Diego and Zion into 2021.

### Inhaled nitric oxide

Early in the pandemic, Viji Sankar, MD, chief of the pulmonary and critical care units at the Kaiser Permanente San Diego and Zion medical centers, became interested in the potential benefits of inhaled nitric oxide for patients with COVID-19. Though often used in neonatal populations and ICU to support oxygen needs in advanced respiratory failure, there had been interest in how inhaled nitric oxide could be used for other settings of respiratory failure.



"I heard about a patient with severe pulmonary hypertension who was on an inhaled nitric oxide platform," she said. "It was a portable device, which made it possible for her to be supported at home."

In late May, Dr. Sankar reached out to the regional clinical trials team to explore the possibility of using the inhaled nitric oxide system under expanded access—a treatment option that allows use of a treatment not yet authorized by the FDA. The FDA had recently cleared the initiation of a phase 3 multicenter randomized, double-blinded, placebo-controlled clinical trial with inhaled nitric oxide in COVID patients with early respiratory failure.

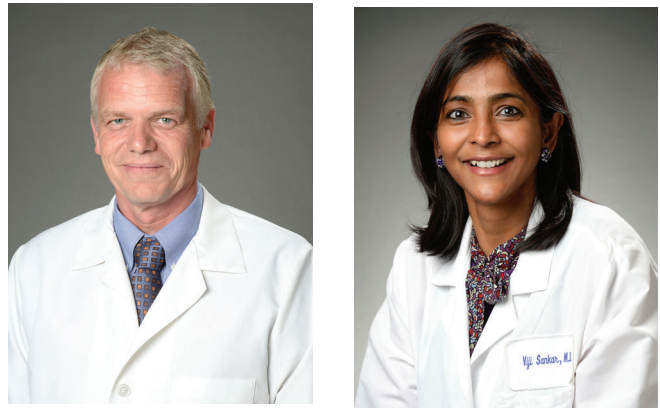
Dr. Sankar worked with the clinical trials team as well as numerous colleagues at the San Diego and Zion medical centers to open the PULSE-CVD19-001 trial. They enrolled their first patient in September.

The trial remained open through mid-November when the study hit its target enrollment of 100 participants. Fifteen of the 17 screened participants were enrolled at San Diego and Zion. Preliminary results did not show any benefit to patients with early-stage respiratory failure.

"Being part of a randomized controlled trial gave us much-needed information that, despite our optimism, this therapy did not actually work," said Dr. Sankar. "This is the way science advances, even in the midst of a pandemic."

Participating in the trial brought other benefits. During an exceptionally difficult time, it strengthened community among the physicians and nurses, giving a sense that everyone was doing all they could to help the patients on their floors. The altruism of the patient participants was also inspiring.

"It often touched me when patients would say to me, 'I know this may not work for me, but I hope it works for someone else,'" Dr. Sankar said. "I am deeply thankful to all of those patients who understood they might not benefit but did this to advance medicine for all future patients."



Dr. Gunter Rieg (left) and Dr. Viji Sankar led clinical trials for oral nucleosides and inhaled nitric oxide

### Oral nucleoside (molnupiravir)

In November, the Kaiser Permanente South Bay Medical Center began enrolling participants in a placebo-controlled trial an oral nucleoside analogue, molnupiravir. First developed in the early 2000s, molnupiravir is a small molecule drug that has proven to work against respiratory diseases from multiple RNA virus families in vitro, including SARS-CoV-2.

Gunter Rieg, MD, an infectious disease specialist, was drawn to the study because it offered one of the first promising oral treatments for COVID-19. Remdesivir and other early authorized treatments had to be delivered intravenously.

"Oral antiviral agents active against SARS-CoV-2 would allow us to treat patients with COVID-19 infection earlier in the disease course when viral replication is the predominant disease mechanism and patients are not sick enough to be hospitalized," Dr. Rieg said.

Early treatment with an antiviral agent may avoid the need for hospitalization, hinder disease progression, and also prevent transmission to others, he noted. While the trial was open to patients while in the hospital, they could be discharged after day 2 of the 5-day course of treatment.

The trial remained open into 2021.



## Vaccines bring hope for end to pandemic

In August, Kaiser Permanente joined the phase 3 clinical trial for a new investigational vaccine developed by Pfizer Inc. and BioNTech. A pop-up clinic at the Kaiser Permanente Los Angeles Medical Center became the primary site for Kaiser Permanente Southern California.

"By that time, more than 16 million people had been infected with COVID-19 around the globe. The pandemic had affected the world profoundly both economically and socially," said Dr. Towner, who served as principal investigator for the vaccine trial in KPSC. "We knew it was imperative that we find a safe and effective vaccine as quickly as possible."

Given Kaiser Permanente's diverse membership, especially in Southern California, the study team quickly turned their focus to recruitment strategies that would support rapid enrollment and foster equitable inclusion of communities of color.

To do that, the team worked with staff from R&E's IT and Communication groups to develop a landing page to host study information and a screening tool along with other recruitment tools. The Regional Research Statistical Services team then pulled information to identify potential participants, tapping into demographic and other information contained in Kaiser Permanente HealthConnect®.

The study team then used the list of identified participants to send more than 70,000 recruitment emails to potential participants. The effort to build an equitable, high-speed recruitment approach was a success. More than 50% of participants came from communities of color.

Due to overwhelming interest, trial enrollment filled quickly. The last patient enrolled at the Los Angeles Medical Center in late September.

By mid-November, preliminary results showed efficacy results of 95%. A month later, the FDA granted emergency use authorization. On December 14, the first COVID-19 vaccine



Celia Garza-Halstead administering a vaccine (or placebo) to Carole Brennan, a participant in Pfizer-BioNTech vaccine trial, at the pop-up clinic at the Los Angeles Medical Center

administered outside of clinical trials in California was administered at the Los Angeles Medical Center.

KPSC's successful participation in the Pfizer-BioNTech trial paved the way for participation in additional COVID-19 vaccine studies in 2021, including a pediatric trial and a study assessing a vaccine booster dose in adults.

"Much as with the AIDS epidemic, the COVID-19 pandemic thrust a light on the importance of rapidly done, high-quality research to help bring critically needed therapies to the public," said Dr. Towner. "It has been incredibly inspiring to see how many people have come together in this historic effort to bring the COVID-19 pandemic to an end."





Staff from across the region jumped in to support clinical trials during the pandemic. Left to right: IT Support Analyst Chris Clendenin; Clinical Trials Operations Manager Tiffany Castanon; LAMC Inpatient Pharmacy Director Dr. David Cheng

## Adapting and innovating during the pandemic

Throughout 2020, the clinical trials program supported more than 400 active protocols. While COVID-19 trials understandably attracted much attention, trials continued across nearly 30 therapeutic disciplines, including oncology, cardiology, neurology, urogynecology, hepatology, infectious diseases, and ophthalmology.

Keeping this broad portfolio of trials available to our membership during a pandemic has involved adaptation and innovation by our clinical trials team.

### Virtual regional command center

During the remdesivir trial, the team established a new centralized process to rapidly enroll hospitalized patients and coordinate with physician investigators and inpatient pharmacies at all 15 Kaiser Permanente medical centers across Southern California. More than 50 staff members from clinical trials and other research divisions staffed the command center 7 days a week, in 12-hour shifts, to support the trial during the 2-month enrollment period.

### Rapid recruitment

The research team developed targeted lists of eligible patients, electronic screening tools, and web-based recruitment tactics to rapidly recruit participants from diverse backgrounds to participate in vaccine and other trials.

### Coordination with home health

To avoid bringing COVID-19-positive patients back to Kaiser Permanente for follow up, the clinical trials team worked with KPSC's home health group to arrange for a nurse to go to the patients' homes to draw blood and collect necessary samples for the monoclonal antibody studies.

### Paperless consent

Throughout the pandemic, new infection control protocols required paperless informed consent. Research IT configured 75 iPads that linked to web-based consent forms to support the remdesivir trial and other COVID-19 trials.

### Pop-up clinic

The team located temporary dedicated space to support high-priority studies that required a high-volume patient enrollment and in-person visits, including the Pfizer-BioNTech vaccine trial.

### Data extraction and entry

Enormous amounts of data are required to support clinical trials quality oversight. Data had to be extracted and entered at unprecedented speed in the pandemic. R&E's statistical services group pulled data electronically for study labs and adverse events. More than 80 research staff manually entered remdesivir trial data into the sponsor's database.

### Home drug delivery

The team used courier services to deliver investigational drugs to patients' homes, mitigating their potential risk of exposure.



Physician scientist Dr. Adam Sharp at the convening stairs in the Medical Education Building at the Kaiser Permanente Bernard J. Tyson School of Medicine, where he is an assistant professor of Health Systems Science

## Searching for evidence to guide COVID-19 care

In April 2020, physician scientist Adam Sharp, MD, MSc, spent his emergency department shifts working in an ambulance bay at the Kaiser Permanente Los Angeles Medical Center, where he evaluated patients who came in seeking care for symptoms that could be COVID-19.

Dr. Sharp recalled, "I remember sitting there, in all my protective gear, thinking, 'How am I supposed to know which of these patients might be most at risk and who really needs to be admitted to the hospital?'"

Emergency physicians across the globe faced daunting constraints in the early stages of the pandemic. Limited testing supplies meant that physicians often had to assess which patients needed to be hospitalized for COVID-19 without having a confirmed diagnosis. Even if a rapid test was available, little was yet known about who might be at greatest risk for deterioration.

The concern Dr. Sharp felt while sitting in the triage tent led to an idea for a new research project. Much of his prior research focused on clinical decision tools, including risk scores. Why not develop a risk score to help physicians determine who might benefit most from hospitalization?

Dr. Sharp and his clinical colleagues began to develop an assessment tool that looked at patient comorbidities, obesity, vital signs, age, and sex. Dubbed the COVAS Score, the tool was developed in a matter of months. By July 2020, it was implemented in the Kaiser Permanente HealthConnect® electronic health record.

"I've used the tool to make informed decisions with my own patients in the emergency room," Dr. Sharp said. "It can help to reassure low-risk patients, and alternatively can encourage those at high risk to receive hospital-based care that may speed their recovery."



## Interest in research surged during pandemic

Dr. Sharp was far from alone in turning to research to resolve the many unanswered questions about COVID-19. Physicians at Kaiser Permanente medical centers across Southern California began to explore ideas for potential research projects. In the early stages of the pandemic, many reached out to Bechien U. Wu, MD, MPH, and other members of the Regional Research Committee.

"The situation with COVID-19 highlighted the important role that research can play," said Dr. Wu, who chairs the committee. "We were dealing with an entirely new disease, with many gaps in our knowledge."

As interest in COVID-19 research surged, concerns arose that projects would overlap and that limited research resources, including our programmers and biostatisticians, would be stretched too thin.

In March, Dr. Steven Jacobsen, then senior director of research, asked epidemiologist Annette Adams, PhD, MPH, to help track COVID-19 research and consult on as much study design as she could. An initial list gathered through phone calls, email inquiries, and an online survey included about 80 study ideas. Dr. Adams discovered significant overlap in research interests, from racial and ethnic disparities to risks and outcomes for pregnant women.

"Some of what I did was matchmaking," said Dr. Adams. "If I heard several investigators expressing a similar idea, I would connect them."

## Matching clinicians and researchers

Meanwhile, Dr. Wu began to do some matchmaking of his own. He saw an opportunity to bring clinicians and researchers together to initiate a series of rapid-cycle research projects. The idea was to conduct research that could be swiftly incorporated into practice.

"We were fielding calls left and right, so it seemed like a natural fit," he said. "We had piloted the concept of rapid-cycle research projects a few years earlier, so we already had a model for accelerated review as well as a funding stream."



Dr. Bechien Wu meets with Research Project Manager Eva Lustigova in the Kaiser Permanente Marilyn Owsley Clinical Research Center

At the end of March, Dr. Wu reached out to Michael K. Gould, MD, MS, then director of the Division of Health Services Research and Implementation Science and leader of the Care Improvement Research Team (CIRT), a group with expertise in bringing together clinicians and researchers to answer important questions and improve care. Dr. Gould quickly agreed.

"We had an opportunity to address urgent research questions and inform our frontline clinical partners, which is the core of our mission as researchers embedded within the care delivery system," said Dr. Gould.

Clinical groups, including emergency physicians, hospitalists, and pulmonologists, reached out with clinical questions. Several research scientists also proposed research ideas.

