DEPARTMENT OF **RESEARCH & EVALUATION**

2022 Annual Report

Kaiser Permanente
Research

Beyond clinic walls:

Research supporting healthy communities

KAISER PERMANENTE®

Contents

Message from the Senior Director

As we entered 2022, COVID-19 continued to dominate much of our attention. The omicron wave was cresting, and we were still learning about it and about the effectiveness of vaccines against the emerging variant. Research from Kaiser Permanente Southern California offered important new insights. Three weeks into the new year, data on vaccine effectiveness against hospitalization from a KPSC-led study were presented at a White House briefing. Throughout the year, our research informed decisions about boosters and effectiveness of the vaccines in vulnerable populations.

But a global pandemic doesn't eliminate the burden from other diseases. Cancer, cardiovascular disease, and obesity continue to affect the lives of our Kaiser Permanente members. New diseases emerge in our communities. Environmental conditions and societal issues influence health.

Amid the pandemic, our scientists and clinician researchers have consistently used research to improve care and health outcomes across a myriad of health conditions. Sometimes, that has involved studying care delivery and treatment within our clinics and hospitals. But often it extends beyond our walls.

Stories in this year's report show the spectrum. A participant from a breast cancer trial shares her experience and her altruistic motivations for taking part in the trial. Clinicians share the story of an innovative program to bring cardiac rehabilitation into people's homes. Researchers share work to improve the total health of patients with cancer.

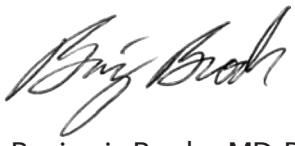
COVID-19 remained a major research focus throughout the year. In addition to multiple vaccine studies, our researchers studied the links between air pollution and COVID-19, partnered with clinical operations to improve vaccine equity, and sought to understand health care utilization in the aftermath of COVID-19.

When mpox (commonly known as monkeypox) emerged as a threat to our communities, our clinical trials team jumped in to help our physicians get access to treatment under expanded access. Scientists in our department responded to the ongoing national epidemic of gun violence with research identifying risk factors for firearm injury and clinical opportunities for prevention. They partnered with health systems across the country to understand racial disparities and outcomes in bariatric surgery.

In 2022, researchers from Kaiser Permanente Southern California published more than 650 journal articles on a wide range of topics. This is the highest annual number to date, prompting us to move our annual publications list online (see page 32 for QR code). Scientists and clinician investigators initiated new projects and clinical trials to study dozens of important health conditions.

Our research program supports health communities far beyond our walls, sharing knowledge that changes clinical practice and health guidelines across the globe. It makes me extremely proud to work with such a talented and dedicated group of people.

Be well,



Benjamin Broder, MD, PhD

Interim Senior Director of Research

To learn more about our research, please visit our website (kp.org/research), subscribe to our *IMPACT* newsletter, or follow us on Twitter (@KPSCalResearch).

Research Highlights

Serving others by joining a cancer clinical trial

At first, Genie Valarao had no interest in joining a clinical trial for her breast cancer.

"It sounded time-consuming," said Genie, an educator who teaches child development and parenting classes at an adult school in the Los Angeles area. "I thought it would be easier just to do my own standard treatment."

It was late 2021, and Genie's breast cancer had begun with a lump. A long-time Kaiser Permanente member, she alerted her primary care physician, who quickly referred her to oncologist Karen Kwan, MD, at the Kaiser Permanente Los Angeles Medical Center.

"I realized that by participating in the trial, there was nothing I could lose but there was something I could give back to other people, something I could leave here on earth to serve others."

Genie's diagnosis: triple-negative breast cancer, stage II. The tumor was removed through surgery, and now it was time to decide on medications to kill any remaining cancer cells. Dr. Kwan told Genie that, by participating in an ongoing clinical trial at Kaiser Permanente, she could get treated while also contributing data to improve treatment for future patients. Genie wasn't able to make the decision in the moment.

But, back at home, she thought of her paternal grandmother who died from breast cancer at the age of 55 – the same age as Genie at her own diagnosis.

"I never got a chance to meet my grandmother," Genie said. "I realized that by participating in the trial, there was nothing I could lose but there was something I could give back to other people, something I could leave here on earth to serve others."

Genie Valarao, shown here tending her succulent garden, participated in a clinical trial for breast cancer at the Los Angeles Medical Center

continued

Genie's clinical trial experience

Genie enrolled in one of the many clinical trials at Kaiser Permanente that are helping to advance cancer treatment. Her trial was designed for people with triple-negative breast cancer whose disease is considered to be particularly high risk.

Beginning in November 2021, through the trial, she received several rounds of different chemotherapy drugs followed by a few rounds of radiation. The trial was testing whether adding the drug carboplatin to an existing treatment regimen would lead to better outcomes.

"Being in a clinical trial ended up being a wonderful experience," Genie said. "The care, attention, and communication were all there. I felt like the team was committed to me, and whenever I had concerns or questions, or didn't know what to expect, they responded right away and relieved my anxiety."

Key to Genie's clinical trial experience was her research nurse Katrina Salgado, RN, who works with the Cancer Clinical Trials Access Program at the Los Angeles Medical Center.

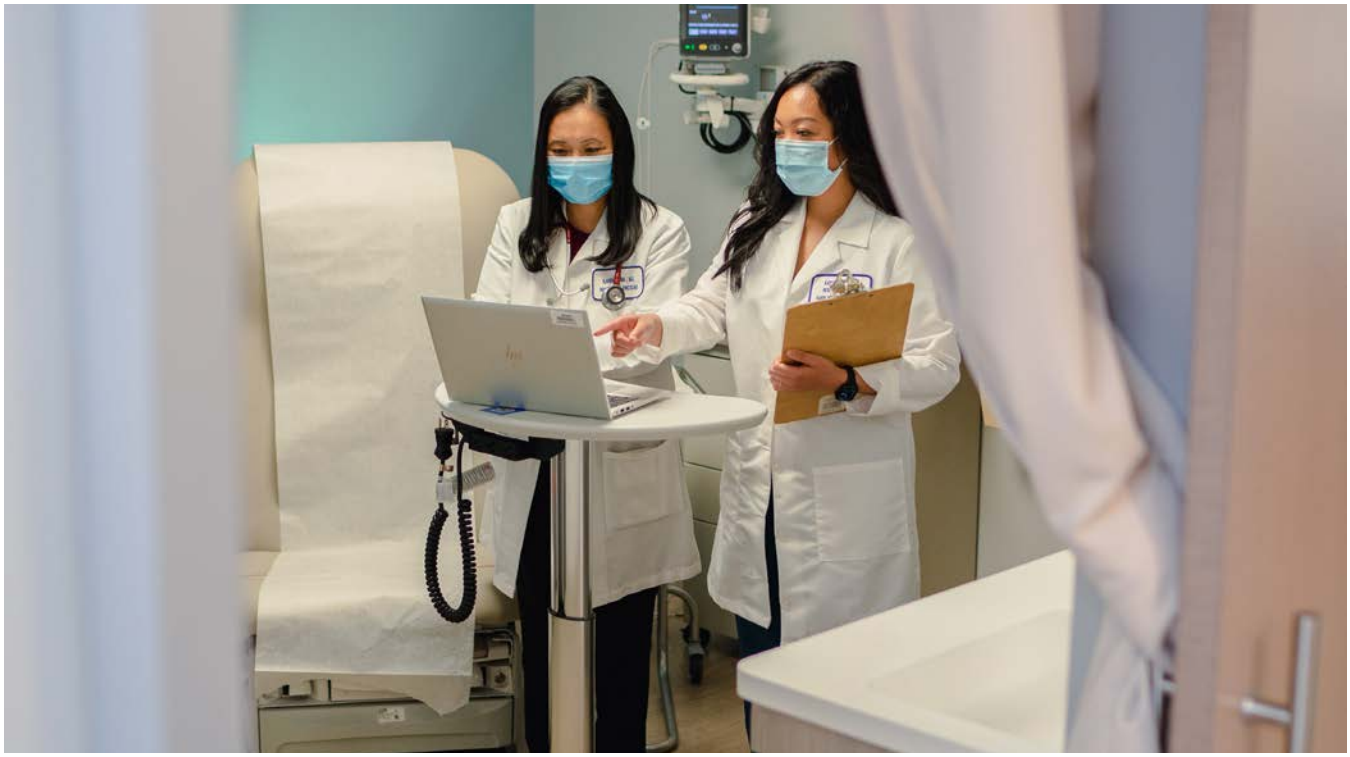
"Katrina was my main contact for communication about any appointments or tests I had coming up, and if I wasn't feeling good or had nausea or other side effects, she was able to give me resources and information," Genie said.

Genie took a break from teaching while enrolled in the trial. "I was blessed to be able to stay home, because my side effects were pretty harsh," she said.

To avoid getting COVID-19 and compromising her treatment, Genie limited her in-person social time, including with her 2 adult children. She also began attending her church remotely via livestream. However, her husband of 27 years provided steady companionship and drove her to her appointments.

Genie's participation in the clinical trial wrapped up in April 2022 and left her cancer free for about 6 months. In fall 2022, her cancer returned. Still, she views her clinical trial experience as a success.

"For someone who is considering a clinical trial, I would say to them that it is a wonderful way to do your part to give back to the community," she said. "Clinical trials move science forward and help give hope to others who are going through similar experiences."



Dr. Karen Kwan and research nurse Katrina Salgado are part of Genie's care team at the Los Angeles Medical Center

Leaving a legacy for future patients

Now, Genie has had a mastectomy and is receiving chemotherapy drugs and an immunotherapy drug known as pembrolizumab.

"It was a smooth transition out of the trial," she said. "Dr. Kwan is still my oncologist, which is great because she already knows my medical history, and I am comfortable with her and trust her."

Genie now has fewer side effects and has started teaching again. She still attends church remotely but is able to see her children in person more often. And while she loves to bake, she has cut down on sugar and has found joy in a new hobby: growing succulents in her garden.

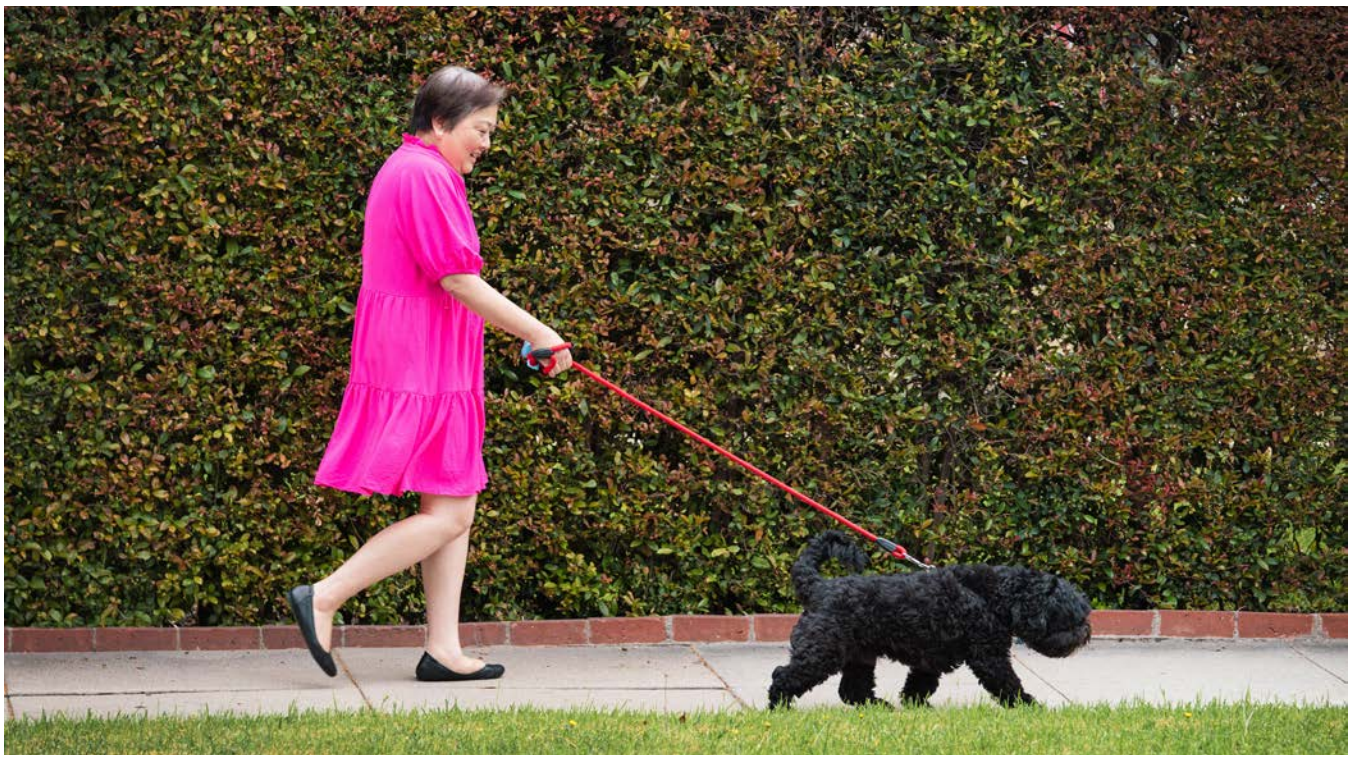
"The way I look at it is, after a storm, there is going to be a rainbow," she said. "The storms make you stronger and make you really thankful for the good things."

In reflecting on her cancer experience, she often thinks of the grandmother she never met. "If she had access to the care I have today, I think I would have gotten the chance to spend time with her," Genie said.

She hopes that, by sharing her own story, she will encourage others to participate in clinical trials. "Sometimes it's more convenient to just think about ourselves, but if we can think about what we can leave for the next generation, that is very powerful."

"Being in a clinical trial ended up being a wonderful experience. The care, attention, and communication were all there."

– Genie Valarao



Genie, shown here walking her dog, sees participating in the clinical trial as a way to give back to the community and give hope to others

The rise of in-home cardiac rehabilitation

If someone had a heart attack today, they might be in and out of the hospital in as little as 24 hours. But there's no rushing the several weeks needed for physical and emotional recovery – doing so could increase the risk of heart problems later on.

To reduce that risk, Kaiser Permanente and other providers have traditionally offered in-person rehabilitation programs to anyone with a heart attack or other serious heart issue or surgery. Three times per week for 12 weeks, patients attend exercise sessions under nurse supervision to ensure the best possible recovery.

While highly effective, however, such programs are not practical for most people.

Now, an innovative in-home program has tripled the percentage of Kaiser Permanente Southern California members who participate in cardiac rehabilitation. And research shows that it can be just as effective as center-based rehabilitation.

"In-home rehab has been overwhelmingly successful," said Columbus Batiste, MD, regional chief of Cardiology and regional medical director of the Kaiser Permanente Southern California Home-Based Cardiac Rehabilitation Program. "Patients have told us how much the program motivates them, and our data show that they are less likely to be readmitted to the hospital."

