



**Caring for
our patients
each other
our community**

2019 Annual Report



Stanford | Department
MEDICINE | of Medicine

Stanford Department of Medicine

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A Look Inside

Welcome to our Department of Medicine annual report for 2019.

You'll see some impressive statistics about us in here: We are 15 divisions comprising 606 faculty, 920 staff and research associates, and 475 trainees. We have 30 endowed professorships. We brought in \$136 million to support our sponsored research. Our work in 2018 included 556 grants from both federal and non-federal entities and clinical trials.



But there's a human side to those numbers, and this year's report reflects that. You'll find an array of stories detailing the activities of the divisions, centers, programs, and institutes that make up the Department of Medicine. We've grouped the articles in this report into three sections reflecting the energy we put into caring for our patients, caring for each other, and caring for communities both local and global.

Much of our work focuses on patients – those who come to Stanford seeking our clinical expertise. We learn about Manali Patel's research into simple ways to improve terminally ill patients' quality of life, and Alan Pao's efforts to help those with kidney stones avoid forming more stones. What better way to teach beginning medical students about interacting with patients than what's described in the Walk with Me article?

Internally, we focus on how we care for our own Department of Medicine community of staff, faculty, trainees, and research associates. Stories like Residency Training with a Side of Wellness describe our attention to wellness and wellbeing. Angela Rogers' resident symposium celebrates the work residents put into their dedicated research month. And from the profile of Tamara Dunn we are encouraged to create an inclusive community, one where people feel strong, accepted, and empowered.

The local communities that we serve are described in stories about the staff-led SCOPE community service program as well as the GI division's move to Redwood City. We learn about the Million Veterans Program, an enormous database that will help both the veterans who contribute their data to it and the entire field of medicine. Our care for global communities is highlighted by Michael Baiocchi's work with at-risk Kenyan girls as well as by Kari Nadeau and Michele Barry's contributions to the study of climate change's effects on children, especially those younger than age five.

This Department of Medicine does amazing work. Read all these articles about our peers and perhaps yourself and take pleasure in the roles many play in what we do. When it comes to the achievements of the Department of Medicine, we all play a part.

Sincerely,
Robert Harrington, MD
Chair, Department of Medicine

Walk with Me:

Early Clinical Experiences for Medical Students

Motivated to integrate the science and art of medicine, incoming medical students at most institutions arrive on campus anticipating opportunities to engage with real patients and their families — at some point in the future. Medical students at Stanford, on the other hand, have an unusual opportunity to interact with patients in their very first month, even as they pursue the critical study of the basic sciences in their first two years.

The Walk with Me class, one offering of Stanford's Patient and Family Engaged Medical Education program, is a student-patient-caregiver partnership experience that offers early, authentic engagement with patients and their families.

Students in the Walk with Me class are the beneficiaries of a key outcome of the Transforming Medical Education Initiative, according to Erika Schillinger, MD, professor of medicine and vice chief for education in the division of primary care and population health. That key outcome suggested that authentic early experiences with patients would put patients and their caregivers center stage from the very start of medical education,



▲ **ERIKA SCHILLINGER, MD** (center right), discusses Walk with Me class topics with (from left) medical students **ISAAC JACKSON**, **MARIJA KAMCEVA**, and **SANDRENE CASSELLS**.

ERIKA SCHILLINGER, MD (right), meets with first-year medical students in a class about patient-physician relationships. ▼



establishing the patient's perspective and experience of health and the health care system as vitally important to being excellent clinicians.

The first practical step in putting early patient experiences in place was to create a curriculum in health systems science and deliver it monthly with didactic workshops, patient perspectives and practical skills building. According to Schillinger, "Health system science has become the essential third pillar of medical education, along with basic science and clinical science. It means everything that anticipates, surrounds, and forms the context for health care."

The course was designed to "prepare students for a 21st-century health system in which they will be leading health care," says Schillinger. Specifically, she continues, "we asked the patient-student pairs to meet a minimum of one hour per month to explore the patient's and caregiver's experiences of the health care system, focusing on the topic of the month with the goal of providing rigor and structure and accountability to their partnership. The result has been a magical, game-changing experience that puts patients and families front and center in medical education from the very beginning."

Three students who enrolled in the course share their experiences.

CROCHETING TOGETHER

Marija Kamceva switched her major at Yale from English to premed following a biology class she took as a junior. Once she got to Stanford and learned about the Walk with Me class, she jumped at the chance to take part because "it seemed like a really good opportunity to understand the role I was about to play either as a primary care physician or a psychiatrist. I thought it would contextualize the rest of my education."

When she learned her patient's name, she says, "I called her, and we met for coffee the first time near Stanford. We bonded really well." Meeting her patient two or three times a month, Kamceva found that they shared many of the same interests, and they even learned to crochet together. "My patient's story was long and interesting," she says, "and this was the first time she had the opportunity to really tell it because it's hard with something so personal to even talk with your friends about it. I feel like I will always have her story with me as I go on and work with patients."

A MIND-BOGGLING MEDICAL HISTORY

Isaac Jackson, an MD/PhD student, plans to be a pediatric oncologist or maybe an obstetrician and gynecologist; he is drawn to research. Early on he wondered what steps he could take "to become a good doctor and a good care provider. I felt that building relationships, getting to know patients, and starting to understand what patients go through was a very important part of that process." Given the specialties he is interested in, he says, "I realized that I was going to be dealing with difficult situations I don't know the first thing about. How do I learn to be empathetic and understanding about something I have no firsthand knowledge about?"

Then he enrolled in Walk with Me. He emailed his patient to get to know her and was invited to an upcoming doctor appointment. To bring him up to speed, his patient partner sent him a summary of her previous appointments and medical history. He found it “mind boggling. It’s easy to read words on this nice crisp page, but then I’m thinking about what that really represents: dozens of rounds of treatment, multiple hospitalizations, four near-death experiences over a few years.”

After several visits with his patient, Jackson could see what he was getting out of the relationship, but he wondered about his patient partner: “What could I offer, as a medical student who just parachuted in years after the start of someone else’s medical journey?” He later learned his patient partner had similar thoughts. “Being so sick for so long became a more and more integral part of her identity. There was family and a significant other, but then there was the sickness. In a way, the relationship we formed illustrated her potential to still form meaningful emotional connections despite such serious illness.”

PANCAKE BREAKFASTS

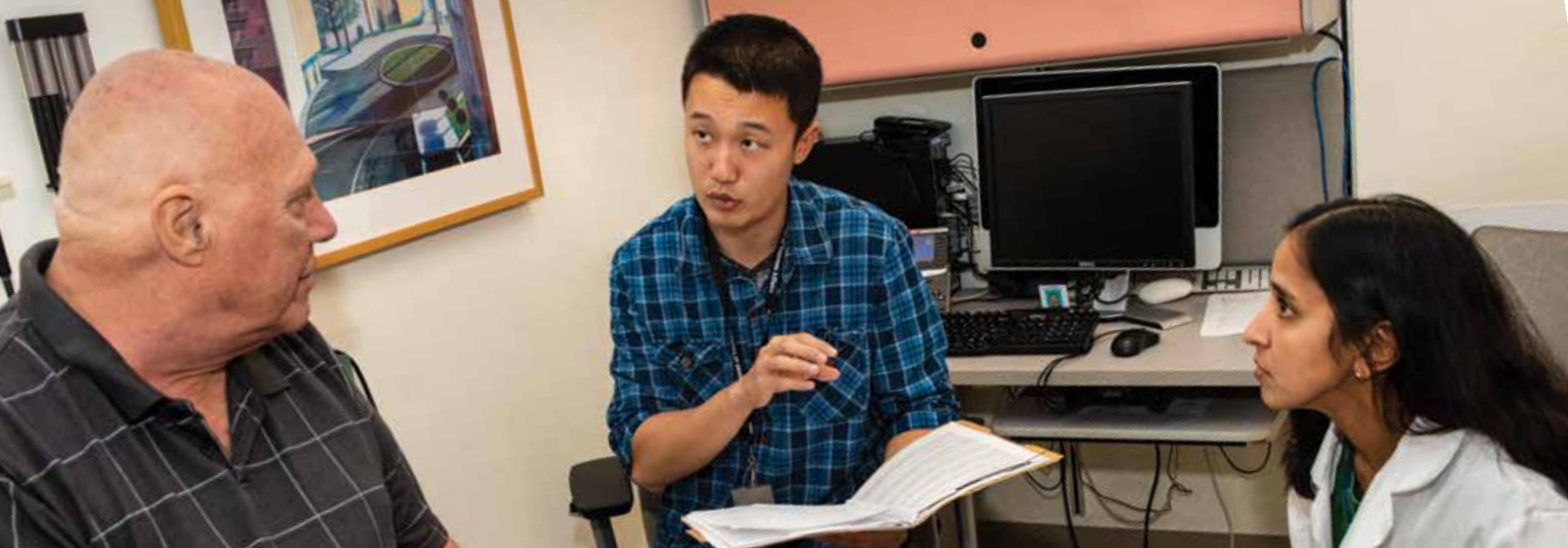
Sandrene Cassells came to medical school after several years teaching high school, where she was used to “being part of the day-to-day experiences of my students, being able to see their academic growth and their personal growth.” Thinking about the first two years of medical school made her realize she “didn’t like not tracking closely with patients until my third year. I was looking for something that would allow me to develop a close relationship with a patient early in my medical school career.”

Then she got involved in Walk with Me. Partnered with a patient undergoing treatment for cancer and sick from chemotherapy, Cassells drove to the patient’s home the first time they met, and they talked and had tea. After that they set up breakfast dates. “We met at a halfway point and we always got pancakes.”

During their year together, Cassells’ patient partner worried about what it would mean when she came to the end of her treatment. At Cassells’ suggestion, “we went together to a nutritionist and explored things she could do in hopes of preventing the cancer from coming back. I felt like I could advocate for her in that situation because we had had all those interactions around food.” In summary, says Cassells, “My entire world has changed from knowing her.”

◀ Current Walk with Me partners: patient **VANESSA DEEN JOHNSON** (left) and medical student **CLAIRE RHEE**.





▲ Lay health worker **GEE ZHU** (center) and **MANALI PATEL, MD** (right) meet with patient **DONALD FREDERICK**.

Delivering Care by Taking a Step Back

Can someone with no medical training improve the quality of life for a terminally ill cancer patient? And will that have any impact on health care costs?

That's what Manali Patel, MD, an assistant professor of oncology, wanted to find out.

During her undergraduate and medical school studies Patel spent time in rural areas overseas where medical technology is scarce, and she noticed how community members without formal medical skills can be effective health workers.

