DEPARTMENT OF **RESEARCH & EVALUATION** 2021 Annual Report

Kaiser Permanente **Research**



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Message from the Senior Director



Reflecting on 2021, it was a tumultuous time. It started with the worst COVID-19 surge to date. Vaccines had just been authorized and were in tight supply, but the pendulum quickly swung the other way. By February we'd begun setting up mass vaccination hubs. Hope rose mid-year that we might be through the worst of it. But then the delta variant surfaced, soon to be followed by omicron, and we began to come to grips with a new reality.

We had to learn new ways of working to continue to provide quality care during the pandemic. For me personally, that meant spending more time caring for patients in our hospitals. It also meant trying to help our region to forecast when the next surge might come, a daunting task.

January 2021 also marked the start of my new role as interim senior scientific director

for the Department of Research & Evaluation. I've had a front row seat as our research program has leapt into action in response to the pandemic, and I'm pleased to be able to share some of that with you in this year's report.

We begin with several stories about vaccine research. Our teams have truly been trailblazers, participating in groundbreaking trials and publishing findings on vaccine safety and effectiveness that have had global influence. We couldn't do any of this, of course, without our patients and study participants. I am particularly thankful to the children who took part in the pediatric trials for the new mRNA vaccines, which were finally authorized in June 2022.

The upheaval of the early days of the pandemic – including new safety concerns, social isolation, and school shutdowns – introduced new health challenges. The pandemic exposed long-standing health inequities. Our researchers have been at the forefront of understanding these consequences and discovering actionable findings.

Our physician researchers are often inspired by questions that arise from daily practice with their patients. Groups like the Regional Research Statistical Support team, the Regional Research Committee, and the Care Improvement Research Team help physician researchers answer those questions to improve care and transform practice.

In 2021, researchers from Kaiser Permanente Southern California published more than 575 journal articles on a wide range of topics. Scientists and physician investigators initiated new projects and clinical trials to study dozens of important health conditions.

I feel privileged to work with you, the trailblazers who make up our research program. You have all worked extremely hard and achieved exceptional results, and you have my deepest gratitude. My wish is that you also take the time to care for yourselves and find time to do the things that matter to you. The pandemic, our careers and our lives are long games, not short ones, and taking care of our own well-being is essential.

Be well,

my bro

Benjamin Broder, MD, PhD Interim Senior Director of Research

For more information about our research, please visit our website (kp.org/research), subscribe to our newsletter IMPACT, or follow us on social media. See back cover for more on how to subscribe to IMPACT or follow us on Twitter and Instagram.

Research Highlights



Patient trailblazers

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Patients are pivotal in COVID-19 vaccine research

One of the most remarkable achievements during the pandemic has been the rapid development of COVID-19 vaccines. This could not have been achieved without the willingness of people around the world to volunteer for vaccine clinical trials.

"The unsung heroes of the pandemic are the people who bravely volunteered to participate in the clinical trials for these new vaccines," said William Towner, MD, FACP, FIDSA, regional physician director for the Division of Clinical Trials Research and the principal investigator for the COVID-19 vaccine trials at Kaiser Permanente Southern California.

Between August 2020 and June 2022, nearly 370 people, including 190 children, volunteered for COVID-19 vaccine trials at the Kaiser Permanente Los Angeles Medical Center.

"In my career, I have never seen so much enthusiasm for participating in clinical trials, including from parents of young children," said Dr. Towner. "I am deeply grateful to each and every one of them. We could not have gotten where we are today without them."

Kids pave the way for peers

Aidan Shih feels strong enthusiasm about his decision to participate in COVID-19 vaccine research.

"I was of course excited that I would get the vaccine – I would be more safe from COVID – but I was also thinking about how a lot of other children my age could get the vaccine if I went to the trial," he said.

In May 2021, Aidan's parents, both physicians with the Southern California Permanente Medical Group, enrolled him and his sister, Avery, in a trial studying the COVID-19 vaccine in children ages 12 and younger. Their mother, Erin, had already participated in a COVID-19 vaccine trial at Kaiser Permanente Southern California in 2020.

Aidan, now 12, said he found participating in the trial to be straightforward. "They told me I was going to get the vaccine and it was going to be a trial, so they would see my reactions to the vaccine. It was very exciting and I thought it would hurt, but it didn't ... My arm was a little sore afterwards, but it was fine overall."

Erin and her husband, Stephen, said that after Avery got her first shot, she asked if she could hug her

grandmother. "The COVID vaccine allows us to do things like that again, like give family members hugs, and go to school in person, and just kind of do normal everyday things again," Erin said.

A return to normalcy is just what kids like Aidan and Avery, now 7, have craved.

"It was definitely hard," Avery said of her time during the pandemic. "We all had our masks on, which we really wanted to take off."

Aidan said they both started off the school year with online learning, which was especially challenging because he had just switched to a new school for fifth grade. "So I was kind of meeting people online, but then we slowly got back into in-person school, which was much better – much, much better," he said.

Would Avery encourage her friends to get vaccinated for COVID-19? "Of course. I mean, it would be great, and it would help," she said.

Aidan agreed: "I definitely would. There's nothing really bad about it," he said. "The vaccine does help you not get COVID, of course, but then also it helps you so you don't spread COVID. So, if enough people get the vaccine, COVID will slow and hopefully eventually stop."

Opposite page: Aidan and Avery Shih, 2 of the early volunteers for the pediatric COVID-19 vaccine trial at LAMC, at home with their parents Drs. Erin and Stephen Shih

Patient trailblazers



Elizabeth Gordon hopes her experience as a study participant will inspire others to get vaccinated

Easing vaccine hesitancy

Deciding to volunteer for COVID-19 research can be far more complicated for people of color due to historic and previous negative experiences with health care. This was true for Kaiser Permanente member Elizabeth Gordon, who is Black.

"I had seen a number of reports of other people who were participating in the trial and hearing their reasoning as to why they wanted to participate," she said. "I thought, 'Wow, I don't know if I could ever do that.' "

That's when Elizabeth happened to receive an email asking if she would like to volunteer for a COVID-19 vaccine trial herself. At the time, she said, she was very distrustful of the U.S. government and, by extension, wary of the vaccines they were helping to create.

"So, I wanted to research for my sake, for my family's sake, to understand how it was being funded, who was making it, and who was designing it," she said. Eventually, she decided, "This is something that's going to be safe, that they're doing it in the right way, for the right reasons." Elizabeth decided to enroll – not only for herself, but because she realized her participation could contribute in a larger way to her community.

"I already knew that there was going to be hesitancy, especially within the Black and brown communities, to take the vaccine," she said. Members of her family have either directly faced discrimination in medical care in the United States or grew up hearing of others' experiences, such as the racist and deadly Tuskegee experiments.

"I wanted to be able to say, 'Look, I've taken it. It's safe. I've done my homework. You can take this and trust that it's going to work for you and protect you.' " – Elizabeth Gordon, Kaiser Permanente member

She received her first dose in September 2020. The side effects were mild; her arm was sore, and she needed some extra sleep for the first 2 days or so. She had a slightly stronger reaction to her second dose, but said that it still did not feel very different from a flu vaccine.

Now, Elizabeth hopes that sharing her experience will encourage others to get vaccinated.

"I don't like having my information or image out there, but if it helps even just one person or one family feel that they can trust this, that they can take this vaccine, that they can protect their family and their loved ones, then it's all worth it," she said.





Mom Tammy Sam with 2 of her children, Joshie and Kylie

Vaccines for the youngest kids

When architect Tammy Sam heard that a clinical trial testing the effectiveness of the COVID-19 vaccine had opened up for children 5 and under, she applied right away.

"I believe in science," Tammy said. "We all need to do our part to help, and I felt confident involving my kids because I had already gotten vaccinated, and we knew it was pretty safe."

Tammy and her husband, Joe, have 3 kids: 5-yearold Kylie, 3-year-old Brucie, and 1-year-old Joshie. Kylie and Joshie are participating in the trial, but Brucie wasn't eligible due to a congenital heart condition.

Kylie and Joshie, who were 4 and younger than 1 when they joined the trial, have each received 2 doses of either the vaccine or a placebo.

"Joshie is, of course, not old enough, and Kylie is not quite old enough, to understand how they are contributing," Tammy said. "I told Kylie she is doing a good thing, and she's like, 'Okay, but this hurts!' I plan to remind them when they're older that they played a small but important part in human advancement." Although Tammy wishes she could have known sooner whether her kids got the vaccine or the placebo, she said the trial has been a smooth experience. The same day she applied, she heard back that Kylie and Joshie had been accepted. And she appreciates the user friendliness of the online tool used by the researchers to routinely capture parents' observations of their children.

"They have made it very simple to answer all the questions about things like whether your kid spiked a fever today, were they in contact with anyone with COVID-19, or were there any changes in health," Tammy said. "I was very impressed by how easy this process is."

Now, the family is making sure to have some fun before Brucie has heart surgery later in the summer. The kids are regulars at their playground and recently visited Legoland.

"It's been hard because Brucie was already quarantined before COVID-19 even came around," Tammy said. "We want to make sure all the kids experience as much as they can – safely – before his next procedure."

Tammy said that enrolling her kids in this trial gave her a newfound appreciation for participants in the initial safety and dosing trials. "It must have been scary to be one of the first to get vaccinated. But they knew that, later, it could potentially save millions of people."



Kaiser Permanente staff speak with a patient about what to expect after getting his COVID-19 vaccine

R&E answers key vaccine safety and effectiveness questions

y mid-March 2021, more than 100 million COVID-19 vaccines had been administered in the United States. The majority of those were mRNA vaccines for which Emergency Use Authorizations had been granted in mid-December 2020. However, there were still several pressing questions about the vaccines' safety and effectiveness: Were the relatively controlled clinical studies of the mRNA vaccines indicative of their performance in the messier real world? If they were safe and effective in the real world, how long would they remain so? And what about the emerging new variants?

Answers to these questions would guide major health policy decisions and influence the personal vaccination choices of millions. The stakes could hardly have been higher. The nation was desperate to get back to work, school, and play. Variants of the coronavirus were appearing on the scene. More than half a million people in the United States had already died from COVID-19, and the number of deaths worldwide exceeded 2.7 million.

"The Kaiser Permanente Southern California Department of Research & Evaluation had been doing postlicensure vaccine safety and effectiveness research for many years before the pandemic. So, we made a natural segue into studying the safety and effectiveness of the COVID-19 vaccines," said Lina Sy, MPH, who is the scientific program manager for vaccine safety and effectiveness research at R&E.

"The main difference with COVID-19 vaccines was the urgency. We had to quickly do the analyses and prepare manuscripts or presentations so the information could be used to help policy or regulatory decision-making in real time," said Sy.

To help provide the answers needed to guide opinion, policy, and regulation, KPSC conducted multiple large, high-impact, multipartner studies in 2021.

Are the mRNA vaccines effective in the real world?

R&E epidemiologist Sara Tartof, PhD, MPH, led an essential early study of the Pfizer-BioNTech vaccine. She and her team looked at its effectiveness, including its protective power against the delta variant. It was clear that delta was dominating infections, which were rising. Many feared that the higher infection rate was due to delta escaping the vaccine. If that were the case, vaccine makers and public health officials would need to seek new interventions. Others suspected that the infection rate was simply a product of the vaccine's waning effectiveness over time after injection. In that case, a booster shot of the same vaccine would be the best way to strengthen protection.

Dr. Tartof's illuminating study, which appeared in *The Lancet* (preprint August 2021, published October 2021) had a major impact. It resolved the question for the Pfizer-BioNTech vaccine. It found that the vaccine remained effective against hospitalization up to 6 months after the second shot. The study also found that decreased effectiveness against infection was likely due to waning rather than due to delta escaping vaccine protection.

Data from the study were cited as demonstrating the validity of the waning hypothesis at the FDA's Vaccines and Related Biological Products Advisory Committee (VRBPAC) meeting. It was also cited at the CDC's Advisory Committee on Immunization Practices (ACIP) meeting. Booster dose recommendations were subsequently made for the Pfizer-BioNTech vaccine in September 2021.

"We could see that the vaccines were working, but we also realized that we had to treat vaccine effectiveness as a moving target, changing over time as well as from variant to variant," Dr. Tartof said.

While Dr. Tartof and her team were assessing the Pfizer vaccine and its effectiveness, Hung Fu Tseng, PhD, MPH, a senior scientist with R&E, was leading a team of researchers looking at the effectiveness of the Moderna COVID-19 vaccine. Their first study was published in November 2021 in *The Lancet Regional Health - Americas* (preprint September 2021).

Katia Bruxvoort, PhD, MPH, an adjunct investigator with R&E, was the first author on the first of these Moderna studies. R&E researchers found that 2 doses of the Moderna vaccine were effective against



Dr. Sara Tartof and Dr. Hung Fu Tseng have led multiple groundbreaking studies on the effectiveness of the Pfizer-BioNTech and Moderna COVID-19 vaccines

asymptomatic and symptomatic COVID-19. They also found that 2 doses provided protection against hospitalization and death for up to 5 months after the second dose.

The study was much larger than studies that led to the Moderna vaccine's Emergency Use Authorization. It included 350,000 recipients who had received 2 doses of the Moderna COVID-19 vaccine between December 2020 and March 2021, and the same number of unvaccinated members.

"The racially and ethnically diverse study population also had a more representative range of underlying conditions, including chronic diseases, immunocompromising conditions, and autoimmune conditions," said Dr. Bruxvoort. People in the Moderna vaccine clinical trial, which was smaller, were mostly younger and healthier.

"This was one of the first studies showing that the Moderna vaccine worked in the real world," said Dr. Tseng, who was the senior author. "It certainly boosted the confidence of the public and of

"We could see that the vaccines were working, but we also realized that we had to treat vaccine effectiveness as a moving target, changing over time as well as from variant to variant."

- Sara Tartof, PhD, MPH



Julia Tubert, Dr. Hung Fu Tseng, Dr. Jennifer Ku, Dr. Ana Florea, Lina Sy, Dr. Bradley Ackerson, Dr. Lei Qian, and Gina Lee are among the physicians, scientists, and staff supporting research into the effectiveness of the Moderna COVID-19 vaccine

physicians using the vaccine to protect patients against infection. Long-term follow-up will continue to evaluate the durability of that protection."

The study was cited in discussions about booster doses at both the VRBPAC and ACIP meetings in October 2021.

Do the mRNA vaccines protect against emerging variants? If so, for how long?

"Whereas other systems had to use proxies such as time periods when certain variants were predominant, our whole genome sequencing work allowed us to precisely ascertain the effectiveness of each vaccine against the different variants," said Sy. "Kaiser Permanente Southern California studies of both mRNA vaccines' effectiveness were instrumental in showing waning protection over time after 2 doses. The studies also demonstrated the potential need for boosters."