A wearable solution

The story of in-home cardiac rehabilitation at Kaiser Permanente began more than 5 years ago when Dr. Batiste treated a young mother for a heart attack at the Kaiser Permanente Riverside Medical Center.

"She was someone we'd now call a frontline worker who was unable to make it to her rehab appointments," Dr. Batiste said. "Despite our efforts, she eventually passed away. It made us wonder: Are we doing everything possible to provide care to our members?"

Michael Flores, a participant in the in-home cardiac rehabilitation program, plays with his dog at home to get a little extra activity

Dr. Columbus Batiste, Dr. Tad Funahashi, and Debora Lahti meet at the Kaiser Permanente Innovation Studio, which played a key role in launching the in-home rehab program

The rise of in-home cardiac rehabilitation

continued

At first, Dr. Batiste was able to significantly boost cardiac rehabilitation enrollment at Riverside by launching an exercise program that patients could do at home with telephone check-ins from clinicians. However, many patients never completed the program after enrolling.

"That's when Columbus came to me and asked if there was an opportunity to work with the Innovation Studio to dramatically change the way we do cardiac rehab," said Tad Funahashi, MD, who is the chief innovation officer for KPSC.

The team realized that tracking patients' physical activity using a smartwatch could be the key to increasing participation in-home cardiac rehabilitation. They developed a smartwatch-based program that mimics the experience of being monitored in real time at a center, while also addressing the unique challenges of rehabilitating at home.

After a successful pilot with 36 Riverside patients, the team officially launched the program across 12 KPSC medical centers in April 2018.

"This project was a truly meaningful harmony between a man with a passion to help his patients and a department that was able to examine the underlying challenges and bring together the resources and talent to find a solution," Dr. Funahashi said.

Rehab that's personal and proven

Prior to the launch of an in-home option, only about 20% of KPSC members who were referred for cardiac rehabilitation actually enrolled. Today, enrollment has reached 65%, and more than 15,000 patients have successfully completed the in-home program, which is free to members.

In August 2022, in the journal *JAMA Network Open,** the team published data from more than 2,500 demographically diverse patients showing that, over a 12-month period, those who did in-home rehabilitation had fewer hospitalizations than those who did traditional center-based rehabilitation.

"This really has transformed our ability to provide rehab for our patients," said Chileshe Nkonde-Price,

"If you need cardiac rehab, you shouldn't have to come to a facility. As a health care organization, we need to figure out how to get that intervention to you."

– Tad Funahashi, MD

MD, MS, FACC, a cardiologist at the Kaiser Permanente West Los Angeles Medical Center, who led the research. She was also the physician lead in launching the program at Antelope Valley, where she previously practiced.

Each patient is fitted with a smartwatch to use during the program, and their physician works with them to design a highly personalized education and exercise plan. "So, activities might include walking your dog around the park, playing basketball for 10 minutes, or doing a few laps around your local Costco," said Dr. Nkonde-Price, who is also a clinician investigator for the Department of Research & Evaluation.

The smartwatch records the patient's activity, which is later reviewed by a nurse who calls the patient weekly to provide coaching and answer questions.

"I think the secret sauce of this program really is the relationship between the nurse and the member," said Debora Lahti, MSN, regional director of the Kaiser Permanente Southern California Home-Based Cardiac Rehabilitation Program, who manages the program's nurses across all 12 centers. "In feedback surveys, patients consistently say their nurse was instrumental in providing the practical and emotional support they needed to get through the program."

To track the program's ongoing success and identify areas for improvement, the team continues to evaluate patient data. Their upcoming publications will highlight the experiences of patients of different ethnicities and genders, for whom enrollment rates have dramatically improved. And, in her role as an assistant professor at the Kaiser Permanente Bernard J. Tyson School of Medicine, Dr. Nkonde-Price is mentoring several students who are examining the program's impact for various subcategories of patients.

"We are an integrated learning health system in which our research should inform our operations," Dr. Nkonde-Price said. "This is Permanente Medicine at its best."

Cardiologist Dr. Chileshe Nkonde-Price, who led a research study on the rehabilitation program, speaks with nurse Ifat Castro Sharabi (shown from behind) at the West Los Angeles Medical Center

Achieving equitable care

When the COVID-19 pandemic began in 2020, at-home cardiac rehabilitation became more important than ever. The only change required was to mail smartwatches to patients' homes instead of doing in-person fittings.

"We never missed a beat, whereas the world had to catch up with us," Dr. Batiste said.

Dr. Batiste and his colleagues believe their smartwatch-based program has the potential to improve cardiac recovery both throughout Kaiser Permanente and across the country.

"At its core, this is all about delivering equitable care within our communities," Dr. Funahashi said. "If you need cardiac rehab, you shouldn't have to come to a facility. As a health care organization, we need to figure out how to get that intervention to you."

He and his colleagues are working with Kaiser Permanente leadership to spread the program throughout all 8 regions. They have also partnered with the Centers for Disease Control and Prevention and its Million Hearts initiative to inspire similar programs nationwide.

"Ultimately, we hope that all the people whose lives we could save are actually touched by programs like ours," Dr. Funahashi said.

*Nkonde-Price C et al. *JAMA Netw Open*. 2022; 5(8):e2228720.

Cancer research focuses on patients' total health

Researchers in the Department of Research & Evaluation see patients as more than a collection of symptoms and possible medical solutions. They focus on the total health of each patient and are working to transform the entire care experience.

In 2022, that passion turned into publications on multiple fronts, including studies focused on improving the lives of patients with breast cancer.

"A person is not just their disease," said Erin E. Hahn, PhD, MPH, a research scientist in the Division of Health Services Research & Implementation in R&E. "Each one is a full, vibrant person who might be diagnosed with something that needs to be treated. And if you focus too narrowly only on the disease or care delivery, all these other things can go unaddressed."

Recent research studies aimed at bettering the lives of breast cancer patients and breast cancer survivors included studies on:

- screening breast cancer patients for depression;
- whether exercise could help breast cancer survivors live longer; and
- how these patients' longevity was affected by chronic conditions such as diabetes, hypertension, and obesity.

"We are interested in holistic care, not just drug treatment," said Reina Haque, PhD, MPH, a research scientist in the Division of Epidemiologic Research in R&E. "We want to help the full person feel better both physically and emotionally."

Increasing breast cancer survival

Dr. Haque focused on breast cancer patients' longevity in 2 of her studies. One examined lifestyle factors that affect longevity among all breast cancer survivors, while the other assessed health conditions that may affect the longevity of women with advanced breast cancer.

Corrine Muñoz-Plaza, Dr. Ernest Shen, and Janet Lee, co-authors on research about screening breast cancer patients for depression, discuss their project at R&E's main office in Pasadena

Cancer research focuses on patients' total health

continued

When diagnosed at an early stage, breast cancer can be managed like a chronic condition. Early-stage breast cancer has 5-year survival rates near 99%, but the 5-year survival rate among women with metastatic breast cancer – breast cancer that has spread to other parts of the body – is only 29%, Dr. Haque said.

This difference can often impact the lives of women of color, who historically have not had their breast cancer diagnosed as early in the disease course as women who are white.

The first of Dr. Haque's studies was published in October 2022 in *Cancer Epidemiology, Biomarkers & Prevention*.[1] It found that the risk of death among women with metastatic breast cancer rises with increasing numbers of chronic conditions, such as diabetes, hypertension, and obesity.

"This study suggested that if we focus on managing chronic medical conditions in patients with metastatic breast cancer, we also may help reduce disparities in mortality," said Dr. Haque, who was the senior author of the study. "With advances in treatment, many women are living longer with metastatic breast cancer, but our findings showed that this is not being realized equally across racial and ethnic groups."

Dr. Haque said the study gave researchers a glimpse into this issue, which will help identify potential ways to solve the disparities in breast cancer survival in the future.

Exercise and breast cancer survival

Dr. Haque also was a senior author of another study that showed that exercise significantly lowers risk of death for breast cancer survivors. While breast cancer survivors, like everyone else, are encouraged to exercise regularly, there had been little research previously on whether exercise helped these patients live longer.

The study was published in November 2022 in *JAMA Network Open*.[2] It followed more than 300 breast cancer survivors for more than 7 years. Moderate physical activity was associated with a 60% lower chance of death in breast cancer survivors.

"One of the most important things we found was that a vigorous workout wasn't necessary to increase longevity. Simply a brisk walk about 6 times a week helped," Dr. Haque said.

"Our study showed that building clinician support and feedback into the depression screening process for cancer patients can create a sustainable program that helps ensure our cancer patients get the mental health support that they need."

– Erin E. Hahn, PhD, MPH

Dr. Reina Haque, who led 2 studies looking at women's lives after breast cancer, working in her office at R&E's main office in Pasadena

She added, "What we learned from both studies is that the conditions that can affect long-term survival can have a behavioral component. So, treating the whole person is critically important."

Living better with breast cancer

The essence of Dr. Hahn's research into screening breast cancer patients for depression began while she was still in graduate school. She read a 2008 report on cancer care and how it often provides state-of-the-science biomedical treatment but fails to address the psychological and social problems associated with the illness.

"I had this realization … we need a more holistic approach," she said.

That idea has inspired much of her work, as well as the study on implementing depression screening for breast cancer patients, which was published in January 2022 in *JAMA*.[3]

"We knew from previous research that breast cancer patients are at greater risk of depression than the general population, but implementing a successful depression screening program within an oncology department focused on beating cancer has been difficult," Dr. Hahn said. "I knew if it can be done anywhere, it could be done here at Kaiser Permanente Southern California because we are an integrated system filled with dedicated people who can connect people to the resources they need – all within the same care network."

Developing a successful screening program

To determine how depression screening could best be implemented, researchers separated medical oncology teams at different locations into 2 groups. In the first group, physicians and nurses received education about depression screening, regular feedback on their performance, and support in determining the best ways to add depression screening into their current workflow. In the second group – the control group – physicians and nurses received only education.

Researchers enrolled 1,436 members: 692 in the control group and 744 in the intervention group. The groups were similar in demographic and cancer characteristics.

Eighty percent of patients in the intervention group completed depression screening versus less than 1% in the control group.

Of the patients in the intervention group, 10% scored in the range indicating a need for referral to mental health services. Of those referred, 75% completed a visit with a mental health provider.

"Our study showed that building clinician support and feedback into the depression screening process for cancer patients can create a sustainable program that helps ensure our cancer patients get the mental health support that they need," Dr. Hahn said.

The new screening initiative was subsequently built into the patient care and daily workflow of medical oncology teams throughout KPSC.

"We have an incredible opportunity right now to be able to treat cancer, and also to make the lives of those living with cancer better," said Dr. Hahn. "Our patients are living longer, fuller lives after cancer; and it is gratifying to be able to find ways to help them beyond the medicine."

[1]Haque R et all. *Cancer Epidemiol Biomarkers Prev.* 2022;31:1935-43.

[2]Haque R et al. *JAMA Netw Open*. 2022;5(11):e2242660.

[3]Hahn EE et al. *JAMA*. 2022;327(1):41-49.

The COVID-19 aftermath: Researchers and physicians seek answers

In 2022, researchers at the Department of Research & Evaluation continued to provide valuable, groundbreaking information on COVID-19 vaccines for policy makers, health care providers, and the public. Also, it was a year when researchers took the time to look at the aftereffects of COVID-19, both on the health system and on patient health.

"In the beginning of COVID-19, everything was so urgent, and we just needed to keep so many people from dying," said Sara Y. Tartof, PhD, MPH, a research scientist in the Division of Epidemiologic Research in R&E. "As we got a few years out, we continued to try to prevent deaths, but we also have been able to look at longer-term questions of health care utilization and see the longer-term impact of the virus on people's health."

Cheng-Wei "Charlie" Huang, MD, a hospitalist at the Kaiser Permanente Los Angeles Medical Center, saw 2022 as a transitional year in which the COVID-19 hospitalization rates dropped compared to 2020 and 2021.

"We saw, however, a sustained increase in health care utilization relative to the pre-COVID-19 era that was no longer driven by acute COVID-19," he said. "There are different theories on this increased utilization, whether it may be due to a direct consequence of COVID-19 or a result of delayed care-seeking for non-COVID-19 health care issues as the pandemic is fading, or a combination of both."

Some of the studies Kaiser Permanente Southern California researchers conducted in 2022 on the aftermath of COVID-19 included the demand that

Physician researchers Dr. Joon Park and Dr. Charlie Huang, pictured here at the Los Angeles Medical Center, worked together on research that identified disease-specific factors associated with lower chances of readmission for patients with COVID-19

continued

COVID-19 patients put on the health care system after infection, how medications might reduce hospital admissions and readmissions, and new ways to identify patterns of the pandemic.

"COVID-19 can have long-term impacts on health care utilization, and ongoing management of patients' health care needs is necessary," said Debbie Malden, DPhil, MSc, epidemiologist and digital surveillance consultant with the Division of Epidemiologic Research in R&E. "Health care organizations and patients should have an awareness of the long-term and multi-organ system effects of post-COVID conditions."

Understanding COVID-19's impact on health care at KPSC

The first of these studies was published in January 2022 in the *Journal of General Internal Medicine*.[1] It showed that patients with COVID-19 put high demands on the health care system whether they had been hospitalized with the disease or not.

"During the pandemic, we recognized that there were many complications associated with COVID-19 infection beyond severe cases requiring hospitalization," said the lead author, Brian Huang, PhD, MPH, who was then a biostatistician with R&E and is now an assistant professor with the University of Southern California Keck School of Medicine. "With the rapidly growing number of infected individuals and the emergence of what is now known as long COVID, we hypothesized that there would be increased utilization and demand for health care resources. At the time, there were many studies on COVID-19-related hospitalization, but there was less information on outpatient and emergency department utilization following COVID-19 infection."

In this study, researchers assessed the medical records of 64,011 KPSC members who had been diagnosed with COVID-19 from March through September 2020. The average number of visits over 30 days after diagnosis was nearly 7 for patients who were not hospitalized, and approximately 12 for those who were admitted. Most of the health care visits after diagnosis were virtual telehealth appointments for COVID-related or respiratory-related reasons.

Dr. Brian Huang said that it had been important to characterize how the pandemic, then still in the early phase, was placing demands on all facets of health care utilization.

Understanding this information would help health care organizations anticipate patient needs and appropriately allocate resources to specific departments and patient populations," he said.

A broader look at health care utilization

Seven months later, a study led by Dr. Tartof was published in *JAMA Network Open*.[2] This study broadened the cohort to 8 different health care systems and extended the time period in which patients were followed after COVID to 6 months.

"Our clinicians had put everything they had into prevention and treatment," Dr. Tartof said. "And we needed to know what to expect as a health care system. As you can imagine, COVID-19 put incredible stress on the health care system."

The study showed that contracting COVID-19 was associated with a 4% increase in the use of health care services during the 6 months following initial infection.

"This study highlighted the potential for COVID-19 to exert an ongoing demand on health care organizations," Dr. Tartof said. "A 4% increase in encounters applied across a large population is a large number of visits associated with substantial cost. In this case, it meant over 27,000 extra encounters among the 8 health care organizations included in this study."