She wondered if it were possible to counteract the U.S. tendency to over-depend on technology by using lay health workers (nonclinical, nonprofessional personnel with no prior experience in the medical field who are trained in specific skills to help deliver various services, including end-of-life care).

That led her to design a randomized clinical trial of 213 patients with late-stage or recurrent cancer at Palo Alto Veterans Affairs.

The primary objective was to see if lay health worker intervention encouraged patients to discuss their personal goals of care with their medical professionals.

Patel split the patients into two groups. While both groups received the standard of care for their disease, one group (the intervention arm) was also paired with lay health workers who were trained to assist patients with establishing end-of-life care preferences.

Patients in the intervention arm could talk about their worries and concerns with their assigned lay health worker on a regular basis and especially during "trigger points" (for example, after receiving results from a medical exam or imaging test that might cause unease). The workers also encouraged their patients to share with their medical professional or team what they were discussing with the worker.

Patel's study, "Effect of a Lay Health Worker Intervention on Goals-of-Care Documentation and on Health Care Use, Costs, and Satisfaction Among Patients With Cancer," was published in the July 26, 2018 issue of *JAMA Oncology*.

The study's results exceeded Patel's expectations. More than 90 percent of the patients who were assigned a lay health worker had the types of discussions described above, while less than 25 percent of the patients without lay health workers had them. The discussions also made patients feel more satisfied with their medical decision making and oncology care.

A startling result of the study was how the lay health worker involvement affected health care costs and use.

"In the last month of life we saw a 95 percent reduction in patients' health care spending, which was largely because patients did not use the emergency department or the hospital," Patel notes.

The drop in spending is consistent with patients feeling more empowered to decline those interventions after clarifying their wishes with their lay health worker.

"In my own practice I can get tunnel vision and focus solely on wanting to eradicate or decrease the size of the cancer in hopes that I can make my patients experience less suffering. But sometimes the treatments may make the patient feel worse, and I need a reminder from the patient that the therapies themselves may not necessarily be achieving the gain," Patel admits.

"The big takeaway from this study is that lay health workers can serve as support for patients to formulate their care preferences and feel encouraged to openly communicate with physicians like myself. Especially when our focus may narrow, our patients allow us to take a step back and think about the big picture," she adds.

Putting Bioethics into Practice

Bioethics is a rapidly evolving, more-relevant-every-day kind of field. And for Kate Luenprakansit, MD, clinical assistant professor of hospital medicine and clinical bioethicist, it has become a major part of her life's work.

Luenprakansit's interest in ethics was sparked when she studied molecular cell developmental biology as an undergraduate at UCLA. "I always felt there was something more to becoming a physician than just knowing the biology, the physiology, the math, and the science. There was even more fundamental knowledge I needed to gain in order to be the best physician I could be," she says.

Her first ethics course during a study abroad program in medical practice and policy in Denmark provided the framework for her higher calling. Questions started to materialize for her about autonomy, beneficence, non-maleficence, and justice and how they play into the doctor-patient relationship. "How do I actually strive to uphold those ideals and principles in medicine?" she asked herself. That first ethics course became the "compass" for her career.

When Luenprakansit started at Stanford as part of the surgical co-management hospitalist group, she brought her interest in ethics with her. "I needed a way to figure out how I could effect change on a larger level," she explains, "and I think Stanford is a phenomenal institution for that work."

Her leaders were Mark Cullen, MD, director of the center for population health sciences and professor of primary care and population health, and Neera Ahuja, MD, clinical associate professor and division chief of hospital medicine. They encouraged and supported her ethics work. David Magnus, PhD, professor of medicine and biomedical ethics, and director of the Stanford Center for Biomedical Ethics (SCBE), helped deepen her understanding of ethics and philosophy. In 2016 she was a summer fellow at the University of Chicago's MacLean Center for Clinical Medical Ethics, and she's been a clinical ethicist and consultant at Stanford ever since.

Luenprakansit's work varies on a day-to-day basis. She fulfills her clinical duties as a hospitalist; conducts research; teaches students, residents, and fellows; and co-teaches two ethics courses — all on top of her ethics consulting work. This past year, she was also one of the ACES (Advancing Communication Excellence at Stanford) facilitators.

Luenprakansit was formally trained in mediation and conflict resolution, both at Stanford and during her summer in Chicago. She now takes part in clinical ethics consults at Stanford Hospital. She helps patients, doctors, and families "reconcile the many ethical concerns and dilemmas that arise in a patient care setting."

Often this means sitting in a room with physicians and patients, trying to work out an "optimal" solution. "Conflict often arises because of a



▲ KATE LUENPRAKANSIT, MD

misunderstanding," she says. "And how we are all communicating with one another can lead to the misalignment of goals and expectations."

"We strive to elicit each party's perspective so that we can achieve some level of mutual understanding," she says.

Mutual understanding is important, but the next step, consensus, may be harder to achieve. Ethics consultants help facilitate a plan and a resolution. "Decisions still need to be made," Luenprakansit states. "At the end of this, there's a patient at the center of all of these discussions."

One of only a few physician ethicists at Stanford, her ultimate goal is to make ethics a part of the larger medical conversation. She wants to engage people, starting as early as medical school, to discuss "the practicality of understanding ethics, and how that affects our decision making: the what, why, and how of medical decision making as clinicians." She concludes, "Through my practice, I have come to appreciate how fundamental ethics is in my role as a physician."



▲ CORNELIA WEYAND, MD

Stanford Vasculitis Clinic: **Infrequently Asked Questions about Uncommon Diseases**

Vasculitis, a group of uncommon diseases characterized by inflammation of the blood vessels, caught the attention of Cornelia Weyand, MD, when she was an immunology and rheumatology fellow at Stanford in the 1980s. Her study of the specialty took her to the Mayo Clinic in Rochester, Minnesota, which gave her access to a large population of vasculitis patients. Weyand returned to Stanford in 2010 as a professor of immunology and rheumatology and started a vasculitis clinic while continuing a wide-ranging research program. During a recent interview, Weyand shared insights about the disease and the clinic, taking us from the time of the Vikings to current-day China.

TO BEGIN WITH, WHAT IS VASCULITIS?

No organ in the body can function without blood supply, which is why blood vessels have a life-sustaining function. Nature has protected blood vessels from inflammatory attacks, but in some patients this protective shield — what we call the immune privilege — fails, and they develop inflammatory disease of blood vessels. When there is an inflammatory attack on the large blood vessels — the aorta or its major branches — it creates a clinically critical situation.

Patients diagnosed with vasculitis and inflammatory blood vessel disease have abnormalities in their immune system. The immune system no longer respects the immune privilege of a blood vessel. In these patients the immune system breaks through that immune privilege and sends inflammatory cells into the blood vessel. Depending on the size of that blood vessel,

the vessel responds differently. Either it becomes damaged and then the consequence is bleeding, or it becomes occluded and then the consequence is lack of oxygen and tissue breakdown.

Inflammation of the aorta is most frequently caused by a disease entity called giant cell arteritis (inflammation of an artery). A variant of that disease is Takayasu arteritis, and we have assembled probably the largest cohort in the country of patients with that diagnosis. Other forms of vasculitis are GPA (granulomatosis with polyangiitis), MPA (microscopic polyangiitis), and Churg-Strauss vasculitis.

HOW DID THE CLINIC GET STARTED?

During my time as a young faculty at the Mayo Clinic I had an opportunity to see many patients with vasculitis in Minnesota. That's because one of the vasculitides — giant cell arteritis — is a Viking disease. When Scandinavian immigrants — descendants from Vikings — came to the United States, they settled in Minnesota and brought the disease with them. That allowed me to develop a research program and clinical expertise that came with me to Stanford in 2010.

Stanford has had a prominent position in cardiovascular disease for half a century. When they began to do heart transplants here, it fueled the development of an outstanding vascular pathology program. Likewise, that our radiologists are so extraordinarily good is a legacy of the development of that prominence in cardiovascular disease.

Because this disease is systemic in nature, but it affects localized organs like the eyes, ears, and nerves, there is a need for expertise in many different areas, which Stanford has.

I took advantage of those areas of expertise and began the multidisciplinary clinic that we have today. This is truly a clinic that not every medical center can have because of the varied expertise required. Our clinic is one of only a few in the nation, and several hundred patients come here on an annual basis.

HOW ARE WE TREATING PATIENTS WITH THIS DISEASE?

Because vasculitis has a component of systemic inflammation, patients with vasculitis often have fevers, weight loss, fatigue, and diffuse aches and pains that are difficult to pinpoint.

All of our patients are chronically sick, so management requires treatment by us over many years. We attempt to inhibit inflammation, but even more so, we attempt to re-educate the immune system of the patient so that when they come out of their therapeutic phase, their immune system is not going to repeat how it has acted in the past.

YOU REFER TO THE MULTIDISCIPLINARY CHARACTER OF THE CLINIC. CAN YOU SAY MORE?

When we are managing patients with these diseases, we almost always work very closely with different specialists, particularly those in cardiology and cardiovascular disease. We have a particular expertise at Stanford in large vessel vasculitis, which is vasculitis of the aorta and its immediate branches. There is a very close connection between the Vasculitis Clinic and the Center for Marfan Syndrome and Related Aortic Disorders, which is run by cardiologist David Liang, MD, PhD, because that center is focused on failure of the aorta. Patients with inflammatory disease of the aorta may need surgery, so we work very closely with our colleagues in cardiothoracic surgery as well.

For diagnostic purposes, we need expertise from two directions — pathology and radiology. We also work very closely with the eye center, ENT, and neurovascular surgery because patients with inflammatory blood vessel disease often have trouble with their eyes, sinuses, ears, and nerves.

WHAT RESEARCH IS THE CLINIC INVOLVED IN?

Another important component of the clinic is an associated research program. We are studying which abnormalities in our patients' immune systems induce these diseases, how we can detect them, and what the mechanisms of the disease are. We also want to know what the immune system is doing wrong to cause inflammation of the aorta or another blood vessel. And we are looking at which type of immunomodulatory therapies can be used so we can stop the immune system from acting the wrong way.

A unique aspect of our research involves a bioengineered mouse that does not have an immune system of its own but serves as a proxy for our patients. We engraft a human blood vessel into the mouse and then we transfuse the blood of our patient, which gives the mouse the immune system of our patient. That way, we can study in the mouse how that patient's immune system would respond to therapy. That has been an extremely

valuable tool for us to examine vasculitis. It is also an excellent example of personalized medicine offered at Stanford: We build a model system that is personalized for one individual to capture the unique aspects of disease and therapeutic responsiveness.

We have published a series of papers having to do with the humanized mouse model, including one that appeared in the July 31, 2018 issue of *Circulation Research*, which featured an image from that paper on its cover.