Another study, published December 2021 in *The BMJ*, showed that 2 doses of the Moderna vaccine were still highly effective against all SARS-CoV-2 variants. However, their effectiveness against infection by the delta variant diminished with time after the second shot. It fell from 94% in the first 2 months to 80% after 6 months. Even after 6 months, though, protection against hospitalization remained high at 98%. This study was also led by Dr. Bruxvoort.

"This was one of the first studies showing that the Moderna vaccine worked in the real world."

- Hung Fu Tseng, PhD, MPH

At the time of *The BMJ* publication, the omicron variant had not yet been found in Southern California. But just a few months later, in early 2022, R&E authors published another paper in *Nature Medicine*. It showed that the Moderna vaccine provided strong protection against infection by the delta variant. But it was less effective at protecting individuals from infection by omicron, the variant that came to dominate at the very end of the year. Individuals in the study were more vulnerable to infection by omicron. However, after 3 doses of the Moderna vaccine, they still had strong protection against hospitalization and death.

The study published in *Nature Medicine*, led by Dr. Tseng, was pivotal. It showed that "third doses may be needed sooner than 6 months after the second dose of the Moderna COVID-19 vaccine for adequate protection against omicron infection," said Dr. Tseng. "It also revealed that 3 doses may not be sufficient to protect people who are immunocompromised from omicron infection."

"Kaiser Permanente Southern California has been studying vaccine safety with the VSD for 30 years. So, we were well prepared for this when the pandemic hit."

- Stanley Xu, PhD, MS

Data from the study were cited at the FDA's April 2022 VRBPAC meeting on COVID-19 vaccine booster doses. Its reach was also international. It was cited by the World Health Organization, Australian policymakers, the European Medicines Agency, and the European Centre for Disease Prevention and Control. It provided evidence of gradual waning of immunity against omicron infection.

Later, research published in *The Lancet Respiratory Medicine* and then supplemented with additional analysis showed that a third dose of the Pfizer COVID-19 vaccine provides strong protection, roughly 80% in the first few months against hospital admissions and emergency department visits caused by the delta and omicron variants. However, against omicron, this protection wanes over time for immunocompromised individuals – even after a third dose.

"A third dose of Pfizer BioNTech COVID-19 vaccine significantly improves protection against omicron, although while that protection stays high for immunocompetent patients, it seems to wane for immunocompromised patients after 3 months," said Dr. Tartof.

Are the mRNA vaccines safe?

R&E's contribution to the COVID vaccine safety studies was an extension of its membership in the Vaccine Safety Datalink (VSD) program. The VSD is a collaboration between the CDC's Immunization Safety Office and 9 health care organizations, the largest of which is KPSC.

The mRNA vaccines were authorized for use based on safety data from robust clinical studies. However, "many people still hesitated to get vaccinated because of fears that the new vaccines were causing blood clots, anaphylaxis, and other serious conditions," said Stanley Xu, PhD, MS, an R&E senior research scientist biostatistician. "Toward the end of spring 2021, vaccination rates began to slow significantly."

"Safety was one of the main reasons given for people's reluctance to get vaccinated," said Dr. Xu.



Dr. Stanley Xu on a video call

"There were reports of death following vaccination, but these were not necessarily caused by vaccination. Without an epidemiologic study using a comparison group, it was unclear whether death rates following COVID-19 vaccination were higher than background rates."

Dr. Xu led a study that relied on data from the VSD to compare 6.4 million vaccinated and 4.6 million unvaccinated Americans. It aimed to determine whether any of the 3 COVID-19 vaccines authorized in the United States caused an increased risk of death.

"Kaiser Permanente Southern California has been studying vaccine safety with the VSD for 30 years," Dr. Xu said. "So, we were well prepared for this when the pandemic hit. We began preparing to do safety studies as soon as the FDA authorized the vaccines," he said.

The study examined all 3 vaccines in use in the United States. It looked at the mRNA vaccines, each of which required 2 doses at the time, and a single dose viral vector vaccine. The study was published in the CDC's *Morbidity and Mortality Weekly Report* in October 2021.

"The results of the analysis were reassuring," said Dr. Xu. "It showed that the vaccines are safe. People who received COVID-19 vaccines in the United States had a lower death rate than those who didn't. That's the case even if you don't count COVID deaths," he said. "I like to think it helped a lot of people with their choice to get vaccinated."

How quickly do new variants spread, and how are they distributed across the population?

Another study, published in CDC's *MMWR* in October 2021, demonstrated how quickly and ably researchers could respond to pressing epidemiologic questions. This study was led by Debbie Malden,



Jeff Slezak, Dr. Sara Tartof, and Vennis Hong are part of the study team evaluating the effectiveness of the Pfizer-BioNTech vaccine

DPhil, MSc. Dr. Malden is a CDC Epidemic Intelligence Service Officer stationed at R&E. Her unique role made it possible to design the study, run the analysis, and publish the report quickly.

This study used a large set of sequencing data, combined with KPSC's extensive medical records, to describe the distribution of SARS-CoV-2 variants circulating in the KPSC population. (See related article on variants on page 16.)

The KPSC study team used sequencing data from almost 7,000 SARS-CoV-2-positive specimens that were linked to members' medical records to establish the distribution of variants and hospitalization rates. The investigators found that the weekly percentage of all infections attributed to the delta variant rapidly increased from 0% to 95% between mid-April and late July 2021. This demonstrated the ability of new variants – and delta in particular – to quickly spread over a large geographic area.

The study also found that SARS-CoV-2 infections attributed to the delta variant were more common among younger members and among non-Hispanic Black members. In addition, the study showed that unvaccinated patients infected with delta were more likely to get sick enough to require hospitalization than unvaccinated patients infected with other variants.

This study showed how important it was to monitor variants for new mutations, and the findings



Julia Tubert and Dr. Lei Qian are part of the large team of biostatisticians supporting KPSC's COVID-19 vaccine safety and effectiveness research

reinforced the continued value of vaccinations, social distancing, and wearing masks to prevent the spread of delta.

KPSC's resources presented a unique opportunity to do this study. The combination of available sequencing data and epidemiologic data from members' electronic health records represents a unique data source that could be used to answer high-priority questions about hospitalization rates and variant distribution.

Addressing the most pressing questions

Together, these studies provided essential answers about vaccine effectiveness against hospitalization and death, the duration of protection, vaccine safety, and the threats posed by variants as they emerged on the scene. Those answers enabled regulators and policy makers to make informed public health decisions, particularly about booster dose recommendations in response to variants and waning vaccine effectiveness.

Over the course of the COVID-19 pandemic, studies from KPSC have enlightened and informed policy makers and the public on the best ways to move toward a safer future. Scientists know, though, that their mission continues. As the pandemic wanes and surges, as new variants emerge, and as public knowledge and opinion shift, the research by KPSC will continue to address the most pressing questions.

Simple text-based platform proves powerful for monitoring symptoms after vaccination

When COVID-19 vaccines rolled out in early 2021, researchers were interested in collecting data on common side effects to help inform policy makers, health systems, researchers, and people who might have concerns.

Kaiser Permanente Southern California researchers worked with the CDC and a coalition of partners within Kaiser Permanente to create an innovative, easy-to-use digital survey tool that would allow patients to send their answers to questions online or via text message. The idea was that this potentially groundbreaking survey tool would record how people felt in the days after their vaccinations and be able to link responses to their health records.

After participating in a competitive process, the KPSC team led by Sara Tartof, PhD, MPH, and Debbie Malden, DPhil, MSc, was awarded a grant from the CDC to develop a digital survey platform that was later used to gather data from patients after they were vaccinated.

Despite many technological hurdles, the researchers sprinted from design to deployment in only a few months. They credit support from a wide range of stakeholders, including contributions by Kaiser Permanente's national information technology, marketing, and legal teams, for the speed from concept to completion. However, it was the support and participation of Kaiser Permanente members that made the novel system a true success.

Named the Kaiser Permanente COVID-19 Vaccine Side Effect Monitoring System, the digital tool included participants across all Kaiser Permanente sites in Southern California. As of May 2022, more than 100,000 people throughout the region had joined. They used a simple text- and web-based digital platform to report any symptoms they experienced after getting their vaccination.

The tool has several important features that the CDC's digital vaccine side effects monitoring tool, called v-safe, did not. Most important, the KP Side Effect Monitor is linked to participants' medical records. So, any exams or treatment following reported symptoms can be tracked and evaluated.

"We had a much higher rate of participation than v-safe, something I attribute to the trust that our members have in us and our integrated health care system," Dr. Tartof said.



Prospective study participant Ramón Arroyo talks with Dr. Debbie Malden about the KP Side Effect Monitor

"We worked through many technological challenges to create this new framework to collect patient-reported outcomes."

- Sara Tartof, PhD, MPH

Also, because participants were recruited from a known population of vaccinated patients, the study team can determine who is participating and who is not. "We can look at participation levels against a true denominator," said Dr. Malden.

Unlike v-safe, the new Kaiser Permanente tool has enhanced accessibility since it does not require a smartphone or internet access to take part; even a flip phone would work.

"As the first of its type to integrate research and IT operations at this scale, this project made huge strides toward providing information on vaccine safety," Dr. Tartof said.

In the future, researchers hope to expand the system to other Kaiser Permanente facilities within the Vaccine Safety Datalink network.

"We worked through many technological challenges to create this new framework to collect patientreported outcomes," Dr. Tartof said. "This system – a first of its kind for Kaiser Permanente and likely other health care institutions – has important implications for potential use in the future with new vaccines as well as new medications and treatments."



Kaiser Permanente nurse helps patients at a drive-through site

Exceptional collaboration tracks emerging variants in real time

n late January 2021, as year one of the COVID-19 pandemic was rounding out, deaths in the United States had just surpassed 400,000, but new infections were declining, thanks largely to effective vaccines. The world was taking tentative, hopeful steps back toward normalcy.

There were, however, ominous signs. The first significant variant of the SARS-CoV-2 virus had appeared in November 2020 in England and shortly after that in the United States. This variant, alpha, seemed to be much more transmissible than the original form. Some feared the virus was developing new characteristics that could move the world back into lockdown.

"We were starting up studies to evaluate the effectiveness of the new vaccines," said Sara Tartof, PhD, MPH, an infectious disease epidemiologist and research scientist with the Kaiser Permanente Southern California Department of Research & Evaluation. "But a super critical question was, how might vaccine effectiveness change for different variants?"

KPSC senior scientist and vaccine researcher Hung Fu Tseng, PhD, MPH, said, "The key was linking the variant data back to the clinical data to find out whether the variants were more virulent or more fatal."

"We needed to know which variants we were seeing among COVID-positive vaccinated individuals and which variants were among COVID-positive unvaccinated individuals," said Katia Bruxvoort, PhD, MPH. She is an epidemiologist and was then a postdoctoral research fellow working with both Dr. Tseng and Dr. Tartof. "Then we would see how the severity or complications of COVID might be different for different variants."

Dr. Tseng said that one way to determine that would be to continuously sequence samples found infecting a wide cross section of the population.



Dr. Michael Aragones and Ana Acevedo working together at the Chino Hills lab

Large, diverse, integrated health system ideal for variants study

In January 2021, the researchers and the vaccine makers, recognizing the value of KPSC's unique potential to track the evolution of coronavirus into new forms, began to converge around the idea of the COVID-19 variants study.

The size and diversity of the Southern California region's patient population and the centralization of Kaiser Permanente's labs made KPSC an ideal location for this kind of study. So did the depth of the electronic health records and the great number of members of all ages that received one of the mRNA vaccines.

Most vaccinated members had avoided infection, but some had not. Some of those who were infected had been hospitalized. And some of them had died. Some members had chosen not to – or were unable to – be vaccinated. Comparing different groups' outcomes to the variants associated with them would yield valuable knowledge to vaccine makers, policy makers, and clinicians.

The 2 major mRNA vaccine makers, Pfizer-BioNTech and Moderna, each reached out to KPSC separately to explore using KPSC's COVID-19 specimens to track and identify emerging variants that might evade, or at least pose new challenges to, their vaccines.

Harpreet Takhar, MPH, a senior research support manager at R&E for the vaccine research teams, was observing a similar request from the researchers and from industry, all pointing to the value of a KPSC COVID-19 variants study. "We could all work together and generate data that everyone could use," he said. "As far as I knew, nothing like this had been done; however, it made sense in terms of efficiency."

Two separate studies, one common aim

It was a simple and elegant plan. But to make it work, all the stakeholders would have to collaborate in unprecedented ways, working hand in hand to sequence the samples, while keeping some elements of the data from the 2 parallel studies – 1 for each of the major mRNA vaccines – separate.

"The clinical side had begun setting the positive specimens aside for us ... So, we had only a week to get the research lab operation up and processing samples and sending them out."

- Michael Aragones, MD

Each study team would be doing its own research, but they would be sharing a lot. Dr. Tartof would be the principal investigator for Pfizer-BioNTech. Dr. Tseng would be the principal investigator for Moderna. The studies would share what data they could, but would keep sensitive and proprietary information separate.

Additionally, the R&E lab would have to be radically scaled up and would have to expand at a second location at the Chino Hills lab, where most of the COVID-19 testing occurred. At first there were only about 1,100 positive samples per week. If there were surges, however – and there soon would be – research lab staff could be processing many thousands of biospecimens a day.

The team brought in Research Lab Manager Michael Aragones, MD, to design, jump-start, and oversee the lab workflow. Dr. Aragones describes his job as "making lab research projects work. Scientists come to me with a study idea, and I figure out how to make it happen."

Devising laboratory solutions in real time

Dr. Aragones described one of his biggest and most important constraints in making research projects work: "Nothing research does can get in the way of the clinical lab's operations – nothing!"

"So, I look for a point of insertion where we won't adversely affect clinical operations. And when we need biospecimens, like we do for the variants study, the best approach may be to collect the specimens once the clinic is finished with them, when they would otherwise have been tossed in the biohazard bin. One person's castoff is another's treasure!"

"The clinical side had begun setting the positive specimens aside for us, and we were not going to waste them. So, we had only a week to get the research lab operation up and processing samples and sending them out," said Dr. Aragones.

While the Central Business Office negotiated an agreement with the vaccine makers and Dr. Tartof and Dr. Tseng laid out strategies for their studies, Dr. Aragones went to see Robert Rabot and Agnes Bautista in the clinical lab in Chino Hills. Dr. Aragones had worked for their team previously. Now his former colleagues offered to carve out a space for research in their area. They also offered to lend the study teams the equipment needed to get started.