"There were many unanswered questions about COVID-19, including how to assess and manage risk for patients with suspected or confirmed COVID-19," said George Yuen, MD, regional chief of pulmonary and critical care medicine. "We hoped these studies would shed much-needed light on the risk factors for severe disease and help inform clinical decisions for our patients."



Dr. Christopher Tenggardjaja, Dr. Jonathan Gullett, and Dr. Katia Bruxvoort at the Molecular Microbiology COVID department at the Regional Reference Laboratory in Chino Hills

## Rapid-cycle research meets urgent need

The rapid-cycle project team brought together nearly 2 dozen scientists and physicians from a wide range of specialties, including pulmonary and critical care, hospital medicine, emergency medicine, cardiology, nephrology, internal medicine, family medicine, pediatrics, neurology, and immunology.

Of the 4 initial projects, 3 have resulted in new clinical decision tools. The first was Dr. Sharp's COVAS model. Early 2021 saw the implementation of 2 tools, one to estimate mortality risk for patients on mechanical ventilation and one to predict which hospitalized patients are at risk for deterioration. For more information on the rapid cycle projects, see page 40.

Even as the first project began to find answers, new questions continued to emerge. In December 2020, regional leaders approved a new round of CIRT projects, including studies focused on household transmission, equitable risk-stratification tools, and understanding and supporting COVID-19 vaccine confidence among health care providers at Kaiser Permanente Southern California.

The Regional Research Committee also supported 5 additional COVID-19 research projects. For more information on those studies and other RRC-funded studies, see page 44.

## Evaluating swabs, saliva to scale up testing

One of the RRC-funded studies was a clinical evaluation of different sample types for SARS-CoV-2 molecular diagnostic testing. Christopher Tenggardjaja, MD, a urologist at Kaiser Permanente Los Angeles Medical Center, initially became interested in the topic for personal reasons. He and his wife were expecting their third child and Kaiser Permanente had recently begun using rapid molecular tests to routinely screen expectant mothers before admission to the hospital.

COVID-19 testing most often involves nasopharyngeal and/or oropharyngeal (NP/OP) swabs, which are inserted deep into the nose and/or throat and must be collected by a health care provider. At the time, there were supply challenges. Dr. Tenggardjaja began to wonder about other testing options.

"I thought we were well positioned to study the sensitivity, or accuracy, of different testing options in our real-world setting, where performance could



differ from highly controlled laboratory studies,” said Dr. Tenggardjaja.

In early April 2020, he reached out to Nancy Gin, MD, regional medical director of Quality and Clinical Analysis, and several other quality and research leaders, who ultimately connected him with Katia Bruxvoort, PhD, MPH, an infectious disease epidemiologist and post-doctoral research fellow, and Jonathan Gullett, MD, physician director of microbiology for the Southern California Permanente Medical Group’s Regional Reference Laboratories.

After exploring several ideas, they initiated a study to determine whether patient-collected saliva or nostril swabs that don’t reach so deep into the nose could be as accurate as NP/OP swabs.

“NP/OP swabs can be really painful for patients, and they have to be administered by a health care provider,” said Dr. Bruxvoort. “There was a need for more flexible options to help scale up testing.”

Other options for testing could help with both supply challenges and safety.

“Another advantage to saliva collection is that it does not rely on swabs or commonly used transport media, both of which have been in relative short supply globally since the beginning of the pandemic,” said Dr. Gullett. “Self-collection, whether at home or in drive-through locations, also offers a safer alternative to both patients and providers alike from the potential further spread of disease.”

### **Data lead to changes in regional lab strategy, EUA application**

In mid-August, the research team launched the study. Patients with COVID-19 symptoms who had orders for the NP/OP test were invited to participate by providing self-collected saliva and nostril swabs. More than 2,000 patients enrolled at 7 Kaiser Permanente emergency departments. The Regional Reference Laboratory team worked closely with the study team to optimize the workflow for testing saliva and nostril swabs. They processed the samples and provided data files daily.



Dr. Benjamin Broder at his office in Walnut Center, Kaiser Permanente’s main administrative building for Southern California

In October, the study team presented its interim results to Dr. Gin and Benjamin Broder, MD, PhD, regional assistant medical director of Quality and Clinical Analysis. The region was in the midst of planning to manage potentially monumental demand for testing in the late fall and winter months.

“Even though our lab capacity had increased, the kind of demand we anticipated would require a lot of personnel, right when we would likely need more people to support direct patient care,” said Dr. Broder. “We were very interested in exploring other testing options.”

Based on the interim results, the regional leaders decided to start using patient-collected saliva at drive-through centers in mid-November. Near the end of the year, the lab team submitted an emergency use application to the Food & Drug Administration, seeking approval to use saliva tests at home, which it received in April 2021.

“Our researchers provide essential insights to our organization by finding evidence that isn’t yet available in the published literature,” said Dr. Gin. “This has been more essential than ever during the pandemic as we deal with a still-new disease with so many unanswered questions.”



Dr. Deborah Cohen observes people for the masking adherence study in Clover Park in Santa Monica, California

## Scientists research masking adherence with communities across the country

When the COVID-19 pandemic closed playgrounds, her research into playground use and physical activity could also have come to a halt. Instead, with the blessing of the National Institutes of Health, which was funding the work, Deborah Cohen, MD, MPH, pivoted to conducting research relevant to lighting the way through the pandemic: Who was adhering to the outdoor masking recommendations, and who wasn't?

"Rather than twiddle our thumbs, we decided to use our skills at systematic observations to impact public health policy," said Dr. Cohen, a research scientist with the Department of Research & Evaluation. "At that point, masks were our best hope of reducing the spread of COVID-19. We

wanted to collect information about usage so we could point out where public health efforts were most needed to increase adherence."

Her team included other researchers at Kaiser Permanente Southern California, researchers from other institutions, university professors, and public health officials. Their first full-scale effort occurred in Philadelphia.

People involved in the Philadelphia study observed more than 4,600 people in 30 outdoor public spaces throughout that city, including commercial streets, neighborhood parks, and playgrounds during 3 weeks in August 2020. The Philadelphia Public Health Department announced results that month.



*"Until vaccination has become near universal, it will still be important for people to wear masks in public settings where they might interact with others to reduce the spread of this deadly disease."*

– Deborah Cohen, MD, MPH

The research was part of an ongoing series of studies called SOMAD (Systematic Observation of Mask Adherence and Distancing). From then through June 2021, 228 researchers across the nation, including in California, recorded their observations of more than 104,000 people in public spaces.

Some of the initial findings, which includes those gathered in California and Philadelphia, showed:

- Women were wearing masks more than men.
- Seniors were the most adherent age group, while teens were least likely to be wearing masks.
- People of Asian descent were more likely to wear masks than other races or ethnicities.
- People were more likely to wear masks in commercial areas than in parks.
- About 20% of people who had masks on were not wearing them properly, for instance had their nose uncovered.
- After the press release went out in Philadelphia, the use of masks increased slightly. It increased much more after President Donald Trump contracted COVID-19.

The disparities in adherence suggest that the information about the risk of exposure is not uniformly appreciated by all groups, Dr. Cohen said. Given that males have more severe consequences from COVID-19 infection than females, a targeted information campaign may be required to motivate greater compliance, she said.



The study showed that women were wearing masks more than men, and seniors were the most adherent age group

After the study was done in Philadelphia, the public health department issued more detailed guidance for mask use.

The first research paper resulting from the work, titled Systematic Observation of Mask Adherence and Distancing (SOMAD): Findings from Philadelphia, was published in the journal *Preventive Medicine Reports*. "Until vaccination has become near universal," Dr. Cohen said, "it will still be important for people to wear masks in public settings where they might interact with others to reduce the spread of this deadly disease."



Research Associate Vanessa Audea and Dr. Conrad Liang at the Fontana Medical Center

## Clinical trials are driving a revolution in stroke care

Stroke is the fifth leading cause of death in the United States, and in the past 5 years, stroke treatment has undergone a renaissance. Clinical trials at Kaiser Permanente Southern California and elsewhere have shown that stroke patients benefit not only from medication, but also from interventional clot removal. The procedure physically removes stroke-causing clots from the brain using small tubes and retrievable stents, and has been shown to reduce death and disability.

The Kaiser Permanente Southern California stroke research program is a collaboration by physician researchers at medical centers around the region led by Navdeep Sangha, MD, a vascular neurologist. Dr. Sangha sees patients physically at the Kaiser Permanente Los Angeles Medical Center and virtually through Telestroke. It is a teleconferencing program throughout the region's 15 medical center emergency departments. With Telestroke, patients can be treated by the stroke specialist and then screened and enrolled into a clinical trial if appropriate, through telemedicine.

"Our stroke program shows how Kaiser Permanente is invested in growing our clinical care through clinical trials. It's really putting us on the map—not just as a place where we provide excellent clinical care, but also as a place where we enroll patients in clinical trials to discover that next level of care," Dr. Sangha said.

### Quick action is key

Acting quickly can help stroke patients get the treatments they need to survive and reduce damage to the brain, according to the Centers for Disease Control and Prevention.

Two million brain cells die every minute until blood flow is restored, according to the American Heart Association. The more quickly symptomatic patients are treated with medication or interventional clot retrieval, the more likely it is that they'll have a good functional outcome. Every 30-minute delay in treatment reduces the chance of good outcome by 10%. New therapies





Dr. Zahra Ajani (right) and Dr. Navdeep Sangha in the Los Angeles Medical Center's Healing Garden



Dr. Navdeep Sangha at the Los Angeles Medical Center

that have been and continue to be tested at Kaiser Permanente Southern California medical centers could expand the potential for treatment, and potentially benefit more patients who have strokes.

"Our goal is to provide the highest-quality, evidence-based care for patients and families dealing with cerebrovascular diseases," said Zahra Ajani, MD, medical director of the Los Angeles Medical Center Comprehensive Stroke Center. "We strive to innovate new methods of diagnosis and treatment through research and clinical trials," she added.

### KPSC medical centers leading enrollment in stroke clinical trials

Kaiser Permanente's research in Southern California allows patients across the region to have access to the newest potential stroke therapies.

Kaiser Permanente Southern California is one of the top enrollers in the TIMELESS trial, a national trial designed to evaluate the use of a clot-busting medication. This success is due to the power of identifying, enrolling, and treating eligible patients at 3 different medical centers (Los Angeles, Fontana, and Anaheim).

In 2020, 21 investigators at the Los Angeles, San Bernardino County (Fontana/Ontario), and Anaheim medical centers oversaw 16 clinical trials. They were sponsored by the National Institutes of Health through the StrokeNET research network or by industry. Two additional medical centers, South

Bay and Baldwin Park, will begin enrollment in stroke clinical trials in 2021.

"Stroke patients are very sick. With Telestroke and clinical trials, we can offer them the best medical care at whichever Kaiser Permanente medical center they go to. That's not something that most other health care systems can offer. This makes us ideally positioned to conduct stroke trials that can potentially change people's lives," said Conrad Liang, MD, PhD. Dr. Liang, a vascular and interventional neurologist at the Kaiser Permanente Fontana Medical Center, said, "In the future we expect to be initiating national stroke clinical trials, not just participating in them."

### Integrating clinical care and clinical trials

The stroke team is a great example of clinical trials being integrated into clinical care, said William Towner, MD, FACP, FIDSA, the regional physician director for the Division of Clinical Trials Research. Dr. Towner also leads the Clinician Investigator Program for the Southern California Permanente Medical Group.

"The clinical trials team is always looking for ways to integrate research into clinical care and our stroke team has achieved that," Dr. Towner said. "They provide new treatment opportunities for patients, while also allowing those patients to be part of determining the best stroke treatments for others."



Dr. Lisa Oakley at a drive-through testing site during a factory workplace outbreak of COVID-19 in eastern North Dakota

## CDC disease detectives at KPSC build bridges to national COVID-19 response

In February 2020, Lisa Oakley, PhD, MPH was in Ghana assisting with a polio vaccination campaign when she heard the news about COVID-19 on TV. “We were seeing the cases in Wuhan, seeing the beginning of the pandemic play out,” she said. “I suspected it would be hitting us about the time I got back home, but I had no idea how big it would become.”

For Dr. Oakley, “back home” meant returning to Kaiser Permanente Southern California, where she was “embedded” in the Department of Research & Evaluation as an Epidemic Intelligence Service (EIS) officer for the Centers for Disease Control and Prevention (CDC). She was only the second EIS officer assigned to work with Kaiser Permanente, in a position created just a few years before.