Paxlovid safety and effectiveness studied

Dr. Tartof worked on other studies related to the aftermath of COVID-19, including 2 examining the effectiveness and safety of Paxlovid for patients who had contracted COVID-19.

In December 2021, the Pfizer-BioNTech medication Paxlovid received emergency authorization as a treatment to prevent severe health problems from COVID-19 that could lead to hospitalization and death. But by May 2022, the medication was being linked anecdotally to a rebound in COVID-19 symptoms following recovery.

The U.S. Centers for Disease Control and Prevention reached out to Dr. Tartof. Could the scientists at R&E harness their research knowledge and robust electronic health records to see if there

were any serious issues? Within 3 weeks, Dr. Tartof and Dr. Malden were able to quickly look at this question within the KPSC patient population.

"We were able to describe the proportion of those who were admitted to the hospital or visited the emergency department for COVID-19-related illness after being treated with Paxlovid," said Dr. Malden. "Our analysis found that less than 1% of patients who received Paxlovid ended up in the hospital or emergency department for COVID-19 in the 5 to 15 days following treatment."

The study was published in June 2022 in the CDC's *Morbidity and Mortality Weekly Report*.[3]

Dr. Tartof went on to also research the effectiveness of Paxlovid in a study that was published in *The Lancet Infectious Diseases*[4] early in 2023. That study showed that receiving Paxlovid within 5 days of the start of COVID-19 symptoms was associated with substantial reductions in the risk of hospital admission or death, she said.

Clinicians also examined COVID-19 aftermath

Dr. Charlie Huang led a study of KPSC members who were hospitalized for COVID-19 that identified disease-specific factors associated with lower chances of readmission.

The study was published in September 2022 in the *Journal of General Internal Medicine*.[5] The findings added to a growing body of research that helped physicians more confidently decide on the best and safest timing for discharging a patient.

"The study was from early in the pandemic, 2020, and found relatively low rates of readmissions; identified the protective benefits of remdesivir treatment prior to discharge; and recognized the importance of symptom duration when determining COVID-19 care," Dr. Charlie Huang said. "These factors can be helpful particularly when there is uncertainty regarding the safety of a COVID-19 patient discharge, and providers can feel even more reassured in today's practice, as overall disease severity has declined since 2020."

Among the other research Dr. Charlie Huang led, one study looked at whether dexamethasone could help prevent deaths of COVID-19 patients if they were prescribed the medication after their release from the hospital. The findings suggested that dexamethasone should not be routinely prescribed beyond discharge for people with COVID-19. The study was published in *JAMA Network Open*[6] in March 2022.

Dr. Sara Tartof and Dr. Debbie Malden, pictured here at R&E's main office in Pasadena, worked together on a study that showed an increase in health care utilization following COVID-19 infection

Moving forward with COVID-19 research

Dr. Malden suggested that one promising direction for future research in the aftermath of COVID-19 is to continue developing and refining Artificial Intelligence (AI) technologies such as natural language processing (NLP) to improve disease identification and characterization, and to estimate the burden of the disease.

She led a study that was published in December 2022 in *JMIR Public Health and Surveillance*.[7]

The findings demonstrated that by "enabling the extraction and analysis of large volumes of electronic health record data, NLP and other AI techniques could help researchers and health care professionals identify emerging patterns of disease," she said.

Dr. Malden added, "This could enhance our ability to prepare for and respond to future disease outbreaks."

[1]Huang BZ et al. *J Gen Intern Med.* 2022; 37:830-837.

[2]Tartof S et al. *JAMA Netw Open.* 2022;5(8):e2225657.

[3]Malden D et al. *MMWR Morb Mortal Wkly Rep.* 2022;71(25): 830-833.

[4]Lewnard J et al. *Lancet Infect Dis.* 2023 March 15. (Epub).

[5]Huang C et al. *J Gen Intern Med.* 2022;37:3973-78.

[6]Huang C et al. *JAMA Netw Open.* 2022;5(3):e221455.

[7]Malden C et al. *JMIR Public Health Surveill.* 2022 Dec 30;8(12):e41529.

Mayra Martinez, Ting Chow, Dr. Margo Sidell, and Dr. Anny Xiang, who worked together on several studies on air pollution and COVID-19, look out at an overcast Pasadena skyline

Uncovering links between air pollution and COVID-19

Air pollution affects the health of millions of people around the world. It may increase the risk or severity of many different conditions, such as stroke, asthma, pneumonia, and lung cancer.

Now, Kaiser Permanente Southern California researchers and their collaborators are discovering links between air pollution and COVID-19.

In one investigation, researchers applied high-resolution air pollution models to estimate individual exposure levels for more than 20,000 KPSC members who had been hospitalized for COVID-19. They found that greater exposure to several different pollutants – including fine particles (PM2.5) – was associated with a greater risk of death from COVID-19. This study was published in January 2023 in *Environment International*.[1]

"The most important message is that air pollution does matter for COVID-19 mortality," said Claudia Nau, PhD, a research scientist in the Division of Behavioral Research in the Department of Research & Evaluation, who helped lead the analysis alongside Deborah Rohm Young, PhD, MBA, director of the Division of Behavioral Research.

Dr. Nau noted that air pollution is just one of many risk factors that could be addressed to reduce COVID-19 deaths. Nonetheless, she said, "Our study adds to mounting evidence that air pollution is bad for our health, and with the future possibility of more respiratory disease outbreaks, it is yet another reason to reduce air pollution."

The study was a collaboration with researchers from the University of California, Los Angeles; UC Davis; UC Berkeley; and the Canadian government. It was funded by the California Air Resources Board, meaning the findings could directly inform future policymaking.

Dr. Claudia Nau, pictured here at R&E's main office in Pasadena, co-led the analysis for another study funded by the California Air Resources Board

Meanwhile, Anny H. Xiang, PhD, MS, director of the Division of Biostatics Research at R&E, was one of the first researchers who received supplemental funding from the National Institute of Environmental Health Sciences to assess connections between air pollution and COVID-19.

Dr. Xiang and her collaborators from the University of Southern California and Sonoma Technology have now published 4 studies on the topic. Dr. Xiang is senior author for all 4 studies. Margo Sidell, ScD, MSPH, a collaborative biostatistician research scientist in the Division of Epidemiologic Research in R&E, co-led the data extraction, analyses, and publications.

Like Dr. Nau's study, these projects harnessed fine-resolution exposure data based on people's residential addresses.

"Most other studies have used larger-scale data," Dr. Xiang said. "By using individual-level data and accounting for demographics and health history, we are addressing many weaknesses of previous studies and contributing a lot more to the current knowledge on this topic."

In the first study, her team found that exposure to traffic-related air pollution was associated with a higher risk of COVID-19 severity and death for 75,010 KPSC members. This study was published in December 2021 in *Environment International*.[2]

Another study, of 4.6 million patients, linked both long-term and short-term exposure to PM2.5 and nitrogen dioxide with a higher risk of COVID-19 infection. This study was published in May 2022 in *Environmental Research*.[3]

Yet another linked PM2.5 and nitrogen dioxide exposure with worse COVID-19 outcomes and a higher risk of death among 74,915 patients. It was published in August 2022 in the *American Journal of Respiratory and Critical Care Medicine*.[4] A fourth showed that COVID-19 vaccination did not appear to mitigate this link among 50,010 patients. It was published in January 2023 in the *American Journal of Respiratory and Critical Care Medicine*.[5]

"Even after controlling for race and ethnicity and other socioeconomic variables, exposure to pollutants was associated with worse outcomes," Dr. Xiang said.

Dr. Nau added that low-income communities and communities of color are more likely to be located near sources of pollution, such as highways. "Addressing air pollution should help address the environmental injustices that impact so many aspects of people's health, including COVID-19," she said.

[1]Jerrett M et al. *Environ Int.* 2023;171: 107675.

[2]Chen Z et al. *Environ Int.* 2021;157:106862.

[3]Sidell MA et al. *Environ Res.* 2022;208:112758.

[4]Chen Z et al. *Am J Respir Crit Care Med.* 2022;206(4):440-448.

[5]Chen Z et al. *Am J Respir Crit Care Med.* 2023;207(2):218-221.

Jorge Arenas Rivera and Dr. Alexander Martos were part of the effort to reduce COVID-19 vaccine disparities, which included using Kaiser Permanente's mobile health vehicle (pictured) to get vaccines to Southern California neighborhoods with the lowest vaccination rates

Increasing vaccine equity in Southern California

In addition to bringing isolation and illness to the world, the COVID-19 pandemic spotlighted the health disparities between Southern California communities.

Getting COVID-19 vaccines to the neighborhoods where they were most needed was one of the greatest challenges health care providers experienced during the pandemic.

At Kaiser Permanente in Southern California, people rallied to address the issue. Their successful quality improvement implementation study outlining these efforts was published in *The Permanente Journal*.*

Many teams worked together to address issue

The effort included team members from National Community Health and the Southern California Permanente Medical Group's regional departments of Complete Care; Equity, Inclusion, and Diversity (EID); and the Department of Research & Evaluation, among others. They were able to align their program with work started by the SCPMG's EID Department in 2019 that was meant to address disparities in flu vaccination.

"Our work was an effort to highlight the concept of 'place equity,' meaning that more of an individual's health can be attributed to their ZIP code than anything else, and that the inequitable distribution of community resources therefore contributes significantly to health disparities," said Alexander Martos, DrPH, a managerial consultant and interim director for SCPMG's EID Department. "We applied this to a real-life crisis during the early pandemic and were able to demonstrate meaningful progress in disparity reduction."

R&E committee stepped up to help

Research & Evaluation formed an EID committee in June 2020 in the wake of the George Floyd murder to increase equity in the workplace and reduce health disparities. By January 2021, when the first COVID-19 vaccines became available to the public, it was clear that some communities with fewer resources were seeing higher rates of illness and death due to COVID-19. Getting vaccines and making them widely available was a challenge in Southern California, as well as across the nation.

"It was an honor to contribute our expertise in research methodology and dissemination to assist the collaborative efforts of our region to improve access to vaccinations for the underserved."

– Angel Alem, MPH, MS

The committee reached out to the SCPMG EID Department to partner on efforts on COVID-19 vaccine distribution.

"It was an honor to contribute our expertise in research methodology and dissemination to assist the collaborative efforts of our region to improve access to vaccinations for the underserved," said research co-author Angel Alem, MPH, MS, a division operations director and EID committee co-leader for Research & Evaluation. "When we had a chance to help with the vaccine equity effort, we didn't hesitate."

The disparities in vaccine access and COVID-19 health burdens in the nation in 2021 were largely driven by inequities in socioeconomic factors and policies, practices, and attitudes that can often result in poor health outcomes for minority populations, said Reina Haque, PhD, MPH, a research scientist with R&E, who was the senior author on the research study.

Hot-spot strategy employed to address inequities

"To address the challenges of inequitable access to the COVID-19 vaccine in Southern California, Kaiser Permanente Southern California applied a community-oriented and geographic strategy aimed at reducing disparities in COVID-19 vaccination by ZIP codes," Dr. Haque said. This became known as the "hot-spot" strategy.

Together, the members of these groups used analytical tools to systematically assess the risk of COVID-19 in different communities within Kaiser Permanente Southern California's 670 ZIP codes. The hot-spot methodology produced monthly lists of ZIP codes that required additional health care resources and vaccination strategies. Then the COVID-19 vaccination teams worked with medical centers in the most challenged ZIP codes to get more people vaccinated. Strategies included sending proactive texts, extending vaccination clinic hours, providing

Angel Alem and Dr. Reina Haque, seen here at R&E's main office in Pasadena, worked with others to reduce disparities in COVID-19 vaccine access during the height of the pandemic

in-home vaccinations for homebound patients, and a mobile health vehicle that drove into the neighborhoods with vaccines. Health care providers at the various pop-up clinics and in the mobile health vehicles vaccinated both Kaiser Permanente members and nonmembers.

The strategy was effective in both creating awareness of inequities and guiding vaccination efforts toward the most vulnerable communities, Dr. Haque said.

Strategy success leads to publication and further efforts

By the end of 2021, this hot-spot strategy helped Kaiser Permanente achieve an overall vaccination rate of 81% among all of its Southern California members. Additionally, 2 out of 3 people who received a vaccine through the hot-spot-guided mobile health vehicle were Hispanic or Black. But the work didn't stop there. This place-based approach to reducing vaccination disparities in underserved communities was quickly adapted to other health disparities, said Dr. Martos.

In 2022, the strategy was rolled out to address disparities in flu vaccination and diabetes control.

"After we had successfully employed this hot-spot vaccination strategy with COVID-19, we were able to refine how we analyzed the data and our approach to the social and economic factors impacting our members," Dr. Martos said. "We are now in the process of operationalizing these hot spots with our vaccination and proactive care teams and look forward to exploring new health equity opportunities in the future."

*Swope M et al. *Perm J.* 2023 Mar 15;27(1):103-112.

Pharmacist Dr. Daniel Ehrlich consults with Regional Chief of Infectious Disease Dr. Elizabeth Hudson and Clinical Trials Research Project Manager Hema Buddha at the Panorama City Medical Center

Responding to a community outbreak through expanded access

On a Friday in late July, Clinical Trials Research Project Manager Hema Buddha, MBBS, received an urgent call from a physician at the Kaiser Permanente South Bay Medical Center.

The physician had a patient with symptoms of mpox, then commonly referred to as monkeypox, and needed help accessing an investigational new drug called tecovirimat.

While the physician waited on blood tests to confirm the diagnosis, Buddha began to navigate the process of obtaining the drug through an expanded access protocol managed by the U.S. Centers for Disease Control & Prevention. A representative of the County of Los Angeles Department of Public Health, which served as a local intermediary for the CDC, provided guidance.

"We were coming up on the weekend, and everybody wanted to get treatment for the patient as quickly as possible," said Buddha, whose primary focus is on helping physicians procure drugs available through expanded access (sometimes called compassionate use). "There were a lot of steps in getting the medication and approvals needed before treatment could be initiated."

Buddha reached out to several resources in Kaiser Permanente Southern California, including the Institutional Review Board, infectious disease specialists, pharmacy staff, and colleagues from the clinical trials team. She traded calls and emails with the Department of Public Health. After a flurry of activity, the process moved forward. Within days, the treatment was started.

Infectious disease physicians, pharmacists jump in to help

Regional Chief of Infectious Disease Elizabeth Hudson, DO, MPH, had been preparing for a local outbreak since late spring, when mpox cases first began appearing in Europe.

"It became imperative for us as infectious disease specialists to understand the disease so we could help our fellow clinicians identify it, especially since the cases we were seeing didn't look like textbook examples," she said. "By late summer, we started seeing an awful lot of cases, particularly in Los Angeles and San Diego counties."

Dr. Hudson and her colleagues worked closely with the clinical trials team to make sure all 51 infectious disease specialists within KPSC had the training and documentation to be able to initiate treatment with tecovirimat. To make sure each specialist could quickly initiate the informed consent process, the clinical trials teams created electronic forms that were individualized to each physician, which could be sent out via patient messages from Kaiser Permanente HealthConnect®.