"It required working very fast," said Dr. Tartof. "Hiring and training people fast. Working out processes – I can't even tell you the number of processes there were. We had to label, aliquot, and store specimens at just the right temperatures. There are so many details when you're working with specimens."

Dr. Aragones said, "Positive samples of different types (some nasal swabs and others saliva) were arriving in different media and in different-size tubes. That made processing, storage, and shipping a challenge. And we were also dealing with a nationwide shortage of tubes and containers." Dr. Tartof said, "We had to build this study while we were running. That's a big difference from clinical trials. We didn't have the established protocols as there would be in a clinical trial. We pretty much had to invent them. There was always a new challenge to overcome. And I think we've met every single one."

Once underway, study shifts into overdrive

The study got underway in March 2021. After obtaining Institutional Review Board approval, R&E employees swept through the clinical labs emptying the bins containing each day's positive samples after they had been read and entered and were considered completed by the clinical team.

Then they brought the samples back to their new Chino Hills workstation. There they de-identified them, aliquoted them, and stored them at the appropriate temperature until they could be shipped to the outside lab contracted to do the sequencing itself. Eventually, housing the tubes of samples required securing an entire freezer trailer that was brought in and parked in the lot outside of the Chino Hills lab.

The third-party lab obtained the sequences and identified the variant causing each infection. They aggregated sequencing data from the samples taken from members who received a Pfizer-BioNTech vaccine but had still been infected. They sent those data to the KPSC study team focused on the Pfizer



Joe Singh and Jared Davis sort positive COVID-19 samples by vaccination status



Samantha Quinones and Kourtney Kottmann prepare COVID-19 samples for aliquoting

vaccine for further analysis. Aggregated sequencing data from those who received the Moderna vaccine, but had still been infected, were sent to the KPSC Moderna vaccine study team. Sequencing data from those who were unvaccinated were shared with both KPSC study teams.

With the emergence of the delta variant in June 2021, the volume of samples rose exponentially. The team ramped up to process as many as 5,700 samples a week. "Our team of research associates worked 6 days a week for 7 weeks to deal with the rise in samples," said Dr. Aragones. "And during omicron, we were handling more than 13,000 samples a week."

Innovative team effort bears groundbreaking, high-impact results

"At the end of the first phase of the sequencing study, even those research associates who were exhausted working on the delta variant over the summer agreed to continue to work on the next phase of the sequencing study," said Takhar.

"Everyone understands how important this work is. That's what helps the lab research associates who are often working overtime shifts. They know their work is making a difference, and I am very grateful for the commitment of our skilled research associates and dedicated project managers to this study's success," he said.

Key publications from the studies have explored the

"At the end of the first phase of the sequencing study, even those research associates who were exhausted working on the delta variant over the summer agreed to continue to work on the next phase of the sequencing study."

- Harpreet Takhar, MPH

effectiveness of vaccines against several specific variants. They have also studied the severity of the disease associated with them. These studies were published in some of the world's most influential medical journals. They were used by decision-makers at the U.S. FDA and CDC and their international counterparts. They helped determine policy, particularly around the need for booster doses to preserve vaccine effectiveness against variants.

"I feel fortunate to be able to use our system in such an elegant, beautiful, helpful, and unprecedented way," said Dr. Tartof. "It would be hard to overstate the importance and influence of the studies this work has already made possible, or of those to come."



Samantha Baluyot, Joanna Truong, and Jared Davis aliquot samples



Katy Taylor and Joe Singh pack samples to be shipped for sequencing



Permanente physician with young patient during the pandemic

Beyond the virus: Health impacts of the pandemic

hen the COVID-19 pandemic began, researchers and physicians at Kaiser Permanente Southern California quickly recognized that its effects would reverberate far beyond the novel respiratory illness itself. This public health crisis would have an unprecedented impact on a range of additional health conditions and health care delivery concerns.

With that foresight, as the pandemic progressed, researchers began to monitor its broader impacts.

One of the earliest secondary effects was a dramatic drop in the number of childhood vaccine doses – including the measles vaccine – administered during the first 6 months of the pandemic, according to Kaiser Permanente research reported in *Pediatrics*. The study found that this decline was less severe and rebounded more quickly for children under 2 than for older children. "At the start of the pandemic, it was immediately clear that fewer parents were bringing their children in for office visits, most likely due to pandemic safety concerns," said the study's lead author, Bradley Ackerson, MD, a Kaiser Permanente South Bay Medical Center pediatric infectious disease specialist and an investigator with the Department of Research & Evaluation.

To understand the pandemic's effects, researchers evaluated vaccinations for nearly 1 million children 18 and younger at Kaiser Permanente Southern California, comparing rates for January through August 2020 with the same timeframe in 2019. They assessed both vaccine uptake, which is the number of children receiving vaccines, and vaccine coverage, the proportion of children of a given age who have been vaccinated with specific vaccines. The analysis showed that uptake of all recommended vaccines declined in early 2020. However, while uptake rebounded completely for children under 2 by May 2020, it only partially rebounded for older kids. In particular, despite some rebound, measles vaccinations remained lower in 2020 than in 2019, causing measles vaccination coverage to decline.

"Decreases in vaccination coverage raised concerns about increased risk of transmission and outbreaks, especially as schools reopened and international travel resumed," Dr. Ackerson said. "We were particularly worried about measles because even small declines in vaccination coverage could lead to exponential increases in outbreaks."

Clinicians at Kaiser Permanente Southern California implemented strategies to ensure ease of access to childhood vaccinations and to alleviate parents' concerns about the safety of medical visits during the pandemic. These included opening drive-through vaccination sites, applying distancing and hygiene measures, and reaching out directly to parents of unvaccinated children.

"In addition, we developed algorithms that alerted providers when children are due for certain vaccines so that at each visit, we never miss an opportunity to keep up with recommended vaccinations," Dr. Ackerson said.

Anxiety, depression, and exercise

As the pandemic set in, people around the world faced a number of stressors, including reduced or altered business practices, financial problems, and fewer opportunities to socialize with friends and family. These factors led to increased symptoms of depression and anxiety.

A Kaiser Permanente study revealed that people who exercised and spent time outdoors experienced lower levels of anxiety and depression.

The research, published in *Preventive Medicine*, was led by Deborah Rohm Young, PhD, MBA, the director of the Division of Behavioral Research for the Department of Research & Evaluation.

"We already knew that physical activity and time spent outdoors are linked to better mental health in nonpandemic times," Dr. Young said. "We saw that these associations held up during the initial pandemic lockdown period."



Dr. Hung Fu Tseng and Dr. Bradley Ackerson frequently collaborate on vaccine research, bringing together scientific and clinical expertise

The study began in April 2020, when researchers launched a series of COVID-19-related surveys to over 200,000 Kaiser Permanente members who volunteered to participate in the Kaiser Permanente Research Bank – an initiative that combines lifestyle surveys with biospecimens. Those with COVID-19 symptoms were excluded from this analysis, leaving a final pool of more than 20,000 participants from 6 regions served by Kaiser Permanente across the United States. They completed at least 4 surveys from April through July 2020.

Overall, anxiety and depression scores decreased over time for the participants, most of whom were older, retired, white women who reported that they had followed "safer-at-home" orders to limit COVID-19 spread. Female and younger participants had higher levels of anxiety and depression, while Asian and Black participants had lower anxiety and depression than white respondents.

People who exercised the most had the lowest anxiety and depression scores. While participants who spent less time outdoors had higher levels of anxiety and depression, those with the greatest increase in time spent outdoors had higher anxiety.



Dr. Deborah Rohm Young discusses the benefits of physical activity and spending time outdoors during the pandemic with colleague Cristine Denver

"The take-home message is that maintaining physical activity during these difficult times has a number of benefits," Dr. Young said. "Regular exercise, even going for a nice, brisk walk every day, is the 'pill' that people need."

The findings also suggest the importance of maintaining safe access to outdoor areas, including parks and trails.

Children gained excess weight

Other researchers were particularly interested in potential secondary effects of pandemic conditions on weight gain in children. A study of Kaiser Permanente Southern California members ages 5 to 17 found that they gained more weight during the pandemic than would normally be expected.

Published in *JAMA*, the analysis showed that children ages 5 to 11 had the greatest excess weight gain. Children in this range would be expected to gain an average of 0.2 pounds during the study's timeframe, but during the pandemic, they gained an average of 5.2 pounds.

"This translated to an increase of nearly 9% in 5- to 11-year-olds who are considered overweight or obese," said the study's senior author, Corinna Koebnick, PhD, MSc, of the Department of Research & Evaluation. "For perspective, over the last 2 decades, we have observed an increase of about 10% in 5- to 11-year-olds who are considered overweight or obese, but during the lockdown, a similar increase happened in just 1 year."

The research team examined the electronic health records of nearly 200,000 children from March 1, 2019, to January 31, 2021. In addition to the findings for younger children, they found a 5% increase in the number of children ages 12 to 15 who were considered overweight or obese, and an increase of 3% among those ages 16 to 17.

"During the pandemic, it has been difficult for many parents to ensure their children have enough opportunities to exercise and eat nutritious meals," Dr. Koebnick said. "As the obesity epidemic worsens, we need to continue monitoring the situation and develop interventions to help children reach and maintain a healthy weight."

Dr. Koebnick is collaborating with Kaiser Permanente clinicians to develop a pediatric weight management program based on a technique known as motivational interviewing.

"Motivational interviewing empowers patients to make their own decisions and changes," Dr. Koebnick said. "We hope that we can train as many doctors as possible to use this powerful tool."

The research team is also analyzing socioeconomic and racial disparities in weight gain among kids during the pandemic, and has been working closely with the CDC on additional research into pediatric weight gain.

Inequities for people of color

Kaiser Permanente research uncovered disparities in COVID-19 outcomes across multiple racial and ethnic groups, pointing to the persistence – and potential worsening – of health inequities during the pandemic.

"We know that there are health inequities across almost all health outcomes. Compared to chronic disease outcomes, the COVID-19 pandemic made these inequities painfully obvious because of how quickly events where unfolding," said the study's lead author, Claudia Nau, PhD, a researcher with the Department of Research & Evaluation. "The stark differences in outcomes we've seen for COVID-19 drive home the existence and seriousness of health disparities."

The study, published in *Annals of Internal Medicine* in August 2021, analyzed the electronic health records of nearly 300,000 KPSC members. It revealed that, compared to white patients, people of color were more likely to be diagnosed with COVID-19. They were also more likely to be hospitalized or to require intensive-level care for COVID-19.

These racial and ethnic disparities – observed for Black or African American, Hispanic, Asian, and Pacific Islander patients – persisted even after accounting for potential preexisting health disparities in obesity, diabetes, and other conditions associated with increased risk and worse outcomes of COVID-19.

"Our study was among the first to examine COVID-19 outcomes for the Pacific Islander population separately from those of the Asian population, and was also one of the first to examine testing, hospitalizations, and deterioration in combination with the same patient population," Dr. Nau said.

The findings emphasize the need for culturally appropriate pandemic response efforts that adequately address distrust of the medical system, resource inequities, language proficiency, and health literacy.



Dr. Claudia Nau and Dr. Corinna Koebnick discuss the health impacts of the pandemic during a break at a scientific conference

"We know that there are health inequities across almost all health outcomes. Compared to chronic disease outcomes, the COVID-19 pandemic made these inequities painfully obvious because of how quickly events where unfolding."

– Claudia Nau, PhD

"As we continue to study the broader impacts of the pandemic at Kaiser Permanente and beyond, it will be important to maintain efforts to understand and mitigate these inequities," Dr. Nau said.

Looking ahead, Dr. Nau and many of her colleagues throughout Kaiser Permanente remain dedicated to tracking the long-term effects of the pandemic as it continues to unfold. By surfacing new insights into health care disparities, care delivery, and the exacerbation of certain conditions, this research will help drive health care improvements around the world – while boosting preparedness for future pandemics.

Physician trailblazers



Physician trailblazers seek answers to improve their patients' health

Physician researchers at Kaiser Permanente Southern California are often motivated to pursue research inspired by questions that spring from their daily practices. The questions they seek to answer are as varied as their clinical backgrounds, but they all share one common goal: finding new and better ways to improve their patients' health.

First same-day discharge for pediatric chest surgery

In 2021, a "dream team" of Kaiser Permanente physician researchers became the first to report that young patients could head home on the same day as their surgery to correct a congenital chest deformity known as pectus excavatum.

"Traditionally, these patients had to be hospitalized for several days in order to manage debilitating pain caused by surgery," said R. Luke Rettig, MD, a resident at the Los Angeles Medical Center's Department of Pediatric Surgery. "Now we send most kids home with little to no pain on the same day."

Pectus excavatum is characterized by a sunken-in chest that results from abnormal development of the breastbone and ribs, leading to symptoms that may include chest pain and breathing problems. Surgery can correct the condition, but postsurgical pain can persist for weeks.

That has now changed, thanks to a new paincontrol strategy developed by the KPSC Pediatric Care Surgical Subspecialties group, which includes Dr. Rettig; Roman Sydorak, MD; Donald Shaul, MD; Franklin Banzali Jr., MD; and Andrew Rudikoff, MD. The groundbreaking protocol involves freezing nerves in the chest to temporarily numb them until the pain subsides, combined with a multimodal analgesia regimen to block short-term pain that occurs before the effects of cryoablation begin.



Dr. Banzali, Dr. Rudikoff, Dr. Rettig, and Dr. Sydorak at the Los Angeles Medical Center

"Families are shocked and very happy that this is now possible," Dr. Rettig said. "Our team has performed about 40 of these procedures, and we're spreading the word to other children's hospitals; some have already adopted our protocol."

The breakthrough required concerted efforts among surgeons and anesthesiologists in the Surgical Subspecialties group, as well as nurses, child life specialists, physical therapists, and more.

"This could not have happened without buy-in and sustained dedication from everyone involved," Dr. Rettig said. "Our team dynamics are truly incredible and key for the success we've seen with our patients."

Opposite page: Dr. Franklin Banzali, Dr. Andrew Rudikoff, Dr. R. Luke Rettig, and Dr. Roman Sydorak are part of a team of Kaiser Permanente physicians who pioneered a new pain control method to make pectus excavatum surgery easier on young patients



Physician trailblazers

Exercise is medicine

From the onset of the pandemic, Robert E. Sallis, MD, suspected that people's COVID-19 outcomes were linked to their levels of physical activity.

"Most diseases associated with severe COVID-19 are also associated with inactive lifestyles," said Dr. Sallis, a family medicine and sports medicine physician at the Kaiser Permanente Fontana Medical Center. "But, early on, the CDC did not identify lack of exercise as a risk factor."