WHAT ABOUT THE FUTURE?

A disease that I mentioned earlier — Takayasu arteritis — was originally described in Japan. It's a disease that is more frequent in young Asian women, and Japanese scientists are seeking collaboration with Stanford in how to diagnose and manage these patients.

While the United States has had an unparalleled ascent in biomedicine, many groups in the world are now participating in the research of vasculitis, from the bench to the bedside. Physician scientists in Shanghai have become important collaboration partners for us. They take care of many patients with vasculitis, and we will work closely with them in exploring the underlying immune defects, diagnostic criteria, and treatment guidelines for diseases that occur in their population, and vasculitis is one of them.



▲ CORNELIA WEYAND, MD (right), works to re-educate the immune system of a patient with vasculitis.



Tackling a Fundamental Disease: Multiple Disciplines Take on Hypertension

A multidisciplinary clinic at Stanford is redefining what it means to live with hypertension.

About one in every three American adults has the condition, generally known as high blood pressure. It's difficult to detect because it typically has no symptoms or warning signs. What's more, a significant proportion of patients aren't fully treated despite taking multiple medications, says Vivek Bhalla, MD, assistant professor of nephrology and co-director of Stanford's Hypertension Center.

The Hypertension Center encompasses 12 specialties including renal, endocrine, and stroke medicine; preventive cardiology; and sleep medicine.

"Treatment always involved multiple specialists, but in the past we never really got together to talk about it. Instead we would view isolated aspects of the problem from different angles," Bhalla says. "But that's not what's best for the patient."

Teaming up with colleagues like center co-director Robert Isom, MD, clinical associate professor of nephrology, Bhalla realized that Stanford had the resources to gather all the necessary experts under one clinical roof.

"There seemed to be somebody in every corner with expertise and/or interest in hypertension," Bhalla says. "So we tried bringing together physicians from these different specialties to create an infrastructure for clinical care of hypertension patients as well as to propagate clinical, translational, and basic research based on shared interest."

For Bhalla, the center's most important feature is having different specialists looking at the same patient and offering various opinions — which results in better overall care. For physicians, trying to lower a patient's blood pressure requires not only medication, but also management of risk factors and secondary causes and consequences of hypertension, like obesity, sleep apnea, or kidney disease.

Center clinicians, along with colleagues in surgical specialties, are conducting a range of studies about hypertension. One study involves correlations between obesity and insulin resistance in patients with high blood pressure. Other research projects, with vascular surgeon Jason Lee, MD, and general

surgeon Electron Kebebew, MD, have looked into the viability of surgical treatments.

The center's research legacy also includes SPRINT — a national systolic blood pressure interventional trial — which focused on whether then-current blood pressure goals for patients with hypertension were insufficient. Led by Glenn Chertow, MD, professor of nephrology, and Randall Stafford, MD, professor of medicine, the trial was supposed to run from 2013 to 2018, but it was halted after just three years because the data so convincingly showed that lower blood pressure targets overwhelmingly improved health.

Just five years ago, guidelines set the upper limit of acceptable blood pressure at 140/90 mm Hg. Bhalla says these conservative guidelines meant that people with moderate hypertension weren't being identified or treated.

"But SPRINT really tested and challenged the prevailing law of the land, showing that a target for systolic blood pressure of 120 mm Hg — versus 140 mm Hg — resulted in an almost 25 percent relative risk reduction in cardiovascular events and mortality," he says.

Inspired in part by SPRINT's success, Bhalla is working with Tara Chang, MD, assistant professor of nephrology, on better tools to measure blood pressure like the AOBP, or automated office blood pressure. This technique reduces sources of measurement error and provides clinicians with a more accurate picture of patients' blood pressure health, enabling them to make informed decisions

regarding diagnoses and therapy plans.

"Not all methods are created equal," Bhalla says. "New methods raise new questions about the best way to measure hypertension, and how often, which ultimately improves treatment."

Members of the center are also working with several Silicon Valley startups on novel devices for measuring blood pressure at home.

"We know that monitoring of blood pressure at home can help control hypertension, and newer devices may facilitate the accuracy and frequency of data that we doctors have to treat our patients," he says.



▲ VIVEK BHALLA, MD

When It Comes to the Kidneys, This Center Leaves No Stone Unturned

How precision medicine is personalizing kidney stone treatment

Half a million Americans go to the emergency room annually for kidney stone issues, and one in every 10 people in the United States will develop a kidney stone during his or her lifetime.

Kidney stones are exactly what they sound like — accumulations of minerals like calcium that crystallize into stone-like masses inside kidneys. Their formation isn't necessarily painful, but passing them can be. If a stone gets lodged in a ureter, it can cause a clog that backs up urine in the kidneys. While stones aren't life-threatening, complications can include kidney injury and increased risk of urinary infection.

Diagnosis and treatment of kidney stones is a two-part process. When patients come in with a painful kidney stone that won't pass on its own, physicians identify and remove it. But removing it doesn't address how to prevent future stones. Patients who've developed one stone have about a 50 percent risk for developing another within the next decade.

Prevention involves taking a detailed dietary and medical history, gathering urine and blood samples for analysis, then implementing appropriate strategies based on those findings. It's a time-consuming and often piecemeal medical assessment that can take weeks, leaving the patient waiting to receive — and understand — the best treatment.

At the Stanford Kidney Stone Center, clinicians are working to provide the best treatment and prevention for kidney stones. In part, that's because the center draws together experts from nephrology, urology, endocrinology, and nutrition.

Alan C. Pao, MD, assistant professor of nephrology, leads the center with Simon Conti, MD, clinical assistant professor of urology.

"Dr. Conti and I decided to divide the work so that the urologists focus on clinical-radiologic correlations and make surgical plans, and the nephrologists analyze the laboratory data and craft prevention strategies," Pao says.

"It's very efficient to discuss medical and surgical options for the same patient at the same time," adds Pao, who is also joined at the center by nephrologists Robert Isom, MD, Pedram Fatehi, MD, and Fahmeedah Kamal, MD.

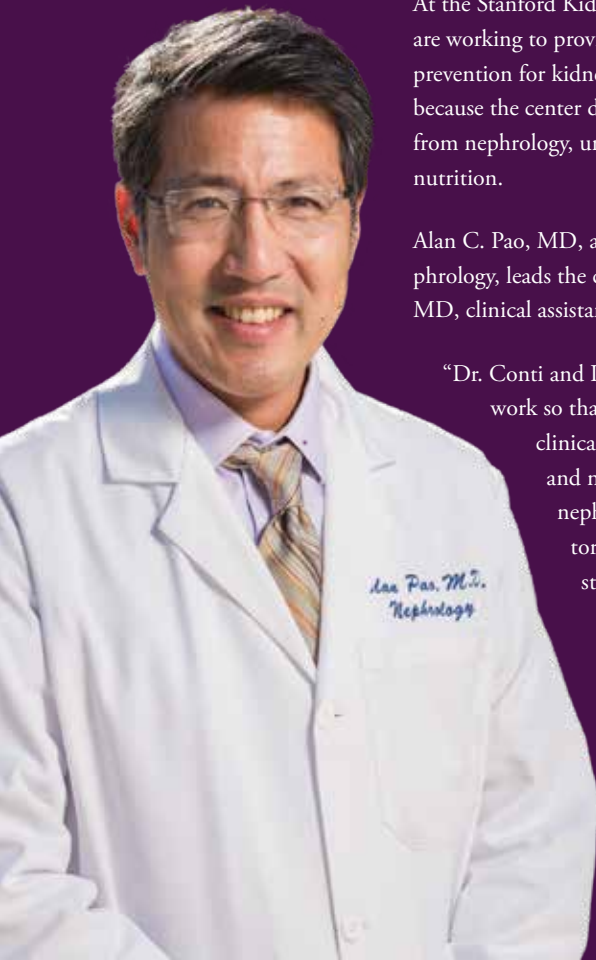
Pao says it's not well understood why kidney stones form, but patients on high-meat and high-sodium diets or who don't drink enough fluids are typically more at risk for stone recurrence. And appropriate treatments to prevent recurring kidney stones aren't one size fits all. In fact, they depend on the diet, health, and stone type of each stone-former.

The secret to preventing stones, Pao says, is in a patient's urine. Urine contents can reveal what minerals are in excess or in deficiency, and those mineral levels can help physicians determine how to help patients. That's why a simple procedure like 24-hour urine collection is so vital — it provides a road map for improved treatment.

Along with John Leppert, MD, associate professor of urology, Pao is analyzing a national database of 120,000 kidney stone patients cared for in Veterans Affairs hospitals. They're examining how frequently stone-formers are getting 24-hour urine collections, and whether subsequent analysis of the urine leads to changes in stone-prevention medications and decreases in stone risks.

Pao is also following the breadcrumbs of other kidney stone mysteries, like why patients with normal-looking 24-hour urine collections still develop recurrent stones. That occasional disconnect has also spurred him to work with another colleague, Joseph C. Liao, MD, associate professor of urology, on a new gadget that will allow patients to spot check their urine throughout the day and provide immediate feedback for how diet and medications are affecting their stone risk.

Undoubtedly, precision medicine has trickled into kidney stone treatment, and Pao's research ensures that patients receive their unique treatments for stone prevention.



◀ ALAN C. PAO, MD

PEDRAM FATEHI, MD ▶



Stanford Amyloid Center: From Start-up to Premier Status

Although Kevin Anderson had committed no crime, he was facing a death sentence when he came to Stanford in 2007.

Anderson was dying from end-stage cardiac amyloidosis, an abnormal accumulation of proteins (amyloid fibrils) in his heart.

He had recently visited the Mayo Clinic in Minnesota to ask about a heart transplant, which at that time was the only viable treatment option for his disease. Because the amyloidosis was mostly in his heart and not in other parts of his body, Anderson qualified for a transplant.

Anderson, a urologist, lived near Sacramento, California. His proximity to Stanford brought him in contact with Ronald Witteles, MD, who at the time was a new faculty member, just starting the Stanford Amyloid Center.

Not long after Witteles met Anderson, the Stanford heart transplant team gave Anderson a second chance at life.

“Without the transplant, Dr. Anderson would not have survived that year. Now, more than a decade later, he remains alive and well, is back to work as a urologist, and he is thriving,” says Witteles, associate professor of cardiovascular medicine.

ANTIBODIES AND LIGHT CHAINS

Anderson was afflicted with AL (primary) amyloidosis, which is related to a type of bone marrow cancer. Normally, plasma cells in the bone marrow produce antibodies. If a plasma cell becomes cancerous, it may produce extra pieces of antibodies called “light chains” (the L in AL amyloidosis). The light chains circulate in the bloodstream and can deposit in the heart and other major organs throughout the body, causing damage.