The clinical trials team worked closely with the infectious disease specialists, pharmacists, and others, meeting at least weekly to develop and refine the workflows that supported access to tecovirimat. Over time, Dr. Hudson noted a reduction in the administrative burden for the infectious disease specialists. Most important, physicians were able to move swiftly to help their patients.

"Patients who had these lesions were very uncomfortable, and that is putting things mildly," she said. "They were calling and emailing us, sometimes telling us they were in excruciating pain. We wanted to get them potential relief as soon as possible."

By the end of 2022, nearly 170 patients had received tecovirimat as treatment at KPSC. This would not have been possible without the clinical trials team, Dr. Hudson noted.

"It is important for folks to know just how robust our expanded access program is, and what an important role it plays in helping us secure access for investigational treatments for our patients," she said. "Expanded access is key to keeping our patients well and staying at the forefront of emerging infectious diseases."

Bringing scientific rigor through a new clinical trial

As valuable as the expanded access program has been in getting patients access to a promising treatment, the medical community still needs data to better understand the safety and efficacy of the drug in treating human mpox.

"Tecovirimat was developed as an antiviral against smallpox, which is in the same family as mpox," said William J. Towner, MD, FACP, FIDSA, physician director of the Division of Clinical Trials Research in the Department of Research & Evaluation. "We won't get the scientific insights we need through data from expanded access. We really need the rigor of a trial."

Buddha works the phone to coordinate the many people and steps involved in getting medication approved under expanded access

In late summer 2022, Dr. Towner and his team heard that the National Institute of Allergy and Infectious Diseases was sponsoring a Phase 3 clinical trial evaluating tecovirimat for treatment of human mpox. The study would be led by NIAID-funded AIDS Clinical Trials Group, also known as ACTG.

KPSC had previously participated in several ACTG studies, including recent trials for COVID-19 treatments. At Dr. Towner's request, Clinical Trials Operations Director Tiffany Castanon, MHA, reached out to see if there might be an opportunity for KPSC to join as a site for the study. A little more than a month later, KPSC had been established as a site for the Study of Tecovirimat for Human Monkeypox Virus, or STOMP.

"Our program had an opportunity to contribute to KPSC and our local community in 2 very important ways, first by facilitating access to an important investigational drug and now by helping to add to the evidence needed to understand its safety and efficacy," said Dr. Towner. "I am so grateful to all of the people across the organization that helped us succeed on both fronts."

By late fall, the number of cases in Southern California began to decline. But infectious disease specialists remain vigilant, aware that cases could begin to climb again if the disease gets a new foothold in our community.

"It is reassuring to know that if we start to see more cases in our area again, our clinical trials division will be able to respond by helping our physicians and patients receive treatment through expanded access and by adding to the scientific evidence about treatment of mpox through participation in this important study," said Dr. Hudson.

Dr. Hui Zhou, Dr. Margo Sidell, Dr. Rulin Hechter, and Dr. Sonya Negriff meet at R&E's main office to discuss a study on risk factors for firearm injury and opportunities for prevention

Research committed to firearm injury prevention

When Kaiser Permanente put out the call for research proposals on firearm injury prevention, Rulin Hechter, MD, PhD, MS, and her colleagues felt there was no choice but to respond.

"Firearm injury is a critical problem in our society that profoundly impacts people's lives," said Dr. Hechter, a research scientist in the Division of Epidemiologic Research in the Department of Research & Evaluation. "We believe it is our responsibility to use our public health expertise to contribute to a solution."

Her multidisciplinary team successfully applied for funding to study risk factors for firearm injury and clinical opportunities for prevention.

In April 2023, in the journal *Academic Pediatrics,*[1] they published their first findings: an analysis of nearly 2 million pediatric Kaiser Permanente members that highlights risk factors associated with children's chances of experiencing a firearm injury.

"Pediatric firearm injury is a public health issue that I feel very strongly about helping to address," said the study's lead author, Sonya Negriff, PhD, a research scientist in the Division of Behavioral Research in R&E. "Our findings bolster confidence in known risk factors and could help target prevention efforts among the most vulnerable youth."

A new endeavor for an experienced team

Most prior research on firearm injury had focused on fairly narrow sets of risk factors using data from small numbers of patients. Larger studies considering a broader constellation of risk factors had been lacking.

To help fill that gap, the team assessed electronic health record data from 1,889,182 children younger than 18 who had received any care at Kaiser Permanente Southern California from 2010 through 2018.

With this data, they investigated potential links between firearm injuries and age, gender, Medicaid status, mental health, substance use disorder, medical comorbidities, and race and ethnicity. Importantly, the study combined those individual-level factors with neighborhood-level data on educational achievement levels in each child's surrounding residential environment.

"Our team had not worked with firearm injury data before," said Margo Sidell, ScD, MSPH, the collaborative biostatistician research scientist and programming lead for the Division of Behavioral Research at R&E. "It was very important to us to take the time needed to validate our measures and ensure quality control of the data."

"We couldn't have done this work without Margo and our programmer Richard Contreras," Dr. Negriff added. "They are essential for projects like this."

Children's risk factors revealed

The analysis showed that children ages 12 to 17 were at significantly higher risk of non-self-inflicted firearm injury than children ages 5 and younger. Being male, being Black or Hispanic (versus white), being a Medicaid recipient, living in a neighborhood with lower education levels, and having a substance use disorder were also linked to higher risk of non-self-inflicted firearm injury.

The only factors significantly associated with self-inflicted firearm injury were being male and being ages 12 to 17. However, Dr. Negriff cautioned, this does not contradict prior studies that have linked mental health to self-inflicted firearm injury.

"Self-inflicted firearm injury is quite rare, which limits our ability to detect statistical associations," she said. "That is why it is important to accumulate evidence from various different studies like ours."

These findings underscore the need to screen pediatric patients for risk of either self-inflicted or non-self-inflicted firearm injury and could help inform efforts to further reduce risk. For instance, in addition to individual screening, medical centers in higher-risk locations could provide services that address risk factors at a broader population level.

"It is important to consider the contextual environment in which non-self-inflicted firearm injuries occur and the systemic factors that contribute to environments where, for instance, kids may face higher risk of firearm injury from just walking to school," Dr. Negriff said.

Building knowledge to inform action

Now, the team is finishing up a similar investigation of risk factors for firearm injuries in adults, as well as a study of trends in firearm injury rates over time with data updated through 2020.

They are also deepening their research with artificial intelligence. In 2022, Fagan Xie, PhD, a principal architect and manager of the Clinical Informatics team in R&E, led the development of an algorithm that detects suicidal ideation and attempts in freely written clinical notes, ensuring such instances are counted even when not formally coded in people's electronic health records.

This summer, the team will present a machine-learning-based model that uses more than 170 predictors in a patient's record to assess potential risk of self-inflicted firearm injury. Construction of the model was led by Hui Zhou, PhD, MS, a collaborative biostatistician research scientist and the biostatistician lead in the Division of Epidemiologic Research at R&E, in close collaboration with Claudia Nau, PhD, a research scientist in the Division of Behavioral Research.

"This model essentially creates a risk score that we are hoping can be adapted for use in the clinic," Dr. Hechter said. "It could serve as a tool to help support more targeted screening."

The importance of such tools was reinforced by the CDC's recent announcement that, as of 2020, firearm injuries surpassed car accidents as the leading cause of death for U.S. children and adolescents.

"Firearm injury is a major component of children's public health in the United States," Dr. Hechter said. "Many people on our team have children ourselves, and we hope our work can help prevent some of the tragedies we hear about all too often."

[1]Negriff S et al. *Acad Pediatr.* 2023;23(3):604-609.

Dr. Karen Coleman stands with Debi Ellis, a bariatric surgery patient, bariatric support group co-leader, and patient advisor, at the Jackie and Mack Robinson memorial across from Pasadena City Hall

Understanding racial disparities and outcomes in bariatric surgery

A study published in *JAMA Surgery found that at 1, 3, and 5 years, Black and Hispanic patients who had bariatric surgery had similar outcomes to white patients for weight loss and type 2 diabetes.**

However, they had higher rates of complications compared to white patients following Roux-en-Y gastric bypass (RYGB), but not the less complex sleeve gastrectomy (SG) surgery.

"Our study across 25 health systems shows bariatric surgery is safe and effective, but some Black and Hispanic patients may be experiencing higher rates of complications with the gastric bypass," said lead author Karen J. Coleman, PhD, a research scientist in the Division of Behavioral Research in the Department of Research & Evaluation. "Based on other research we have conducted, we don't believe the differences between racial groups are due to the bariatric operations themselves. We think they're because of issues of access to post-surgery care and to systemic racism that may make it difficult for some patients to get healthy foods and engage in the kind of self-care necessary to recover from major surgery."

Black and Hispanic patients suffer disproportionately from severe obesity. Dr. Coleman noted that surgery is the most effective intervention for severe obesity, but only 2% of people in the United States have the surgery. The rates are even lower for patients from racial and ethnic minority groups.

"Our research program is designed to address this disparity and improve outcomes from bariatric surgery for those who need it most," she said.

This retrospective study included 36,871 adult and adolescent patients – 43% of whom were Black or Hispanic – who underwent a primary RYGB or SG operation between January 1, 2005, and September 30, 2015, at 25 health systems in the National Patient-Centered Clinical Research Network (PCORnet).

"As we move forward, clinicians and researchers should focus on improving pre- and post-operative care for diverse populations," Dr. Coleman said. "It's also important to create a system of shared decision-making that takes into consideration which bariatric operations are best for each patient."

*Coleman K et al. *JAMA Surg.* 2022;157(10):897-906.

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

31 FULL-TIME RESEARCH SCIENTISTS

300+ PHYSICIAN RESEARCHERS

Includes clinical trials principal investigators and sub-investigators, as well as retired and affiliated SCPMG 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, and communications staff

20 RESEARCH SCIENTISTS

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

Projects

500+ ACTIVE STUDIES

Throughout Kaiser Permanente Southern California. Funded by external sources. Projects may include multiple protocols.

350+ ACTIVE CLINICAL TRIALS PROTOCOLS

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

Publications

650+ JOURNAL ARTICLES

110+ CARDIOVASCULAR DISEASE

90+ CANCER

80+ COVID-19

60+ IMMUNIZATION

25+ DIABETES

25+ MENTAL HEALTH

To view the full list of 2022 publications, go to:

Financial overview

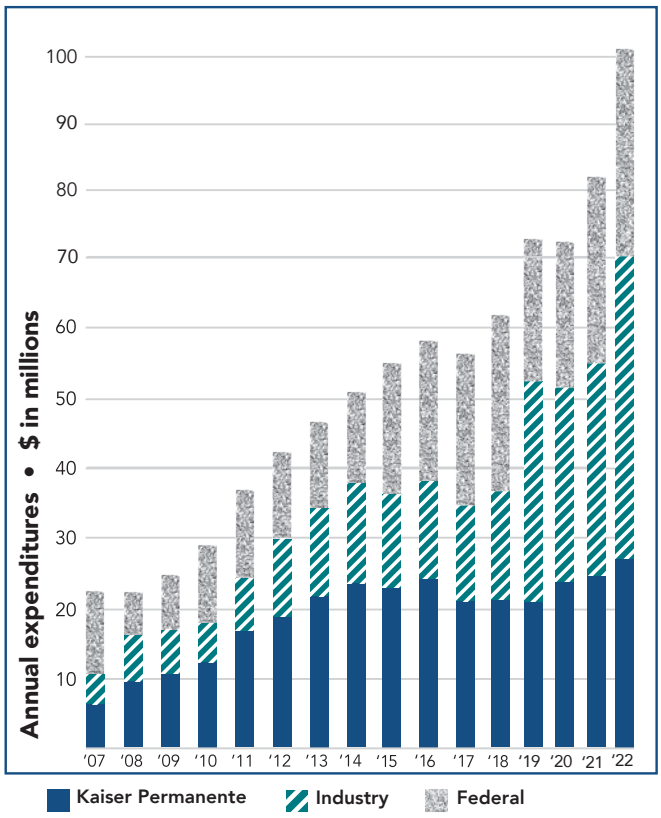
Funding for research at Kaiser Permanente Southern California has increased consistently over the past 2 decades to support a growing portfolio of innovative and clinically relevant research.

Total research funding: $100+ million

Federal grants: $32 million

Industry/non-federal contracts: $46 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.



2022 grant and contract submissions

(new grants only, external only)

150 SUBMITTED

91 AWARDED

New grants and contracts

(all years, includes clinical trials)

Direct costs:	$51.6 million
Indirect costs:	$30.2 million
Total:	**$81.8 million**

Continued grants and contracts

(all years, includes clinical trials)

Direct costs:	$169.5 million
Indirect costs:	$88.3 million
Total:	**$257.8 million**

Selected findings

In 2022, Kaiser Permanente Southern California scientists and clinician researchers made important findings in a variety of areas. The following is a small sample of some of these discoveries.

Cancer

Antidepressants linked to lower risk of prostate cancer recurrence

Prescribing antidepressants to patients who have depression in addition to prostate cancer decreased the risk of a cancer recurrence. Published in September 2022, this study aimed to increase awareness of the potential benefits of antidepressants in cancer and depression outcomes. It is unknown how antidepressants might influence prostate cancer recurrence, but behavioral and/or biochemical factors are suspected. The study underscored the importance of screening and treating prostate cancer patients for depression. Researchers suggested that mental health should be evaluated as a routine part of prostate cancer diagnosis.

Haque R et al. Cancer Causes Control. 2022;33:1363-1372.

New approach reduces colon cancer deaths

A comprehensive, novel approach to improving colon cancer care at Kaiser Permanente Southern California between 2009 and 2018 resulted in a 24% decrease in mortality over 7 years. The approach focused on a variety of care process improvements beyond improving rates of screening and follow-up and sought to improve any care element that could increase overall survival. The approach included follow-up of rectal bleeding and presumed iron deficiency anemia, improving postsurgical surveillance reliability, decreasing time from surgery to chemotherapy, expanding surgical referrals for advanced cases, increasing vitamin D and aspirin use, and monitoring and increasing the adenoma detection rate.

Kanter M et al. Jt Comm J Qual Patient Saf. 2022;48(8):388-394.

Cardiovascular disease

Heart attacks increased in the 5 days after 2020 election

Hospitalizations for heart attack, stroke, and heart failure were 17% higher in the 5 days following the 2020 presidential election than in the same period 2 weeks before the vote. This study of more than 6 million people from Southern and Northern California reinforced findings of a similar 2016 presidential election study that found increased rates of acute cardiovascular disease after voting results. The study underscored the impact of emotional stress on heart disease, and the recognition that political events can cause excitement and anxiety in some people.

Mefford M et al. JAMA Network Open. 2022;5(4):e228031.