EIS officers, better known as CDC disease detectives, spend 2 years serving at various training sites throughout the country, mostly at CDC headquarters in Atlanta or in public health departments throughout the country. KPSC is the only site in the country where an EIS officer works within a health care delivery system rather than a governmental organization.

In general, the role of these disease detectives is to investigate the sources and spread of disease and devise innovative approaches to prevention and control. An EIS officer working within KPSC has the unique opportunity to work alongside the organization’s research epidemiologists and clinicians, blending the investigation of infection with the delivery of health care directly to Kaiser Permanente members.



"I was able to work with researchers and clinicians to explore health on the larger population level, looking at how we can protect our members all around, and not just when they come in to see the doctor," said Dr. Oakley, who now works as an epidemiologist at the CDC. "From that perspective, Kaiser Permanente is truly practicing a public health approach."

### Bringing experience back to colleagues

During their 2-year experiential training, EIS officers may be called upon to respond to an urgent public health need, outside of their initial assignment. Dr. Oakley was no exception, deploying not only to Ghana, but then to Seattle, on a mission that turned out to be incredibly important in the early days of the COVID-19 pandemic.

In Seattle, she served on a team of CDC infection prevention and control experts alongside the Seattle-King County Public Health Department as part of the first efforts to test asymptomatic residents and health care workers in long-term care facilities.

"We started getting a sense that the situation was going to be bigger than we anticipated it would be," she said about the data they were collecting. "It really was a time of learning how the virus is transmitted and what kind of symptoms are associated with it."

As a result of this investigation, Dr. Oakley co-authored one of the first publications describing COVID-19 transmission among people who weren't showing symptoms. That finding has become vital to the public health response in this pandemic. She then went to North Dakota, where she investigated an outbreak of COVID-19 in a long-term care facility and guided testing strategies to help the employer quickly identify people who were infected and isolate them from other staff and residents.

Once she returned to California, Dr. Oakley developed strategies to support Kaiser Permanente members across the nation



Dr. Lisa Oakley in a near-deserted airport on her way to North Dakota, one of her deployments as an EIS officer at KPSC

sharing households with residents who had tested positive for COVID-19 infection. In these consultations, she advised members how to isolate, how to appropriately wash hands and wear masks, and how to safely carry out other essential household activities.

"I was so fortunate to have gained the experience of supporting this emergency response," said Dr. Oakley. "It really informed my understanding of how to support members at an early stage when we didn't have a lot of information about virus transmission within a household."

### Passing the torch

Dr. Oakley's tenure as an EIS officer at KPSC ended in June 2020 as she completed her EIS fellowship. During her last few months, she joined another regional team that laid the groundwork for a digital COVID-19 surveillance tool that proactively prompts members regarding symptoms and triages them for appropriate care via text or email. When Dr. Oakley's successor, Debbie Malden, DPhil, MSc, took the reins in August, she sprang into action as disease detectives do, linking up with



Dr. Debbie Malden and Dr. Sara Tartof, one of her supervisors, near the department offices in Pasadena

a group of colleagues who were just piloting the tool among Kaiser Permanente members in Washington state.

"I was able to jump in at the right time and with the right skill set to help them meet their goal of reaching more members to capture the real-time prevalence of COVID-19 symptoms, particularly among members who have typically been under-represented in medical research involving digital health interventions previously," said Dr. Malden, who came into EIS equipped with a background in epidemiology.

The digital surveillance tool, known as the Voluntary Symptom Reporting tool, or VSR, queries Kaiser Permanente members via text or email (based on the member's preference) asking if they're experiencing COVID-19 symptoms. If they are, the tracker asks more questions to triage the member appropriately, sometimes to a physician for consult or to the emergency department.

### **Collaboration with IT proved invaluable**

One aspect of the project that was particularly exciting for Dr. Malden was being able to bring

*"I was able to jump in at the right time and with the right skill set to help them deliver on their goal toward reaching more members to capture the real-time prevalence of COVID-19 symptoms..."*

*— Debbie Malden, DPhil, MSc*

the VSR tool to full potential by working with Kaiser Permanente's seasoned information technology experts and platforms.

"I got to work hand in hand with the software engineers and make recommendations from a public health standpoint," she said. "The collaboration between Kaiser Permanente IT and the Community Health team was truly remarkable. The team's ability to approach the VSR project with tactful creativity and a bold application of novel techniques, together with their unified drive to improve health, was inspiring. It felt like, working together, we could really enhance the design of the tool for the benefit of public health at large. It was a real team effort."



Dr. Malden presented the VSR tool to her EIS colleagues at the CDC in the fall. “It was really valuable not only to gather opinions from my fellow EIS officers but also to see what they’ve been doing and to get input from them and the surveillance experts across the agency,” she said, noting that she was able to incorporate that input when making improvements to the VSR tool.

“The main finding is that it’s feasible to target texts and emails, get responses in real time, and communicate with members in a way that affects their behavior and their interaction with the health care services,” she said. “And this is independent of what information we’re trying to record.”

In other words, the symptom reporter can be used in any public health context, regardless of the disease or symptoms being tracked. In fact, the work done for the VSR laid the groundwork for the Kaiser Permanente COVID-19 Side Effect Monitoring System, which was implemented in 2021 as part of a collaboration with the CDC.

Dr. Malden’s supervisor, Sara Tartof, PhD, MPH, who herself went through the EIS fellowship before joining KPSC, couldn’t be prouder of her trainee’s work.

“What this means, essentially, is that our Kaiser Permanente EIS officer is able to leverage work and models done by Kaiser Permanente in other regions into a similar system the CDC is developing that could ultimately have a worldwide impact,” Dr. Tartof said. “Both Lisa and Debbie have been a really important link between the CDC and Kaiser Permanente on COVID-19 efforts.”

### EIS alums advocate for KPSC position

When Dr. Tartof was an EIS officer, she and her then-colleague Jean Lawrence, ScD, MPH, MSSA—also a CDC EIS alum—were instrumental in the creation of the EIS officer position at KPSC. Being familiar with the EIS fellowship, they knew that such a collaboration had enormous potential. “The caliber of professionals in the EIS fellowship is really tremendous,” Dr. Tartof said.



Dr. Sara Tartof, Dr. Debbie Malden, and Research Associate Sylvia Kim at a vaccine site in Baldwin Park

“They’re highly trained and really motivated. And this position allows them to see how their work can impact population health through a variety of avenues, including patient care. It’s not an academic exercise here. It has real medical and public health value.”

After several years of discussion within KPSC and with the CDC, the role was created in 2016. The next step, Dr. Tartof said, was to recruit one of those highly trained and motivated officers to fill it. Dr. Tartof described the recruitment process as something resembling medical residency matching: representatives from the host sites sit at tables and answer questions from prospective recruits, after which the EIS officers are matched with one of the host sites that suits their training needs and expectations.

It was challenging to find an officer willing to take the plunge on a newly created position, said Dr. Tartof, especially given that KPSC was (and still is) the only site unaffiliated with local, state, or federal government. “There was no history. We couldn’t answer questions about what the experience had been like for previous officers,” she said.

## A unique opportunity

But Drs. Tartof and Lawrence successfully matched with Gloria Chi, PhD, MPH, a newly minted PhD graduate from the University of Washington. Dr. Chi recognized that, with access to Kaiser Permanente's electronic health records and research expertise, she could take on investigations that wouldn't be possible in other places. Combining that opportunity with the chance to be a government representative working in a non-governmental environment elevated the potential. "I could see how the position would enable me to conduct research that applied directly to improving health care and health care delivery," said Dr. Chi.

Dr. Chi came to the new position with an interest in investigating the health impacts of environmental pollutants. "Even though that type of data isn't usually available in medical records, using Kaiser Permanente's data we were still able to conduct a study in that area."

For example, during her tenure from 2016 to 2018, shortly after lead was discovered in the water in Flint, Michigan, Dr. Chi was able to study trends in blood lead levels in children living in the KPSC region and create a more streamlined process for getting kids from across the region tested.

## Reflecting on valuable KPSC experience

The richness and accuracy of Kaiser Permanente's data has been a draw for Drs. Chi, Oakley, and Malden. That data, layered on top of the opportunity to collaborate and do field work with health officials in the country's most populous county, makes a good argument for an EIS "datahead" to choose Kaiser Permanente as their host site.

Dr. Chi said that combining that data with the skills of an EIS officer really helps bring out the potential for new understanding. "You can have a lot of data, but analyzing it isn't always straightforward," she said. "Having an EIS officer



Dr. Gloria Chi presents at a research seminar in Pasadena in 2018 during her tenure as an EIS officer at KPSC

working in R&E allows that person not only to access the data, but to address research questions that have direct relevance to clinical practice."

Now a senior data scientist at Genentech, Dr. Chi said that every day, she employs the data analysis skills she learned during her time with KPSC.

Dr. Oakley agrees. Reflecting on her time spent as a CDC disease detective with Kaiser Permanente, both before COVID-19 and during the public health response, she said the EIS position is a real opportunity for public health and health care systems to learn from each other.

"I was able to bring my experience from boots-on-the-ground CDC deployments back to inform my work at Kaiser Permanente, just as my population-level health research in the Division of Epidemiologic Research helped to inform my work in the field."

"Building stronger relationships between health care and public health serves to strengthen the whole system," she said.



# ACCOMPLISHMENTS & MILESTONES





# Kaiser Permanente Southern California research

Research at Kaiser Permanente Southern California is conducted through collaboration between scientists and physicians, and supported by a large skilled staff, resources, and rich data from Kaiser Permanente's electronic health record system. The program publishes hundreds of studies each year. Many study results are put into clinical practice quickly to improve care and outcomes for Kaiser Permanente members and knowledge is shared with the larger medical community.

## Research program overview

### Investigators & Staff

**40+** SCIENTISTS



Includes full-time staff scientists, adjunct investigators, and trainees (post-doctoral research fellows and Epidemic Intelligence Service officer). Eight are on faculty of the Kaiser Permanente Bernard J. Tyson School of Medicine

**250+** PHYSICIAN RESEARCHERS

Includes 180+ conducting clinical trials, plus active and retired SCPMG physicians

**~400** RESEARCH AND SUPPORT STAFF

Includes research project managers and research associates, clinical trials support staff, programmers, biostatisticians, and clinical informatics personnel. Plus division administration, business office, operations, research IT, and communications staff

### Projects & publications



**1,250+** active protocols  
Includes 400+ active clinical trial protocols

**25+** Regional Research Committee-funded projects

**10+** Care Improvement Research Team studies

**475+** original research papers published  
(In medical and scientific journals. Excludes case reports, editorials, and letters.)

### COVID-19 research

**84** studies initiated

**15+** studies published

**20+** vaccine safety and effectiveness studies

**9** clinical trials

**178** participants in Pfizer-BioNtech vaccine trial

**588** participants in remdesivir trial (KPSC was one of largest-enrolling sites in the world)

**3** new clinical decision tools developed via rapid-cycle research



### Southern California research environment

#### FACILITIES

**15** medical centers

**235** medical offices

**7,600+** physicians

**27,000** nurses

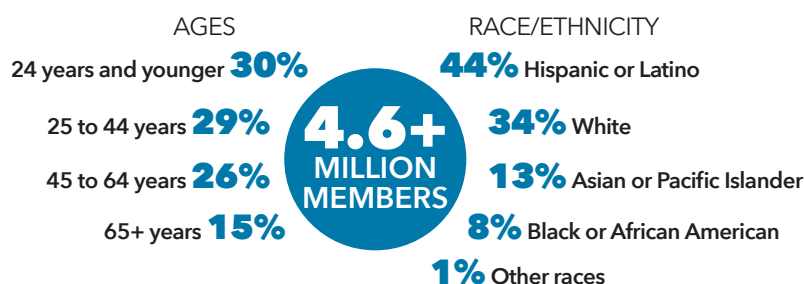
**75,000** employees

**33.9 million** outpatient prescriptions filled

**11.7 million** prescriptions filled by mail order



## Southern California member population



#### SEX

**52%** Female

**48%** Male

#### MEMBERSHIP RETENTION RATES

**92%** remain with Kaiser Permanente  
**more than 1 year**

**82%** remain with Kaiser Permanente  
**after 3 years**

**73%** remain with Kaiser Permanente  
**after 5 years**



# Financial overview

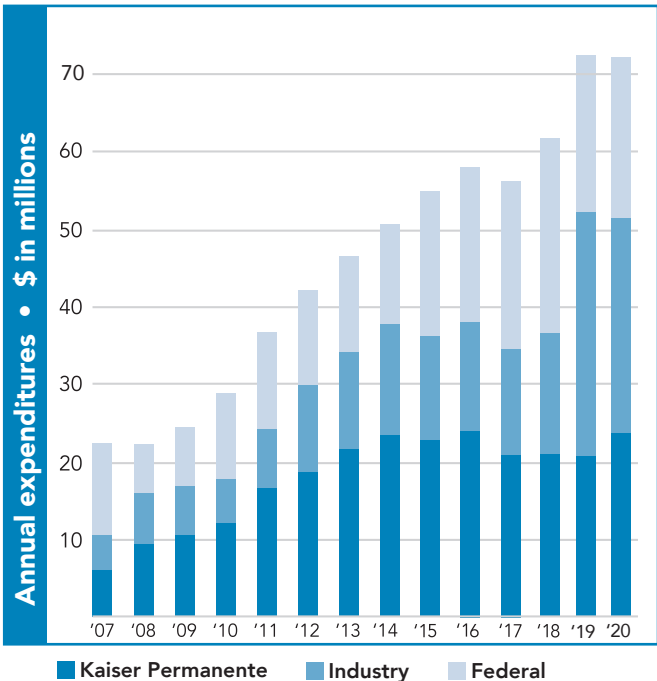
Funding for research at Kaiser Permanente Southern California has increased consistently over the past 15 years to support a growing portfolio of innovative and clinically relevant research.