“A generation ago, a diagnosis of AL amyloidosis often was a death sentence, particularly when it involved the heart, but in the last 10 years treatments have improved by leaps and bounds so we can now give very effective treatments to many patients with the disease,” Witteles says.

Transthyretin (TTR) amyloidosis is the other main type of the disease. It is not related to cancer, and one of its two forms is inherited from those carrying a genetic mutation. The mutation is present in about 1 in 30 African Americans in this country; about 7 percent of the people with the mutation will develop the disease. Another form of TTR amyloidosis, which is not hereditary, first strikes people usually between ages 60 and 80 and causes mainly heart dysfunction. Up to a quarter of men in their 80s and 90s have significant deposits present in their hearts.



▲ **RONALD WITTELES, MD**, performs a patient exam in the Stanford Amyloid Center. Inset: Patient **KEVIN ANDERSON** tells his story in a YouTube video.

A SYNERGISTIC APPROACH

AL amyloidosis, the bone marrow type of the disease, is by definition a cancer, but it endangers other organs — including the heart, the kidneys, the liver, the gastrointestinal tract, and the nerves. Optimum patient care requires a true multidisciplinary approach in which amyloidosis specialists closely collaborate with experts in various medical specialties.

Witteles had that approach in mind when he first contacted Stanley Schrier, MD, professor of hematology, about an opportunity for a Stanford team to form a multidisciplinary group to battle this disease. Colleagues in other disciplines also expressed interest, including Richard Lafayette, MD, professor of nephrology; Sally Arai, MD, associate professor of blood and marrow transplantation; and Gerald Berry, MD, professor of pathology. That first group of physicians wanted to learn everything they could about the disease, and they were willing to work collaboratively to contribute to the body of knowledge. That meant patients who would be coming from great distances could see all their specialists in one coordinated visit.

FROM A MODEST START, THE CENTER QUICKLY GREW

“It turned out that there were many more of these patients than anyone realized, and there was no other center for the disease within a thousand miles of here. Also, by luck of timing, the formation of our center occurred just as new treatments for AL amyloidosis were poised to take off and

newer treatments for TTR amyloidosis were being studied and ultimately would be successful and on their way to approval,” Witteles says.

ELUCIDATING THE BASIC MECHANISMS OF THE DISEASE

Then came the recruitment in 2017 of Ronglih Liao, PhD, a professor of medicine whose expertise is in the basic science of amyloidosis.

“She and a very talented trainee, Kevin Alexander, MD, a fellow in advanced heart failure and transplant cardiology, moved their lab from Brigham and Women’s Hospital in Boston to Stanford to continue doing remarkable work in elucidating many of the basic mechanisms of the disease,” says Witteles.

The lab has been at the forefront of investigating questions like how amyloid deposits injure organs and why amyloidogenic immunoglobulin light chain proteins are so much more toxic than transthyretin.

The devotion of the Stanford Amyloid Center physicians and staff as well as the leadership in the Department of Medicine were factors that attracted Liao to Stanford.

“I was impressed with the recognition of the critical importance of basic and translational research. There is an understanding of how that research contributes to the continued success in providing top-quality patient care,” Liao says. “We are optimistic that at this center our scientific discoveries can rapidly be translated back to the clinic and we can use our patients to

accelerate the discovery process, with each part helping the other. This will set up a feed-forward system that we hope will allow us to develop new therapies in record time.”

ENRICHING THE REPUTATION

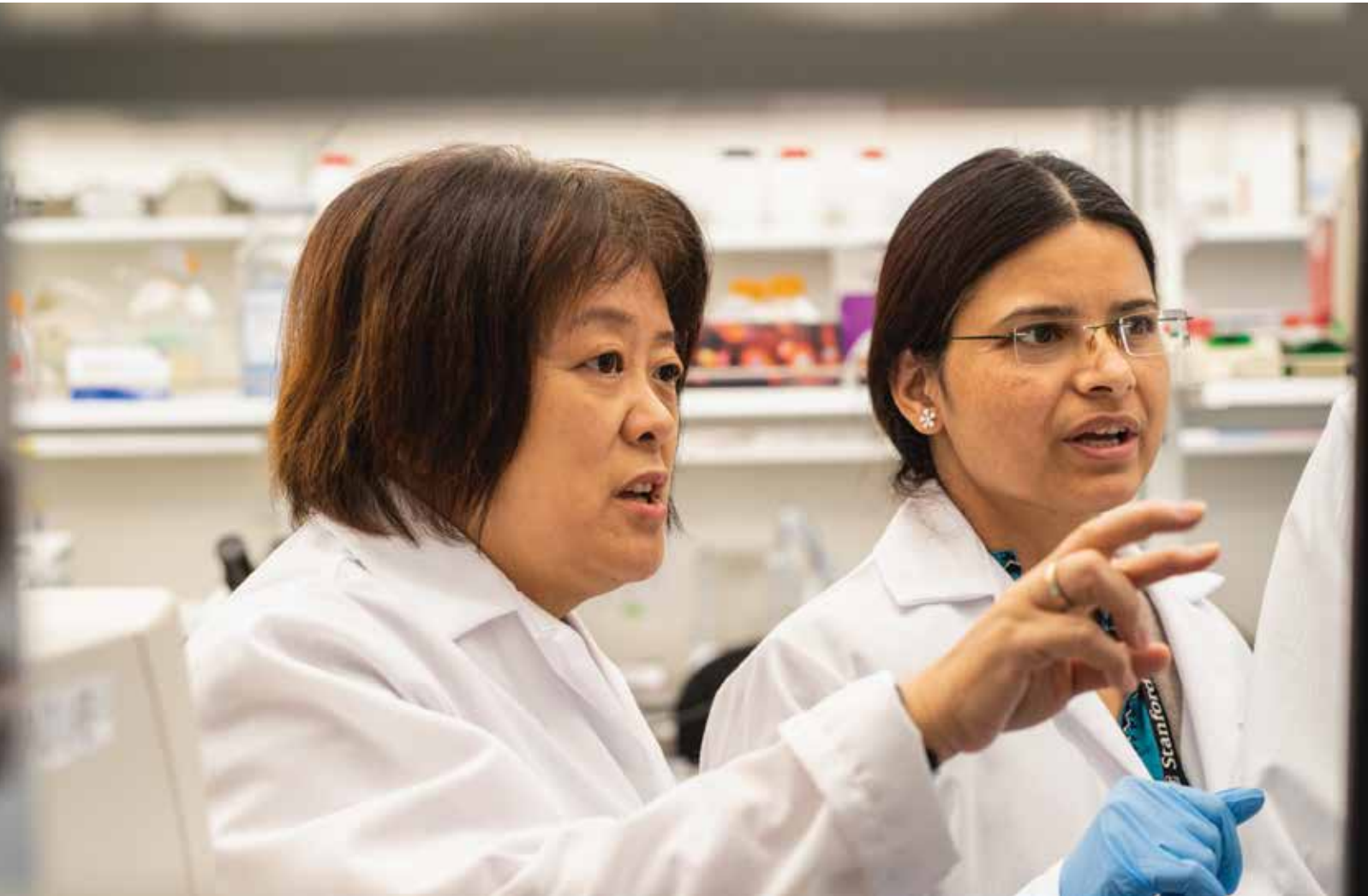
Prior to Liao’s arrival, Stanford was known for being on the cutting edge of some clinical treatments like transplants and newer chemotherapy approaches. Now, the basic science expertise is enriching its reputation.

Today, with about 125 new amyloidosis patients per year, several hundred others receiving regular care, and many enrolled in various clinical trials, the Stanford Amyloid Center is one of the largest such centers in the world. Witteles and Liao lead the center along with Michaela Liedtke, MD, associate professor of hematology. The staff includes 14 faculty from three departments and five divisions in the Department of Medicine, a dedicated clinical trials coordinator, and two full-time nurse coordinators.

In August 2018 the FDA approved the first drug ever for treating TTR amyloidosis, and two more drugs are expected to receive approval in the coming year. All three of these drugs and many more that are on the way, including AG-10, which was first identified at Stanford, represent classic bench-to-bedside development: An initial understanding of the mechanism of the disease led to treatment approaches based entirely on that understanding.

What that all means is a leading role for the Stanford Amyloid Center in promising bright futures for patients like Kevin Anderson.

▼ **RONGLIH LIAO, PHD** (left), reviews research data with lab instructor **SEEMA DANGWAL, PHD**.





▲ DAVID MIKLOS, MD, PHD

A Breakthrough Drug Facilitates Safer Bone Marrow Transplants

Within the walls of the Center for Clinical Sciences Research, scientists are hard at work developing life-saving treatments for patients with blood and bone marrow cancers.

Since 1987, Stanford has performed more than 7,000 adult bone marrow transplants, long considered the gold standard for treating people with these cancers. However, a potentially serious complication of bone marrow transplantation is graft versus host disease (GVHD).

GVHD is caused when immune cells from a donor start attacking the normal tissues of a recipient. This can lead to painful, debilitating problems in organs from the skin and mouth to the liver and lungs, including itchy rashes, nausea and vomiting, muscle weakness, and breathing difficulty.

For those needing a bone marrow transplant, the ideal option is to find a donor within the patient's family, but the odds for a match of antigens between family members are at best only one in four. The next best option is a transplant of cells from an unrelated donor, known as a hematopoietic cell transplant. However, the risk for GVHD increases with unrelated donors.

Corticosteroids were the conventional treatment for GVHD, but the long-term use of steroids has many side effects, and GVHD frequently re-emerges when steroids are stopped.

Researchers had been working for years to find a more reliable treatment than steroids, and they found it in ibrutinib, the first drug approved by the U.S. Food and Drug Administration (FDA) for the treatment of GVHD.

A team led by David Miklos, MD, PhD, associate professor of blood and marrow transplantation, contributed greatly to the development of ibrutinib.

"We'd been looking for a long time for targeted effective therapies to get patients with chronic GVHD off steroids. But other drugs, even those that showed early promise, all ended up failing to show benefit in randomized clinical trials," Miklos says.

Miklos discovered that B lymphocytes — one type of immune cell — are critical to the development of chronic GVHD. Blocking B cell activity, he hypothesized, could prevent or treat the disease. Ibrutinib — a drug first developed to treat B cell cancers and already approved for multiple cancer types — was able to potentially deplete B cells from a hematopoietic cell transplant donor. Miklos approached Pharmacyclics, the Sunnyvale-based company that makes ibrutinib, about launching a clinical trial of the drug for GVHD; the company agreed.