COVID-19

More exercise linked to less severe COVID-19 outcomes

Kaiser Permanente members who were physically active prior to being diagnosed with COVID-19 had a lower risk of severe outcomes. In this study, researchers analyzed the electronic health records of 194,191 adult patients at Kaiser Permanente Southern California who were diagnosed with COVID-19 between January 2020 and May 2021, before widespread COVID-19 vaccination. The study showed an association between physical activity and improved COVID-19 outcomes across major demographic groups, regardless of whether patients had chronic medical conditions. While Black, Hispanic, and Asian patients had a greater risk of adverse outcomes compared with white patients, exercise was still associated with less severe COVID-19 outcomes in every racial and ethnic group.

Young, D et al. Amer J Prev Medicine. 2023;64(4):492-502. Epub in 2022.

Public policy can improve pandemic masking adherence

A yearlong study of mask adherence and social distancing among more than 100,000 people in 126 U.S. cities found that people were 3 times more likely to wear masks correctly in places where mask-wearing was mandated. This national observational study was conducted from September 2020 through August 2021. It found that 48% of people in public spaces wore masks correctly, with the highest adherence among females, teens, and seniors. The lowest adherence was among white people, people who were engaged in vigorous exercise, and people in large groups. The study concluded that city, county, and state leaders can influence whether people wear masks.

Cohen D et al. Am J Infect Control. 2023;64(3):326-333. Epub in 2022.

COVID-19 during pregnancy may increase risks for newborn adverse outcomes

This study found that babies born to mothers who had COVID-19 during pregnancy had higher rates of heart issues, preterm births, and congenital abnormalities. Prior studies have demonstrated that COVID-19 patients are at an increased risk for physiological and psychological stress that may impact pregnancy outcomes. This retrospective cohort study of women who delivered at Kaiser Permanente Southern California hospitals from April 2020 to February 2021 showed that the chance of specific adverse outcomes was greater when a mother was infected earlier in pregnancy and the likelihood of vertical transmission from the mother to the fetus was low (0.3%). The findings suggested that pregnancy complications resulting from SARS-CoV-2 infection posed more risk to the baby than transplacental viral transmission.

Getahun D et al. Am J Perinatol. 2022;Jun 23. Epub ahead of print.

Child abuse–related emergency department visits increased after pandemic lockdown

The rate of emergency department visits for child abuse or neglect doubled immediately after the March 2020 stay-at-home order began. The increase was highest among younger children, girls, and children who were Black or Hispanic. Through September 2021, visits slowly decreased to pre-lockdown rates. Researchers noted that typically teachers are one of the most frequent reporters of suspected child abuse, but because school was virtual during the lockdown, this didn't happen. This study showed that overlapping systems of care for children are needed during a community health crisis. This was the first study of its kind to examine potential disparities in child abuse risk by race, age, and gender.

Negriff S et al. Child Abuse & Neglect. 2022;132:105821.

Omicron variant infections less severe than delta

When both the SARS-CoV-2 delta and omicron variants were circulating in December 2021, patients with omicron had substantially lower risk of severe illness and shorter hospital stays than those with delta. In this study, researchers sought to understand whether new COVID-19 variants differ in severity or susceptibility to vaccine-derived immunity to help inform public health approaches. The primary aim was to understand how the omicron variant affected the severity of illness. Patients infected with omicron were 41% less likely to be admitted to the hospital and had a 25% shorter stay than those infected with delta. The study showed that changes in variant distributions can affect health and health care.

Lewnard J. et al. Nat. Med.2022;28:1933-1943.

Down syndrome linked to higher risk of severe COVID-19

The first large study of Down syndrome and COVID-19 found that before the vaccines became available, people with Down syndrome were less likely to be diagnosed with the virus. The study determined that people with Down syndrome faced a 6-times-higher risk of being hospitalized due to COVID-19, and an even higher risk of dying from the disease, compared to those without Down syndrome. These results highlighted the need to pay particular attention to prevention, monitoring, and prompt treatment of COVID-19 in patients with Down syndrome, along with promoting vaccination.

Ku J et al. J Infect Dis. 2022;226(5):757-765.

Health equity

Comparative safety and effectiveness of bariatric surgery across racial and ethnic groups

This large retrospective study offered insight into comparative differences in weight loss, diabetes outcomes, and safety for the 2 most common bariatric operations in the United States across different racial and ethnic groups, some of whom suffer disproportionately from the burden of severe obesity. The research looked at a diverse cohort of over 36,000 adult bariatric surgery patients (43% of whom were Black or Hispanic) in the National Patient-Centered Clinical Research Network (PCORnet). At 1, 3, and 5 years, weight loss and reductions in hemoglobin A1C were larger for Roux-en-Y gastric bypass (RYGB) than sleeve gastrectomy (SG) in all racial and ethnic groups. The magnitude of these differences was small among races and ethnicities. However, Black and Hispanic patients who had RYGB had more safety concerns when compared to SG. These findings can inform shared decision-making for diverse patients choosing between bariatric operations.

Coleman K et al. JAMA Surg. 2022;157(10): 897-906.

Barriers and facilitators to use of PrEP among transgender and gender-diverse adults

Transgender and gender-diverse individuals experience health disparities, including a higher prevalence of HIV. This study underscored the low use of pre-exposure prophylaxis medication (PrEP) to reduce HIV risk among transgender and gender-diverse individuals, despite prevalent HIV risk factors. Earlier limited studies in this vulnerable population reported barriers to PrEP uptake such as stigma, cost, concern about side effects and drug interactions, and mistrust of health care systems. Researchers on this study identified barriers to PrEP use and care retention at the patient, provider, and health system levels, which can be addressed by training and supporting providers, increasing PrEP awareness among transgender and gender-diverse individuals, and streamlining PrEP care in primary care.

Bruxvoort K et al. AIDS Behav. 2023;1-13. Epub in 2022.

Vaccine safety and effectiveness

COVID-19 boosters shown to be effective for adolescents

Teens who received 3 doses of the Pfizer–BioNTech COVID-19 vaccine were better protected against infection than those who received 2. The study of more than 3,000 Kaiser Permanente members ages 12 to 17 underscored the importance of boosters for teens and helped doctors better understand vaccine protection for this age group. Before this study published in August 2022, most vaccine studies had focused on adults, and of those that did focus on teens, few had explored the waning of effectiveness of 2 doses over time. This study revealed that 2 doses of the vaccine were 89% effective against delta infection and 73% effective against omicron within the first 2 months after vaccination. However, by 6 months and later, effectiveness had waned to 49% for delta and 16% for omicron.

Tartof S et al. JAMA Netw Open. 2022;5(8):e2225162.

COVID-19 vaccine protection against hospitalization wanes for the most vulnerable

A Pfizer–BioNTech COVID-19 booster provided strong protection against hospital admissions and emergency department visits caused by the delta and omicron variants. But this protection waned over time for immunocompromised people who were infected with omicron, even after a third dose. The study focused on patient records between December 2021 and March 2022, when the delta and omicron variants were circulating. The study showed that the Pfizer COVID-19 protection levels against omicron after 3 doses were much higher than those seen after 2 doses, although they were less than those observed for delta or other COVID-19 strains at the time. Further, people who were immunocompromised appeared at greatest risk of waning immunity.

Tartof S. The Lancet Respir Med. 2022;10(7):e61-e62.

3 doses of Pfizer-BioNTech COVID vaccine better than 2

Three doses of the Pfizer-BioNTech COVID-19 vaccine were more effective in preventing infection and hospitalization after 1 month than 2 doses. This study assessed the effectiveness of 2 vaccinations against infection, hospitalization, and death for up to 8 months, and the effectiveness of 3 doses for up to 3 months. Researchers evaluated electronic health records of 3.1 million Kaiser Permanente members in Southern California from December 2020 to December 2021 during the delta variant outbreak. The results underscored previous studies that showed meaningful improvement in vaccine effectiveness against a broad range of SARS-CoV-2 outcomes with 3 doses.

Tartof S et al. Lancet Reg Health Am. 2022;9:100198.

Shoulder pain rare after vaccination

There have been reports of shoulder pain and injury following upper-arm intramuscular vaccination. In a study of 3.7 million vaccinations given from April 2016 to December 2017, Kaiser Permanente Southern California researchers found that the incidence of shoulder injuries is less than 1 in 10,000 vaccinations. The risk was much lower in

the pediatric population (5 in 1 million). Older adults, women, people who had multiple outpatient visits in the 6 months before vaccination, people with comorbidities, and people receiving the pneumococcal conjugate vaccine were the most at risk for shoulder injuries. The most likely cause is needle overpenetration–induced immune-mediated inflammation.

Zheng C et al. Ann Intern Med. 2022;175(5):634-643.

3 doses of Moderna COVID-19 vaccine highly effective against hospitalization from omicron or delta

Moderna COVID-19 vaccine protection was strong against coronavirus infection by the delta variant, but not as strong against infection from the omicron variant. Researchers determined that 3 doses of the Moderna COVID-19 vaccine were highly effective against hospitalization caused by infection from either omicron or delta. The monthlong December 2021 study included 26,683 patients who tested positive for COVID-19, 16% of whom had delta infections and 84% of whom had omicron infections. Results suggested that third doses may be needed sooner than 6 months after the second vaccine dose to protect against omicron infection.

Tseng HF et al. Nat Med. 2022;28:1063-1071.

Substance abuse

Prescription guidelines help decrease opioid use

Implementing evidence-based clinician interventions and adopting national guidelines in health care systems can lead to sustained decline in chronic and high-dose prescription opioid use. Researchers evaluated trends in opioid use following implementation of national guidelines in 2016 (and Kaiser Permanente Southern California's own system-wide Safe and Appropriate Opioid Prescribing Program in 2010). Researchers reviewed the medical and pharmacy records of more than 88,500 Kaiser Permanente Southern California adult members between 2013 and 2020 for the study. They concluded that the implementation of guidelines led to a decrease in both prevalent and incident chronic use (i.e., taking opioids daily for 90 days or more). There was also a decreasing trend in people consistently having a daily dose ≥50 morphine milligram equivalent (MME) for 183 days or more, especially those with a daily dosage ≥90 MME and concurrent use of benzodiazepines.

Hechter R et al. Am J Prev Med. 2022;64(2):167-174.

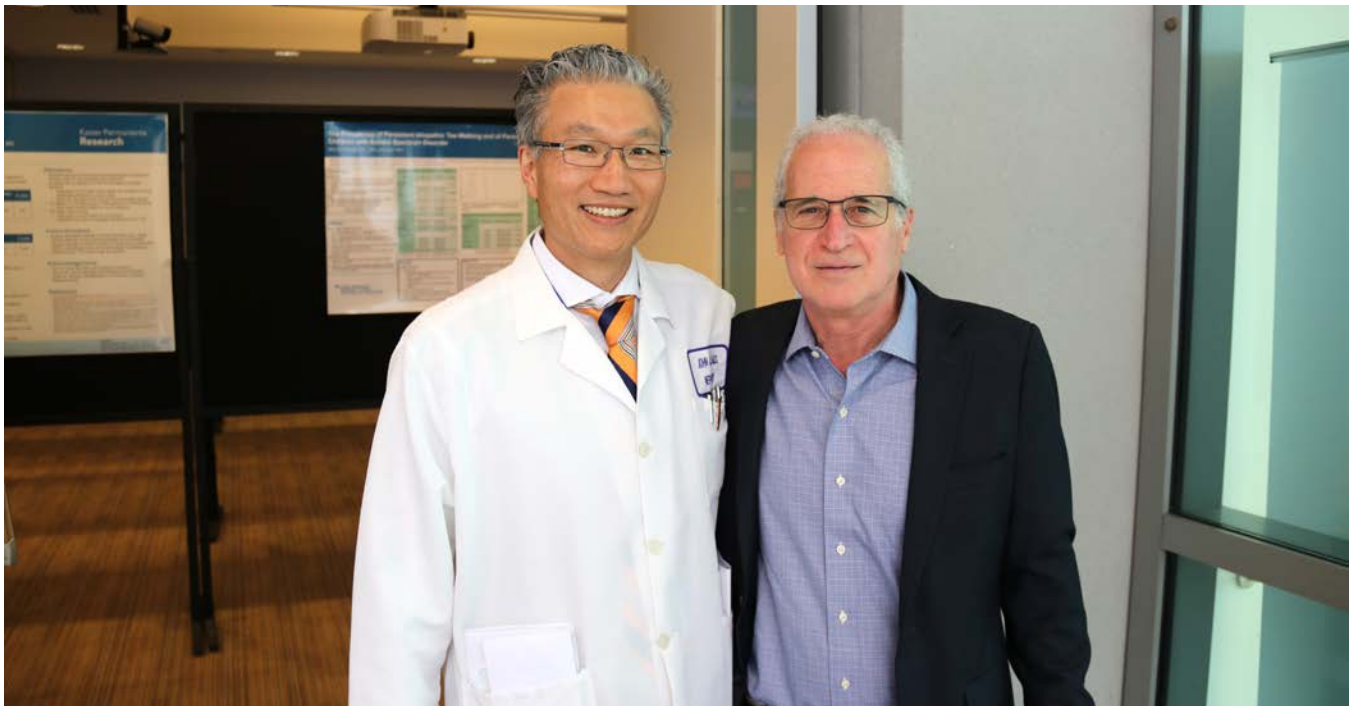
Alerts may improve safety in opioid prescribing

On-screen prompts for providers support safe prescribing habits that can mitigate opioid overdose risk and death. In 2018, California passed a bill that mandated the opioid overdose reversal drug naloxone be prescribed alongside opioids for patients at high risk for overdose. Researchers evaluated the impact of the law and found that decision support tools decreased long-term, high-dose opioid prescriptions, and increased orders for naloxone. Researchers suggested that behavioral interventions and strategic tools can facilitate compliance with public health policies and improve patient outcomes.

Duan L et al. JAMA Netw Open. 2022;5(5):e229723.

Selected grants and contracts

Our scientists and clinician researchers lead studies that have the potential to change practice well beyond the walls of our clinics and hospitals. Many studies receive external funding from federal agencies, nongovernmental organizations, and industry sponsors. The following is a selection of new 2022 awards for federal- and state-funded projects led by Kaiser Permanente Southern California investigators.



Multilevel intervention strategies to transform kidney care and improve pursuit of transplant in an integrated health care delivery system

Chronic kidney disease affects 15% of the total U.S. population. Patients whose kidneys fail have better outcomes if they receive a kidney transplant than if they remain on dialysis. This study will refine and tailor a multilevel intervention to improve care for patients with chronic and end-stage kidney disease, conduct a stepped-wedge cluster randomized controlled trial of the intervention within KPSC, and examine the heterogeneity of treatment effects to guide further improvements. Researchers will develop tools and resources to help spread implementation of the intervention, with the aim of improving care inside and outside of the Kaiser Permanente system.