**\$73** MILLION: TOTAL RESEARCH FUNDING

Federal grants: \$21 million

Industry contracts: \$28.7 million

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



## 2020 grant and contract submissions

(new grants only, external only)

Submitted: 238

Awarded: 127

Kaiser Permanente Southern California was the lead, or prime, institution for 56% of all grants and contracts submitted, and was the subcontractor institution for the remaining 44%.



## New grants and contracts

(all years, includes clinical trials)

Direct costs: \$43.4 million

Indirect costs: \$25.4 million

**Total: \$69.1 million**

## Continued grants and contracts

(all years, includes clinical trials)

Direct costs: \$112.1 million

Indirect costs: \$51.3 million

**Total: \$163.4 million**

## Selected findings

In 2020, 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.

### Does election stress affect health?

In this study of adults in Kaiser Permanente Southern California, researchers examined the rate of heart attacks and strokes before and after the 2016 U.S. presidential election. In the 2 days after the election, the rate of hospitalization for heart attacks or strokes was 1.62 times higher than in the same 2 days the week before the election. Other research has shown that the risk of cardiovascular events increases after significant public events like earthquakes or terror attacks, but little was known about how sociopolitical stress, like election stress, affects health. Although more research is needed to better understand the interplay between these factors, people should be aware that sources of stress like an election can affect their cardiovascular health.

*Mefford et al. Proc Natl Acad Sci. 2020 Oct;117(43):27054-27058.*

### Femur fracture risk with bisphosphonate use

Although atypical femur fractures (a break in the middle of the thighbone) are rare with the use of osteoporosis medications called bisphosphonates, KPSC researchers found that the risk for these fractures increases with longer bisphosphonate use, especially after 5 years. The risk was higher in Asian women than in white women. The researchers examined fracture risk in a large ethnically and racially diverse patient population of nearly 200,000 women. However, because women are still more likely to sustain a “typical” hip fracture than an atypical femur fracture, they should not avoid treating their osteoporosis with bisphosphonates. These findings can help physicians develop personalized treatment plans for their patients.

*Black et al. N Engl J Med. 2020 Aug;383:743-753.*



Dr. Paul Lee and Dulce Hayes

### Declines in heart attacks greater in men

The number of heart attacks experienced by men and women enrolled in KPSC declined from 2000 to 2014. Men saw a steady decline during the study period of about 4.7% per year. In women, however, heart attacks declined by about 4.6% annually from 2000 to 2008 and then by only 2.3% annually from 2009 to 2014. The research findings highlight that a better understanding of the factors that lead to sex-based differences in heart attack is needed. Women especially should talk with their doctors to find out what they can do to reduce their risk of heart attacks.

*Mefford et al. Circulation. 2020 Feb;141:509-519.*



## Differences in how myopia progresses

Myopia, or nearsightedness (when objects far away appear blurry), worsens at different rates in children according to race/ethnicity. In this study, children of East and Southeast Asian descent showed significantly faster myopia progression over time. Myopia appeared to progress independently of the age of myopia onset in white children but varied by age of onset in East and Southeast Asian children. A strength of the study was the large, real-world population studied. The value of using real-world population data is that selection bias and confounding, which lead to errors in analysis, can be reduced. Information from this study may help in designing racially and culturally specific interventions and in planning clinical trials.

*Luong TQ et al. Invest Ophthalmol Vis Sci. 2020 Nov;61(13):20.*

## Insomnia and depression after breast cancer

Breast cancer survivors with insomnia were 6 times as likely to report symptoms of depression as were survivors who did not have insomnia. Researchers at KPSC and the UCLA Geffen School of Medicine interviewed 315 breast cancer survivors to determine whether insomnia, which affects about 40% of these women, was a factor correlated with depression and fatigue. A strength of the cohort studied was its diverse makeup: 30% of the group were women of color. Screening for insomnia should be considered to improve the quality of life of long-term breast cancer survivors.

*Haque R et al. J Womens Health. Published online October 9, 2020. doi:10.1089/jwh.2019.8135*

## Physicians can influence patient weight loss

Findings from a survey of more than 2,800 patients showed that patients who have overweight or obesity, but not aware of it, or whose primary care provider had not talked with them about weight, were less likely to have attempted weight loss in the previous year. People who have overweight or obesity may not realize the effect of weight on their health, such as increasing their risk for



Tiffany Castanon and Oliva Bravo

cardiovascular disease and diabetes. The study findings are especially relevant for physicians. By talking to their patients about weight, physical activity, and diet, primary care providers may motivate their patients to consider weight management strategies.

*Young DR et al. Obes Res Clin Pract. 2020;14(5):449-455.*

## Real-world evidence on herpes zoster

Researchers estimated the incidence of herpes zoster, or shingles, and the proportion of patients who experienced complications, were hospitalized, or died. The research was conducted among adults 50 years and older who had never been vaccinated against shingles. The people studied also had to be immunocompetent, meaning they could mount a normal immune response. In this population, the risk of hospitalization or death from shingles was low. Population-based data in unvaccinated, immunocompetent adults are needed to assess the effectiveness of vaccination with the newest shingles vaccine available to patients.

*Tseng HF et al. J Infect Dis. 2020 Sep;222(5):798-806.*

For a full list of 2020 publications, please see the bibliography starting on page 66.

## Selected grants and contracts

Our scientists and clinician researchers lead studies that have potential to change practice well beyond the walls of our organization. Many studies receive external funding from federal agencies, non-governmental organizations, and industry sponsors. The following is a selection of federally funded projects led by Kaiser Permanente Southern California investigators.



Marissa Barron, Vanessa Audea, Ashima Sharma, Pamela Pyrzynski, Catherine Lui, and Elizabeth Castorena

### Ambient air pollution and COVID-19 disease severity or death among confirmed cases in Southern California

Recent studies suggest that long-term ambient air pollution may contribute to mortality from COVID-19. Researchers at KPSC and USC will collaborate on this study, which will assemble a large cohort to investigate contributions of air pollution to the severity of the pandemic. This study is expected to identify key environmental factors that may contribute to COVID-19 infection and its progression.

*Principal investigators: Anny Xiang, PhD, MS (KPSC), and Zhanghua Chen, PhD (USC)*

*Funding agency: National Institute of Environmental Health Sciences*

### The EPICS (Engaging Primary Care in Cancer Survivorship) study: A trial of novel models of care for cancer survivors

As the number of patients treated for cancer continues to rise, challenges have emerged in caring for an increasing number of survivors. This study will compare a primary care physician-led model of survivorship care, where PCPs receive survivorship training and support, to the traditional oncology-led model for survivors of early-stage colorectal cancer and breast cancer. Findings will provide more definitive evidence on the effectiveness of a scalable model of PCP-led survivorship care.

*Principal investigator: Erin Hahn, PhD, MPH*

*Funding agency: National Cancer Institute*



### Clinical care gaps and unmet needs in adolescent and young adult cancer survivors: Patterns of care and patient experiences during early survivorship among AYA cancer survivors

Little is known about the patterns of care provided for survivors of adolescent and young adult (AYA) cancers. This project will investigate patterns of health care utilization among AYA survivors, explore patient-reported care experiences and barriers to care, and examine the relationship between adherence to clinical care guidelines and patient-reported outcomes. Findings from this study, which is part of a program grant to understand clinical care gaps and unmet needs in AYA survivors, will provide crucial insights to improve care and outcomes for this population.

*Principal investigator: Erin Hahn, PhD, MPH*

*Funding agency: National Cancer Institute*

### Risk prediction of breast cancer treatment-related cardiotoxicity

Nearly 20% of breast cancer survivors in the United States have cardiovascular disease but there are no standard risk models to predict cardiovascular events associated with adjuvant breast cancer therapies.

Researchers at KPSC and Georgetown will develop risk prediction models for cardiovascular events following adjuvant breast cancer therapy, ranging from 1 year to

15 years post-treatment. Findings will provide new information to guide clinician and patient decisions about adjuvant therapy use and cardiovascular care.

*Principal investigators: Reina Haque, PhD, MPH (KPSC), and Arnold Potosky, PhD, MHS (Georgetown University)*

*Funding agency: National Heart, Lung, and Blood Institute*



### Primary prevention to reduce cardiovascular morbidity and optimize cancer outcomes

Recommended strategies to prevent cardiovascular problems for patients with cancer include prescribing primary prevention medications and adjusting oncology regimens to protect heart health. KPSC researchers will evaluate the comparative and cost effectiveness of these strategies on short- and long-term cardiovascular, cancer, and economic outcomes. Findings will guide policy on primary prevention and cardio-protective regimens, help improve patient outcomes, and identify groups that may benefit the most from different strategies.

*Principal investigator: Aniket Kawatkar, PhD, MS*

*Funding agency: National Heart, Lung, and Blood Institute*

### Impact of sugary beverage taxes on weight and health outcomes

One potential strategy to address the prevalence of obesity is to implement excise taxes on sugar-sweetened beverages. Researchers from KPSC and KPNC will examine whether taxes in several California

cities that have implemented taxes on sugar-sweetened beverages are associated with any changes in body mass index or diabetes incidence in those communities. This study will be one of the first to include control cities without similar taxes in an investigation of health outcomes related to the taxes.

*Principal investigators: Deborah Rohm Young, PhD, MBA (KPSC) and Monique Marie Hedderson, PhD (Kaiser Permanente Northern California)*

*Funding agency: National Institute of Diabetes and Digestive and Kidney Diseases*



## Linking DNA methylation with child maltreatment and mental health across adolescence

Epigenetics, or the processes that influence gene expression, is crucial to our understanding of how child maltreatment influences later health outcomes, including mental health. In this study, researchers from KPSC and USC will examine the pathways that connect childhood maltreatment to DNA methylation and mental health outcomes. Data from this study, which is a continuation of a longitudinal study begun in 2002, will allow researchers to compare changes in DNA methylation over time and identify factors that may have influenced those changes, potentially leading to future interventions.

*Principal investigators: Sonya Negriff, PhD (KPSC) and Ferol Mennen, PhD, LCSW (USC)*

*Funding agency: Eunice Kennedy Shriver National Institute of Child Health & Human Development*

## Assessing the burden of diabetes by type in children, adolescents, and young adults (DiCAYA) - Component B (18-<45 years)

Young adults between the ages of 18 and 45 years account for about 3 million diagnosed cases of diabetes in the United States, but information on diabetes type is limited for this age group. KPSC researchers will assess the trends of the prevalence, incidence, and early clinical characteristics of young adults in our racially and ethnically diverse membership population. Findings will assist in identifying groups that may benefit from focused efforts to prevent or delay onset of diabetes and reduce co-morbidities and diabetes-related complications.