Dr. Sallis was well poised to mobilize an investigation. He has an extensive history of collaboration with the Department of Research & Evaluation; and in 2009, he pioneered the Exercise Vital Sign, which captures information on people's weekly physical activity at every outpatient encounter within KPSC. To study links with COVID-19, Dr. Sallis led an analysis of Exercise Vital Sign data for nearly 50,000 members who had COVID-19 between January and October 2020.

The findings revealed strong associations between continued on page 28

Strategic action on a serious liver condition

Several years ago, Amandeep Sahota, MD, experienced a career-shifting wake-up call.

"My son was on the high school football team, and after they had a brief break, I was alarmed to see that he and his teammates had suddenly gained considerable weight," she said.

Dr. Sahota, who directs the Department of Hepatology at the Kaiser Permanente Los Angeles Medical Center, had increasingly been hearing about nonalcoholic steatohepatitis (NASH) – excessive buildup of fat in the liver that may progress to life-threatening disease.

"One in 4 U.S. adults has a fatty liver and does not realize that they are well on their way to NASH," she said. "I was worried that my son might be too."

Galvanized by her concerns, Dr. Sahota led a study that uncovered a rise in nonalcoholic fatty liver disease – which can progress to NASH – in young adults. Meanwhile, she spoke with her son and his friends about their weight.

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Physician trailblazers



Fostering trainee-led discovery

Mingsum Lee, MD, PhD, is not one to seek the spotlight. Nonetheless, she is building a powerful legacy through her dedication to mentoring the next generation of physician researchers.

"For residents and fellows, the opportunity to lead research can be transformative, because they realize that while they're caring for the patient in front of them, their research could help many more," said Dr. Lee, a cardiologist at the Los Angeles Medical Center and a clinician investigator for the Department of Research & Evaluation.

As program director for the Cardiovascular Disease Fellowship Training Program, she helps residents and fellows pursue questions that move and intrigue them.

For instance, after caring for patients who developed myocarditis after getting a COVID-19 vaccination, 2 fellows became concerned about a potential connection. With Dr. Lee's guidance, they analyzed Kaiser Permanente member data and published widely

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Dramatic strides in infant lung disease

In 2009, rates of an infant lung condition known as bronchopulmonary dysplasia seemed to be rising at the Kaiser Permanente Panorama City Medical Center neonatal intensive care unit. Maria Fe Bellen Villosis, MD, was inspired to pursue a bold vision: to not only stem the rise but to drastically reduce these rates – at Kaiser Permanente and beyond.

Infants with bronchopulmonary dysplasia experience breathing problems that raise their risk of other serious conditions, such as high blood pressure and developmental delays. This disorder may develop as a result of lung underdevelopment or injury from the machines, and oxygen treatments used to help preterm babies breathe.

"There is no quick fix," said Dr. Villosis, a neonatologist who has directed the Panorama City NICU for over a decade. "But I've always believed that prevention is the best care."

These days, Dr. Villosis and her colleagues report that rates of bronchopulmonary dysplasia have plummeted

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2

Exercise is medicine

regular physical activity and lower odds of being hospitalized, being admitted to an intensive care unit, or dying from COVID-19. People who exercised inconsistently were still more protected than people who were completely inactive, even after accounting for other factors including diabetes, smoking, and obesity.

"Our research was a linchpin in convincing the CDC to recognize inactivity as a major COVID-19 concern," Dr. Sallis said.

The study adds to a large body of evidence on the health benefits of exercise compiled by Dr. Sallis over his 3-decade career at Kaiser Permanente. Much of this research has been powered by data from the Exercise Vital Sign, which has also been adopted by other major health care systems across the United States.

"By prescribing exercise, doctors can often do more good for their patients than by just focusing on traditional treatments," Dr. Sallis said. "I've been incredibly lucky to collaborate with worldclass colleagues at the Department of Research & Evaluation on exercise research that influences clinical practice across the country."

Dramatic strides in infant lung disease

from 31% to less than 2% among very preterm babies at the Panorama City NICU. In contrast, the statewide rate for California remains at about 20%.

This dramatic improvement was the result of a comprehensive system of clinical care and team management practices originally developed by Dr. Villosis and her colleagues in 2009, and continually refined since then. Central to this approach is the care team's shared belief that bronchopulmonary dysplasia is, indeed, preventable.

"It has been amazing to see how that shared mindset enabled our team to work so effectively," Dr. Villosis said. "We're proud that Kaiser Permanente has taken a leading role in the prevention of bronchopulmonary dysplasia."

She and her colleagues are sharing their strategies in the form of a road map and bronchopulmonary dysplasia prevention bundle that other NICUs can follow.

"Change doesn't happen overnight, and there were times early on when we almost felt hopeless," she said. "But our hard work paid off, and I hope to inspire other NICUs around the world that this is possible for them too."

Strategic action on a serious liver condition

"Fortunately, NASH can be managed by controlling cholesterol and blood pressure, eating healthy, and losing weight," she said. "After we spoke, my son and his teammates lost weight, and I lost 30 pounds myself."

Dr. Sahota's personal journey sparked a new commitment to raise awareness about NASH and improve treatment for this little-known disease. Now she leads 2 clinical trials on medications for NASH and liver fibrosis in adults.

"We not only want to test these promising treatments but also boost NASH awareness," she said. "Some patients have actually ended up being too healthy to participate in the trials because they were motivated to get healthier during the screening process."

Additionally, Dr. Sahota has developed tools to help clinicians address NASH more effectively by raising its profile in primary care, rather than confining it to gastrointestinal or hepatological care.

"This work is exactly why I came to Kaiser Permanente – because of the rich opportunities to help as many people as possible," Dr. Sahota said.

Fostering trainee-led discovery

discussed findings stating that vaccine-related myocarditis is rare and mild, and the benefits of vaccinations still outweigh the risks.

"This was a great illustration of how, as frontline physicians, our clinical observations can inspire research that broadly informs care," Dr. Lee said.

In another project, Dr. Lee has guided residents as they lead research into Takotsubo syndrome, a condition resembling a heart attack. So far, they have published 3 papers, including 1 linking beta blockers to better survival outcomes.

"I hope they're as proud as I am about the advancements they've made," Dr. Lee said.

She also recently mentored 2 fellows who are passionate about tackling health inequities. They published findings highlighting disparities in post-heart attack survival between Black and white patients living in low-resource neighborhoods. Now they're working with Kaiser Permanente leadership to translate the findings into clinical practice.

"It is quite rewarding for trainees when their research has immediate implications for patient care," Dr. Lee said. "And for me, mentorship is a 2-way street; while I provide guidance on research, I learn from their unique talents and expertise."

Accomplishments & Milestones



Research program at a glance

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

33 FULL-TIME RESEARCH SCIENTISTS

300+ PHYSICIAN RESEARCHERS

Includes 88 clinical trials principal investigators and 240+ sub-investigators, as well as retired and affiliated Southern California Permanente Medical Group physicians

390+ RESEARCH AND SUPPORT STAFF

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

19 RESEARCH SCIENTISTS

On faculty of Kaiser Permanente Bernard J. Tyson School of Medicine

Projects & publications

500+ active studies

Throughout KPSC. Projects may include multiple protocols

~450 active clinical trials protocols

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

2,800+ patients enrolled in clinical trials across 30 therapeutic areas

575+ journal articles

Southern California research environment

15 medical centers

236 medical offices (including retail or employer clinics)

7,800+ physicians

75,000+ employees (including technical, administrative, and clerical employees, nurses, and nonphysician caregivers)

22.3 million outpatient prescriptions filled

11.8 million prescriptions filled by mail order

Southern California member population SFX 52% Female RACE/ETHNICITY AGES 24 years and younger **29% 41%** Hispanic or Latino 29% White 25 to 44 years 29% **MILLION 11%** Asian or Pacific Islander 45 to 64 years 26% **MEMBERS** 7% Black or African American 65+ years 16% **12%** Multiple or other

43% Male
MEMBERSHIP RETENTION RATES
93% 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 2 decades to support a growing portfolio of innovative and clinically relevant research.

Total research funding: \$83 million

Federal grants: \$27.6 million

Industry contracts: \$31.3 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.



2021 grant and contract submissions

(new grants on	ly, external only
Submitted:	221
Awarded:	113

Kaiser Permanente Southern California was the lead, or prime, institution for 64% of all grants and contracts submitted, and was the subcontractor institution for the remaining 36%.

\$

New grants and contracts

(all years, includes clinical trials)Direct costs: \$39.3 millionIndirect costs: \$18.0 millionTotal: \$57.3 million

Continued grants and contracts

(all years, includes clinical trials)
Direct costs: \$156.8 million
Indirect costs: \$75.4 million
Total: \$232.2 million

Selected findings

In 2021, Kaiser Permanente Southern California scientists and clinician researchers made important findings in a variety of research areas, including research related to COVID-19. The following is a small sample of some of these discoveries.

COVID-19 research

Mortality study reinforces safety of COVID-19 vaccinations

Kaiser Permanente researchers reported that people who were vaccinated for COVID-19 had lower non-COVID-19 death rates than did people who were not vaccinated. The study, which was published in October 2021, covered the period from December 2020 through July 2021 and examined the electronic health records of more than 11 million persons. Few studies to date have evaluated mortality from causes other than COVID-19. The study findings provide reassurance that vaccines are safe and can help allay concerns about vaccine safety, which contribute to vaccine hesitancy. (See related story on page 10.)

Xu et al. MMWR Morb Mortal Wkly Rep. 2021 Oct;70(43):1520-1524.

COVID-19 delta variant associated with increased risk for severe disease

Researchers from the CDC and KPSC found that COVID-19 cases caused by the delta variant increased rapidly from 0% to 95% of all infections from April 15 to July 21, 2021. Infections attributed to the delta variant were particularly common among persons ages 18 to 44. The study was published in October 2021. The findings reinforce the importance of continued monitoring of new variants of SARS-CoV-2, in conjunction with effective preventive measures, to control the COVID-19 pandemic. (See related story on page 10.)

Malden et al. MMWR Morb Mortal Wkly Rep. 2021 Oct;70(40):1415-1419.



Dr. Debbie Malden

COVID-19 severity associated with air pollution from nonfreeway traffic

A study of KPSC members diagnosed with COVID-19 found that patients who had recently lived in areas with high levels of air pollution from roadways other than freeways had a higher risk for severe outcomes. Using a patient's residential address history in the electronic health record, the researchers found that patients exposed to more air pollution were more likely to have received intensive respiratory support, been admitted to an intensive care unit, or died of COVID-19. The study findings bring new attention to the importance of air pollution from neighborhood streets and major roads with many stoplights.

Chen et al. Environ Int. 2021 Dec;157:106862.

Risk of severe COVID-19 higher for patients who recently needed asthma care

A study of KPSC members diagnosed with COVID-19 found that patients with active asthma – that is, those who had visited a health care provider for asthma care in the previous 12 months, had a higher risk for severe COVID-19 outcomes than patients without asthma. Among patients with active asthma, using asthma medications lowered the risk for severe outcomes. Earlier studies of associations between asthma and COVID-19 severity had not considered whether patients had active disease. The findings suggest that patients with asthma, especially those who require clinical care, should continue taking their control medications during the COVID-19 pandemic.

Huang BZ et al. J Allergy Clin Immunol Pract. 2021 Oct;9(10):3621-3628.e2.

Pfizer-BioNTech COVID vaccine effectiveness wanes over time

In a study published in October 2021, KPSC researchers reported that the Pfizer-BioNTech COVID-19 vaccine is highly effective against hospitalization for 6 months after full vaccination, even in the midst of widespread transmission of the delta variant. However, vaccine effectiveness against infection started very high and declined over time. If the delta variant had escaped protection from the vaccine, researchers would have seen low vaccine effectiveness at all time points. The findings suggest that reductions in vaccine effectiveness against SARS-CoV-2 infections over time is primarily due to waning immunity rather than the delta variant escaping vaccine protection. (See related story on page 10.)

Tartof SY et al. Lancet. 2021 Oct;398(10309):1407-1416.

Pneumonia vaccine may affect course of COVID-19

KPSC researchers found that one type of pneumonia vaccine, the PCV13 vaccine, may affect the course of COVID-19 for some older adults. Bacteria like Streptococcus pneumoniae, called pneumococci, are known to interact with influenza, respiratory syncytial virus, and several other viruses in the airway, but their contribution to SARS-CoV-2 infection and



Jessica Alvarez, Ageo Fernando, and Jasper Ancheta

pathogenesis has not been widely investigated. In this study, researchers found that the PCV13 vaccine, which protects against 13 types of pneumococci, lowered the incidence of COVID-19 diagnoses along with hospitalizations and death in older adults.

Lewnard JA et al. J Infect Dis. 2021; jiab 128.

Vulnerable populations sought virtual care during pandemic

In a study that spanned age, race/ethnicity, and income groups, researchers found that Hispanic patients and low-income patients had the largest increase in telehealth visits in response to the COVID-19 pandemic. Telehealth visits increased in these patient groups by about 300% compared with the prepandemic period. Although it was known that outpatient visits decreased dramatically and telehealth visits increased during the pandemic, it was unclear whether these changes differed according to patient demographics and socioeconomic status. The findings on the use of telehealth visits during the pandemic suggest that virtual care may be a way to reduce health care disparities.

Qian et al. J Med Internet Res. 2021;23(9):e29959.

Young children gained weight during the pandemic

Children, especially those ages 5 to 11 years, gained excess weight during the COVID-19 pandemic. In a study of nearly 200,000 children published in JAMA, researchers also reported that the number of the youngest children who fell into the categories of being overweight and obese increased by almost 9%. Few studies had previously focused on the weight of U.S. children and adolescents during the pandemic. If generalizable to all children in the United States, the findings suggest that intervention efforts to address weight gain related to COVID-19 may be needed. (See related story on page 20.)

Woolford SJ et al. JAMA. 2021;326(14):1434-1436.

COVID-19 outcomes are more severe for people of color

A study published in Annals of Internal Medicine found that Hispanic patients were more likely to test positive or be diagnosed with COVID-19 than white patients; and Asian, Black, and Pacific Islander patients were more likely to have severe outcomes than white patients. These disparities remained even after adjustment for known health risk factors. Prior research was limited by small, nondiverse samples, a shortcoming that researchers addressed in this study by using electronic health record data from the diverse KPSC membership. The findings underscore health inequities during the COVID-19 pandemic and the need for culturally appropriate pandemic responses and vaccination strategies. (See related story on page 20.)

Nau C et al. Ann Intern Med. 2021 Aug;174(8):1183-1186.