Principal investigators: Brian S. Mittman, PhD, and Amy D. Waterman, PhD, FAST (Houston Methodist)

Funding agency: Agency for Healthcare Research and Quality

Using a virtual screening and care program to increase access to treatment for urinary incontinence in women

Nearly 50% of adult women experience urinary incontinence, or accidental leaking of urine, with prevalence increasing with age. Although nonsurgical treatments are available, most women do not receive treatment, and many clinicians do not screen for urinary incontinence symptoms. This project will implement a text message- and computer-based self-care screening and care program with a goal of increasing recognition and treatment of urinary incontinence for women who are 60 or older and are from diverse racial and ethnic backgrounds. The project will leverage KPSC's innovative online Personal Action Plan and bidirectional text messaging capabilities to deliver care to tens of thousands of patients whose symptoms would likely go undetected and untreated.

Principal investigators: Brian S. Mittman, PhD, and Shawn A. Menefee, MD

Funding agency: Patient-Centered Outcomes Research Institute

New risk models for diabetes complications using electronic health records

Diabetes outcome prediction and simulation models can predict a person's risk for diabetes complications and death. However, many existing models rely on a study conducted in the United Kingdom that included mostly white British citizens. Capitalizing on data from Kaiser Permanente's vast electronic health records and legacy systems in Southern California, researchers have identified more than 500,000 patients with incident diabetes who were diagnosed and treated in KPSC from 1993 to 2020. The cohort includes a much more diverse population (34.5% Hispanic, 12.7% African American or Black, and 10.6% Asian). Using this data to update risk equations will allow researchers to identify disparities in diabetes and improve prediction of diabetes outcomes for diverse population groups. Findings from this study will help to update existing models and support more timely and equitable clinical decision support and patient education.

Principal investigator: Claudia Nau, PhD

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

Childhood maltreatment and disease risk in young adulthood: The role of HPA regulation in adolescence

Child maltreatment has a pervasive effect on short- and long-term physical and mental health. Delineating the pathways through which maltreatment contributes to the risk of disease and identifying opportunities for prevention is critical to improving health and mortality in this vulnerable population. This study will examine the role of the hypothalamic-pituitary-adrenal (HPA) – a major neuroendocrine system that controls reactions to stress – in the transmission of maltreatment experiences into disease. Findings will provide new evidence as to whether recalibration of the HPA axis during adolescence can mitigate the effects of early trauma on disease risk, informing intervention efforts.

Principal investigator: Sonya Negriff, PhD

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

A risk-varying and perturbed self-controlled case series design for assessing the safety of COVID-19 vaccines in a large health care system

Robust evaluation of vaccine safety is central to public confidence in COVID-19 vaccination, a vital tool in ending the pandemic. Rigorous safety monitoring may help address vaccine hesitancy, but there are multiple methodologic challenges such as multi-dose administration, unknown risk intervals for novel vaccines, potential overlapping risk intervals, and the impact of prior adverse events on subsequent vaccination. KPSC researchers will develop innovative approaches to detect serious adverse events that may occur after vaccination. They will apply the new approaches to existing data within KPSC to evaluate vaccine safety. By applying these approaches to a large racially and socioeconomically diverse population, researchers may identify rare adverse events that were not detected in clinical trials. Findings from this study will provide important information about the safety of COVID-19 vaccines to the public and policymakers and may help clinicians deliver appropriate care to those who may be at risk for serious adverse events.

Principal investigator: Stanley Xu, PhD, MS

Funding agency: National Institute of Allergy and Infectious Diseases

Improving the detection of hypertension and its control

Blood pressure measured in the office is used to diagnose hypertension and guide blood pressure management for adults taking antihypertensive medication. Guidelines recommend using ambulatory or home blood pressure monitoring to confirm blood pressure taken in the office across multiple visits. But the evidence supporting this recommendation is weak. This study will compare 3 approaches for measuring blood pressure, including measurements taken in the office setting over 3 visits; measurements using a device that measures blood pressure every 30 minutes over a 24-hour period; and self-measurement at home by the participant over the course of a week. Findings will determine the best approach to diagnosing and managing hypertension, which has the potential to improve health for millions of adults in the United States.

Principal investigators: Kristi Reynolds, PhD, MPH; Daichi Shimbo, MD (Columbia University); and Paul Muntner, PhD (University of Alabama at Birmingham)

Funding agency: National Heart, Lung, and Blood Institute

Influence of comorbidities on survival disparities in women with metastatic breast cancer

Breast cancer mortality rates have been declining over time, but improvements have not been equally realized across racial and ethnic groups. The extent to which common comorbidities may influence mortality or contribute to racial and ethnic disparities in survival is unknown. This study will evaluate the influence of comorbidities on mortality risk and examine whether disparities in mortality can be mitigated by better management of common comorbidities. Findings will help fill a critical gap in knowledge about the role of comorbidities in influencing mortality risk among women with metastatic breast cancer and clarify whether better management of comorbidities may reduce disparities in survival.

Principal investigator: Reina Haque, PhD, MPH

Funding agency: California Breast Cancer Research Program

Vaccine Safety Datalink

The Vaccine Safety Datalink is a partnership between the Centers for Disease Control and Prevention's Immunization Safety Office and integrated health care organizations across the country. KPSC has been a fully participating study site for the VSD for the past 15 years. This award, which extends from September 2022 through 2027, will support planned immunization safety studies as well as timely investigations of hypotheses that arise from review of medical literature, reports to the Vaccine Adverse Event Reporting System (VAERS), changes in immunization schedules, or the introduction of new vaccines. The CDC also funds essential infrastructure activities of the VSD site at KPSC. This infrastructure allows investigators to react quickly to evolving needs for vaccine safety research.

Principal investigator: Hung Fu Tseng, PhD, MPH

Funding agency: Centers for Disease Control and Prevention

Selected clinical trials

In 2022, the Kaiser Permanente Southern California clinical trials program supported more than 350 protocols across 30 therapeutic areas. Participation in these pivotal clinical trials keeps Kaiser Permanente at the leading edge of medicine. It also supports access for Kaiser Permanente members to participate in groundbreaking trials for investigational drugs, devices, and vaccines.

KPSC remains a top enroller in many important clinical trials, including those for stroke, cardiac devices, and cancer treatments, and has been recognized for its success in enrolling ethnically diverse study participants. The program continued to open new trials in 2022 to advance prevention and treatment of many different conditions, from macular degeneration to mpox.

Clinical trials at KPSC receive funding from industry sponsors, foundations, research networks, and federal agencies. In 2022, federal funding sources included the National Cancer Institute, the National Institute for Allergy and Infectious Diseases, the National Institute of Neurological Disorders and Stroke Trials Network, and the Eunice Kennedy Shriver National Institute of Child Health and Human Development, among others.

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

CANCER

Gastrointestinal oncology

Durvalumab or placebo in combination with gemcitabine/cisplatin in patients with first-line, advanced biliary tract cancer

This Phase 3 trial randomized, double-blind, placebo-controlled study evaluated the use of durvalumab, an immunotherapy, in combination with 2 chemotherapy drugs, gemcitabine and cisplatin, to treat advanced, unresectable biliary tract cancer. KPSC was a high enroller for this study, which has resulted in changes to the standard of care for patients who have this disease. KPSC investigators are co-authors for several publications on the study findings.

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

Participating locations: Baldwin Park, Downey, Los Angeles, Orange County, Riverside County, San Bernardino County, San Diego, South Bay, West Los Angeles

NCT03875235

Genitourinary oncology

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

This study examined the safety and anticancer activity of an experimental drug, enfortumab vedotin, given intravenously as a monotherapy and in combination with other anticancer therapies as first- and second-line treatments of urothelial cancer. KPSC was one of the high accrual sites. In April 2023, the U.S. Food and Drug Administration granted accelerated approval to enfortumab vedotin-ejfv with pembrolizumab for patients with locally advanced or metastatic urothelial carcinoma who are not eligible for cisplatin-containing chemotherapy.

Principal investigator: Helen Moon, MD

Participating locations: Baldwin Park, Downey, Los Angeles, Orange County, Riverside County, San Bernardino County, San Diego, South Bay, West Los Angeles

NCT03288545

Neuro-oncology

Testing the use of immunotherapy drugs ipilimumab and nivolumab plus radiation therapy compared to the usual treatment for newly diagnosed MGMT unmethylated glioblastoma

This Phase 2/3 trial compares the usual treatment (radiation therapy and temozolomide) for patients with newly diagnosed MGMT unmethylated glioblastoma to radiation therapy in combination with 2 immunotherapy drugs (ipilimumab and nivolumab). The goal is to determine whether dual checkpoint inhibitor therapy is more effective than standard of care for patients who are newly diagnosed. Kaiser Permanente was a high enroller in this study.

Principal investigator: Richard Green, MD

Participating location: Los Angeles

NCT04396860

Standard chemotherapy vs. chemotherapy guided by cancer stem cell test in recurrent glioblastoma

The purpose of this clinical study is to confirm the validity of chemosensitivity tumor testing (ChemoID) on cancer stem cells as a predictor of clinical response in poor-prognosis malignant brain tumors such as recurrent glioblastoma and recurrent World Health Organization grade III glioma. Findings from the study were published in abstract form at the 2022 annual meetings of the American Society of Clinical Oncology and the American Association for Cancer Research.

Principal investigator: Richard Green, MD

Participating location: Los Angeles

NCT03632135

Radiation Oncology

De-escalation of breast radiation trial for hormone-sensitive, HER-2 negative, oncotype recurrence score ≤ 18 breast cancer

This Phase 3 trial evaluates whether breast conservation surgery and endocrine therapy results in rate of invasive or noninvasive ipsilateral breast tumor recurrence (IBTR) that is noninferior (not worse) than breast conservation with breast radiation and endocrine therapy. This study will help determine whether de-escalating treatment for patients with low-risk, early-stage breast cancer is appropriate. If radiotherapy can be omitted, it could potentially reduce future risk of secondary malignancies, radiotherapy-associated heart disease, and cosmetic complications associated with adjuvant radiotherapy.

Principal investigator: Michael R. Girvigian, MD, DABR

Participating location: Los Angeles

NCT04852887

Cardiology

The ENCIRCLE Trial

This study will establish the safety and effectiveness of the SAPIEN M3 System – a minimally invasive transseptal mitral valve replacement therapy – in participants with mitral regurgitation for whom commercially available surgical or transcatheter treatment options are deemed unsuitable. This may be the only treatment available to patients who are high risk and are not candidates for surgical mitral valve replacement. KPSC has developed a robust screening process for the study, which remained open to enrollment through early 2023.

Principal investigator: Somjot S. Brar, MD, MPH

Participating location: Los Angeles

NCT04153292

AMPLATZER PFO Occluder post approval study

This post-approval study seeks to assess the safety and effectiveness of 2 cardiac device systems, the Amplatzer™ Talisman™ PFO Occlusion System and the Amplatzer PFO Occluder. The device systems are designed to treat people with patent foramen ovale (PFO) – a hole in the heart that doesn't seal after birth – who have had a stroke and are at risk of another. In 2022, Kaiser Permanente Los Angeles exceeded its enrollment targets, holding on to its spot as top enroller since the study launched.

Principal investigator: Somjot S. Brar, MD, MPH

Participating location: Los Angeles

NCT03309332

Infectious disease

A study of vaccination with ExPEC9V in the prevention of invasive extraintestinal pathogenic E. coli disease in adults aged 60 and older with a history of urinary tract infection in the past 2 years

This randomized, placebo-controlled, Phase 3 study will assess the efficacy, safety, and immunogenicity of vaccination with ExPEC9V in the prevention of invasive extraintestinal pathogenic E. coli disease, which is the leading cause of bloodstream infections resulting in increased hospitalizations and deaths in patients over 60. The study is part of the KPSC clinical trials program's effort to expand its vaccine portfolio, building on its success with the COVID-19 vaccine studies.

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

Participating location: Los Angeles

NCT04899336

Study of tecovirimat for human monkeypox virus

This randomized, placebo-controlled, double-blind study seeks to establish the efficacy of tecovirimat for the treatment of people with laboratory-confirmed or presumptive human mpox disease. Tecovirimat, or Tpoxx, was developed originally to treat smallpox but has never been studied in a randomized clinical trial in humans. The study, sponsored by the National Institute of Allergy and Infectious Diseases, along with the Expanded Access team's efforts to facilitate use of Tpoxx, were part of a larger effort to aid the organization when KPSC members began to experience mpox in summer 2022 (see story on page 26).

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

Participating location: Los Angeles

NCT05534984

Ophthalmology

Pivotal 2 study of RGX-314 gene therapy in participants with nAMD

This study will assess a new gene therapy, RGX-314, which is being developed as a novel one-time gene therapy for the treatment of neovascular (wet) age-related macular degeneration (nAMD).

Recent developments in gene therapy have shown some very promising therapeutic results by greatly reducing the burden of frequent injections for those with nAMD, one of the leading causes of blindness in Western society.

Principal investigator: Vivienne S. Hau, MD, PhD

Participating location: Riverside

NCT05407636

Safety and efficacy of ADVM-022 in treatment-experienced patients with neovascular age-related macular degeneration

This study will assess the safety, tolerability, and efficacy of a single intravitreal (IVT) injection of another gene therapy, ADVM-022, in patients who have had treatment with an antivascular endothelial growth factor agent for neovascular (wet) age-related macular degeneration. Current standard of care includes a burdensome regimen of IVT injections every 4 to 8 weeks, with complications and risks of increased IVT injections. ADVM-022 offers the potential for sustained treatment delivery and improved outcomes for people who face vision loss from the disease.

Principal investigator: Vivienne S. Hau, MD, PhD

Participating location: Riverside

NCT05536973

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 the following projects during 2022.

Discontinuing car seat tolerance screening: Effect on postdischarge adverse outcomes

–David Braun, MD

The American Academy of Pediatrics has recommended car seat tolerance screening (CSTS) for preterm newborns without evidence that CSTS programs improve outcomes. For this reason, the Kaiser Permanente Southern California health care system discontinued CSTS in about 2017. In this study, researchers compared outcomes of infants born in hospitals practicing CSTS to infants born in hospitals when CSTS was no longer practiced. The primary outcome was the composite frequency of death; 911 calls; readmissions for respiratory, apnea, and apparent life-threatening events; or brief, resolved, unexplained event-related diagnostic codes within 30 days of discharge. They found no statistically significant difference in the primary outcome or across related outcomes. Researchers concluded that CSTS as a standard predischarge practice needs to be reconsidered.

Retrospective regional review of risk factors for intracranial hemorrhage, morbidity, and mortality in transported preterm infants of 32 weeks gestation or less, as compared to a control group

–Kim Chi Bui, MD, FAAP

Infants born at 32 weeks gestational age or less may require transport to a tertiary level NICU after birth. Within KPSC, approximately 25% to 30% of infants born at ≤32 weeks or with a birth weight ≤1,500 grams are transported each year for a variety of reasons: tertiary care, subspecialty consultation, or lower level of care. This project sought to determine whether neonatal transport is an independent risk factor for intraventricular hemorrhage (IVH) and mortality associated with neonatal transport. They found that mortality was lower in the transported group. Morbidities and IVH rate were higher in the transported group. However, most transports (58%) occurred after 7 days of age with IVH present before transport. They were not able to reach any

conclusions about IVH risk related to transport because the diagnosis was linked to timing of head ultrasound studies, which were often obtained after transport in patients transported before 7 days of age. Researchers say their insights may help increase neonatal transport safety.