*Principal investigator: Jean Lawrence, ScD, MPH, MSSA\**

*Funding agency: Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion*

*\*Transitioned to Kristi Reynolds, PhD, MPH, after Dr. Lawrence left KPSC*



Diane Avilez, Ana Martinez, Alex Carruth, Nehaa Khadka, I-Chun Jennifer Lin, and Jessica Moore



### ParkRx, physical activity and other health benefits for low income children

Park agencies, health care providers, and community organizations developed Park Prescriptions (ParkRx) in order to promote both physical activity and exposure to nature among low-income populations. In collaboration with Unity Health, a federally qualified community health center in Washington, D.C., researchers will conduct a randomized controlled trial to evaluate ParkRx's impact on physical activity and health outcomes among pediatric patients. The results will help to quantify the effectiveness of ParkRx and inform its future dissemination.



*Principal investigator: Deborah Cohen, MD, MPH*

*Funding agency: National Heart Lung, and Blood Institute*

### Standardizing portion sizes

Given that restaurant serving sizes vary greatly and often include more food than customers can burn, offering portions that are standardized and predictable could help Americans reduce their risk for being overweight or obese. This planning grant will support the development of a randomized controlled trial to test the impact of standardized portions, determine what standard portion sizes should be, develop practical methods by which restaurants can adopt standardized portions, and develop and test methods for recruitment of participants.



*Principal investigator: Deborah Cohen, MD, MPH*

*Funding agency: National Heart, Lung, and Blood Institute*

### A new approach to an old problem: Redesigning latent tuberculosis screening and treatment

More than one-quarter of the world's population is infected with *Mycobacterium tuberculosis*, but most of these people have what is called latent TB. Researchers in KPSC and KPNC will identify gaps in screening for latent TB, develop more effective screening guidelines, and create patient education tools to improve initiation and completion of treatment for TB. Findings will be used to improve identification and treatment of latent tuberculosis, supporting the California Department of Public Health's goal to eliminate TB in the state by 2040.

*Principal investigator: Sara Tartof, PhD, MPH*

*Funding agency: National Institute of Allergy and Infectious Diseases*

### Assessing changes in health care utilization during the COVID-19 pandemic in the Vaccine Safety Datalink

At its outset, the COVID-19 pandemic caused an abrupt drop in use of in-person health care and a sharp rise in use of telehealth services. Prior to the pandemic, the Vaccine Safety Datalink—a longstanding research partnership between the Centers for Disease Control and Prevention and 9 health care organizations—had relied primarily on in-person health care visits to identify possible adverse events after vaccinations. This study will explore available telehealth visit data across VSD sites, assess the impact of the pandemic on health care utilization and on the baseline rates of adverse events in vaccine safety studies, and evaluate the quality of telehealth data across the VSD sites for identifying adverse events. Results will help identify evidence-based guidelines to use electronic health record data to identify adverse events in vaccine safety studies during the COVID-19 pandemic.

*Principal investigator: Stanley Xu, PhD, MS*

*Funding agency: Centers for Disease Control and Prevention*

## Rapid-cycle research projects

Early in the pandemic, the Regional Research Committee and the Care Improvement Research Team joined forces to initiate a series of rapid-cycle research projects focused on COVID-19 (see related story on page 18). These studies helped our researchers and clinicians better understand the prognosis for patients with suspected or confirmed COVID-19 and spurred the development of several new clinical decision tools.

### Patients suspected for COVID-19 at elevated risk for adverse events: The COVAS score

– Adam L. Sharp, MD, MSc

**Background:** COVID-19 can result in life-threatening critical illness, but most patients recover without medical treatment. An understanding of which patients are at greatest risk, and who may safely recover at home, is needed to inform decisions about hospitalization.

**Key results:**

- Investigators derived and validated the COVAS (Comorbidities, Obesity [BMI], Vital signs, Age, and Sex) score to predict a patient's risk for needing critical respiratory care within 7 days.
- The score performed well among 26,600 emergency department patients with COVID-like symptoms.
- After the initial rollout, investigators adjusted how vital signs were scored in order to improve its performance.
- They also further validated the score among patients in both the emergency room and urgent care who had been tested for COVID-19. The score demonstrated continued high performance.

**Impact:** The COVAS score has been implemented into Kaiser Permanente HealthConnect®. The tool includes thresholds—developed with input from clinical leaders—to identify patients at low, moderate, and high risk. Individual patient scores guide patient and clinician decisions about care in emergency departments and urgent care settings throughout the region.

### Estimating prognosis in hospitalized patients with COVID-19 and acute respiratory failure

– Michael K. Gould, MD, MS

**Background:** COVID-19 patients with acute respiratory failure, including those receiving mechanical ventilation, have high mortality. Being able to accurately estimate prognosis can help physicians communicate with families and inform decisions about withholding or withdrawing life-supporting therapies at various points during hospitalization.

**Key results:** Researchers derived a simple model to accurately estimate prognosis and risk of death on day 8 of invasive mechanical ventilation in patients with respiratory failure due to COVID-19. Similar models to estimate prognosis on day 1 of high-frequency noninvasive ventilation or invasive mechanical ventilation were less accurate. The day 1 invasive mechanical ventilation model overestimated the likelihood of death for patients in the higher risk categories.

**Impact:** A novel model was developed to more accurately estimate prognosis for patients with respiratory failure due to COVID-19. The team implemented the day 8 model in Kaiser Permanente HealthConnect early in 2021.





Bertin Valdez and Amanda McDonald

## Early deterioration index for hospitalized patients: COVID-EDI

– Claudia Nau, PhD

**Background:** Some COVID-19 patients who require ICU admission decline rapidly. A decision support tool that identifies patients at high and low risk of deterioration can facilitate communication with families and inform clinical care decisions, such as whether a patient may be considered for discharge or may need monitoring and care to mitigate deterioration.

**Key results:** The team used machine learning and regression modeling to develop a risk score that predicts the risk of a patient (1) requiring ICU level of care, (2) requiring mechanical ventilation, (3) requiring high-flow oxygen, or (4) possibly dying within 72 hours. COVID-EDI significantly outperforms existing published models to identify high and low risk patients. It contains only 7 variables and can be easily integrated into electronic health record systems.

**Impact:** A high-performing model was developed to identify patients at risk of early deterioration from COVID-19. The COVID-EDI was implemented in Kaiser Permanente HealthConnect in the first quarter of 2021.

## Risk of severe morbidity and mortality in patients taking antihypertensive medications

– Jaejin An, PhD

**Background:** The COVID-19 pandemic has generated concerns that use of angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin receptor blockers (ARBs) may be associated with increased risk of COVID-19 infection or disease severity. The team studied the risk of COVID-19 infection, and the risk of severe morbidity and mortality, among a racially and ethnically diverse group of patients.

### Key results:

- Neither ACEI nor ARB use was associated with increased likelihood of COVID-19 infection.
- The decreased odds of infection among adults ages 85 years and older using ACEIs warrants further investigation.
- The likelihood of infection among those not taking antihypertensive medications was higher than in those taking calcium channel blockers, beta-blockers, or thiazide diuretics.

**Impact:** The results support KPSC clinicians' decisions to prescribe antihypertension medication as appropriate. Patients can confidently continue their ACEIs or ARBs as recommended (see related story on page 6).

## Care Improvement Research Team projects

The year 2020 propelled everyone to change and adapt. The Care Improvement Research Team was no exception. Michael K. Gould, MD, MS, CIRT's director since its inception, transitioned to a full-time position at the new Kaiser Permanente Bernard J. Tyson School of Medicine. Adam L. Sharp, MD, MSc, is the new director.

In addition to the rapid-cycle research projects collaboration with the Regional Research Committee, CIRT initiated or accomplished other key projects in 2020 as highlighted below.

### Changing to an age-adjusted D-dimer threshold in the emergency department

– Adam L. Sharp, MD, MSc

**Background:** The team studied whether changes to KPSC laboratory D-dimer thresholds (a laboratory value for patients with suspected pulmonary embolus, or a blockage in a lung artery) for patients over age 50 years affected 30-day patient outcomes or use of advanced diagnostic imaging.

#### Key results:

- Increasing the D-dimer laboratory threshold was safe and did not increase 30-day adverse events.
- Use of advanced imaging declined after intervention, but not significantly, which indicates an opportunity for improvement with future implementation strategies.

### Optimizing care delivery, quality, and outcomes for people living with dementia

– Huong Q. Nguyen, PhD, RN

**Background:** This study aims to investigate how home-based primary care and hospital-at-home services are used by a unique and hard-to-reach population of geographically remote patients with Alzheimer's disease-related dementias and memory loss, and their caregivers.

#### Key results:

Opportunities exist for cognitive screening of high-risk patients and for earlier diagnosis of dementia, but the value for the KPSC health system remains uncertain.

Earlier diagnosis may translate to funding for more ancillary support for dementia care.

There is an opportunity to revamp the approach to the Medicare Wellness Exam for cognitive screening and appropriate follow-through.

### Improving care transitions and reducing readmissions

– Huong Q. Nguyen, PhD, RN

**Background:** This project is evaluating the effectiveness of interventions to improve care transitions and reduce avoidable readmissions. Key research questions include:

Which patients will benefit most (as measured by shorter hospital stays) from post-discharge telephone calls and follow-up clinic visits?

In adults discharged for sepsis, is the type of follow-up care associated with readmission?

#### Key results:

- Associations between completion of follow-up visits and readmission are lessened in those with dementia compared with those without.
- Follow-up clinic visits are more strongly associated with lower readmission risk, but telephone visits could serve as a substitute in certain patient groups.
- Greater use of telephone visits improves access and reduces cancellations.
- The pattern of home care service does not seem to matter as much as the in-person follow-up visits by a provider, which KPSC is already doing routinely.

### Access to tailored autism integrated care (ATTAIN) phase III pilot

– Karen J. Coleman, PhD, MS, and Brian S. Mittman, PhD

**Background:** This study pilot tested an innovative, integrated model for the mental health care of children with autism spectrum disorder (ASD). The 8-step model aimed to enhance mental health screening in primary care and linkage to mental health services for children with ASD.





Justine De Jesus and Dr. Adam Sharp

#### Key results:

- Annual completion of the pediatric symptom checklist (PSC-17) improves linkage to mental health services. More automated support is warranted to ensure that PSC-17 screening is completed.
- The pilot provided primary care providers with a new way to talk about mental health.
- Some children with positive PSC-17 scores were not referred for follow-up care, likely because of misunderstanding about ASD versus mental health services; already being connected to services or not interested in a new referral; or having screened negative with a different test.

### Preventing venous thromboembolism in abdominal surgery

– Michael K. Gould, MD, MS

**Background:** This project builds on ongoing work by the CIRT in collaboration with the Regional VTE Steering Committee to prevent venous thromboembolism (VTE) and improve patient outcomes by extending the data collection and analysis to high-risk abdominal surgery patients.

#### Key results:

In patients undergoing inpatient abdominal surgery for cancer:

- VTE events were higher than benchmarks from randomized controlled trials.
- VTE risk seemed to be highest for exploratory (laparoscopy/otomy) procedures and for patients with pancreatic cancer.

- Strong risk factors included prior VTE and albumin  $\leq 2.5$  gm/dl.
- Over 90% of patients received medications to prevent VTE.
- About half of all VTE events occurred more than 30 days after discharge.

### Implementing systematic depression screening in medical oncology

– Erin E. Hahn, PhD, MPH

**Background:** Implementing systematic screening for depression in medical oncology is an evidence-based, guideline-recommended practice. Our recent pragmatic trial found that we can integrate this practice with minimal workflow disruption while effectively identifying and referring highly distressed patients.

#### Key results:

- The team conducted qualitative interviews and surveys with stakeholders at each oncology department. These findings were used to develop workflows specific to each site.
- The screening intervention was spread across KPSC medical centers and the team is evaluating uptake of the program.
- An alert was developed that will be available in 2021 to assist in referral and use of behavioral health services.

## Projects funded by the Regional Research Committee

The Regional Research Committee awards funds from Kaiser Permanente's Community Health program 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 2020, in addition to the rapid-cycle research collaboration with CIRT, the committee awarded funds to the following studies.