Child vaccination rates recovering since pandemic's early days

A study of trends in the vaccination of children compared 3 timepoints during the pandemic in 2020 – before the declaration of a national state of emergency, during the stay-at-home order, and during reopening - with similar timepoints in 2019. Even though the number of children being vaccinated recovered in younger children during reopening, vaccination coverage did not return to prepandemic levels in most age groups and continued to decline in some. The findings imply



Lina Sy and Gina Lee

that additional strategies like immunization tracking and reminders for needed vaccinations - particularly during virtual visits - will be required during a pandemic to reduce the risk of outbreaks of vaccinepreventable diseases. (See related story on page 20.)

Ackerson BK et al. Pediatrics. 2021;148(1):e2020047092.

Physical activity may reduce the risk of poor **COVID-19 outcomes**

Using data on physical activity collected during outpatient visits, researchers found that regular physical activity provided strong protection from hospitalization, intensive care unit admission, and death from COVID-19. The study of nearly 50,000 people with COVID-19 found that even exercising inconsistently lowered the odds for severe COVID-19 outcomes compared with people who were not active at all. Other than being over the age of 60 or having a history of organ transplantation, being consistently inactive conferred the highest risk of death from COVID-19. Physical activity can be an important component of recommendations to reduce severe COVID-19 outcomes. (See related story on page 24.)

Sallis R et al. Br J Sports Med. 2021;55:1099-1105.

Impact of COVID-19 on cervical cancer screening rates

During California's stay-at-home order in 2020, cervical cancer screening rates in about 1.5 million women in the KPSC network decreased by about

80% and then returned to near normal after reopening. The COVID-19 pandemic has highlighted a critical need for effective cancer screening methods for patients who cannot or prefer not to have inperson appointments. Health care systems can take steps such as enhancing efforts to reach overdue patients, evaluating women at high risk first, and using telemedicine or other innovative technologies to reach women.

Miller MJ et al. MMWR Morb Mortal Wkly Rep. 2021;70:109-113.

Real-world effectiveness of the Moderna COVID-19 vaccine against COVID-19

The interim results of a study conducted by KPSC reearchers, first published as a preprint in September 2021, confirmed high Moderna COVID-19 vaccine effectiveness up to 5 months after the second dose. The study findings, from a large, diverse population with a broad range of underlying conditions, add to the evidence for the real-world effectiveness of the Moderna COVID-19 vaccine. Effectiveness was 87% against COVID-19 infection, 96% against COVID-19 hospitalization, and 98% against COVID-19 death. Vaccine effectiveness remained high across age, sex, and racial/ethnic subgroups. (See related story on page 10.)

Bruxvoort KJ et al. Lancet Regional Health Americas. 2021;100134. doi:10.1016/j. lana.2021.100134

Effectiveness of the Moderna COVID-19 vaccine against emerging variants of SARS-CoV-2

A study published in December 2021 found that 2 doses of the Moderna COVID-19 vaccine were highly effective against SARS-CoV-2 variants circulating at the time. Vaccine effectiveness against hospital admission was 97.5%. Of cases admitted to the hospital with the delta variant, only 3.5% had received 2 doses of the vaccine, and no hospital deaths occurred among people who had received 2 doses. Vaccine effectiveness against infection with the delta variant moderately declined with time since vaccination. These findings, published in December 2021, add to the literature specific to the Moderna COVID-19 vaccine and support recommendations for a booster dose. (See related story on page 10.)

Bruxvoort KJ et al. BMJ. 2021;375:e068848.

Rates of acute myocardial infarction during the COVID-19 pandemic

Among KPSC patients, rates of hospital admissions or emergency department visits for heart attacks dropped significantly after the implementation of stay-at-home orders during the COVID-19 pandemic. Researchers compared rates of heart attacks in adults before and during the COVID-19 pandemic in 2020 and during the same period in 2019. The findings suggest that public health messaging encouraging people to seek emergency care for life-threatening conditions – even during stay-at-home orders – is necessary and important.

Mefford MT et al. Perm J. 2021;25:21.074.

Associations of physical activity, time spent outdoors in nature, and symptoms of depression and anxiety during COVID-19 quarantine

During the lockdown period of the COVID-19 pandemic, people who reported no mild, moderate, or vigorous exercise had higher depression and anxiety scores than people who exercised more. Less time spent outdoors was also associated with higher depression and anxiety scores compared with no change in time outdoors. More than 20,000 people without COVID-19 symptoms from 6 regions served by Kaiser Permanente participated in the study. The findings suggest that even during an active pandemic or other public health crisis, people should be encouraged to be physically active to help maintain their physical and mental health. (See related story on page 20.)

Young DR et al. Prev Med. 2022;154:106863.



Dr. Deborah Rohm Young

Selected findings | continued



Dr. Maria Fe Bellen Villosis and Dr. David Braun

Dr. Robert Cooper

Other clinical research

Sleep aids increase fracture risk in breast cancer survivors

About 40% of breast cancer survivors use prescription medications to alleviate sleep problems, but these medications can increase their risk for bone fractures, according to research from KPSC. Breast cancer survivors are more likely to have insomnia than the general population, and they may be vulnerable to bone fractures because certain cancer treatments like aromatase inhibitors can weaken bones. Sleep problems among women who have survived breast cancer might be better resolved by nonmedical approaches, such as cognitive behavioral therapy, increasing daytime physical activity, and limiting caffeine and alcohol use.

Haque R et al. Breast Cancer Res Treat. 2021;190:541-548.

Kaiser Permanente members have higher survival rates after cancer diagnosis

Among insured cancer patients in Southern California, those who were diagnosed and treated at Kaiser Permanente had better survival rates, especially Black and Latinx patients, a difference that held within each age category, racial/ethnic group, and stage at diagnosis. Inadequate health insurance coverage is a major contributor to disparities in cancer outcomes. The study findings suggest that vertically integrated health care delivery systems like KPSC may be well positioned to help reduce disparity gaps in cancer outcomes.

Cooper RM et al. Am J Manage Care. 2021;27(5).

Infant lung disease rates drop dramatically over 10-year effort

Neonatologists at KPSC completed a quality improvement study of a new system of care for prematurely born infants that led to a drop in bronchopulmonary dysplasia (BPD), a chronic lung condition in preterm infants, from 31% to less than 2%. Rates of BPD have changed little in the United States over the last decade. The new system includes a comprehensive clinical decision road map and BPD prevention bundle. The adoption of a proactive care approach through a multidisciplinary team could have huge benefits for infants and their families within Kaiser Permanente neonatal intensive care units and throughout the country. (See related story on page 24.)

Villosis MFB et al. JAMA Netw Open. 2021;4(6):e2114140
Bariatric surgery associated with better health for mothers

Women with obesity who undergo bariatric surgery before pregnancy may have improved outcomes, such as a reduced risk for serious pregnancy-related blood pressure conditions and lower instances of a newborn needing care in the neonatal intensive care unit. However, these women may also be at increased risk of heavy bleeding and of delivering small infants. The study fills a gap in research on the effects of bariatric surgery on perinatal outcomes. Women with severe obesity who undergo bariatric surgery may experience several benefits on pregnancy outcomes but should be monitored closely.

Getahun et al. Am J Obstet Gynecol. June 30, 2021.

Where people live may affect long-term survival after a heart attack

A study of approximately 31,000 KPSC members showed that Black patients from disadvantaged neighborhoods were significantly more likely to die within 5 years of surviving a heart attack than white patients. To explore sociodemographic factors outside the health system, investigators considered the effects of neighborhood resources on patient outcomes using a metric of neighborhood disadvantage called the Area Deprivation Index. Because all patients in the study were KPSC members, they had equal access to health care and were treated at the same medical facilities. The findings suggested that the neighborhoods in which patients live may affect their long-term health outcomes. (See related story on page 24.)

Goitia JJ et al. J Am Coll Cardiol. 2021 Aug;78(6):632-633.

Researchers examine association of preterm birth and chemicals in flame-retardant fabrics

Chemical pollutants, such as polybrominated diphenyl ethers (PBDEs) that are widely used as flame retardants, may increase the risk for preterm birth. In this study, KPSC researchers found that pregnant women with high levels of PDBE-47 were at increased risk of giving birth early in the pregnancy. Nearly all plasma samples from the women had detectable levels of PBDE-47 in the first trimester. High levels of PBDEs had previously been associated with lower birth weight, but the effects on preterm birth had been less clear. One way to reduce exposure to PBDEs is to replace furniture containing flameretardant material.

Peltier MR et al. J Perinat Med. 2021 Jan 4;49(4):439-447



Dr. Maereg Wassie, Dr. Mingsum Lee, and Dr. Jesse Goitia



Dr. Kristi Reynolds and Dr. Matthew Mefford

Rates of heart failure deaths lower at Kaiser Permanente Southern California than U.S. overall

Age-adjusted rates of death from heart failure were lower among KPSC members ages 45 and older from 2001 to 2017 than in the general U.S. population. Although mortality due to cardiovascular disease has declined in past decades, death from heart failure has begun increasing. Researchers designed this study to compare mortality in KPSC members and the populations of California and the United States. Given the aging of the U.S. population and the increasing prevalence of heart failure, findings such as these can help inform health care policy and practice.

Mefford MT et al. BMC Cardiovasc Disord. 2021;21:261.

Most patients' end-of-life care wishes are met

To answer the question of how well patients' end-oflife care wishes are met, researchers surveyed next of kin about their loved ones' experiences during the last year of life. The findings suggest that most older adults (89%) are receiving care in line with their wishes. In addition, more than 80% of respondents in the study reported that their loved ones had participated in end-of-life discussions and had received the right amount of care. Clinician training on end-of-life care should continue to encourage physicians to start informed discussions with patients about their preferences at the appropriate time.

Glass DP et al. JAMA Netw Open. 2021;4(4):e213053.

Diabetic eye damage reflects future cardiovascular risks

Researchers reported that people with more severe diabetic retinopathy, an eye condition that can lead to vision loss, are at greater risk for heart attacks, strokes, congestive heart failure, and death, even after accounting for traditional diabetic and cardiovascular risk factors. The new study builds on earlier research showing an association between diabetic retinopathy and the risk of vascular events, demonstrating that higher risks of retinopathy may confer higher risk of future systemic disease. Incorporating retinal information into clinical risk prediction tools could help to predict which patients with diabetes are most at risk for future disease.

Modjtahedi BS et al. Ophthalmology. 2021 Aug;128(8):1169-1179.

Self-order option boosts colorectal cancer screening rates

A study of KPSC members showed that allowing patients to self-order a colorectal cancer screening test online improves rates of testing completion. Members who ordered a testing kit directly from the Kaiser Permanente patient portal using an embedded order button were more likely to take the test and send it in than those mailed a test when they were due for screening. Despite a significant investment in colorectal cancer screening, 40% of U.S. adults are not up to date. The ability to self-order screening kits may act as a "commitment device" that can complement existing colorectal cancer outreach strategies.

Hahn EE et al. J Gen Intern Med. 2021;36:952-960.

Gastric bypass vs. vertical sleeve gastrectomy for hypertension remission and relapse

In a study of almost 5,000 patients with high blood pressure who underwent either vertical sleeve gastrectomy (VSG) or Roux-en-Y gastric bypass (RYGB) surgery, researchers found that both operations were equally effective for hypertension remission (43% for VSG, 42% for RYGB) after 5 years. However, many patients experienced a relapse of their high blood pressure, so the durable remission rate was only 18% for VSG and 17% for RYGB. The research was part of the ENGAGE CVD cohort study. Future studies will examine why most bariatric patients did not experience durable remission of their high blood pressure.

Reynolds K et al. Hypertension. 2021 Sep;78(4):1116-1125.



Dr. Kristi Reynolds and Allan Slatkin

Does hospital admission for chest pain improve patient outcomes?

Among patients presenting to 1 of 13 KPSC emergency departments (EDs) with chest pain who were not diagnosed as having a heart attack, patient outcomes did not differ according to whether the patients were admitted for observation or discharged for outpatient follow-up. The risk for major adverse cardiac events appears to be quite low in ED patients with chest pain who are not having a heart attack. These results question why chest pain is the top reason for hospitalization or observation in the United States, when it is unclear how hospitalization improves patient outcomes.

Sharp AL et al. J Gen Intern Med. 2021 May 14. doi: 10.1007/s11606-021-06841-2

Selected grants and contracts

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



Gabriela Jimenez, Dr. Jeniffer Kim, Dr. Sally Shaw, Dr. Sara Tartof, Ashley McDaniel, Alexandria Reyes, and Raul Calderon

COVID-19 studies

Environmental and social health determinants of pregnancy outcomes related to the COVID-19 pandemic

Adverse pregnancy outcomes such as gestational diabetes, preeclampsia and eclampsia, preterm birth, antepartum depression, and postpartum depression are likely worsened by the COVID-19 pandemic, and ambient air pollution may increase this risk further. In an extension of a previous study, investigators will examine the link between air pollution and adverse pregnancy outcomes during the pandemic, taking into account maternal comorbidities and sociodemographic factors. The study results can help inform public health practices to reduce adverse pregnancy outcomes, particularly while COVID-19 transmission remains widespread.

Principal investigators: Darios Getahun, MD, PhD, MPH, and Jun Wu, PhD (University of California, Irvine)

Funding agency: National Institute of Environmental Health Sciences

Evaluating influenza and COVID-19 vaccine effectiveness in preventing laboratoryconfirmed illness in a Southern California population

The U.S. Flu VE (Vaccine Effectiveness) Network provides estimates of the vaccine effectiveness of licensed flu and COVID-19 vaccines by age group and by influenza type and subtype. As one of 7 study sites in the network, KPSC will evaluate vaccine effectiveness for influenza and COVID-19. These studies help to determine the effectiveness of the vaccines used in clinical practice and monitor health problems after vaccination.

Principal investigator: Sara Tartof, PhD, MPH

Funding agency: Centers for Disease Control and Prevention



Ashley McDaniel

Text and web-based data collection for adverse events after SARS-CoV-2 vaccination in the Vaccine Safety Datalink

The Vaccine Safety Datalink (VSD) is a collaborative project between the Immunization Safety Office of the CDC and 9 health care organizations to monitor the safety of vaccines and conduct studies about rare and serious adverse events after immunization. In this project, investigators from KPSC will design, test, and expand a vaccine safety monitoring system for COVID-19 vaccines that uses text messaging and web applications. Collecting data on adverse events through the use of digital tools will allow the VSD to rapidly monitor and identify potential safety problems and provide timely information on COVID-19 vaccines. (See related story on page 15.)

Principal investigator: Sara Tartof, PhD, MPH Funding agency: Centers for Disease Control and Prevention

Other clinical studies

Implementation strategies for improving HPV vaccination

Millions of U.S. teens remain at risk of developing human papillomavirus (HPV)-related cancers because they do not complete the recommended



Dr. Corinna Koebnick and Dr. Margo Sidell

series of HPV vaccinations. Researchers at KPSC will study whether tailoring an intervention to a specific location and context can better remove barriers to HPV vaccinations and improve recommendations made by health care providers. The study findings can provide much-needed guidance on strategies for optimizing HPV vaccinations.