Miklos and his colleagues presented favorable results of that trial at an annual meeting of the American Society of Hematology. On the heels of that research, the FDA fast-tracked its approval process, and in August 2017 the FDA approved ibrutinib for the treatment of patients with chronic GVHD who have failed at least one systemic treatment.

More recent insights come from senior scientist Bitu Sahaf, PhD, who has worked in the Miklos lab since 2007. Sahaf presented the mechanism for ibrutinib chronic GVHD during a top abstracts session at the combined annual meetings of the Center for International Blood & Marrow Transplant Research and the American Society for Blood and Marrow Transplantation in early 2018.

"Our research is focused on B and T cells, two important components of the immune system. The overall research goal is the characterization of adaptive B and T cell immune responses that cure cancer while avoiding GVHD," Miklos explains.

Now, Miklos and his colleagues are working on a randomized placebo-controlled trial of 185 patients to see if ibrutinib is effective in patients with earlier stages of GVHD. They expect to have results by the end of 2019.

"Perhaps most exciting, the Stanford Bone Marrow Transplant program has initiated its own clinical trial to see if ibrutinib immediately following transplant can prevent chronic GVHD from developing months later," Miklos says.

Integrating Medicine with Basic Science

Justin Annes, MD, PhD, assistant professor of endocrinology, gerontology and metabolism, and ChEM-H faculty fellow, feels that he owes a great deal of credit for his unique research program to the ChEM-H Institute, which stands for Chemistry, Engineering & Medicine for Human Health. “What they do,” he says, “is take a physician scientist like me and enable me to bring chemistry into the laboratory in a really significant way.”

Envisioned by Chaitan Khosla, PhD, professor of chemistry, ChEM-H is co-directed with Carolyn Bertozzi, PhD, professor of chemistry, “both outstanding scientists and wonderful leaders,” Annes says.

He continues: “ChEM-H has allowed me to unleash chemistry in an informed and supported way. One important person for me has been Mark Smith, PhD, director of the ChEM-H Medicinal Chemistry Knowledge Center, who is an engaged partner in our drug-development programs. Another is Justin Du Bois, PhD, associate professor of chemistry, who has generously provided the chemists in my group an environment and culture of chemistry. We recently developed a first-generation ‘smart drug’ that applies the principles of chemistry to selectively target a regenerative medicine to insulin-producing β -cells. We hope someday this medicine will be used to reverse diabetes.”

Annes has also developed an interdisciplinary research effort that integrates engineering, chemistry, and biology. “My collaboration with Amin Arbabian, PhD, an electrical engineer, and Richard Zare, PhD, a chemist, aims to develop a new nanoparticle-based drug-delivery microdevice to reverse life-threatening hypoglycemia in diabetic patients. This is a uniquely Stanford project as it reaches across scientific disciplines that normally don’t interact. My role as leader of the Stanford Diabetes Research Center enrichment program, which fosters cross-disciplinary work, was instrumental in developing this collaboration.”

Annes’ research and clinical interests, which are in diabetes and hereditary endocrine disorders, have led him to work with patients who have two neuroendocrine tumor-related conditions, pheochromocytoma and paragangliomas. While at Brigham & Women’s Hospital, says Annes, “I became the pheochromocytoma and paraganglioma guy, and when I came to Stanford I continued to see these patients, extending my practice to neuroendocrine tumors in general. I got to know Pam Kunz, MD, assistant professor of oncology, a leader in neuroendocrine tumors on the oncology side. Over the years we’ve brought our clinics together, and now we have an endocrine cancer clinical program.”

When not seeing patients, Annes can be found in his lab where, he says, “our driving principle is to harness the power of chemistry to deliver new insights into biologic function and to develop a regenerative therapeutic for diabetes and improved chemotherapeutics for our neuroendocrine tumor patients.”

His lab spans the spectrum of preclinical drug development. His biologists, chemists, and biochemists work with animal models to understand pathophysiology and identify the molecular basis of disease, in-vitro systems to identify lead compounds for therapeutic targets, and test tubes where they build drugs from individual components. And then they take those drugs back into cell systems and animal models to demonstrate their activities.

Asked to describe a good day, Annes returns to the lab: “One of my favorite days is when I go into the lab, and a couple of my graduate students are trying to stay calm despite being exuberant about a new experimental result. I get to sit down and see what the science is, what they’ve discovered, how fulfilled, motivated, and off-the-wall happy they are by the new discovery.”

“This is one of the great joys of being in an academic institution: discovery and mentorship all in one moment.”



JUSTIN ANNES, MD, PHD ►



▲ TAMARA DUNN, MD

Tamara Dunn in Focus

A steady hum of energy and activity seems to constantly surround Tamara Dunn, MD, clinical assistant professor of hematology. Perhaps it's the time of day — it's early evening, a notoriously hectic time, and she's toggling between the end of her work day, her children's after-school commitments, patients' schedules, and her dog's veterinary appointment. But, after an hour of conversation, it becomes clear that this is a more permanent state — a reflection of the passion and attention she brings to each sphere of her busy life.

Dunn was one of those kids who “always knew” she wanted to be a physician. She was raised in Kansas City, and her father's job as a dentist gave her an insider's glimpse into the medical field.

“My dad had a lot of friends who were physicians. In fact, his best friend was my pediatrician,” she explains. “I was very fortunate to be surrounded by this group of black professionals who inspired me.” The early exposure

planted the seeds for what would become one of her causes: building — and fostering — inclusive communities in medicine.

After a post-college break spent living in France and New York, performing “off-off-Broadway,” singing with a band, and toying with a career as a financial trader, Dunn found her way back to her childhood love — medicine.

She received her MD from SUNY Downstate Medical Center and came to Stanford for her residency, where she's remained ever since, treating patients at Veterans Affairs, working alongside residents and fellows on the diversity council, and playing a role in the establishment of the Adolescent and Young Adult Cancer Program. In the process, she's emerged as a champion for diversity and inclusion — at Stanford, at the American Society of Hematology, and beyond. Dunn shared more about performing, medicine, and diversity in a recent interview.

HOW DID YOU BECOME INTERESTED IN MEDICINE?

I always wanted to be a physician, but I took a very unconventional path. When I arrived at Stanford as an undergraduate I was taking premed courses — I began as a human biology major — but I changed my major after my sophomore year to French. I had already performed quite a bit in high school, but I really cultivated my abilities during this time. I was in an a cappella group that performed world music focusing on the African-American diaspora, I was involved in Stanford's theatrical society, and I was in a funk band. My mother died when I was 15, and I realized how quickly life could change. Since then I've had a "carpe diem" attitude and have never taken anything for granted — I believe in following your passion and that anything is possible.

After graduation, I went to performing arts school at the American Musical and Dramatic Academy in New York City, and did some more theater work — performing off-off-Broadway and auditioning. Then, I took a 180 degree turn into finance. I got licensed and was working on the trading floor on the sales side. I was offered a position in the trader training program but had already enrolled in the post-bac pre-med program at Hunter College.

WHAT DREW YOU TO HEMATOLOGY?

It was always an interest of mine. I was just excited to look at blood smears — I thought the cells looked so beautiful on the slide. And all the diseases intrigued me, especially leukemia. I fell in love with how intense the field was and how deep of a relationship you form with your patients and their families. So, I went right into a hematology sub-specialty training program at Stanford, and I loved it.

WHAT DOES AN AVERAGE WORK DAY LOOK LIKE?

One thing I love about my job is that every day is unique. Some days I'm focused on my clinic patients, some days I'm performing inpatient consults at the VA or Stanford Hospital, some days are fellowship heavy. I also work on research for our Adolescent and Young Adult (AYA) Cancer Program. I recently did a study where we gave all the AYA patients receiving therapy Fitbits and an iPad to encourage physical activity because we believe it can improve cancer-related fatigue and quality of life. We also gave our patients a quality of life assessment tool, and using the technology did in fact improve their score.

YOU'VE BECOME A VOICE FOR DIVERSITY AND INCLUSION IN THE DEPARTMENT OF MEDICINE. HOW ARE YOU BRINGING COMMUNITIES TOGETHER?

I've been working alongside Wendy Caceres, MD, clinical assistant professor of primary care and population health, as a faculty advisor on the diversity council, which is composed mostly of residents and fellows. Having a community is one thing — we know we should improve our diversity — but I think making the people who are currently here feel comfortable is where the inclusion piece comes in. Once the community is formed and people are feeling acclimated, strong, and important, that's when you start to attract more underrepresented minorities.

I've hosted informal get-togethers at my home where we share dinner and discussion, and that is a valuable space. We have a few initiatives in the

pipeline: We're trying to incorporate diversity into the weekly medicine grand rounds by encouraging a more diverse speaker roster. We also have taken a larger role in the recruitment process. We're doing more distance travel meetings and making sure that we're bringing diverse faculty to the table. I am also a member of the Graduate Medical Education's Diversity and Inclusion Committee where we are trying to promote diversity on a broader level.

YOU WERE RECENTLY NAMED AN AMERICAN SOCIETY OF HEMATOLOGY (ASH) AMBASSADOR. WHAT WILL THIS NEW JOB ENTAIL?

The ASH ambassador program is in its inaugural year, and Stanford was chosen to be one of 16 participating institutions. The ambassadors serve as liaisons between the society and trainees. The goal of the program is to recruit and retain diverse trainees into hematology.

Underrepresented minorities are even more underrepresented in subspecialties like hematology, and representation decreases from med school, to residency, to fellowship, to faculty positions. ASH has established a minority recruitment initiative, and the ambassador program is a function of this. One of our primary goals is getting the word out about ASH awards — for example, their minority medical student awards programs. These awards not only provide funding for students, but more importantly, they provide mentorship.

WHAT DO YOU CONSIDER TO BE SOME OF THE BIGGEST CHALLENGES AND THE BIGGEST SUCCESSES IN YOUR DIVERSITY WORK?

It's hard to talk about diversity-related issues, because we know we have a lot of work to do. We all have biases, which are a natural thing, but defensiveness does not allow us to make progress. Research shows that we are all better when our environments and communities are more diverse — we're better doctors, better people, and better researchers.

I'm proud to be an underrepresented minority in a leadership position, because I know that impacts people who are applying. This year the hematology division has more female fellows than male fellows, and it's wonderful to see young women achieving so much. The men are outstanding as well; it's just that since I can remember the men have outnumbered the women disproportionately. I'm heartened that diversity and inclusion have come to the forefront of discussion at Stanford, and that Stanford is showing that these issues are important.



▲ Left to right: **ANGELA ROGERS, MD**; **LEE BROCKUS, MD** and his wife; **ROBERT HARRINGTON, MD**; **SHRIRAM NALLAMSHETTY, MD**; **KAI SWENSON, MD**.