### COVID-19 studies

#### Hospital Medicine

Outcomes of hospitalized COVID-19 patients following discharge

*Principal investigator: Cheng-Wei Huang, MD  
Los Angeles*

#### Laboratory

COVID-19 prognosis and von Willebrand factor antigen

*Principal investigator: Darryl Palmer-Toy, MD, PhD  
Regional Reference Laboratory*

#### Psychiatry

The effect of COVID exposure/quarantine on the mental health/wellness of resident physicians across different specialties within Kaiser Permanente SCPMG

*Principal investigator: Devin Walker, DO  
San Bernardino County*

#### Urology

Clinical evaluation of SARS-CoV-2 molecular diagnostic tests

*Principal investigator: Christopher  
Tenggardjaja, MD  
Los Angeles*

Patient experience and satisfaction of care during pandemic, phase I

*Principal investigator: Gary Chien, MD  
Los Angeles*

### Traditional grant studies

#### Anesthesiology

Retrospective evaluation of a comprehensive surgical and anesthesia perioperative treatment plan for maxillary and mandibular osteotomies to reduce opioid administration, hospital length-of-stay and hospital costs

*Principal investigator: Jammie Ferrara, MD  
Los Angeles*

#### Cardiac catheterization

Association between fluoroquinolone use and clinically significant aortic dissection

*Principal investigator: Somjot Brar, MD, MPH  
Los Angeles*

#### Cardiology

Clinical, quality, and safety outcomes among patients enrolled in the Kaiser Permanente home-based cardiac rehabilitation program: The Virtual Cardiac Rehab Study

*Principal investigator: Chileshe Price, MD, MS,  
MRCP (UK)  
West Los Angeles*

Long-term effect of continuous positive airway pressure (CPAP) on cardiovascular outcomes after acute myocardial infarction (AMI) in obstructive sleep apnea (OSA) patients

*Principal investigator: Jie Ren, MD, PhD, FACC  
San Bernardino County*



## Emergency medicine

Opioid-overdose related hospitalizations before and after implementation of California State Law AB 2760, requiring prescribers to offer naloxone to high-risk patients

*Principal investigator: Ali Ghobadi, MD, CPPS  
Orange County*

## Family Medicine

Adherence and method of prescription contraception by women of reproductive age with alcohol disorder compared to those without

*Principal investigator: Lidia Liang, DO (resident physician)  
Los Angeles*

Efficacy of a longitudinal, group-based lifestyle medicine intervention for reversal of type II diabetes

*Principal investigator: Steven A Lawenda, MD  
Antelope Valley*

Racial and ethnic disparities in prescribing practice of opiates in HIV-positive patients

*Principal investigator: Janelle Rodriguez, MD  
Los Angeles*

## Gastroenterology

Identification of care needs in patients with irritable bowel syndrome

*Principal investigator: Christine Yu, MD  
Los Angeles*

## Hematology-Oncology

Timing and acceptance of bilateral prophylactic salpingo-oophorectomy among BRCA1 and BRCA2 mutation carriers enrolled in an integrated community-based health care system

*Principal investigator: Karen W. Kwan, MD  
Los Angeles*

## Obstetrics-Gynecology

Posterior tibial nerve stimulation for overactive bladder utilizing a generic neurostimulator

*Principal investigator: John Nguyen, MD  
Downey*

Gender and racial microaggressions toward surgeons: The KP experience

*Principal investigator: Emily L. Whitcomb, MD  
Orange County*

## Ophthalmology

Assessing outcomes of a clinic-based vision screening program at Southern California Permanente Medical Group

*Principal investigator: Shaival S. Shah, MD  
Orange County*

## Pediatric Endocrinology

Nine years of a secondary screening program for congenital hypothyroidism in high-risk neonates

*Principal investigator: Alan B. Cortez, MD  
Orange County*

### Pediatric Oncology

A study of health disparities in cancer patients

*Principal investigator: Robert Cooper, MD  
Los Angeles*

### Pediatrics

Review of risk factors associated with high-grade retinopathy of prematurity requiring treatment. A regional retrospective study in premature infants below 1500 grams birthweight

*Principal investigator: Kim-chi T. Bui, MD  
Los Angeles*

### Plastic Surgery

Baseline characteristics of transgender patients seeking gender-affirming services: The Southern California Kaiser Permanente Transgender Cohort Study

*Principal investigator: Holly H. Kim, MD  
West Los Angeles*

### Pulmonary, Critical Care Medicine

Exploring novel effects of different statins on ICU admission for sepsis

*Principal investigator: Kenneth Wei, MD  
Los Angeles*

### Sleep Medicine

Using artificial intelligence to improve the triaging of patients with suspected sleep disordered breathing into the proper sleep Diagnostic testing pathway

*Principal investigator: Dennis Hwang, MD  
San Bernardino County*

### Urology

Improving diagnostic accuracy and care quality for bladder cancer: a study to assess the frequency and variation in the use of restaging tumor resections

*Principal investigator: Philip H. Kim, MD  
San Diego*



## RRC-GME Research Program Development Grant

### Family Medicine

Safety of tizanidine and baclofen in elders (STaBE): a retrospective cohort study

*Principal investigator: Monique George, MD  
Woodland Hills*

## RRC COVID-19 Grant

### Hospital Medicine

Outcomes of hospitalized COVID-19 patients following discharge

*Principal investigator: Cheng-Wei Huang, MD  
Los Angeles*

### Laboratory

COVID-19 prognosis and von Willebrand factor antigen

*Principal investigator: Darryl Palmer-Toy, MD, PhD  
Regional Reference Laboratory*

### Psychiatry

The effect of COVID exposure/quarantine on the mental health/wellness of resident physicians across different specialties within Kaiser Permanente SCPMG

*Principal investigator: Devin Walker, DO  
San Bernardino County*

### Urology

Patient experience and satisfaction of care during pandemic, phase I

*Principal investigator: Gary Chien, MD  
Los Angeles*

Clinical evaluation of SARS-CoV-2 molecular diagnostic tests

*Principal investigator: Christopher Tenggardjaja, MD  
Los Angeles*

## RRC-CIRT Collaboration - Rapid Cycle Research Program Grant

### Emergency Medicine

Identifying patients with COVID-19 symptoms at high risk for adverse events

*Principal investigator: Adam Sharp, MD, MSc  
Los Angeles*

### Pulmonary / Research & Evaluation

Incidence and Outcomes of Patients with Coronavirus 2019 (COVID-19)

*SCPMG principal investigator: George Yuen, MD, Irvine*

*KPSC co-principal investigator: Michael K. Gould, MD, MS, Pasadena*

Hospitalized patients with confirmed or suspected COVID-19

*Study lead: Claudia Nau, PhD, Pasadena*

Patients with hypertension and confirmed or suspected COVID-19

*Study leads: Kristi Reynolds, PhD, MPH, and Jaejin An, PhD, Pasadena*

# 2020 Regional Research Committee

Bechien U. Wu, MD, MPH, Chair

## Antelope Valley

Jonathan Truong, MD, Area Research Chair  
David Bronstein, MD, Vice Area Research Chair

## Baldwin Park

Gaurav Khanna, MD, Area Research Chair  
Bobeck Modjtahedi, MD, Vice Area Research Chair

## Downey

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

## Fontana/San Bernardino

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

## Kern County

Michael J. Fassett, MD, Area Research Chair

## Los Angeles

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

## Orange County

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

## Panorama City

Shireen Fatemi, MD, Area Research Chair  
David Manela, MD, Vice Area Research Chair

## Regional Laboratory

Darryl Palmer-Toy, MD, PhD, Area Research Chair

## Riverside/Palm Springs

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

## San Diego

Shawn A. Menefee, MD, Area Research Chair  
Marco Tomassi, MD, Vice Area Research Chair

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William W. Crawford, MD, Vice Area Research Chair

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Daniel T. Lang, MD, Vice Area Research Chair

## Woodland Hills

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

## Department of Research & Evaluation

Steven J. Jacobsen, MD, PhD, Area Research Chair  
Deborah R. Young, PhD, MBA,  
Vice Area Research Chair  
Stephanie Tovar, MS, Regional Research Committee  
Project Manager



# INVESTIGATORS





# Overview of our investigators and scientific divisions



## Steven J. Jacobsen, MD, PhD

Dr. Steven Jacobsen joined Kaiser Permanente in March 2006 with a mission to grow the Southern California research program, increase clinical research within the organization, and increase research that has a demonstrable positive impact on care delivery. During his 15-year tenure, the faculty, staff, funding, clinical collaboration, and research portfolio grew significantly. The program's discoveries are being implemented broadly to improve the health and well-being of Kaiser Permanente Southern California members and in the community. Dr. Jacobsen left Kaiser Permanente in January 2021.

Dr. Steven Jacobsen outside his office at the main Pasadena research building. Photo taken in December 2019, prior to the pandemic.

Our research program includes 5 scientific divisions as well as affiliated researchers (see page 51).

## Epidemiologic Research (page 51)

Our epidemiologists apply rigorous research methods to address important health questions that have the potential to change clinical practice and health care delivery. The division's research portfolio spans the care continuum, from etiology and prevention to survivorship and quality of life. Current research areas include cancer, cardiovascular disease, COVID-19, diabetes, infectious disease, molecular epidemiology, orthopedics and bone health, perinatal health, pharmacoepidemiology, and vaccines.

## Behavioral Research (page 53)

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

## Biostatistics Research (page 54)

Our collaborative biostatistician research scientists work closely with investigators in other scientific divisions, as well as physician researchers at medical centers across Kaiser Permanente

Southern California. They provide expertise and guidance on study design, power and sample size calculations, data management, data analysis and interpretation, and statistical methodology.

## Health Services Research & Implementation Science (page 55)

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

## Clinical Trials Research (page 56)

The Division of Clinical Trials Research advances medical innovation by supporting evaluation of new drugs, therapies, and devices to prevent and treat health problems. Our physician investigators work with cooperative groups and industry sponsors to conduct clinical trials for investigational drugs, biologics, and devices. In addition, the division develops pragmatic trials that help answer questions about care delivery. See our clinical trials principal investigators by specialty on page 62.



# Division of Epidemiologic Research

## Research scientists



**Kristi Reynolds, PhD, MPH**

*Director*

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



**Darios Getahun, MD, PhD, MPH**

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



**Annette L. Adams, PhD, MPH**

- Osteoporosis and bone health
- Injury epidemiology



**Reina Haque, PhD, MPH**

- Cancer epidemiology and health disparities
- Cancer survivorship and late treatment effects
- Biomarkers of cancer outcomes
- Pharmacoepidemiology



**Jaejin An, PhD**

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



**Rulin Hechter, MD, PhD, MS**

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



**Chun Chao, PhD, MS**

- HPV vaccine; cervical cancer
- Adolescent and young adult cancer and survivorship
- Lymphoid malignancies
- Chemotherapy toxicity



**Jean M. Lawrence\*, ScD, MPH, MSSA**

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

\*Dr. Lawrence left KPSC in 2020.



**Wansu Chen, PhD, MS**

- Risk prediction using machine learning and statistical methods
- Pancreatic cancer; acute and chronic pancreatitis
- Asthma and chronic cough
- Gastric cancer



**Sara Y. Tartof, PhD, MPH**

- Infectious diseases
- Antibiotic resistance
- Hospital infections
- COVID-19



**Hung Fu Tseng, PhD, MPH**

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



**Lisa P. Oakley\*, PhD, MPH**

- Maternal and child health
- Infectious disease
- Social epidemiology
- Health equity

\*Dr. Oakley left KPSC in 2020.

## Post-doctoral research fellows



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

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

\*Dr. Becerra-Culqui left KPSC in 2020.



**Debbie Malden, DPhil, MSc**

- Large-scale prospective cohort studies
- Obesity and cardiovascular disease
- Outbreak response
- Genetic epidemiology



**Katia Bruxvoort, PhD, MPH**

- Infectious diseases
- Vaccine safety and effectiveness
- Screening and diagnostics
- Antimicrobial treatment and adherence



**Ana Florea, PhD, MPH**

- Vaccine safety and effectiveness
- Infectious diseases
- Cancer epidemiology
- Chronic kidney disease



**Matthew T. Mefford, PhD**

- Cardiovascular disease
- Treatment, outcomes, and effectiveness
- Health disparities and equity
- Medication adherence



## Division of Behavioral Research

### Research scientists



**Deborah Rohm Young, PhD, MBA**

*Director*

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



**Claudia Nau, PhD**

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



**Deborah A. Cohen, MD, MPH**

- Obesity, diet
- Physical activity
- Parks and urban design
- Food retail outlets, food environment



**Sonya Negriff, PhD**

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



**Corinna Koebnick, PhD, MSc**

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

## Division of Biostatistics Research

### Research scientists



**Anny H. Xiang, PhD, MS**

*Director*

- Biostatistics: design and analysis
- Diabetes, gestational diabetes, and obesity
- Pregnancy and women's and children's health



**Margo A. Sidell, ScD, MSPH**

- Biostatistics
- GIS mapping and spatial analysis
- Behavioral health and preventive care
- Social determinants of health



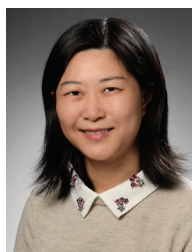
**Heidi Fischer, PhD**

- Multilevel modeling
- Functional data analysis
- Observational data
- Biostatistics



**Jeff Slezak, MS**

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



**Lei Qian, PhD**

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



**Stanley Xu, PhD, MS**

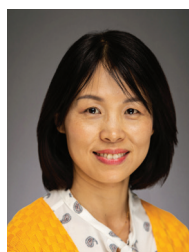
- Analytic methods
- Vaccines
- Pharmacoepidemiology
- Overdose prevention



**Jiaxiao Shi\*, PhD**

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

\*Dr. Shi moved to a new position in the department in 2020.