Principal investigators: Chun Chao, PhD, MS, and Erin E. Hahn, PhD, MPH

Funding agency: National Cancer Institute

Evaluating broad-spectrum antibiotic use and high birth weight as potential risk factors for early-onset colorectal cancer

The incidence of colorectal cancer in adults younger than 50 (called early-onset colorectal cancer) has been rising, but it is not known why. By studying more than 1,000 people diagnosed with this disease, researchers will test whether risk factors such as greater exposure to broad-spectrum antibiotics and high birth weight increase risk. The insights gained can help explain the increase in cases of early-onset colorectal cancer and improve early screening and prevention.

Principal investigator: Chun Chao, PhD, MS Funding agency: National Cancer Institute

Selected grants and contracts

continued

Reducing childhood obesity through motivational interviewing

Rates of childhood obesity in the United States remain at historic highs, and although successful treatment approaches that rely on engaging and motivating parents exist, duplicating these approaches in real-world settings remains a challenge. In 18 randomly chosen pediatric clinics in KPSC, researchers will use motivational interviewing of parents by primary care practitioners and trained wellness coaches. If successful, the intervention will be shared with other providers and translated for use in other settings to reduce obesity in children. (See related story on page 20.)

Principal investigator: Corinna Koebnick, PhD, MSc

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

Improving blood pressure screening and treatment strategies in young adults

About 20% of young adults in the United States have high blood pressure (BP), but the best ways to screen and treat high BP in young adults are unknown. To address this lack of evidence, researchers will study optimal screening intervals and identify subgroups of young adults at high risk for heart disease who may benefit the most from BP-lowering medications. The study findings can help inform future guidelines, reduce health inequities by directing screening and treatment to high-risk subgroups, and improve the heart health of young adults in the United States.

Principal investigators: Jaejin An, PhD, and Yiyi Zhang, PhD, MS (Columbia University)

Funding agency: National Heart, Lung, and Blood Institute



Jasper Ancheta, Huong Ly, Robert J. Elazegui, Dr. Jonathan Gullett, Jessica Vega, and John Mark Viray



Dr. Sally Shaw and Dr. Sara Tartof

Optimizing risk assessment for incident and recurrent atherosclerotic cardiovascular disease

Current cholesterol treatment guidelines rely on risk assessment to guide decisions about lipid-lowering therapies, but the tools used for risk prediction lack data on social determinants of health and important U.S. ethnic groups. Using large, contemporary sources of data that are racially and ethnically diverse, researchers will develop more refined approaches to risk assessment. By improving the precision of cholesterol treatment guidelines, the study findings can help direct lipid-lowering therapies to high-risk groups, ultimately improving health outcomes and narrowing health inequities.

Principal investigators: Jaejin An, PhD, and Yiyi Zhang, PhD, MS (Columbia University)

Funding agency: National Heart, Lung, and Blood Institute

Air pollution and pregnancy complications in complex urban environments

Pregnancy complications such as gestational diabetes, gestational hypertension, and preeclampsia and eclampsia are major causes of morbidity and mortality in pregnant women. Previous studies that examined how air pollution affects pregnancy had limitations. To address these limitations, KPSC researchers will use state-of-the-art modeling and statistical methods, such as measuring individual pollutants instead of mixtures and considering the effects of the weather, the built environment (like the greenness or walkability of a neighborhood), and socioeconomic status. The data can help identify pregnant women at risk and inform decisions about how to protect these women from the adverse effects of environmental pollution.

Principal investigators: Darios Getahun, MD, PhD, MPH, and Jun Wu, PhD (University of California, Irvine)

Funding agency: National Institute of Environmental Health Sciences

Food prescriptions to promote affordable healthy diets in multigenerational Latino households

Latino families are unequally affected by obesity, type 2 diabetes, nonalcoholic fatty liver disease, and dyslipidemia, and diet is a major contributing factor to these disparities in chronic disease risk. In this trial, multigenerational Latino households will be provided with culturally sensitive meal planning – including information on portion sizes – and grocery delivery. The study researchers will assess whether such "food prescriptions" can improve diet quality, weight control, and chronic disease risk. Food prescriptions could provide a scalable and sustainable model to improve diet, health, and well-being in Latino families.

Principal investigator: Deborah A. Cohen, MD, MPH

Funding agency: National Institute on Minority Health and Health Disparities



Alicia Torres, Alexandria Reyes, and Raul Calderon

Selected clinical trials

In 2021, the Kaiser Permanente Southern California clinical trials program supported almost 450 protocols across 30 therapeutic areas. About 60% of the trials were for cancer in adults and children. More than 2,800 patients were enrolled, including nearly 700 newly enrolled patients in 2021.

Clinical trials at KPSC receive funding from industry sponsors, foundations, research networks, and federal agencies. In 2021, federal funding sources included the National Cancer Institute, the National Institute of Neurological Disorders and Stroke, the Foundation for the National Institutes of Health, and the Eunice Kennedy Shriver National Institute of Child Health and Human Development.

The studies below are a small selection of the clinical trials that were open to patients at Kaiser Permanente Southern California during 2021. More information about each trial can be accessed using the National Clinical Trials (NCT) number included with each entry.

COVID-19

Evaluation of the safety, tolerability, efficacy, and immunogenicity of BNT162b2 boosting strategies against COVID-19 (NCT04955626)

Principal investigator: William J. Towner, MD, FACP, FIDSA

Participating medical center: Los Angeles

A study to evaluate safety and effectiveness of mRNA-1273 COVID-19 vaccine in healthy children between 6 months of age and less than 12 years of age (NCT04796896)

Principal investigator: William J. Towner, MD, FACP, FIDSA

Participating medical center: Los Angeles

A study of rivaroxaban to reduce the risk of major venous and arterial thrombotic events, hospitalization, and death in medically ill outpatients with acute, symptomatic COVID-19 infection (PREVENT-HD) (NCT04508023)

Principal investigator: William J. Towner, MD, FACP, FIDSA

Participating medical center: Los Angeles

I-SPY COVID-19 Trial: An adaptive platform trial for critically ill patients (I-SPY COVID) (NCT04488081)

Principal investigator: Kenneth Wei, MD Participating medical center: Los Angeles

Efficacy and safety of molnupiravir in hospitalized adult participants with COVID-19 (NCT04575584)

Principal investigator: Gunter K. Rieg, MD Participating medical center: South Bay

Cardiology

Abbott Vascular Medical Device Registry (NCT04573660)

Principal investigator: Somjot S. Brar, MD, MPH Participating medical center: Los Angeles

AMPLATZER PFO Occluder Post-Approval Study (NCT03309332)

Principal investigator: Somjot S. Brar, MD, MPH Participating medical center: Los Angeles

Stroke

Accelerating COVID-19 therapeutic interventions and vaccines 4 ACUTE (ACTIV-4A) (NCT04505774)

Principal investigators: Conrad Liang, MD, PhD, and Zahra A. Ajani, MD

Participating medical centers: Fontana and Los Angeles

Tenecteplase in stroke patients between 4.5 and 24 hours (TIMELESS) (NCT03785678)

Principal investigator: Navdeep Sangha, MD

Participating medical centers: Los Angeles, Fontana, Ontario, Anaheim, and South Bay



Kylie Buonya, Tammy Sam, Joshie Buonya, and Elena Hinkle

Statins in intracerebral hemorrhage (SATURN) (NCT03936361)

Principal investigators: Harsimran S. Brara, MD, FAANS, and Mazen Noufal, MD

Participating medical centers: Los Angeles and Fontana

Hepatology

Metabolic interventions to resolve nonalcoholic steatohepatitis (NASH) with FIBROSIS (NCT04321031)

PI: Amandeep Sahota, MD Participating medical center: Los Angeles

Ophthalmology

Study of a high-dose aflibercept in participants with diabetic eye disease (PHOTON) (NCT04429503)

Principal investigator: Vivienne S. Hau, MD, PhD Participating medical center: Riverside

The safety and efficacy of SYD-101 in children with myopia (NCT03918915)

Principal investigator: Michelle Britt, MD Participating medical center: Baldwin Park (Irwindale Medical Offices)

Nephrology

EMPA-KIDNEY (The Study of Heart and Kidney Protection) (NCT03594110)

Principal investigator: Hui Xue, MD, MMSc

Participating medical center: San Diego (Viewridge Medical Offices)

Pelvic Floor Disorders Network

Pivotal study of eCoin for overactive bladder with urgency urinary incontinence (NCT03556891)

Principal investigators: John N. Nguyen, MD, and Kimberly Ferrante, MD, MAS

Participating medical centers: Downey and San Diego (Point Loma Medical Offices)



Elizabeth Gordon

Sling versus Botox for mixed incontinence (MUSA) (NCT04171531)

Principal investigator: Shawn A. Menefee, MD

Participating medical centers: Downey and San Diego (Point Loma Medical Offices)

Rheumatology

A study to evaluate the efficacy and safety of obinutuzumab in patients with ISN/RPS 2003 class III or IV lupus nephritis (REGENCY) (NCT04221477)

Principal investigator: Steve S. Lee, DO Participating medical center: Fontana

Study to demonstrate the efficacy, safety, and tolerability of an intravenous regimen of secukinumab compared to placebo in subjects with active axSpA (NCT04156620)

Principal investigator: Swati S. Medhekar, MD Participating medical center: Irvine (Barranca Medical Offices)

Oncology

Cancer control

NCI COVID-19 in cancer patients study (N-CCaPS) (NCT04387656)

Principal investigator: Gary L. Buchschacher Jr., MD, PhD

Participating medical centers: Anaheim, Baldwin Park, Bellflower, San Diego, San Marcos, Fontana, South Bay, Irvine, Ontario, Panorama City, Riverside, Los Angeles, West Los Angeles, and Woodland Hills

Umbrella study

Tumor-agnostic precision immuno-oncology and somatic targeting rational for you (TAPISTRY) platform study (NCT04589845)

Principal investigator: Gary L. Buchschacher Jr., MD, PhD

Participating medical centers: Anaheim, Baldwin Park, Bellflower, San Diego, San Marcos, Fontana, South Bay, Irvine, Ontario, Panorama City, Riverside, Los Angeles, West Los Angeles, and Woodland Hills

Colon Cancer

Circulating tumor DNA testing in predicting treatment for patients with Stage IIA colon cancer after surgery (NCT04068103)

Principal investigator: Gary L. Buchschacher Jr., MD, PhD

Participating medical centers: Anaheim, Baldwin Park, Bellflower, San Diego, San Marcos, Fontana, South Bay, Irvine, Ontario, Panorama City, Riverside, Los Angeles, West Los Angeles, and Woodland Hills



Dr. Harsimran Brara, Dr. Nancy Gin, and Dr. Jonathan Finkelstein

Esophageal cancer

Assessing durvalumab and FLOT chemotherapy in resectable gastric and gastroesophageal junction cancer (MATTERHORN) (NCT04592913)

Principal investigator: Gary L. Buchschacher Jr., MD, PhD

Participating medical centers: Anaheim, Baldwin Park, Bellflower, San Diego, San Marcos, Fontana, South Bay, Irvine, Ontario, Panorama City, Riverside, Los Angeles, West Los Angeles, and Woodland Hills

Renal cell carcinoma

Nivolumab in treating patients with localized kidney cancer undergoing nephrectomy (NCT03055013)

Principal investigator: Helen Moon, MD

Participating medical centers: Anaheim, Baldwin Park, Bellflower, San Diego, San Marcos, Fontana, South Bay, Irvine, Ontario, Panorama City, Riverside, Los Angeles, West Los Angeles, and Woodland Hills

Immunotherapy with nivolumab and ipilimumab followed by nivolumab or nivolumab with cabozantinib in patients with advanced kidney cancer (NCT03793166)

Principal investigator: Helen Moon, MD

Participating medical centers: Anaheim, Baldwin Park, Bellflower, San Diego, San Marcos, Fontana, South Bay, Irvine, Ontario, Panorama City, Riverside, Los Angeles, West Los Angeles, and Woodland Hills

Urothelial cancer

A study of enfortumab vedotin alone or with other therapies for treatment of urothelial cancer (NCT03288545)

Principal investigator: Helen Moon, MD

Participating medical centers: Anaheim, Baldwin Park, Bellflower, San Diego, San Marcos, Fontana, South Bay, Irvine, Ontario, Panorama City, Riverside, Los Angeles, West Los Angeles, and Woodland Hills



Dr. William Towner and Randi Kendrick

Germ cell tumors

A study of miRNA 371 in patients with germ cell tumors (NCT04435756)

Principal investigator: Helen Moon, MD

Participating medical centers: Anaheim, Baldwin Park, Bellflower, San Diego, San Marcos, Fontana, South Bay, Irvine, Ontario, Panorama City, Riverside, Los Angeles, West Los Angeles, and Woodland Hills

Breast cancer

Clinical trial of neoadjuvant chemotherapy with atezolizumab or placebo in patients with triple-negative breast cancer followed after surgery by atezolizumab or placebo (NCT03281954)

Principal investigator: Lara Durna, MD, MS

Participating medical centers: Anaheim, Baldwin Park, Bellflower, San Diego, San Marcos, Fontana, South Bay, Irvine, Ontario, Panorama City, Riverside, Los Angeles, West Los Angeles, and Woodland Hills

Study of adagloxad simolenin (OBI-822)/OBI-821 in the adjuvant treatment of patients with globo H-positive triple negative breast cancer (NCT03562637)

Principal investigator: Lara Durna, MD, MS

Participating medical centers: Anaheim, Baldwin Park, Bellflower, San Diego, San Marcos, Fontana, South Bay, Irvine, Ontario, Panorama City, Riverside, Los Angeles, West Los Angeles, and Woodland Hills

Pediatric oncology

A study to investigate blinatumomab in combination with chemotherapy in patients with newly diagnosed B-lymphoblastic leukemia (NCT03914625)

Principal investigator: Robert M. Cooper, MD

Participating medical centers: Los Angeles, Anaheim, Downey, Fontana, and San Diego



Dr. Bruno Lewin and Dr. Lei Qian

Inotuzumab ozogamicin and post-induction chemotherapy in treating patients with highrisk B-ALL, mixed phenotype acute leukemia, and B-LLY (NCT03959085)

Principal investigator: Robert M. Cooper, MD

Participating medical centers: Los Angeles, Anaheim, Downey, Fontana, and San Diego

A study to compare standard chemotherapy to therapy with CPX-351 and/or gilteritinib for patients with newly diagnosed AML with or without FLT3 mutations (NCT04293562)

Principal investigator: Robert M. Cooper, MD

Participating medical centers: Los Angeles, Anaheim, Downey, Fontana, and San Diego

Surgical radiation oncology

Testing the use of the immunotherapy drugs ipilimumab and nivolumab plus radiation therapy compared to the usual treatment (temolzolomide and radiation therapy) in patients with newly diagnosed MGMT unmethylated glioblastoma (NCT04396860)

Principal investigator: Richard Green, MD Participating medical center: Los Angeles Standard chemotherapy versus chemotherapy chosen by cancer stem cell chemosensitivity testing in the management of patients with recurrent glioblastoma multiforme (NCT03632135)

Principal investigator: Richard Green, MD Participating medical center: Los Angeles

Expanded access

Provide Stamaril vaccine to persons in the United States for vaccination against yellow fever

Principal investigators: Bruno Lewin, MD; Lisa Andelin, MD; Clifford Clinton, MD; Jose Dryjanski, MD; and Spencer Rickwa, DO

Participating medical centers: Los Angeles, West Los Angeles, Orange County, Woodland Hills, South Bay, Fontana, and San Diego

Care Improvement Research Team projects

The Care Improvement Research Team works to build capacity for research embedded in clinical practice. CIRT aims to improve the access, quality, and affordability of care delivery and the health of patients, families, and communities. CIRT initiated and continued 13 projects during 2021.