Residency Training with a Side of Wellness

It's a crisp, bright Sunday morning in Palo Alto, and over a dozen residents have congregated at the entrance to the Dish, a satellite structure reached by a popular 3.9-mile hiking trail that winds through the foothills behind Stanford's campus. They're joined by Robert Harrington, MD, the Arthur L. Bloomfield Professor of Medicine; Angela Rogers, MD, assistant professor of pulmonary and critical care medicine; Shriram Nallamshetty, MD, clinical assistant professor of cardiology; and several staff members from the Internal Medicine Residency Program.

This group has gathered for the pleasure of exercising and socializing, of course, but also to recognize the importance of well-being.

Over the last year, events like this one have happened with increasing frequency. They're part of a new initiative called REACH (Resiliency, Education, Advocacy, Community, Health), which is committed, broadly, to resident wellness.

It's no secret that medical residency training is intense, and the structure — long hours, compromised sleep, packed schedules — leaves little time for self-care. REACH, Karina Delgado-Carrasco, the residency program manager, says, is designed to help mitigate these stressors.

The program began as many in academia do: with a review of current research on the topic. "We read lots of publications on residency wellness and identified several domains that we wanted to cover," Delgado-Carrasco details. These findings were shared and discussed with the Internal

Medicine Residency Wellness Committee — composed primarily of current residents and "everyone we identified as important to resident well-being." The result? A multifaceted approach to wellness and burnout built on five pillars that Delgado-Carrasco believes "touch different aspects of residents' lives."

FOSTERING RESILIENCY WITH LAUGHTER

Resiliency — the ability to recover, and learn from, stressful circumstances and adversity — is a prized characteristic in the medical field, and one that's difficult to cultivate during stressful residency years. REACH is taking steps to change that through a monthly lecture series entitled "Residency Resilience" and other initiatives.

"Building resiliency skills can help prevent burnout and also promote a consistent feeling of wellness," notes Neera Ahuja, MD, clinical professor of hospital medicine and associate residency program director. "A large part of resilience is being able to see life through a positive lens: being optimistic about the future and believing that one can overcome any obstacle and learn from the process."

A key component to fostering this mindset, Ahuja explains, is to "seek and savor positive moments throughout one's day." To that end, the REACH program strives to "creatively sprinkle" exciting team-building activities throughout a resident's work day. These moments create an opportunity for house staff to "laugh and bond together — even for only 15 minutes before returning to the wards — which can have a lasting, positive impact."

PRIORITIZING EDUCATION THROUGH MENTORSHIP

Faculty mentorship is seen as a way to supplement residents' education and propel them into successful professional and academic careers. Mentors meet with mentees throughout a resident's career, collaborating on research and providing career guidance. Other events, like the first-ever Residency Research Symposium, provide a forum for trainees to share their work with the broader Stanford community.

SUPPORTING ADVOCACY BY PROVIDING A SEAT AT THE TABLE

Through internal REACH advocacy committees, such as the Committee on Residency Reform and the Diversity Group, residents are provided avenues to effect change and make their voices heard.

"The committee is composed of elected resident class representatives, chief residents, and program directors and administration," says Ron Witteles, MD, associate professor of cardiology and the residency program director. "It allows for a true 'ground-up' approach to program reform and is designed to turn feedback quickly into action. Residents work really hard; it's important for them to know they have an outlet to effect change."

Additional opportunities for advocacy abound and extend beyond the Stanford campus: A new diversity lecture series trains residents to better care for diverse patients, and tracks like Homeless Outreach and Social Medicine prime residents to care for the broader Bay Area community.

BUILDING COMMUNITY OVER QUALITY COFFEE

On September 28, 2018, as bleary-eyed residents filed into Stanford's Grant building for their morning report, they were met with a small surprise: artisanal coffee that had been brought in for them to celebrate National Coffee Day. Another morning, they received boba tea. At a scheduled lunch, unknowing residents were paired to complete an Amazing Race-style scavenger hunt all over campus.

These events, known informally as "pop-ups," are an important tenet of REACH and have a marked positive impact on residents. Delgado-Carrasco explains the thought process behind these small gestures: "It's about surprising residents to show that we appreciate them, to let them know that we know how hard they're working."

Other, larger events — like free tickets to Stanford's homecoming football game — are specifically designed to connect residents with each other and the community around them, to carve out space for them to build rapport.

"These events bring people together so they can meet and support each other," Delgado-Carrasco says. "That's how we build community."

CARING FOR RESIDENTS' HEALTH ON — AND OFF — THE YOGA MAT

REACH provides myriad ways for residents to care for their physical — and mental — health. Yoga aficionados can expect an opportunity to

unroll their mats and take a private yoga class taught by Ahuja. And each year, residents can lace up their sneakers and hit the softball field with their families, interns, program directors, and faculty for annual softball days. "It's fun to get everyone and their families out to that event," Delgado-Carrasco says.

REACH prioritizes mental health by clearly communicating available resources and destigmatizing the process of asking for help. Delgado-Carrasco elaborates: "We let all the residents know what's available to them through Stanford Hospital — like access to mental health programs and wellness coaches. We post these resources on a poster board every day. We want them to know that if you need to reach out to someone, there are people — and resources — available."

At the end of the Dish hike, residents, faculty, and program administrators chat with each other before heading home to enjoy the rest of their respective weekends. Pictures from the event broadcast the group's enthusiasm — everyone has wide grins and cheeks flushed from outdoor exercise. This happy image is one Delgado-Carrasco is committed to continuing as REACH looks into the future. "We're committed to supporting our residents during their time here and promoting their wellness, and we want them to know that everyone is invested in their well-being."



▲ ROBERT HARRINGTON, MD (far left) and ANGELA ROGERS, MD (far right) hike alongside residents.

The group stops for a photo in front of the dish satellite structure. ▼





New Cardiology Faculty

The cardiovascular medicine division has added two new faculty members, both of whom have skills that complement and supplement those of the rest of the division. Both Nitish Badhwar, MD, and Fatima Rodriguez, MD, MPH, have hit the ground running and are greatly enjoying their challenges and accomplishments.

▲ **NITISH BADHWAR, MD** (left), in the electrophysiology lab.

Nitish Badhwar

An Experienced Cardiologist with Sought-After Expertise

Nitish Badhwar is busily settling in as clinical professor of cardiovascular medicine. “I came to Stanford in part because of my expertise in ablating complex cardiac arrhythmias, particularly catheter ablations of ventricular tachycardia, and in part because of my interest in leading a fellowship program to develop future electrophysiologists. There is no shortage of patients with challenging arrhythmias, and the fellowship program will soon be expanding.”

One obvious reason for the growth in the arrhythmia population is the success cardiologists have had in treating other heart conditions. “In cardiology we have increased the lifespan of patients through drug therapy and preventive cardiology,” says Badhwar. “As patients who might have died in their sixties are now getting older, they are developing arrhythmias that affect their quality of life.”

Stanford has a large heart failure population and a very busy cardiac transplant center; the first U.S. adult heart transplant was completed at Stanford 50 years ago. For those who cannot qualify for a heart transplant, there are other options, including left ventricular assist devices (LVADs), which help with the pumping function of a weakened heart, and bi-ventricular implantable cardioverter defibrillators (ICDs), which are internal devices that stop deadly arrhythmias by delivering a shock to the heart.

“Most patients with severe heart failure have ventricular tachycardia,” explains Badhwar, “and that leads to shocks from ICDs or makes LVADs less efficient. Ultimately, the ventricular tachycardia (VT) has to be treated, but medications are not that effective. We often end up taking the patient

to the electrophysiology lab to eradicate the ventricular tachycardia by ablating it when possible.”

Another of Badhwar’s interests is idiopathic VT, where patients have normal heart function as opposed to heart failure. Badhwar has published the characteristics of idiopathic VT arising from the crux of the heart and, he says, “for this arrhythmia I am collaborating with my colleague, Marco Perez, MD, assistant professor, on a research project to identify the culprit genes.”

Badhwar has had a great deal of experience with atrial fibrillation (Afib), an increasingly common arrhythmia that puts patients at risk of stroke from blood clots that arise in the atrial appendage. While at UC-San Francisco, he helped develop and publish a new technique to control the rhythm of the heart in patients with persistent Afib. This technique uses a catheter-based approach through a vein in the leg to tie off the left atrial appendage. A multicenter clinical trial called the aMAZE trial is currently testing the technique. “The trial is very near and dear to my heart,” says Badhwar. “Stanford is recruiting patients now.”

LEADING A FELLOWSHIP PROGRAM

The fellowship program for electrophysiology (EP) trainees plays a large role in Badhwar’s work. “Because I had enjoyed training EP fellows at UCSF, I wanted to develop the electrophysiology training program here. One of my passions is teaching fellows, and it’s been very satisfying for me since I’ve been here. At UCSF I worked with Dr. Melvin Scheinman, one of the pioneers in this field, and I was very proud to use unique training tools such as teaching anatomy using cadaveric hearts in collaboration with pathology. I’ve also started intracardiac conferences for EP fellows and a national cardiology EP fellows program.”

The EP training program is also likely to expand because, says Badhwar, “It is clear that we are going to be doing more complex and novel procedures. My focus will be to make Stanford a magnet for U.S. and international fellows for world class electrophysiology training.”



▲ **FATIMA RODRIGUEZ, MD, MPH** (center), rounding with residents **ERIK ECKHART, MD** (left) and **KYLE CATABAY, MD** (right).

Fatima Rodriguez

A New Cardiology Faculty Member with Much-Needed Experience

The influences in Fatima Rodriguez's life began early. A child of immigrants, she was raised by a single mother who developed a pivotal illness: "My mom had rheumatic heart disease discovered when I was 15. I wanted to be just like her cardiologist who had made a life-changing diagnosis with just the use of his stethoscope." Additional influences came her way at Harvard Medical School, where she arrived wanting to "just be a good clinical doctor."

"There I had wonderful mentors who opened my eyes to public health research as well as taking care of individual patients. I received a Zuckerman Public Policy Fellowship in the John F. Kennedy School of Government, where I got to work with people across such sectors as business and law with a common goal of improving parts of health care that are not related to the medical system."

Today, Rodriguez is a new assistant professor in the cardiovascular division with a particular interest in health disparities and improving cardiovascular risk prediction for understudied populations. As a general and preventive cardiologist, she encounters her research subjects at every clinic and during each two-week period of inpatient care. "My clinical work always influences my research questions," she says. And, with 75 percent of her time devoted to research, she is able to think broadly about, and often test, new approaches to improving the health outcomes of her patients.