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

–Karen J. Coleman, PhD, MS

Depression will be the greatest global disease burden by 2030, disproportionately affecting Black, Hispanic, and Asian communities. This project created patient-centered approaches to depression treatment that emphasized cultural values and humility. Researchers examined if new patient-centered approaches could be implemented with minimal impact on workflows and providers. They found that clinical partners were critical to designing and implementing culturally relevant care processes with standardized materials. Researchers also determined that telehealth has some disadvantages for depression screening, symptom monitoring, and medication-related treatment. They recommend additional work to ensure that research teams are embedded in clinical teams.

Evaluating COVID-19 decision-support tools (COVAS, COVID-HDI, and COVID-IMV)

–Beth Creekmur, MA

Early in the pandemic, KPSC created 3 risk prevention models for COVID-19: the COVAS Score (Comorbidity Obesity Vital Signs Age Sex), COVID-HDI (Early Deterioration Index for Hospitalized Patients), and COVID-IMV (COVID Invasive Mechanical Ventilation). This project aimed to evaluate utilization and validate performance using noncontemporaneous data. Researchers found that penetration of the COVID-HDI and COVID-IMV models was limited across regional medical centers. Where the COVAS and COVID-HDI models were used, the trends aligned with COVID-19 surges. Models performed better after launch than during the initial development phase because of improvements made during implementation. Researchers said that providers can be confident in using these 3 models for decision support and resource allocation as COVID-19 challenges continue.

Enhanced implementation of lung cancer screening

–Michael K. Gould, MD, MS

Low-dose computed tomography (LDCT) screening has been shown to reduce lung cancer mortality by at least 20% in high-risk smokers, but a variety of factors have hindered uptake in the target population. This project aims to improve screening of people within KPSC who smoke or previously smoked. The project team introduced several interventions in 2022 to reduce inappropriate screening and provide educational decision aids to patients. However, screening remained suboptimal, and inappropriate screening continued to be problematic. Additional interventions, including centralization of core functions supporting lung cancer screening, may be necessary to meet goals. Researchers will continue to monitor progress in 2023.

Prevention of venous thromboembolism in abdominal cancer surgery

–Michael K. Gould, MD, MS

Venous thromboembolism (VTE) is a frequent and potentially serious but preventable complication following major abdominal surgery for cancer. This study evaluated the effect of interventions to increase extended duration thromboprophylaxis in patients discharged after high-risk abdominal cancer surgery. Interventions included informal provider notification and education and implementation of a

new standardized discharge order set to increase the use of postdischarge prophylaxis. As of late 2022, the study found a 65% improvement in the use of postdischarge prophylaxis with no observable effect on the frequency of perioperative VTE or bleeding. Researchers plan to continue monitoring and measuring outcomes through June 2023.

Implementing systemic depression screening in medical oncology

—Erin E. Hahn, PhD, MPH

Depression screening in oncology is recommended by the American Society of Clinical Oncology and others. This implementation study drew on strategies developed in an earlier cluster-randomized pragmatic trial to introduce depression screening at medical oncology departments across all 15 KPSC medical centers. By the end of 2022, more than 11,000 members diagnosed with cancer had been screened for depression. Of those, 16% scored in the range requiring referral, and 60% were referred to behavioral health care within 10 days. Nearly 80% of those with moderate or high scores had not previously been seen in behavioral health. Researchers noted that sustaining this screening program is dependent on local resources and requires ongoing support and training.

Next-generation sequencing to inform clinical decision-making for non-small cell lung cancer treatment in a large integrated health care delivery system

—Reina Haque, PhD, MPH, and Eric McGary, MD, PhD, MPH

Next-generation sequencing (NGS) of lung cancer can identify mutations and match them with an FDA-approved targeted therapy, improving efficacy of treatment. KPSC implemented NGS testing of tumor tissue for patients diagnosed with non-small cell lung cancer in 2019. Researchers evaluated the quality and timeliness of NGS results obtained from an outside vendor and examined how clinicians utilized results to guide first-line treatment decisions. They found the average time for NGS results was 25 days. Clinicians began treatment in 52% of patients before receiving results; 29% were subsequently found to have a targetable mutation on NGS. Based on these findings, the KPSC Cancer Care Program is taking steps to accelerate the turnaround time for NGS results, including implementing NGS testing from blood.

Medication initiated at discharge to reduce readmission and mortality in heart failure (MIDTERM-HF)

—Cheng-Wei "Charlie" Huang, MD

Guideline-directed medical therapy (GDMT) and other interventions have been shown to improve outcomes for patients with heart failure but have also been reported to be underutilized. This study sought to identify potential care gaps in coronary artery disease (CAD) testing and initiation of GDMT medications. Researchers found multiple factors associated with CAD testing, suggesting that testing reflected clinical decision-making and goals of care. They concluded that a push for increased testing may not be warranted in KPSC. They also found no benefit to simultaneous or rapid sequence initiation of mineralocorticoid receptor antagonists (MRA) in addition to beta blockers and renin angiotensin system inhibitors during acute heart failure hospitalization in terms of postdischarge outcomes. They recommended that initiation of MRA during hospitalization and/or at discharge may be safely deferred until the outpatient setting when there is concern with its initiation during hospitalization.

Endoscopy first versus surgery first: An analysis of organ-sparing tissue resection techniques across the gastrointestinal tract versus comparative surgery in an integrated health care organization

–Karl Kwok, MD

Historically, large polyps and early cancers in the esophagus, gastrointestinal system, or colon have been treated surgically. While effective, surgeries have high morbidity and drive high health care utilization. This study assessed the impact of an "endoscopy first" approach. It compared clinical outcomes and 5-year mortality of patients who underwent organ-preserving endoscopic mucosal resection (EMR) versus traditional surgery. It also compared health care utilization, including emergency visits, operating room use, and days in the hospital. EMR saved nearly 6 days in the hospital. Procedures were 3 times faster, and fewer units of blood were transfused. No operating rooms were used, freeing up space for other surgeries. Results from this timely study may be used to help create a standardized referral policy.

ASCVD safety program: Statin initiation and follow-up of lipid panels among patients with high LDL-C

–Matthew T. Mefford, PhD

Statins are effective at lowering high low-density lipoprotein-cholesterol (LDL-C) and reducing cardiovascular risk but remain underutilized. This study evaluated a patient safety net program (KP SureNet) that facilitates high-intensity statin orders and lipid panel orders to determine if the program improved rates of statin initiation and lab completions. The study compared patients before and after SureNet implementation. Researchers found that eligible adults had a higher likelihood of receiving and filling their prescription, completing their lipid panel; and improving their LDL-C after SureNet implementation (36%, 32%, 41%, and 21%, respectively). Researchers concluded that the SureNet program was effective and recommended expanding its eligibility and providing patient reminders to maximize the impact of this successful program.

Development of an equitable COVID-19-compatible risk stratification tool to support reporting and planning of specialty palliative care services

–Claudia Nau, PhD

Models to identify patients in need of specialty palliative care (SPC) can support timely referrals and staff planning, but existing models lacked sensitivity, had not been assessed for statistical fairness, and had not accounted for COVID-19. Researchers collaborated with KPSC's palliative care leadership to build a high-performing, statistically fair risk model that addressed these issues. The tool improved sensitivity by 30% to 50% compared with other models while maintaining comparable positive predictive values of approximately 30%. Researchers also used natural language processing to identify seriously ill patients who were homeless or at risk of homelessness. They found emergency visits were 4 times higher in this high-risk population. As of the end of 2022, options to fund implementation of the new risk model were being explored.

Implementation and evaluation of an enhanced adverse childhood experiences (ACES) screening and referral system in pediatric primary care

–Sonya Negriff, PhD

There is a clear link between adverse childhood experiences (ACEs) and poor physical and mental health outcomes over a person's life span. In California, screening in pediatric primary care is recommended to combat these negative sequalae. This study examined the impact of ACEs screening on the rate of referrals and visits to social work and behavioral health. Researchers found a small but not statistically significant increase in rates of visits to social work and behavioral health providers after ACEs screening was implemented in 28 clinics. Researchers noted that this increase was manageable, indicating that there should not be a large influx of patients after instituting screening. Findings supported a continuation of the regional rollout.

Improving care transitions and reducing readmissions: Impact of posthospitalization home-delivered meals for Medicare members

–Huong Q. Nguyen, PhD, RN

Reducing avoidable readmission without causing patient harm is a high priority for KPSC. This study evaluated a Medicare 4-week, posthospitalization, home-delivered meal benefit introduced in 2021. Researchers examined uptake and satisfaction with meals as well as readmission rates. Half of referred members accepted the meals, with more than two-thirds reporting high satisfaction. Patients experiencing financial strain or food insecurity were more likely to accept and be satisfied with the meals. Meal recipients had lower odds of 30- and 60-day readmission and mortality, but the effects were attenuated in patients admitted for heart failure compared with other medical conditions. Researchers recommended continuing to optimize the meals benefit to accrue larger sample sizes, and to repeat analyses in 2023.

Prevalence, trend, care delivery, and disparity in mental health conditions in children, adolescents, and young adults among KPSC members

–Anny H. Xiang, PhD, MS

As rates of childhood depression rise, it is critical for health care providers to identify children currently in need. This study assessed the prevalence, incidence, and trend of depression and anxiety in children, teens, and young adults up to age 22 within KPSC. Preliminary data showed that both the prevalence and incidence of depression and anxiety increased substantially between 2017 and 2021. Rates of depression were higher among adolescents, with a steeper increase in girls. Those affected by obesity, overweight, or underweight also had higher rates of depression. Researchers will continue the study in 2023 and examine clinical care trajectories, screening rates, adherence to follow-up, and potential disparities.

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

–Hui Xue, MD, MMSc

Cardiovascular morbidity and mortality rates are 10 to 30 times higher for patients receiving hemodialysis. Intradialytic hypotension (IDH) occurs in 20% to 40% of dialysis treatments, potentially impairing perfusion in major organs. Cooling dialysate – the fluid used during dialysis – to less than 36.5 degrees Celsius has been used to reduce IDH in the outpatient treatment for decades. But the effect is unknown in hospitalized patients, who experience IDH more frequently. This study randomized 8 hospitals at KPSC to use dialysate at different temperatures for 3 months; then each hospital serves as its own control for months 4 through 6 using a different temperature. Researchers will analyze the impact of temperature on IDH and evaluate morbidity and mortality rates. Findings from this study could potentially change the practice of inpatient hemodialysis if lower temperatures are found to be protective.

Investigating disparities in telephone and video appointment visits among patients with chronic kidney disease

–Hui Zhou, PhD, MS

Regular follow-up visits play a critical role in preventing progression of chronic kidney disease (CKD) and related medical complications. As a trend toward telehealth visits, including telephone appointment visits (TAVs) and video appointment visits (VAVs) as alternatives to in-person visits, accelerated during the pandemic, researchers sought to identify barriers to successful telehealth visits as well as potential differences in health outcomes for patients with CKD. About 74% of patients with CKD had at least one successful TAV/VAV during the study period. Patients who spoke a language other than English or who were older, Asian, or male had lower success rates. Those with Medicaid coverage or kp.org access had higher success rates. The study identified no significant neighborhood, socioeconomic, or technology barriers to telehealth. Patients who had telehealth and no in-person visits had higher rates of non-COVID-related death or hospitalization, major cardiovascular events, and CKD progression. Findings can be used to improve outreach and promote more successful telehealth visits, especially among seniors and non-English speakers. They added that enhanced follow-up may be needed to achieve telehealth care as efficient as in-person care.

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 2022, the committee awarded funds to the following studies.

Traditional grant studies

Dermatology

Health disparities in melanoma patients: Understanding the influence of comorbidities on survival among our poorest patient populations

Principal investigator: Christina Kim, MD
Los Angeles

Outcomes of skin-directed and systemic therapies of mycosis fungoides: A longitudinal, retrospective analysis from an integrated health care system

Principal investigator: Riana Sanyal, MD, MSc (resident)
Los Angeles

General Surgery

The impact of COVID-19 on appendicitis and cholecystitis management

Principal investigator: Janice Verham, 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

Internal Medicine

Occupational therapy-led intensive lifestyle intervention clinic: A retrospective observational cohort study

Principal investigator: Ramez Ethnasios, MD
West Los Angeles

Obstetrics-Gynecology

Long-term reoperation risk after augmented versus native tissue level I transvaginal prolapse repair

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

Referral and treatment for stress urinary incontinence stratified by race and ethnicity

Principal investigator: Brittni Boyd, MD (resident)
Orange County

Ophthalmology

Disparities in cataract surgery prior to and during the era of COVID

Principal investigator: Brian Lee, MD
West Los Angeles

Prognostic socioeconomic factors in the treatment and management of rhegmatogenous retinal detachments

Principal investigator: Vivienne S. Hau, MD, PhD
Riverside

The impact on visual acuity and macular thickness when patients return to intravitreal bevacizumab after being treated with intravitreal aflibercept for neovascular NAMD

Principal investigator: Amila Silva, MD
San Bernardino County

Orthopedic Surgery

Effect of adverse childhood events on outcomes following arthroscopic hip surgery

Principal investigator: Brett Shore, MD
Panorama City

Pediatrics

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

Principal investigator: Alan Cortez, MD
Orange County

Pediatric depression and suicide risk screening outcomes during COVID-19

Principal investigator: Yvonne Tsai, 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

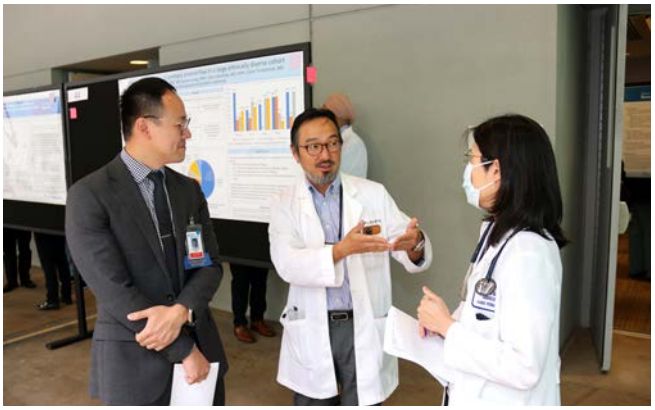
Follow-up care of patients with newly diagnosed depression after widespread implementation of telemedicine

Principal investigator: Vidush Athyal, MD, MPH, FAAFP
San Diego

Head and Neck Surgery

Assessment of "real world" management of patients with chronic rhinosinusitis: From primary care to subspecialty clinic

Principal investigator: Frederick Yoo, MD
Orange County



Nephrology

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

Principal investigator: Richard Treger, MD
Los Angeles

Pediatric oncology

Expanding our understanding of health disparities in cancer patients

Principal investigator: Robert M. Cooper, MD
Los Angeles

Pediatrics

Predictive variables associated with pediatric hospital readmissions

Principal investigator: Paul Han, MD
Los Angeles

Urology

Are there socioeconomic disparities in reconstructive surgery for pelvic organ prolapse in a managed care setting?