**Hui Zhou, PhD, MS**

- Biostatistical method and study design
- Risk prediction modeling
- Chronic kidney disease and end-stage renal disease
- Cardiovascular disease



# Division of Health Services Research & Implementation Science

## Research scientists



**Michael K. Gould\*, MD, MS**

*Director*

- Lung cancer
- Venous thromboembolism
- Effectiveness and outcomes
- Implementation science

\*Dr. Gould moved to the Kaiser Permanente School of Medicine in 2020.



**Aniket A. Kawatkar, PhD, MS**

- Health economics
- Patient preferences
- Comparative effectiveness



**Karen J. Coleman, PhD, MS**

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



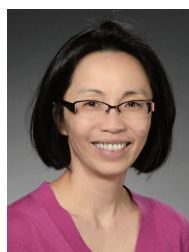
**Brian S. Mittman, PhD**

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



**David Glass, PhD**

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



**Huong Q. Nguyen\*, PhD, RN**

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

\*Dr. Nguyen became interim division director in 2020.



**Erin E. Hahn, PhD, MPH**

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



**Adam L. Sharp, MD, MSc**

- Health services research, implementation science
- Health system science, emergency medicine
- Equity, inclusion, social risks and diversity

## Division of Clinical Trials Research

### Portfolio principal investigators



**William J. Towner, MD, FACP, FIDSA**

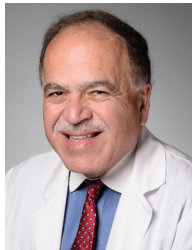
*Regional Physician Director*

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



**Gary L. Buchschacher Jr., MD, PhD**

- Medical oncology
- Clinical trials
- Gastrointestinal cancers
- Molecular medicine and gene therapy



**Vicken Aharonian, MD**

- Cardiac catheterization
- Interventional cardiology



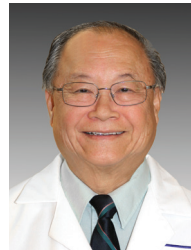
**Jeffrey Cavendish, MD**

- Interventional cardiology
- Structural heart disease
- Peripheral vascular disease, renal artery stenosis, and stenting
- Cardiovascular event prevention and risk factor reduction



**Zahra A. Ajani, MD**

- Comprehensive stroke care
- Diagnosis and treatment of cerebrovascular diseases
- Systems of care and quality improvement



**Sirichai Chayasirisobhon, MD, FAAN**

- Epilepsy



**Ashraf R. Aziz, MD**

- Hematology
- Oncology
- Breast cancer clinical trials



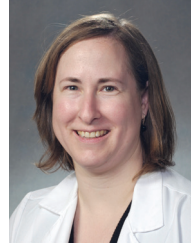
**Robert M. Cooper, MD**

- Cancer clinical trials
- Cancer outcomes



**Somjot S. Brar, MD, MPH**

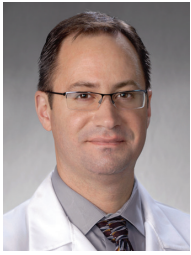
- Cardiovascular disease and risk factors
- Medical devices and interventional procedures
- Clinical trials and meta-analysis



**Lara Durna, MD, MS**

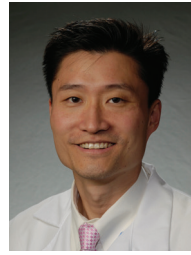
- Breast cancer therapeutic clinical trials
- Breast cancer survivorship and quality-of-life trials
- Medical oncology
- Hematology





**Michael R. Girvigian, MD**

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



**Steve S. Lee, DO**

- Axial spondyloarthritis
- Systemic lupus erythematosus
- Psoriatic arthritis
- Rheumatic arthritis



**Nigel Gupta, MD**

- Clinical cardiac electrophysiology
- Cardiac implantable electronic devices and catheter ablation
- Sponsor- and investigator-initiated clinical trials
- Fellowship mentorship, teaching



**Scott E. Lentz, MD, FACS**

- Gynecologic oncology
- Hereditary cancer syndromes
- Surgical innovation



**Suresh Gurbani, MD**

- Pediatric epilepsy
- Neuromodulation in epilepsy therapy
- Clinical trials



**Eric McGary, MD, PhD, MPH**

- Clinical trials of investigational cancer drugs
- Real-world data and real-world evidence-based clinical studies
- Precision medicine and molecular diagnostic platforms in oncology



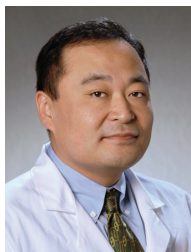
**Vivienne S. Hau, MD, PhD**

- Age-related macular degeneration
- Diabetic macula edema
- Diabetic retinopathy
- Vitreoretinal surgery



**Shawn A. Menefee, MD**

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



**Han A. Koh, MD**

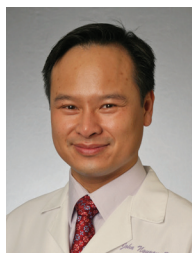
- Lung cancer
  - Benign hematology
- \*Dr. Koh retired from KPSC in January 2021.



**Helen Moon, MD**

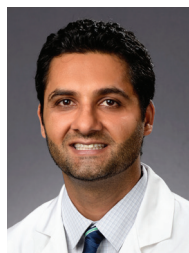
- Genitourinary cancer
- Melanoma
- Immuno-oncology

## Portfolio principal investigators



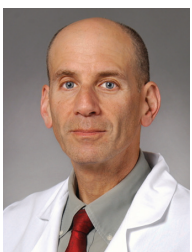
**John Nguyen, MD**

- Female pelvic medicine and reconstructive surgery
- Pelvic organ prolapse and urinary incontinence treatment
- Clinical instructor
- Minimally invasive surgery



**Navdeep Sangha, MD**

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



**Jonathan Polikoff, MD**

- Breast cancer
- General oncology
- General hematology



**Ricardo T. Spielberger, MD**

- Hematopoietic cell transplant
- Transplant side effects
- Opportunistic infections



**Muhammad Saeed, MD**

- Cystic fibrosis clinical trials
- Psychosocial impact of cystic fibrosis newborn screening
- Quality improvement



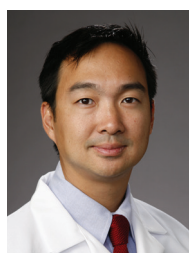
**Devansu Tewari, MD, MBA**

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



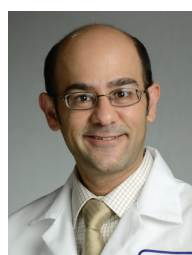
**Amandeep Sahota, MD**

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



**Bechien U. Wu, MD, MPH**

- Pancreatology
- Acute and chronic pancreatitis
- Early detection of pancreatic cancer
- Gastrointestinal cancer screening and prevention



**Kapil M. Sampat, DO**

- Retinal disease
- Retina vitreous surgery



## Affiliated researchers

### Affiliated investigators



**Donald S. Fong, MD, MPH**

- Myopia
- Diabetic retinopathy
- Care redesign
- Retinal degenerations



**Lisa Nyberg, MD, MPH**

- Hepatology risk and treatment
- Non-alcoholic fatty liver disease



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

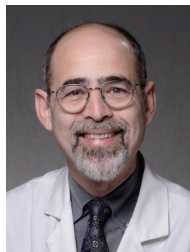
- MS susceptibility, prognosis, and treatment
- Migraine-care models
- Comparative effectiveness and safety of treatments
- Alzheimer's disease care models



**David A. Sacks, MD**

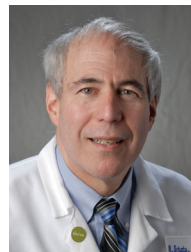
- Diabetes and pregnancy

### Associate investigators



**David Braun, MD**

- Factors influencing NICU admission and length of stay
- Degree and effects of regionalized perinatal care
- Antibiotic stewardship in the NICU
- Cross-disciplinary clinical research collaboration



**Michael Schatz, MD, MS**

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



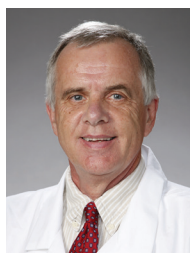
**Michael Kanter, MD**

- Quality improvement
- Patient safety
- Patient engagement
- Models of care for chronic conditions



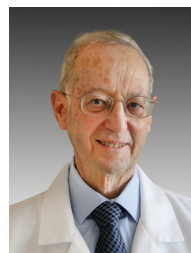
**Joanne Schottinger, MD**

- Colorectal cancer screening
- Medical oncology
- Hematology



**Anders Nyberg, MD, PhD**

- Hepatology risk and treatment
- Hepatology clinical trials



**Robert S. Zeiger, MD, PhD**

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

**Adjunct investigators**



**Dennis Black, PhD**

- Osteoporosis
- Fracture risk
- Clinical trials



**Paul Muntner, PhD**

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



**Soo Borson, MD**

- Dementia screening and care
- Late-life cognitive and mood disorders in patients with neurodegenerative diseases



**Lauren P. Wallner, PhD, MPH**

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



**Kristen Choi, PhD, MS, RN**

- Health services research
- Child behavioral health
- Trauma and violence
- Nursing



## Clinician investigators



**Kimberly Ferrante, MD, MAS**

- Pelvic floor disorders in women
- Prevention of recurrent urinary tract infections
- Treatment of genitourinary syndrome of menopause



**Chunyuan Qiu, MD, MS**

- Anesthesiology
- Pain medicine
- Perioperative medicine



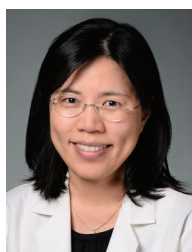
**Dennis Hwang, MD**

- Health care delivery innovation
- Big data and machine learning
- Automation and population health management innovation
- Integration of medical and consumer health technologies



**Joan J. Ryoo, MD, MSHS**

- Radiation oncology
- Cancer care outcomes



**Mingsum Lee, MD, PhD**

- Cardiovascular disease
- Medication adherence and drug safety
- Health care utilization and outcomes



**Hui Xue\*, MD, MMSc**

- Dialysis outcomes
- Chronic kidney disease
- Glomerular disease
- Bone mineral metabolism

\*Dr. Xue also participated in the Clinician Investigator Program in 2016-2017.