As a general cardiologist in a tertiary care center, Rodriguez works on the general cardiology service as an inpatient consultant and as part of a team that includes residents and medical students. She also has two weekly clinics: "I have an outpatient clinic in prevention focusing on risk

factor control and risk assessment, and I see patients with advanced lipid disorders. I also have a general cardiology clinic, where I have a particular interest in caring for Spanish-speaking patients, since limited English proficiency directly impacts patient health and adherence."

Dealing with patients' medications is often a challenge. She explains: "In cardiology we have many very wonderful medications, and most of them are generic and therefore cheap and readily accessible. But they can't work if you don't take them. I often struggle with patients about their resistance to taking statins, which unfortunately get such bad press. I have a deal with my patients where I usually don't start a new medication without taking something else away."

TAKING ON TELEMEDICINE

Proximity to Silicon Valley has had an effect on Rodriguez as well.

"I am the research director of our telemedicine clinic, which is called CardioClick. We are piloting it in the Stanford South Asian Translational Heart Initiative (SSATHI), a program designed for South Asians because of their higher risk of heart and vascular disease than any other ethnic group. Once CardioClick shows that it helps the SSATHI population understand their risk factors and develops targeted treatment plans for them, we will expand the services to the rest of preventive cardiology. We want to show not only that it's convenient, because our patients can access us on the computer or iPhone, but also that it improves clinical outcomes. We're also tracking patient satisfaction and engagement, factors that are important for the expansion of the program."

Having had wonderful mentoring throughout her early career, Rodriguez naturally drifted toward passing it forward. "What is becoming important to me now is mentoring others," she says, "especially underrepresented minorities and women. I hope to be able to continue to support people in that way."

Showing a Commitment to Cost Savings and High-Value Patient Care

As Stanford Health Care strives to be increasingly innovative and efficient, front-line providers develop and implement collaborative initiatives aimed at saving money and increasing high-value care. Two such programs illustrate those efforts.

THE COST SAVINGS REINVESTMENT PROGRAM

Leaders at Stanford Hospital expend a fair amount of time and energy figuring out how to improve the delivery of high-value care and patient outcomes and, when possible, to reduce costs. One such effort is the Cost Savings Reinvestment Program (CSRP), which Paul Heidenreich, MD, professor of cardiovascular medicine and vice chair for quality in the Department of Medicine, describes as a “Stanford Health Care–led initiative which asks faculty to come up with a cost-saving idea or intervention, and if it is approved and put in place, rewards those who carry it out with a 25 to 50 percent share of the savings in the first year.”

The funds cannot be used as any form of salary support or compensation for physicians, but they can be used at the discretion of the departments for supplies, research-related expenses, and continuing education.

THE APPROPRIATE USE OF ACCOMMODATIONS PROJECT

One project under the CSRP addressed a significant source of inpatient costs: the level of in-hospital care to which patients are assigned. A patient occupying an intensive care unit bed who does not require specialized personnel and equipment associated with such accommodations is

mismatched. Lisa Shieh, MD, PhD, clinical professor of hospital medicine, and David Svec, MD, MBA, assistant professor of hospital medicine, saw mismatching as expensive and wasteful. Besides simply saving money, says Svec, “We believed that using these extremely expensive resources appropriately would improve the value of the care patients receive.”

After exhaustively gathering data about accommodation costs and the distribution of patients in different levels of accommodation, Shieh and Svec estimated that assigning patients to more intensive levels of care than necessary was costing Stanford Hospital millions every year. They designed a project that would ensure appropriate levels of care for all patients by engaging physicians responsible for patients’ levels of care.

To effect meaningful change, they first had to get buy-in from all departments that assign accommodations, which meant meeting with the chair-people of those departments and convincing them to delegate a faculty member to drive their part of the project.

Shieh and Svec’s next step was to create a set of alerts to increase awareness about levels of care. The first alert they created asks — every day — whether a patient who is on cardiac monitoring still needs it. A response from a caregiver is required, causing that caregiver to think about whether the use is appropriate according to Stanford and national guidelines. A second alert reminds caregivers that their patient’s level of care is the intermediate intensive care unit, a fact sometimes missed because rooms on different levels look the same.

The results are positive so far. The CSRP project is likely to save the millions Shieh and Svec estimated, and they look forward to working on additional projects to provide higher value care for Stanford patients.

THE IMPROVEMENT CAPABILITY DEVELOPMENT PROGRAM

The Improvement Capability Development Program (ICDP) is a joint venture between the Department of Quality for Stanford Health Care and the School of Medicine. Its premise: Stanford Health Care commits to returning 1 to 2 percent of a department’s clinical revenue to help develop and execute far-reaching quality improvement (QI) projects, depending on its level of commitment and outcomes or deliverables. Although these funds cannot be distributed as a bonus to department faculty, they can support faculty conducting improvement work, including research and education related to quality.

According to Stephanie Harman, MD, clinical associate professor of primary care and population health, it has been a challenge for clinical departments to fund QI initiatives “because clinicians are bootstrapping projects with unfunded time and no project management support. With ICDP, Stanford Health Care is funding the time and project management it takes to lift up a new project that aims to improve the care we give.”



◀ PAUL HEIDENREICH, MD



▲ **WINNIE TEUTEBERG, MD** (left), and **STEPHANIE HARMAN, MD**, discuss the difficult conversations project.

DIFFICULT CONVERSATIONS WITH SERIOUSLY ILL PATIENTS

One ICDP project has to do with seriously ill patients. After learning that there are many patients with serious illness who have no advanced directives or other documentation of what matters most to them, Harman realized that important conversations with patients were not happening. “These are conversations that many physicians see as challenging and time-intensive, but the system wasn’t built for them to happen in busy clinic settings,” she says. The serious illness conversation project was developed to bring advance care planning to more patients and families and to integrate it into the standard work of the clinic.

To get the project off the ground, its leaders entered into a partnership with Ariadne Labs — a joint health system innovation center of Brigham & Women’s Hospital and the Harvard T. H. Chan School of Public Health — founded by Atul Gawande, MD, to help with training and workflow redesign. Harman explains the need for such help: “Left to our own devices, we would have been reinventing the wheel. We didn’t know what resources it would take to carry out the project on a large scale, for instance. The

ICDP project funding has paid a fee to join, which covers team training and coaching, the implementation of workflow redesign, and our membership in a collaborative national group. Those funds also support part of a physician leader’s time as well as true project management support.”

Harman says that while the program is still in the early stages, “it’s going well. The emphasis on implementation and workflow redesign ensures that physicians aren’t the sole holders of these conversations and ensures that they happen. Everything else we do in the clinic is team-based, and so should this be. The feedback from several groups of physicians, nurses, social workers, and clinic managers who underwent training is that they are 100 percent likely to recommend it.”

The physician leader of the project is Winnie Teuteberg, MD, clinical associate professor of primary care and population health. Her responsibility entails partnering with the project manager to implement the program. The hardest part, she believes, “is selling the program. We’re asking doctors to change a part of their job that deals with an emotionally-charged subject.”

The project uses a guide developed by Ariadne Labs, which Teuteberg describes as “having a list of about 10 questions that go through information sharing and patient preferences. It includes ways for providers to share a prognosis if that’s appropriate. Then it talks about hopes and goals, fears and worries. The ultimate wrap-up is the physician pulling the information together and making a recommendation about where to go next.”

Ann Weinacker, MD, senior vice chair of medicine for clinical affairs, reflects on the fundamental value of programs such as the CSRP and ICDP: “What is really exciting about these programs is that they actively engage physicians and School of Medicine clinical departments in improvement work that aligns with the goals of Stanford Medicine, an alliance between the School of Medicine and the hospitals. The development of ICDP and CSRP was born of the recognition that the commitment of physicians to this work is essential to increasing the value of the care we deliver.”

Staff meet to discuss the appropriate use of accommodations project. From left: **ARPITA PATEL, RN; ROSDY PAMATIAN, RN; LISA SHIEH, MD, PHD; DAVID SVEC, MD, MBA; PAUL GEORGANTES, MSN, RN, CNL.** ▼





▲ **KEN MAHAFFEY, MD** (right), discusses site-based research with **REBECCA MCCUE**.

Stanford Center for Clinical Research: **The Engine That's Powering Clinical Research**

The Stanford Center for Clinical Research (SCCR) is the “operational engine” that enables many faculty throughout Stanford to drive robust clinical research enterprises, according to Kenneth Mahaffey, MD, professor of cardiovascular medicine, vice chair of clinical research in the Department of Medicine, and director of SCCR.

Since its inception in late 2014, SCCR has grown to 70 staff and partnered with more than 50 faculty and 25 fellows on 82 research projects.

SCCR has three foundational enterprises:

1. A site-based research program led by Rebecca McCue to support projects in which Stanford researchers enroll Stanford patients in clinical trials.
2. A coordinating center led by Amol Rajmane, MD, to help design and conduct multicenter registries, trials, and outcome programs.
3. An educational component led by Kiera Larsen, RN, which has created preceptorships and a large portfolio of educational opportunities — including scientific seminars and Good Clinical Practice workshops for research staff — and educational events for industry.

SUPPORTING FACULTY ACROSS THE SCHOOL OF MEDICINE FOR SITE-BASED RESEARCH

SCCR works with faculty to understand research interests and then develop their research portfolios to support the desired vision. SCCR hires, trains, manages, and mentors research staff to navigate complex processes, letting faculty focus on their scientific and clinical care activities.

“SCCR doesn’t remove the faculty member from the key relationship with research coordinators, but we take on a lot of the administrative burden,”

McCue, the associate director for SCCR’s site-based research projects, points out.

In just a few years, SCCR’s partnership with the division of gastroenterology and hepatology has helped the division’s research portfolio grow from 10 studies to more than 50. The SCCR team works with 22 principal investigators and 11 dedicated research staff in the division. Key achievements for the division include: collaboration with the Research Management Group to determine the appropriate funding for studies, a streamlined budgeting and contract process that has led to earlier initiation of studies, improved financial metrics, the adoption of a central Institutional Review Board process, and a culture of collaboration and efficiency.

SCCR teams support many types of research — drug, medical device, and mobile/digital technology trials; investigator-initiated studies; and multisite registries. Investigators collaborate across divisions and departments in the School of Medicine, with groups such as neurosurgery; vascular surgery; radiology; biodesign; athletics; infectious diseases; and Spectrum, the Stanford Center for Clinical and Translational Research and Education — furthering a holistic and multidisciplinary approach.

Sanjiv (Sam) Gambhir, MD, PhD, professor and chairman of radiology, helped launch Project Baseline, one of the largest projects that SCCR works on. Project Baseline is a collaborative effort among Stanford Medicine, Duke University School of Medicine, Verily, and Google. The researchers plan to enroll approximately 10,000 participants with an extraordinarily detailed evaluation of each participant; the idea is to characterize what it means to be healthy and to capture changes during a transition to disease.