Principal investigator: Christopher Tenggardjaja, MD
Los Angeles

2022 Regional Research Committee

Bechien U. Wu, MD, MPH, Chair

Antelope Valley
Jonathan Truong, MD, Area Research Chair

David Bronstein, MD, MS, 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, Vice Area Research Chair

Fontana/San Bernardino
Conrad Liang, MD, PhD, Area Research Chair

Steve S. Lee, DO, Vice 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

Panorama City
Shireen Fatemi, MD, Area Research Chair

Ahmed Dehal, 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
Marco Tomassi, MD, Vice Area Research Chair

South Bay
David Cohen, MD, Area Research Chair

William W. Crawford, MD, Vice Area Research Chair

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

Daniel T. Lang, MD, Vice Area Research Chair

Woodland Hills/Ventura County
Armen Aboulian, MD, Area Research Chair

Monique George, 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

Investigators

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

In 2022, our research program included 5 scientific divisions as well as affiliated researchers (see page 65). In 2023, the department is creating a new Division of Clinician Research.

Epidemiologic Research (page 57)

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 portfolio spans the care continuum from etiology and prevention to survivorship and quality of life. 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 59)

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

Biostatistics Research (page 60)

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 61)

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 62)

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 68.

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 fractures in older adults
- Pharmacologic influences on bone health
- Atypical femoral fractures
- 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 and dementia 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 risk factors and outcomes
- Chronic disease epidemiology
- Health disparities
- Medication adherence

Sara Y. Tartof, PhD, MPH

- Infectious diseases
- Antibiotic resistance
- Vaccine effectiveness
- COVID-19

Hung Fu Tseng, PhD, MPH

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

Post-doctoral research fellows

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
- Antimicrobial treatment and resistance
- Pharmacoepidemiology

Nana Mensah, PhD, MPH

- Maternal and child health
- Fetal substance exposures
- Preterm birth

Amrita Mukherjee, PhD, MPH

- Human papillomavirus–associated cancers
- Comorbidities in cancer patients
- Risk prediction models
- Electronic health records data

Adovich Rivera, MD, PhD

- HIV
- Cardiovascular health
- Health disparities
- Sexual and gender minorities

Epidemic Intelligence Service officer

Debbie Malden, DPhil, MSc*

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

* Dr. Malden's assignment as EIS officer ended in August 2022, when she became an epidemiologist and digital surveillance consultant with R&E.

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

Deborah A. Cohen, MD, MPH

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

Corinna Koebnick, PhD, MSc

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

Claudia Nau, PhD

- Health equity and patient social needs
- Food insecurity and diabetes outcomes
- End-of-life care
- Predictive modeling and statistical fairness

Sonya Negriff, PhD

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

Post-doctoral research fellow

Titilola Labisi, PhD, MHA, MPH

- Health behaviors: sexual, diet, and physical activity
- African American health and disparities
- Community engagement interventions
- Implementation and dissemination science

Division of Biostatistics Research

Research scientists

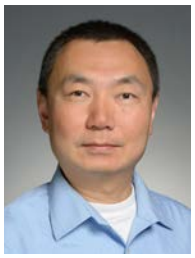
Anny H. Xiang, PhD, MS

Director

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

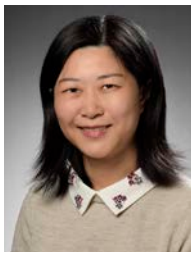
Heidi Fischer, PhD

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



Bing Han, PhD

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



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, design, and analysis
- GIS mapping and spatial analysis
- Applied statistical methodology
- Predictive modeling

Ernest Shen, PhD

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

Jeff Slezak, MS

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

Stanley Xu, PhD, MS

- Analytic methods
- Vaccine safety
- Pharmacoepidemiology
- Overdose prevention

Hui Zhou, PhD, MS

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

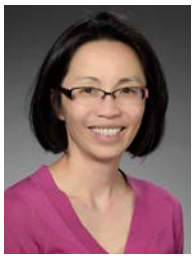
Post-doctoral research fellow

Sarah Carter, DPhil, MA

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

Division of Health Services Research & Implementation Science

Research scientists



Huong Q. Nguyen, PhD, RN

Interim Director

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

Karen J. Coleman, PhD, MS

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

David Glass, PhD*

- COVID long-haulers
- Primary care sustainability
- End-of-life values and quality performance
- Global health

* Dr. Glass passed away in early 2023. See memoriam on page 70.

Erin E. Hahn, PhD, MPH

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

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

Post-doctoral research fellow

Lewei Duan, PhD, MS*

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

* Dr. Duan left Kaiser Permanente in 2022.

Division of Clinical Trials Research

Portfolio principal investigators

William Towner, MD, FACP, FIDSA

Physician Director

- HIV therapeutics
- Infectious disease
- Vaccine safety and effectiveness

Zahra A. Ajani, MD

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

Ashraf R. Aziz, MD

- Medical oncology
- Hematology

Somjot S. Brar, MD, MPH

- Cardiovascular disease
- Medical devices and interventional procedures
- Cardiac catheterization
- Cardiac electrophysiology

Harsimran S. Brara, MD, FAANS

- Neurosurgery
- Stroke treatment and prevention
- Spine surgery

Gary L. Buchschacher Jr., MD, PhD

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

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
- Hematology

Kimberly Ferrante, MD, MAS

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

Michael R. Girvigian, MD, DABR

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

Richard Green, MD

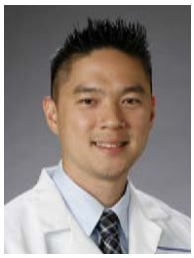
- Neuro-oncology
- Glioblastoma
- Central nervous system malignancies
- Primary CNS lymphoma

Nigel Gupta, MD

- Clinical cardiac electrophysiology
- Cardiac implantable electronic devices and catheter ablation
- Left atrial appendage occluder closures
- Atrial fibrillation treatments

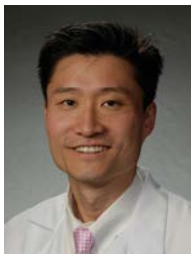
Vivienne S. Hau, MD, PhD

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



Kevin T. Kao, MD

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

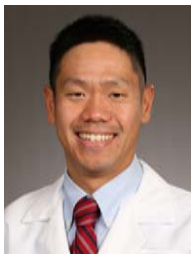


Steve S. Lee, DO

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

Scott E. Lentz, MD, FACS

- Gynecologic oncology
- Hereditary cancer syndromes
- Surgical innovation



Conrad Liang, MD, PhD

- Stroke and interventional neurology
- Medical devices and interventional procedures

Eric McGary, MD, PhD, MPH

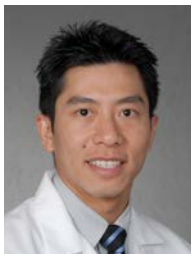
- Medical oncology
- Lung cancer
- Real-world data and real-world evidence-based research
- Precision medicine and molecular diagnostic platforms in oncology

Shawn A. Menefee, MD

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

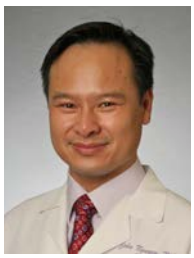
Helen Moon, MD

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



Andrew Nguyen, MD

- Systemic lupus erythematosus
- Giant cell arteritis
- Psoriatic arthritis
- Rheumatoid arthritis
- Osteoarthritis



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
- Liver transplant
- Biliary cholangitis and cirrhosis
- Overt hepatic encephalopathy
- Alpha-1 antitrypsin deficiency

Portfolio principal investigators

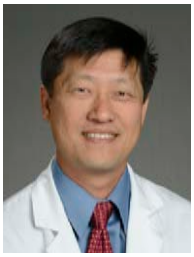
Kapil M. Sampat, DO
- Retinal disease
- Retina vitreous surgery

Jonathan Truong, MD
- Infectious disease
- Valley fever

Navdeep Sangha, MD
- Vascular neurology
- Ischemic stroke and intracerebral hemorrhage
- Hospital systems of care

Divya Vats, MD
- Rare diseases
- Gaucher disease
- Phenylketonuria (PKU)
- Fabry disease
- Pompe disease

John J. Sim, MD
- Glomerular diseases
- Polycystic disease
- Chronic kidney disease epidemiology and outcomes



Kenneth Wei, MD
- Pulmonary diseases
- Early lung cancer detection
- Pulmonary atrial hypertension
- Acute respiratory distress syndrome (ARDS)

Ricardo T. Spielberger, MD
- Hematopoietic cell transplant
- Transplant side effects
- Opportunistic infections

Abel Wu, MD
- Neuromuscular disorders
- Amyotrophic lateral sclerosis (ALS)
- Muscular dystrophy

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 and associate investigators

David Braun, MD

- Degree and effects of regionalized perinatal care
- Factors influencing NICU admission and length of stay
- Evaluation of NICU quality improvement initiatives

Michael Kanter, MD

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

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

- Multiple sclerosis susceptibility, prognosis, and treatment
- Comparative effectiveness and safety of treatments
- Alzheimer's disease care models
- Racial and ethnic disparities in MS

Anders Nyberg, MD, PhD*

- Hepatology risk and treatment
- Hepatology clinical trials

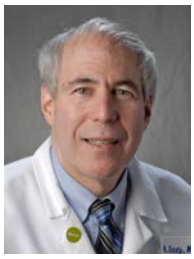
* Dr. Nyberg passed away in early 2023. See memoriam on page 71.

Lisa Nyberg, MD, MPH

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

David A. Sacks, MD

- 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

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

Katia Bruxvoort, PhD, MPH

- Infectious diseases
- Vaccine uptake, safety, and effectiveness
- HIV prevention
- Malaria

Kristen Choi, PhD, MS, RN

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

Michael K. Gould, MD, MS

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

Paul Muntner, PhD

- Hypertension
- Lipids
- Cardiovascular disease
- Kidney disease
- Epidemiology methods

Adam L. Sharp, MD, MSc

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

Clinician investigators

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 ehealth
- Artificial intelligence/machine learning

Chileshe Nkonde-Price, MD, MS, FACC

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

Chunyuan Qiu, MD, MS

- Anesthesiology
- Pain medicine
- Perioperative medicine

Previous appointments

Raymond Chen, MD, DPhil (2016–2018)

Kimberly Ferrante, MD, MAS (2019–2021)

Dennis Hwang, MD (2019–2021)

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

Bone Marrow Transplant

Ricardo T. Spielberger, MD, Los Angeles Medical Center

Cardiology

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

Jeffrey Cavendish, MD, San Diego Medical Center

Nigel Gupta, MD, Los Angeles Medical Center

Jonathan Neyer, MD, Los Angeles Medical Center

COVID-19

Adam Schwartz, MD, MS, San Diego Medical Center

Dermatology

Kim Chong, MD, Los Angeles Medical Center

Gastroenterology

Gareth S. Dulai, MD, Downey Medical Center

Kevin T. Kao, MD, Downey 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 Sim, MD, Los Angeles Medical Center

Hui Xue, MD, MMSc, San Diego Medical Center

Neurology

Zahra 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

Scott E. Lentz, MD, FACS, Los Angeles Medical Center

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

Head and Neck Surgery

Rohit Garg, MD, MBA, Anaheim Medical Center

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

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

Elisabeth McLemore, MD, FACS, 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 I. Kessler, MD, Los Angeles Medical Center

Pediatric Oncology

Robert M. Cooper, 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

Rheumatology

Steve S. Lee, DO, Fontana 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

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

John N. Nguyen, MD, Downey Medical Center

Christopher Tenggardjaja, MD, Los Angeles Medical Center

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

Vascular Surgery

Catherine Chang, MD, San Diego Medical Center

Linda Chun, MD, Los Angeles Medical Center

Edward Plecha, MD, San Diego Medical Center

IN MEMORIAM

David Glass, PhD

Dr. David Glass, a research scientist in the Division of Health Services Research, passed away on March 2, 2023.

He made many contributions to Kaiser Permanente over his career of 33 years, almost 12 of which were with the Department of Research & Evaluation. As an operational research scientist, he worked closely with senior leadership in the Southern California Permanente Medical Group and focused his research on strategic issues, from long COVID to end-of-life care.

His work even took him to Ghana, where he had hoped to establish a program that would bring SCPMG physicians to support and train local doctors serving cocoa farmers in an impoverished area. He recently played a vital role in the Kaiser Permanente Bernard J. Tyson School of Medicine by developing the global health curriculum for students.

Before joining Research & Evaluation, Dr. Glass was the executive director of National Market Research for Kaiser Permanente. One of his proudest accomplishments was directing the research that led to the highly successful Thrive marketing campaign. Wherever he went, he sought opportunities to improve the services and quality of care for Kaiser Permanente members.

Dr. Glass had an infectious laugh that could be heard by his research colleagues across the floor in the offices in Pasadena. He was warm, personable, and inquisitive; and always seemed to be able to make time for a conversation with a colleague, whether it was about focus groups, political science, or tennis matches.

IN MEMORIAM

Anders Nyberg, MD, PhD

Dr. Anders Nyberg, a hepatologist at the Kaiser Permanente San Diego Medical Center and longtime researcher, passed away on March 14, 2023. He officially retired from the Southern California Permanente Medical Group in 2015 but continued to work on a per-diem basis until 2022.

He joined Kaiser Permanente in 1995 in Continuing Care and Hospice and later joined the Department of Gastroenterology and Hepatology. He won numerous awards for his compassionate care and his excellence in clinical research.

Dr. Nyberg was principal investigator for about 20 studies at Kaiser Permanente and a co-investigator on another 50. His work helped bring medications that ultimately saved the lives of many patients over the years. He cared for many patients before and after liver transplantation, skillfully guiding their care and helping to save many lives.

Along with his wife, Lisa Nyberg, MD, MPH, he led numerous clinical trials and epidemiologic studies on therapies for hepatitis C, other liver diseases, and gastrointestinal disorders. Their most recent paper – on the value of direct-acting antivirals for hepatitis C – was accepted for publication in the *American Journal of Managed Care* just a few weeks before his death.

Dr. Nyberg was a compassionate human being and a brilliant physician who generously shared his knowledge. He had his own unique sense of humor and tended to make jokes at serious moments, making it hard for others to keep a straight face. His contributions to science and medicine will make a difference in the lives of patients – his own and many others – for years to come.

Additional photo captions

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Inside back cover: Allan Slatkin, Dr. Kim Kaiser, Dr. Hai Linh Kerrigan, and Annie Chen

Credits

Research Communications, Department of Research & Evaluation
Cristine Denver, Dani Dodge Medlin, Lisa Killen, and Steven Kirk

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Wendy Healy, Jill Kramer, and Sarah Stanley

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Vision

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

Mission

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

kp.org/research
research-communications@kp.org

@KPSCalResearch

@kaiserpermanenteresearch

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