**Bobeck S. Modjtahedi, MD**

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

## Previous appointments

**Raymond Chen, MD, DPhil** (2016-2018)

**Casey K. Ng, MD** (2017-2019)

**Navdeep Sangha, MD** (2017-2019)

**John J. Sim, MD** (2016-2018)

**Devansu Tewari, MD, MBA** (2016-2018)

**Emily L. Whitcomb, MD, MAS** (2016-2019)

**Bechien U. Wu, MD, MPH** (2017-2019)

## Clinical trials investigators by specialty

### Allergy

Robert S. Zeiger, MD, PhD, San Diego Medical Center

### Bone Marrow Transplant

Ricardo T. Spielberger, MD, Los Angeles Medical Center

### Cardiology

Vicken Aharonian, MD, Los Angeles Medical Center

Somjot S. Brar, MD, MPH, Los Angeles Medical Center

Jeffrey Cavendish, MD, San Diego Medical Center

Nigel Gupta, MD, Los Angeles Medical Center

Naing Moore, MD, MRCP, FSCAI, Los Angeles Medical Center

Jonathan Neyer, MD, Los Angeles Medical Center

Morris Salem, MD, Los Angeles Medical Center

### COVID-19

Gunter K. Rieg, MD, South Bay Medical Center

Viji Sankar, MD, San Diego Medical Center

Adam Schwartz, MD, San Diego Medical Center

David J. Silberstein, MD, Los Angeles Medical Center

### Dermatology

Kim Chong, MD, Los Angeles Medical Center

### Endocrinology

Dasia E. Esener, MD, San Diego Medical Center

Patricia Wu, MD, San Diego Carmel Valley Medical Offices

### Gastroenterology

John M. Iskander, MD, Los Angeles Medical Center

Kevin Kao, MD, Downey Medical Center

Mun-Wah Ng, MD, Fontana Medical Center

Suresh Pola, MD, San Diego Medical Center

Bechien U. Wu, MD, MPH, Los Angeles Medical Center

### Hepatology

Mamie Dong, MD, San Diego Medical Center

Amandeep Sahota, MD, Los Angeles Medical Center

### Infectious Diseases

William J. Towner, MD, FACP, FIDSA, Los Angeles Medical Center

### Interventional Neuroradiology

Lei Feng, MD, Los Angeles Medical Center

Conrad Liang, MD, PhD, Fontana Medical Center

Mazen Noufal, MD, Fontana Medical Center

### Metabolic/Genetics

Divya Vats, MD, Los Angeles Medical Center

### Nephrology

John Sim, MD, Los Angeles Medical Center

Hui Xue, MD, MMSc, San Diego Medical Center

### Neurology - Pediatric

Sirichai Chayasirisobhon, MD, FAAN, Anaheim Kraemer Medical Offices

Suresh Gurbani, MD, Anaheim Medical Office

### Neurology - Stroke

Zahra Ajani, MD, Los Angeles Medical Center

William Neil, MD, San Diego Medical Center

Navdeep Sangha, MD, Los Angeles Medical Center



## Neurological Surgery

Harsimran S. Brara, MD, Los Angeles Medical Center  
Vaninder Chhabra, MD, Fontana Medical Center

## Gynecologic Oncology

Melissa Hodeib, DO, Riverside Medical Center  
Scott E. Lentz, MD, FACS, Los Angeles Medical Center  
Devansu Tewari, MD, MBA, Irvine Medical Center,  
Alton/Sand Canyon Medical Offices

## Head and Neck Surgery

David Keschner, MD, San Canyon Medical Offices

## Hematology Oncology

Ashraf R. Aziz, MD, Anaheim Medical Center  
Gary L. Buchschacher Jr., MD, PhD, Los Angeles  
Medical Center  
Lara Durna, MD, MS, South Bay Medical Center  
Han A. Koh, MD, Downey Medical Center  
Eric McGary, MD, Los Angeles Medical Center  
Helen Moon, MD, Riverside Medical Center  
Jonathan Polikoff, MD, San Diego Medical Center

## Neuro-Oncology

Richard Green, MD, Los Angeles Medical Center

## Radiation Oncology

Michael R. Girvigian, MD, Los Angeles Medical Center

## Surgical Oncology

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

## Ophthalmology

Michelle Britt, MD, Irwindale Medical Offices  
Vivienne S. Hau, MD, PhD, Riverside Medical Center  
Damien Rodger, MD, PhD, Los Angeles Medical  
Center  
Kapil M. Sampat, DO, Riverside Medical Center  
Neil M. Vyas, MD, Panorama City Medical Center

## Orthopedics

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

## Pediatric Oncology

Robert M. Cooper, MD, Los Angeles Medical Center  
Hung Ngoc Tran, MD, Los Angeles Medical Center  
Lisa Mueller, MD, Los Angeles Medical Center

## Pediatric Pulmonology

Muhammad Saeed, MD, Los Angeles Medical Center

## Pulmonology

Aung Htoo, MD, Kern County  
Jonathan Truong, MD, Antelope Valley  
Kenneth Wei, MD, Los Angeles Medical Center

## Physical Medicine

David M. Nguyen, MD, South Bay Medical Center

## Rheumatology

Steve S. Lee, DO, Fontana Medical Center  
Swati Medhekar, MD, Anaheim Medical Center

## Sleep Medicine

Prasanth Manthena, MD, Los Angeles Medical Center

### Urology/Reproductive/Gynecological Disorders

Keisha Dyer, MD, San Diego Point Loma Medical Offices

Kimberly Ferrante, MD, San Diego Medical Center

Karl Luber, MD, San Diego Medical Center

Shawn A. Menefee, MD, San Diego Point Loma Medical Offices

John Nguyen, MD, Downey Medical Center

Jasmine Tan-Kim, MD, San Diego Point Loma Medical Offices

Christopher Tenggardjaja, MD, Los Angeles Medical Center

Neha Trivedi, MD, San Diego Medical Center

Emily L. Whitcomb, MD, MAS, Irvine Medical Center

### Vascular Surgery

Catherine Chang, MD, San Diego Medical Center

Linda Chun, MD, Los Angeles Medical Center

Edward Plecha, MD, San Diego Medical Center

Elena Rakhlin, MD, San Diego Medical Center



# PUBLICATIONS





## 2020 Publications

Scientists, clinicians, and other health professionals from Kaiser Permanente Southern California authored original research papers on a wide range of topics in 2020, from allergy and asthma to women's health.

### Aging and Geriatrics

Aguila E, Park JH, Vega A. Living arrangements and supplemental income programs for older adults in Mexico. *Demography*. 2020 Aug;57(4):1345-1368.

Haagsma JA, Olij BF, Majdan M, van Beeck EF, Vos T, Castle CD, Dingels ZV, Fox JT, Hamilton EB, Liu Z, Roberts NLS, Sylte DO, Aremu O, Bärnighausen TW, Borzi AM, Briggs AM, Carrero JJ, Cooper C, El-Khatib Z, Ellingsen CL, Fereshtehnejad SM, Filip I, Fischer F, Haro JM, Jonas JB, Kiadaliri AA, Koyanagi A, Lunevicius R, Meretoja TJ, Mohammed S, Pathak A, Radfar A, Rawaf S, Rawaf DL, Riera LS, Shiue I, Vasankari TJ, James SL, Polinder S. Falls in older aged adults in 22 European countries: incidence, mortality and burden of disease from 1990 to 2017. *Inj Prev*. 2020 Oct;26(Suppl 1):i67-i74. PMID: PMC7571349

Lee EA, Brettler JW, Kanter MH, Steinberg SG, Khang P, Distasio CC, Martin J, Dreskin M, Thompson NH, Cotter TM, Thai K, Yasumura L, Gibbs NE. Refining the definition of polypharmacy and its link to disability in older adults: conceptualizing necessary polypharmacy, unnecessary polypharmacy, and polypharmacy of unclear benefit. *Perm J*. 2020;24:18.212. PMID: PMC6972545

Phan DQ, Rostomian AH, Schweis F, Chung J, Lin B, Zadeegan R, Lee MS. Revascularization versus medical therapy in patients aged 80 years and older with acute myocardial infarction. *J Am Geriatr Soc*. 2020 Nov;68(11):2525-2533.

Rashid R, Chang C, Niu F, Deguzman L, Draves M, Awsare S, Hui R. Evaluation of a pharmacist-managed nonsteroidal anti-inflammatory drugs deprescribing program in an integrated health care system. *J Manag Care Spec Pharm*. 2020 Jul;26(7):918-924.

### Allergy and Asthma

Caspard H, Ambrose CS, Tran TN, Chipps BE, Zeiger RS. Associations between individual characteristics and blood eosinophil counts in adults with asthma or COPD. *J Allergy Clin Immunol Pract*. 2020 May;8:1606-1613.e1. ePub.

Cloutier MM, Akinbami LJ, Salo PM, Schatz M, Simoneau T, Wilkerson JC, Diette G, Elward KS, Fuhlbrigge A, Mazurek JM, Feinstein L, Williams S, Zeldin DC. Use of national asthma guidelines by allergists and pulmonologists: a national survey. *J Allergy Clin Immunol Pract*. 2020 Oct;8(9):3011-3020.e2. PMID: PMC7554121

Cloutier MM, Dixon AE, Krishnan JA, Lemanske RF, Pace W, Schatz M. Managing asthma in adolescents and adults: 2020 asthma guideline update from the National Asthma Education and Prevention Program. *JAMA*. 2020 Dec;324(22):2301-2317.

Decuyper II, Green BJ, Sussman GL, Ebo DG, Silvers WS, Pacheco K, King BS, Cohn JR, Zeiger RS, Zeiger JS, Naimi DR, Beezhold DH, Nayak AP. Occupational allergies to cannabis. *J Allergy Clin Immunol Pract*. 2020 Nov-Dec;8:3331-3338. PMID: PMC7837257

Fitzpatrick AM, Bacharier LB, Jackson DJ, Szeffler SJ, Beigelman A, Cabana M, Covar R, Guilbert T, Holguin F, Lemanske RF, Martinez FD, Morgan W, Phipatanakul W, Pongratic JA, Raissy HH, Zeiger RS, Mauger DT. Heterogeneity of mild to moderate persistent asthma in children: confirmation by latent class analysis and association with 1-year outcomes. *J Allergy Clin Immunol Pract*. 2020 Sep;8(8):2617-2627.e4. PMID: PMC7483393

Haselkorn T, Szeffler SJ, Chipps BE, Bleecker ER, Harkins MS, Paknis B, Kianifard F, Ortiz B, Zeiger RS. Disease burden and long-term risk of persistent very poorly controlled asthma: TENOR II. *J Allergy Clin Immunol Pract*. 2020 Jul-Aug;8(7):2243-2253.

Kosinski M, Nelsen L, Rizio AA, Lay-Flurrie J, von Maltzahn R, Jacques L, Schatz M, Stanford RH, Svedsater H. Psychometric properties of the Asthma Control Test in 2 randomized clinical trials. *J Allergy Clin Immunol Pract*. 2020 Aug;S2213-2198(20)30798-4.

Lee LK, Ramakrishnan K, Safioti G, Ariely R, Schatz M. Asthma control is associated with economic outcomes, work productivity and health-related quality of life in patients with asthma. *BMJ Open Respir Res*. 2020 Mar;7(1):e000534. PMID: PMC7101043

Litonjua AA, Carey VJ, Laranjo N, Stubbs BJ, Mirzakhani H, O'Connor GT, Sandel M, Beigelman A, Bacharier LB, Zeiger RS, Schatz M, Hollis BW, Weiss ST. Six-year follow-up of a trial of antenatal vitamin D for asthma reduction. *N Engl J Med*. 2020 Feb;382(6):525-533. PMID: PMC7444088

Lu M, Litonjua AA, O'Connor GT, Zeiger RS, Bacharier L, Schatz M, Carey VJ, Weiss ST, Mirzakhani H. Effect of early and late prenatal vitamin D and maternal asthma status on offspring asthma or recurrent wheeze. *J Allergy Clin Immunol*. 2020 Aug 19;S0091-6749(20)31164-7.



Murphy KR, Chipps B, Beuther DA, Wise RA, McCann W, Gilbert I, Eudicone JM, Gandhi HN, Harding G, Coyne KS, Zeiger RS; US PRECISION Advisory Board. Development of the Asthma Impairment and Risk Questionnaire (AIRQ): a composite control measure. *J Allergy Clin Immunol Pract*. 2020 Jul-Aug;8(7):2263-2274.e5.

Nelsen LM, Kosinski M, Rizio AA, Jacques L, Schatz M, Stanford RH, Svedsater H. A structured review evaluating content validity of the Asthma Control Test, and its consistency with U.S. guidelines and patient expectations for asthma control. *J Asthma*. Published online December 30, 2020. doi: 10.1080/02770903.2020.1861624

Sullivan PW, Ghushchyan VH, Skoner DP, LeCocq J, Park S, Zeiger RS. Complications and healthcare resource utilization associated with systemic corticosteroids in children and adolescents with persistent asthma. *J Allergy Clin Immunol Pract*. Published online December 5, 2020. doi: 10.1016/j.jaip.2020.11.049

Zeiger R, Sullivan P, Chung Y, Kreindler JL, Zimmerman NM, Tkacz J. Systemic corticosteroid-related complications and costs in adults with persistent asthma. *J Allergy Clin Immunol Pract*. 2020 Nov-Dec;8:3455-3465.e13.

## Bone Health and Orthopedics

Black DM, Geiger EJ, Eastell R, Vittinghoff E, Li BH, Ryan DS, Dell RM, Adams AL. Atypical femur fracture risk versus fragility fracture prevention with bisphosphonates. *N Engl J Med*. 2020 Aug;383(8):743-753.

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## Additional photo captions

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## Vision

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

## Mission

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

# Kaiser Permanente Research

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