Dr. Bruno Lewin, Dr. Matthew Mefford, Jessica Vallejo, Angel Alem, Dr. Hui Zhou, Thearis Osuji, Dr. Bing Han, Dr. Huong Nguyen, Dr. Ernest Shen, In-Lu Amy Liu, Dr. Stacy Park, Dr. Benjamin Broder, Natalie Firmeza, and Dr. Claudia Nau

Ongoing projects

Developing and testing an equitable risk stratification tool to identify patients for serious illness care in the era of COVID-19

– Claudia Nau, PhD

Patients with serious illness often receive SPC (Specialty Palliative Care) at the end of life. Kaiser Permanente Southern California wanted to participate in national efforts to develop a decision-support tool for planning and early identification of patients who need SPC, including those with COVID-19. This study supports the Kaiser Permanente regional Dignified Journey team in evaluating and comparing end-oflife indices, including the EPIC End of Life Care Index and other usable, diverse, and inclusive tools.

Implementing systematic depression screening in medical oncology

– Erin Hahn, PhD, MPH

The American Society of Clinical Oncology and other organizations recommend screening cancer patients for depression. Kaiser Permanente Southern California understands that addressing depression can improve patient outcomes and foster excellence in cancer care. The study partnered with the Southern California Permanente Medical Group to launch a depression screening program for all newly diagnosed cancer patients. It includes technology to support the implementation of a screening system, the training of oncology and depression-care teams, and the rollout and monitoring of a well-functioning system.

Observed role of cooling on hemodynamics in inpatient dialysis (ORCHID)

– Hui Xue, MD, MMSc

Hemodialysis patients are 10 to 30 times more likely to have cardiovascular morbidity and mortality. Intradialytic hypotension occurs in 20 to 40% of all dialysis treatments. Cooling dialysate to <36.5°C has improved outcomes for outpatients, but little is known about inpatients in acute physiologic distress who are at maximum vasoconstriction. This study tested whether cooling dialysate in the inpatient setting prevents intradialytic hypotension.

Piloting approaches to improve cultural sensitivity and humility in the care of patients with depression

– Karen J. Coleman, PhD, MS

The study set out to develop a culturally sensitive shared decision-making process to improve depression treatment options in primary care. It also focused on creating a system to train therapists and depression-care managers in cultural humility principles to improve therapeutic alliance and patient adherence to depression treatment.

Venous thromboembolism prevention in high-risk abdominal surgery patients

– Michael K. Gould, MD, MS

Kaiser Permanente implements safety measures to prevent VTE (venous thromboembolism), or blood clots, during hospitalization. VTE is especially common following discharge after abdominal surgery for cancer and other nonelective abdominal procedures. Patients who have extended preventive treatment at home can reduce VTE by 50%, and avoid bleeding complications. Kaiser Permanente Southern California designed, implemented, and evaluated an at-home intervention to prevent VTE that includes extended chemical prevention with heparin.



Angel Alem and Natalie Firmeza



Dr. Deborah Rohm Young, Dr. Anny Xiang, Dr. Huong Nguyen, and Dr. Kristi Reynolds

Enhanced implementation of lung cancer screening and pulmonary nodule evaluation

– Michael K. Gould, MD, MS

As part of its National Strategic Plan for Cancer Care, Kaiser Permanente Southern California is committed to reducing lung cancer deaths. The organization is improving its regional lung cancer screening practices, including processes for patient selection, test ordering, results reporting, and follow-up. In addition, Kaiser Permanente Southern California wants to improve benchmarking data, and to develop standardized practices to evaluate pulmonary nodules detected by screening.

Implementation and evaluation of an enhanced Adverse Childhood Experiences (ACEs) screening and referral system in pediatric primary care

– Sonya Negriff, PhD

Children who have ACEs (adverse childhood experiences) have poor physical and mental health, especially in minority and low-income families. Screening children for ACEs at a pediatric visit is recommended throughout California. The study tested an individualized approach to screen children with ACEs, and a referral process using a socialworker triage system. The study also assessed the effectiveness of case-manager follow-up services.



Dr. Kim Kaiser, Dr. Hai Linh Kerrigan, Annie Chen, and Allan Slatkin

Improving care transitions and reducing (re) admissions

– Huong Q. Nguyen, PhD, RN

Since 30-day readmission rates affect Medicare 5-star ratings and financial penalties, reducing avoidable readmission without causing patient harm is a high priority for Kaiser Permanente Southern California. This study describes the sociodemographic and clinical factors associated with the completion of inperson and telehealth follow-up visits within 7 days of hospital discharge, and the association between visit completion and 30-day readmissions. The study also assessed patient satisfaction with a new posthospitalization, home-delivered meal benefit, and sought ways to improve implementation of the program.



A Bayesian latent phenotype model to estimate risk for COVID-19 in the presence or multiple and/or missing biomarker data

– Ernest Shen, PhD

COVID-19 knowledge has improved markedly over the last year and has resolved some drawbacks to testing and diagnostic data. But work still remains. Building on the efforts of a COPD cohort at Kaiser Permanente Southern California, this study developed a Bayesian Latent Variable (LV) model that incorporates various and potentially different clinical indicators of COVID-19, including missing diagnostic markers and relevant patient covariates. The team used a COVAS (Comorbidities, Obesity [BMI], Vital signs, Age, and Sex) cohort of suspected COVID-19 cases. COVAS is an assessment tool developed by Kaiser Permanente to ensure that patients with COVID-19 symptoms get the right care by accurately predicting the probability of experiencing severe disease or death. Since Kaiser Permanente has goldstandard measurements for phenotyping a subset of the COVAS cohort, this should avoid previous issues for latent phenotype models.

Dr. Lewei Duan, Dr. Nana Mensah, and Dr. Jennifer Ku

Completed projects

COVID long-hauler study: Patient-reported outcomes

– David Glass, PhD

A portion of COVID-19 survivors, known as longhaulers, experience symptoms and complications weeks and months after recovery. Kaiser Permanente Southern California sought to better understand who becomes a long-hauler and why, and how many COVID survivors still feel ill months after recovery. The study focused on survivors 2 to 10 months after testing positive for COVID-19.

Evaluating the impact of high-sensitivity Troponin implementation on patient outcomes and health care utilization for Kaiser Permanente Southern California members

– Adam L. Sharp, MD, MSc

Chest pain accounts for 8 million annual emergency department visits, and is a leading cause of mortality and morbidity. It's unclear how changing standard Troponin testing will impact serious patient outcomes and Kaiser Permanente Southern California care. The study compared the impact of high-sensitivity Troponin versus the conventional Troponin decisionsupport algorithm on 30-day outcomes, and highsensitivity Troponin versus the conventional Troponin decision-support algorithm on hospitalizations and cardiac testing.



To scan or not to scan: Utilization of transient elastography in a tertiary care center before and after implementation of an electronic medical record-based clinical decision support tool

– Amandeep Sahota, MD

More than 450,000 Kaiser Permanente Southern California patients are diagnosed with fatty liver disease. More patients will likely request earlydetection liver screening, especially since drugs are being approved to fight fatty liver disease. Kaiser Permanente Southern California sought a unified strategic approach to screen patients, assure quality of care, and foster access. The study looked at the benefits of the Fib-4 Aura-based clinical decision support tool with fibrosis calculator, the most common way to assess liver disease.

Understanding and supporting COVID-19 vaccine confidence among health care providers at Kaiser Permanente Southern California

– Katia Bruxvoort, PhD, MPH

Vaccine hesitancy is a major threat to controlling the COVID-19 pandemic. Health care providers are patients' trusted sources for COVID-19 vaccination recommendation. High vaccine confidence among health care providers can increase the number of patients getting vaccinated. Prior vaccine studies have found that a provider's recommendation is a strong predictor of a patient's willingness to be vaccinated. To inform strategies to increase COVID-19 vaccine uptake and boost provider certainty in recommending the vaccine, this mixedmethod study examined vaccine confidence among health care providers and their adolescent children. The study asked their opinion on the vaccination, how willing they were to recommend it, what influenced hesitancy, and how to improve their certainty on safety and effectiveness.

Justine De Jesus and Dr. Adam Sharp

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 at 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 2021, the committee awarded funds to the following studies.

Traditional grant studies

Cardiology

Telehealth in Patients with Coronary Artery Disease (CAD) and Heart Failure (HF) during the COVID-19 pandemic and its short-term clinical outcomes

Principal investigator: Pauline Woo, MD, FACC Baldwin Park

Family Medicine

The impact of obesity and ethnicity on hospitalization, ventilation, and mortality with COVID-19

Principal investigator: Hemesh Patel, DO

Orange County

Geriatrics, Palliative, and Continuing Care

Clinical outcomes of a joint ICU and Palliative Care multidisciplinary rounding model

Principal investigator: Dov Shalman, MD Los Angeles

Hematology-Oncology

Impact of an oral chemotherapy pharmacist telehealth program on patient safety and satisfaction

Principal investigator: Rashmi Menon, MD Woodland Hills

Infectious Diseases

HIV/STI screening and diagnoses before and during the COVID-19 pandemic in a large, integrated health system

Principal investigator: Jennifer Chang, MD Los Angeles

Obstetrics-Gynecology

Efficacy of vaginal estrogen in the prevention of recurrent urinary tract infection in hypoestrogenic women

Principal investigator: Jasmine Tan-Kim, MD, MAS San Diego

Reoperation rate for apical suspension procedures in female pelvic reconstructive surgery

Principal investigator: Nemi Shah, MD (fellow) San Diego

Ophthalmology

Rate of acute endophthalmitis after intravitreal injection under a universal masking mandate compared to prior

Principal investigator: Damien Rodger, MD, PhD Los Angeles

The comparative risk of acquiring SARS-CoV2 after surgical and nonsurgical care

Principal investigator: Sean Tsao, MD Orange County



Christina Lim and Huong Ly

Pathology

Efficacy of COVID-19 convalescent plasma for the treatment of COVID-19 at Kaiser Permanente Southern California

Principal investigator: Allison Zemek, MD Downey

Pediatrics

Identification and treatment of children with familial hypercholesterolemia using KP-SCAL lipid screening guidelines

Principal investigator: Alan Cortez, MD Orange County

Sleep Medicine

Evaluating the impact of obstructive sleep apnea and positive airway pressure on health care costs

Principal investigator: Joseph Kim, MD San Bernardino County

RRC-GME Research Program Development Grant

Family Medicine

Follow-up care of patients with newly diagnosed depression after widespread implementation of telemedicine

Principal investigator: Vidush Athyal, MD, MPH, FAAFP

San Diego

Nephrology

Unmeasured organic anions as predictors of clinical outcomes in lactic acidosis due to sepsis

Principal investigator: Richard Treger, MD Los Angeles

Pediatrics

Expanding our understanding of health disparities in cancer patients

Principal investigator: Robert M. Cooper, MD Los Angeles

2021 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 S. Modjtahedi, MD, Vice Area Research Chair

Downey

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

Fontana/San Bernardino

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 Mingsum Lee, MD, PhD, Vice Area Research Chair

Orange County

Emily L. Whitcomb, MD, MAS, Area Research Chair Ali Ghobadi, MD, Vice Area Research Chair Patrick J. Van Winkle, 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, PhD, Vice Area Research Chair

San Diego

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

South Bay

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

West Los Angeles

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

Woodland Hills

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

Department of Research & Evaluation

Deborah Rohm Young, PhD, MBA, Area Research Chair Stephanie Tovar, MS, Regional Research Committee Project Manager



Overview of investigators and scientific divisions

Benjamin I. Broder, MD, PhD

Interim Senior Director of Research



Dr. Broder is a practicing hospitalist at the Kaiser Permanente Baldwin Park Medical Center, double board certified in Family Medicine and Clinical Informatics, the regional assistant medical director of Quality and Clinical Analysis for the Southern California Permanente Medical

Group, and a certified professional in patient safety, a credential of the Institute for Healthcare Improvement.

In his role as interim senior director of research and as a sponsor of the Care Improvement Research

Team, Dr. Broder supports the team's work to build capacity for research embedded in clinical practice at Kaiser Permanente Southern California. He connects researchers with clinicians to identify key questions and secures organizational support to get studies underway. Through this bridging of research and clinical practice, clinically relevant findings can be put into practice to improve the delivery of care.

In addition, Dr. Broder is an investigator with research interests in:

- Evidence-based practice
- Patient safety
- Preventive medicine
- Clinical informatics
- Predictive analytics

Our research program includes 5 scientific divisions as well as affiliated researchers (see page 67).

Epidemiologic Research (page 59)

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 61)

Our behavioral scientists focus on research that has the potential to reduce disease risk by identifying modifiable risk factors and encouraging healthpromoting 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 62)

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 63)

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 64)

The Division of Clinical Trials Research advances medical innovation by supporting the 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. Clinical trials investigators have made especially valuable contributions testing COVID-19 vaccines and treatments that have informed national policy during the pandemic. In addition, the division develops pragmatic trials that help answer questions about care delivery. See our clinical trials principal investigators by specialty on page 70.

Division of Epidemiologic Research

Research scientists



Kristi Reynolds, PhD, MPH

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

Annette L. Adams, PhD, MPH

- Osteoporosis and bone health
- Injury epidemiology



Jaejin An, PhD

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

Chun Chao, PhD, MS

- HPV vaccine; cervical cancer
- Adolescent and young adult cancer and survivorship
- Lymphoid malignancies
- Early-onset colorectal cancer



Wansu Chen, PhD, MS

- Risk prediction using machine learning and statistical methods
- Pancreatic cancer early prediction
- Asthma and chronic cough management
- Stroke prevention in patients with silent cerebrovascular disease











Darios Getahun, MD, PhD, MPH

- Women's and children's health
- Adverse pregnancy outcomes and health disparities
- Fetal origin of childhood diseases
- Environmental exposure during pregnancy and maternal/child outcomes

Reina Haque, PhD, MPH

- Cancer epidemiology
- Cancer survivorship and health disparities
- Pharmacoepidemiology

Rulin Hechter, MD, PhD, MS

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

Matthew T. Mefford, PhD

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

Sara Y. Tartof, PhD, MPH

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

Division of Epidemiologic Research

continued



Hung Fu Tseng, PhD, MPH

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



Epidemic Intelligence Service officer

Debbie Malden, DPhil, MSc

- Large-scale observational studies
- Vaccine safety monitoring
- Digital health surveillance tools
- Outbreak response

Post-doctoral research fellows



Katia Bruxvoort, PhD, MPH*

- Infectious diseases
- Vaccine uptake, safety, and effectiveness
- Screening and diagnostics
- Antimicrobial treatment and adherence
- * Dr. Bruxvoort left KP in 2021 and is an adjunct investigator.



Ana Florea, PhD, MPH

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



Jennifer Ku, PhD, MPH

- Infectious diseases
- Vaccine safety and effectiveness
- Tuberculosis/nontuberculous mycobacterial infection
- Pharmacoepidemiology

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

- Pediatric obesity and chronic disease epidemiology
- Health services research
- Primary care-based behavioral interventions
- Pediatric mental health

Division of Biostatistics Research

Director

Research scientists



Anny H. Xiang, PhD, MS

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



Jeff Slezak, MS

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



Heidi Fischer, PhD

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



Stanley Xu, PhD, MS

- Analytic methods
- Vaccine safety
- Pharmacoepidemiology
- Overdose prevention



Bing Han, PhD

- Applied statistical methodology
- Behavioral health
- Health services research
- Epidemiology



Hui Zhou, PhD, MS

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

Post-doctoral research fellow

Sarah Carter, DPhil, MA

- Maternal and child health
- Labor induction, epidural, and operative childbirth
- Environmental and social influences on health
- Health care systems, access to care



Lei Qian, PhD

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



Margo A. Sidell, ScD, MSPH

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





Division of Health Services Research & Implementation Science

Research scientists



Huong Q. Nguyen, PhD, RN

Interim Director

- Healthy aging; health promotion
- Chronic and serious illnesses; palliative care
- Home and community-based support and services
- Program evaluation; implementation science



Karen J. Coleman, PhD, MS

• Implementation research

• Primary care sustainability

• End-of-life values and quality

• COVID long-haulers

performance

- Mental health
- Health equity

David Glass, PhDGlobal health

• Weight loss surgery



Aniket A. Kawatkar, PhD, MS

- Health economics
- Patient preferences
- Comparative effectiveness



Brian S. Mittman, PhD

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

Adam L. Sharp, MD, MSc

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

Post-doctoral research fellow



Erin E. Hahn, PhD, MPH

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



Lewei Duan, PhD, MS

- Health economics and health policy
- Geriatrics care and palliative care
- Statistical methodology
- Cardiology and dementia

Division of Clinical Trials Research

Portfolio principal investigators



William J. Towner, MD, FACP, FIDSA

Regional Physician Director

- HIV therapeutics
- Infectious disease vaccine safety and effectiveness



Harsimran S. Brara, MD, FAANS

- Neurosurgery
- Spine surgery



Vicken Aharonian, MD

- Cardiac catheterization
- Interventional cardiology



Gary L. Buchschacher Jr., MD, PhD

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



Zahra A. Ajani, MD

Ashraf R. Aziz, MD

• Hematology

Medical oncology

- Stroke
- Diagnosis and treatment of cerebrovascular diseases
- Systems of care and quality improvement



Jeffrey Cavendish, MD

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

Sirichai Chayasirisobhon, MD, FAAN*

- Neurology
- Epilepsy
- * Dr. Chayasirisobhon retired from Kaiser Permanente in 2021.

Somjot S. Brar, MD, MPH

- Cardiovascular disease and risk factors
- Medical devices and interventional procedures



Robert M. Cooper, MD

- Medical oncology
- Pediatrics hematology
- Cancer outcomes



Lara Durna, MD, MS

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



Michael R. Girvigian, MD, DABR

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

Clinical cardiac electrophysiology

• Cardiac implantable electronic

devices and catheter ablation



Kevin T. Kao, MD

- Ulcerative colitis
- Post-polypectomy-induced ulcers
- Colorectal cancer prevention



Steve S. Lee, DO

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

Scott E. Lentz, MD, FACS

- Gynecologic oncology
- Hereditary cancer syndromes
- Surgical innovation



Suresh Gurbani, MD

Nigel Gupta, MD

- Pediatric epilepsy
- Neuromodulation in epilepsy therapy



Conrad Liang, MD, PhD

- Stroke and interventional neurology
- Medical devices and interventional procedures



Vivienne S. Hau, MD, PhD

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



Eric McGary, MD, PhD, MPH

- Medical oncology
- Lung cancer
- Real-world data and real-world, evidence-based research
- Precision medicine and molecular diagnostic platforms in oncology

Portfolio principal investigators



Swati Medhekar, MD

- Rheumatology
- Active ankylosing spondylitis or nonradiographic axial spondylarthritis
- Giant cell arteritis



Shawn A. Menefee, MD

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



Helen Moon, MD

- Medical oncology
- Genitourinary cancer
- Melanoma
- Immuno-oncology
- Robotic surgery



John N. Nguyen, MD

- Ob-gyn urogynecology
- Female pelvic medicine and reconstructive surgery
- Pelvic organ prolapse and urinary incontinence treatment
- Minimally invasive surgery



Muhammad Saeed, MD

- Pulmonology
- Cystic fibrosis
- Psychosocial impact of cystic fibrosis newborn screening
- Quality improvement



Amandeep Sahota, MD

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





- Retinal disease
- Retina vitreous surgery



Navdeep Sangha, MDVascular neurology

- Ischemic stroke and intracerebral hemorrhage
- Hospital systems of care
- Primary biliary cirrhosis
- Alpha-1-antitrypsin deficiency

Ricardo T. Spielberger, MD

- Hematopoietic cell transplant
- Transplant side effects
- Opportunistic infections



Devansu Tewari, MD, MBA

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

Bechien U. Wu, MD, MPH Acute and chronic pancreatitis Early detection of pancreatic cancer

 Gastrointestinal cancer screening and prevention



Affiliated researchers

Affiliated investigators



Donald S. Fong, MD, MPH

- Myopia
- Diabetic retinopathy
- Care redesign
- Retinal degenerations



Lisa Nyberg, MD, MPH

- Hepatology epidemiology studies
- Non-alcoholic fatty liver disease
- Hepatitis C epidemiology, treatment, and cost effectiveness



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

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

Associate investigators



David Braun, MD

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



Michael Kanter, MD

- Quality improvement
- Patient safety
- Diagnostic errors
- Models of care for chronic conditions



Anders Nyberg, MD, PhD

- Hepatology risk and treatment
- Hepatology clinical trials





• Diabetes and pregnancy







Michael Schatz, MD, MS

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

Joanne E. Schottinger, MD

- Colorectal cancer screening
- Medical oncology
- Hematology

Robert S. Zeiger, MD, PhD

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

Affiliated researchers

continued

Adjunct investigators



Dennis M. Black, PhD

- Osteoporosis
- Fracture risk
- Clinical trials



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Soo Borson, MD

- Early detection of dementia as a public health and health systems issue
- Population-based and clinical models of care for people with dementia and their care partners





- learning health care system
- Implementation science and outcomes research
- Lung cancer screening, diagnosis, and staging
- Venous thromboembolism

Paul Muntner, PhD

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



Kristen Choi, PhD, MS, RN

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



Lauren P. Wallner, PhD, MPH

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

Clinician investigators



Kimberly Ferrante, MD, MAS

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



Chileshe Nkonde-Price, MD, MS, FACC

- Cardiovascular disease
- Cardiac rehabilitation
- Health care utilization and outcomes



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



Mingsum Lee, MD, PhD

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



Bobeck S. Modjtahedi, MD

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



Chunyuan Qiu, MD, MS

- Anesthesiology
- Pain medicine
- Perioperative medicine

Previous appointments

Raymond Chen, MD, DPhil (2016-2018) Casey K. Ng, MD (2017-2019) Joan J. Ryoo, MD, MSHS (2018-2020) Navdeep Sangha, MD (2017-2019) John J. Sim, MD (2016-2018) Devansu Tewari, MD, MBA (2016-2018) Emily L. Whitcomb, MD, MAS (2017-2019) Bechien U. Wu, MD, MPH (2017-2019) Hui Xue, MD, MMSc (2016-2018, 2018-2020)

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

Viji Sankar, MD, San Diego Medical Center Adam Schwartz, MD, MS, San Diego Medical Center David J. Silberstein, MD, Los Angeles Medical Center Gunter K. Rieg, MD, South Bay 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

Gareth S. Dulai, MD, Downey Medical Center John M. Iskander, MD, Los Angeles Medical Center Kevin T. 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, PhD, 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 J. 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 A. Ajani, MD, Los Angeles Medical Center Pamela Cheng, DO, Los Angeles Medical Center William Neil, MD, San Diego Medical Center Navdeep Sangha, MD, Los Angeles Medical Center

Neurological Surgery

Harsimran S. Brara, MD, FAANS, 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 Alton/Sand Canyon Medical Offices

Head and Neck Surgery

Rohit Garg, MD, MBA, Anaheim Medical Center David Keschner, MD, Irvine Alton/Sand 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

Eric McGary, MD, PhD, MPH, 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, DABR, Los Angeles Medical Center

Surgical Oncology

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

Jeffrey Kessler, MD, Los Angeles Medical Center Gregory Maletis, MD, Baldwin Park Medical Center Anshuman Singh, MD, San Diego Medical Center

Pediatric Oncology

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

Investigators

Clinical trials investigators by specialty

continued

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, MAS, San Diego Medical Center

Karl Luber, MD, San Diego Medical Center

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

John N. 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 Alton/Sand Canyon Medical Offices

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

X

2021 Publications

Scientists, clinicians, and other health professionals from Kaiser Permanente Southern California authored journal articles on a wide range of topics in 2021, from allergy and asthma to women's health.

Allergy and Asthma

Carra S; Schatz M; Mertes PM; Torres MJ; Fuchs F; Senna G; Castells MC; Demoly P; Tanno LK. Anaphylaxis and pregnancy: a systematic review and call for public health actions. *J Allergy Clin Immunol Pract*. Published online 2021 Aug 5. doi: 10.1016/j.jaip.2021.07.046

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Dhudasia MB; Spergel JM; Puopolo KM; Koebnick C; Bryan M; Grundmeier RW; Gerber JS; Lorch SA; Quarshie WO; Zaoutis T; Mukhopadhyay S. Intrapartum group B streptococcal prophylaxis and childhood allergic disorders. *Pediatrics*. 2021 May;147(5). Epub 2021-04-08. PMCID: PMC8085997

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Knihtilä HM; Stubbs BJ; Carey VJ; Laranjo N; Chu SH; Kelly RS; Zeiger RS; Bacharier LB; O'Connor GT; Lasky-Su J; Weiss ST; Litonjua AA. Low gestational vitamin D level and childhood asthma are related to impaired lung function in high-risk children. *J Allergy Clin Immunol*. Published online 2021 Jan 21. doi: 10.1016/j. jaci.2020.12.647 PMCID: PMC8315297

Lu K; Sidell M; Li X; Rozema E; Cooper DM; Radom-Aizik S; Crawford WW; Koebnick C. Self-reported physical activity and asthma risk in children. *J Allergy Clin Immunol Pract*. Published online 2021 Sep 15. doi: 10.1016/j.jaip.2021.08.040

Luo G; Nau CL; Crawford WW; Schatz M; Zeiger RS; Koebnick C. Generalizability of an automatic explanation method for machine learning prediction results on asthma-related hospital visits in patients with asthma: quantitative analysis. *J Med Internet Res.* 2021 Apr 15;23(4):e24153. Epub 2021-04-15. PMCID: PMC8085752

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IN MEMORIAM



Samuel O. Sapin, MD

Sam Sapin, MD, a Southern California Permanente Medical Group quality, medical education, and clinical research pioneer, died on January 10, 2021. He was 96.

Dr. Sapin became SCPMG's first regional director of the Department of Education and Research in 1972. He was appointed associate medical director of Clinical Services in 1982, when education and research activities were folded into the department. The Department of Research & Evaluation was established in 1988.

Dr. Sapin's career at Kaiser Permanente began in 1955 when he joined the young Southern California Permanente Medical Group as a pediatrician in Los Angeles. He went on to serve as chief of Pediatrics for the Panorama City Medical Center and maintained an active practice until his retirement in 2000. He was SCPMG's first pediatric cardiologist, and conducted related research throughout his career. He was the primary or co-author of dozens of peer-reviewed medical publications between 1949 and 2005.

Known as a humble and compassionate man, Dr. Sapin was the ultimate caring physician to his patients, treating them with dignity, equity, and respect, and was a passionate teacher that listened because he thought "everyone had a story to tell." He remained in contact with many of his pediatric patients for decades, as they grew from children to adults with families of their own.

Over his 6-decade career, Dr. Sapin was instrumental in bringing a number of innovations to Kaiser Permanente Southern California. He started Panorama City's nurse practitioner program, which was later expanded throughout the region, and established and expanded programs in physician and patient education. He pioneered SCPMG's early quality assurance methods, was involved in creating and refining quality improvement methods, and was a trailblazer in Kaiser Permanente's efforts to ensure appropriate use of medical technology. He served 2 terms on the SCPMG Board of Directors, and was a passionate advocate for Kaiser Permanente in both academic and community settings.

Oliver Goldsmith, MD, SCPMG executive medical director from 1994 to 2003, said of his good friend and mentor that Dr. Sapin "was one of those important early SCPMG physicians for several reasons: He was a superb clinician, pediatrician, and cardiologist, and encouraged SCMPG to participate and lead quality and research efforts."

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Credits

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Contributing writers and editors Sarah Stanley, Gordy Slack, Wendy Healy, and Jill Kramer

Photography & Design

The Studio, Kaiser Permanente Southern California Quon Design and Communication Inc.

Produced August 2022

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.

Trailblazers



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