“A large part of Project Baseline deals with trying to understand the transition from health to disease on a personal level, which integrates precision medicine, preventive health, and mobile and digital technologies,” Mahaffey says.

To help with study recruitment, SCCR leaders launched a Community Advisory Board for Clinical Research in 2015, which allows faculty to engage community members as partners. The aim of the advisory board is to bridge the gap between researchers and the community to enhance clinical research.

MULTISITE RESEARCH PROJECT COORDINATION

SCCR’s Coordinating Center helps faculty design and run multisite research projects, as its project managers provide input on protocols, assist with FDA and Institutional Review Board submissions, shape sustainable study budgets, and manage sites. It also offers core lab administration, safety desk work, event adjudication, and data safety monitoring committee management.

The Apple Heart Study, conducted to learn if an app can use data from the Apple Watch to identify irregular heart rhythms, is one example of how SCCR works with Stanford researchers and sponsors to leverage technology and innovation to rigorously test drugs, devices, and other interventions.

“We have a portfolio of five studies relating to mobile and digital technologies created in part by an intense interest in these technologies by many Stanford faculty and by a strategic partnership with the Center for Digital Health,” says Rajmane, SCCR’s associate director for the Coordinating Center.

The Coordinating Center is also managing the research operations for a study evaluating concussions using an innovative mouth guard with local high school football programs. Partners include leading concussion experts from Stanford: bioengineer David Camarillo, PhD; neurosurgeon Gerald Grant, MD; and neuroradiologist Michael Zeineh, MD, PhD.

Every clinical research project involves tasks like project management, site start-up and initiation, oversight for recruitment and retention, data collection, core lab activities, safety event reporting, and quality and compliance oversight. For faculty who want to lead multicenter clinical research projects, SCCR eliminates the need to outsource those tasks.

“Faculty can lead these large projects without worrying about the operational administration and coordination, and as the activities are performed by a Stanford team and not by an outside entity, it’s easy for them to coordinate and work with the team. Faculty can have a much higher profile in these projects because all the research activities are being done here at Stanford,” Mahaffey says.

David Maron, MD, a clinical professor of cardiovascular medicine, notes how SCCR is readily available to round out his research team by helping complete proposals. He recalls

an instance when a research application required detailed information about a committee to adjudicate clinical events and notes how “SCCR provided a description of the organization, the budget, and the personnel that was required in the application.”

PARTNERSHIPS AND TEAM SCIENCE

Mahaffey describes the importance of having SCCR collaborate with institutional resources like the Research Management Group, the Institutional Review Board, and the Privacy Office.

“We work with these resources to understand how to oversee new types of research protocols to make sure processes are appropriate. We want them to adhere not only to institution policies and standards, but also to external requirements from the FDA and NIH,” he says.

On the subject of partnership, Mintu Turakhia, MD, associate professor of cardiovascular medicine and director of the Center for Digital Health, describes his relationship with SCCR.

“Working with SCCR has been seminal to my career progression. I’ve had the privilege of working with Ken [Mahaffey] and his outstanding team for over four years now on a series of clinical trials that range from traditional small, single-center trials all the way to the Apple Heart Study, a massive virtual clinical trial. In the early days of SCCR, it was a handful of us working together — much like a startup — to get the job done. Now the group has about 70 people and is a remarkably well-oiled machine,” Turakhia says.

SCCR is involved with faculty who are experts in a variety of therapeutic subjects and areas of practice. “We have projects that really epitomize team science, with faculty from multiple disciplines and research staff from multiple areas, including data scientists, project managers, information technology experts, biostatisticians, and bioinformaticians,” Mahaffey says.

He describes how SCCR’s activities over the past four years speak to its mission of “conducting and promoting high-impact, innovative clinical research to improve human health.”

▼ Apple Heart Study Project Manager **NISHA TALATI, MBA** (left), reviews data with **AMOL RAJMANE, MD**.





◀ **MAGGIE NING, MD**, presents her work to **SHRIRAM NALLAMSHETTY, MD**.

Conference Showcases Residency Research

Wearing a black Stanford Medicine fleece over his blue scrubs, third-year internal medicine resident Gilad Jaffe, MD, stood in front of a poster that described his research on screening rates for primary aldosteronism in patients with resistant hypertension.

He shared the specifics of his findings with a roomful of attendees at the first-ever Stanford Medicine Residency Research Symposium.

Jaffe was one of 49 residents who participated in the event, which was designed to “highlight the remarkable things our residents are doing,” says Angela Rogers, MD, an assistant professor of pulmonary and critical care medicine and the associate program director of the Stanford Internal Medicine Residency Program, who oversaw the symposium.

“More than 80 percent of Stanford residents take a dedicated research month during their time here,” she explains, “and they are amazingly productive. The amount of work and research that they do on their nights and weekends is worth celebrating.”

Resident Jimmy Tooley, MD, one of the leaders of the Stanford Internal Medicine Research Interest Group who helped organize the event, agreed with Rogers, adding: “There is a lot of great mentorship and research going on. I am so impressed and inspired by all the amazing work being done by my peers.”

During the event, faculty judges, mentors, and fellow residents walked up and down several aisles of poster boards, pausing to ask questions, give insights and feedback, and take notes.

The projects on display spanned disciplines, fields, and diseases — investigating topics ranging from advanced care planning to complications of cirrhosis. “Essentially every specialty within medicine was represented,” recalls Rogers. “It was an opportunity for residents to show each other their work, and there aren’t a lot of avenues for that.”

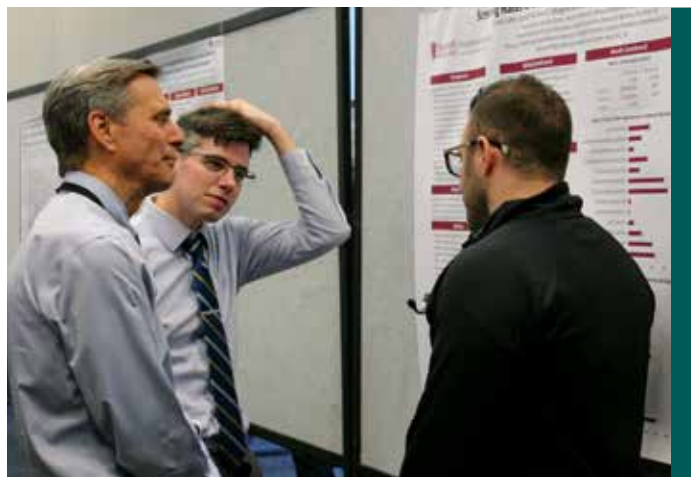
It was also an opportunity to highlight the important role that mentorship and guidance play throughout the Stanford residency experience. “The

projects that were presented involved 25 mentors — it’s a testament to how many faculty give their time,” says Rogers. “This type of long-term relationship with a single mentor can be instrumental, and it’s something we pride ourselves on.”

Jaffe has seen the benefits of this long-term mentorship firsthand. He’s been working alongside his mentor, Vivek Bhalla, MD, an assistant professor of nephrology, since the start of his intern year in 2016. “Dr. Bhalla is an outstanding teacher, mentor, and physician,” Jaffe explains. “He is extremely supportive of me and my goals. He worked with me closely and guided me through the process, but also gave me room to spread my wings and figure out the research landscape. He always made time for our research, even if it meant talking to him on his personal time at home.”

At the end of the event, the judges picked 10 winners who received small monetary prizes, but it was clear from the palpable energy and excitement in the room that it was a valuable experience for all involved. “It was spectacularly successful, and we plan to host it every year,” Rogers confirms. “The enthusiastic response from residents and faculty made the event celebratory and supportive.”

From left: **DAVID MARON, MD**, and **ALEXANDER PERINO, MD**, ask **GILAD JAFFE, MD**, about his research poster. ▼



A Portfolio to Capture Faculty's Inventive Side

As faculty members are being considered for promotion, they compile their CVs, including their publications and lists of professional activities, to paint a holistic picture of their academic achievements. But for some Stanford faculty, who live and work in the heart of Silicon Valley amid its booming tech industry, those quotidian check boxes don't capture their whole story. That's why a group of professors in the Department of Medicine are developing an "innovator's portfolio," much like an artist's portfolio, which showcases technologies that a faculty member has piloted.

Ryan Van Wert, MD, clinical assistant professor of pulmonary and critical care medicine, was one of the first faculty members to try filling in the innovator's portfolio. His portfolio includes Vynca, a company he founded to manage advance directive documentation [see sidebar].

Van Wert credits Paul J. Wang, MD, professor of cardiovascular medicine, with the success of the innovator's portfolio.

"There was a recognized need for an environment and training pathway for faculty to become innovators," Wang says.

"It was equally recognized that innovation as an endeavor is different than typical academic pursuits. But we wanted to go deeper than just encouraging faculty to say 'I patented X,'" Wang adds.

The innovator's portfolio is intended to capture what the impact of that patent is — for example, how many patients are affected by the technology, how it's related to new diagnoses and treatments, whether it decreases health care costs, and if it generates additional intellectual property.

Wang and Van Wert are collaborating with Robert Harrington, MD, the Arthur L. Bloomfield Professor of Medicine, and Paul Yock, MD, professor of medicine, of bioengineering, and, by courtesy, of mechanical engineering. They all presented the innovator's portfolio as a pilot program at the 2018 Faculty Forum on Clinical Research in the department.

Andrew Hoffman, MD, professor of endocrinology and vice chair for academic affairs in the department, is supportive of the idea and intends to incorporate it into faculty evaluations soon.

"As faculty, we don't have a mechanism to present ourselves this way, and Andy said that promotion committees don't have a means of interpreting it," Wang says. "So we're creating that common language."

Ultimately, Van Wert wants his colleagues' innovator's portfolio concept to persist along the entire span of a clinician's promotion cycle. "It's designed to be relevant from assistant to associate to full professor," he says. "The portfolio will recognize a career of innovation during which the bar appropriately rises at every level."

RYAN VAN WERT, MD ▼

VYNCA ENCOMPASSES THE SPIRIT OF SILICON VALLEY

In 2013, Ryan Van Wert, MD, was an innovation fellow in the Stanford Biodesign Program, now the Stanford Byers Center for Biodesign. His time in the program spurred him to help create Vynca, a company that uses cloud-based technology to aggregate and corroborate documentation and care instructions for families of terminally ill patients.

Vynca manages 420,000 advance care planning documents for patients at 60 hospitals using cloud-based technology. It not only helps patients understand their different choices (like power of attorney or do-not-resuscitate forms), but it can also share those documents between hospitals and nursing homes, while reconciling different copies of the same document signed in different locations. "We aggregate them in a single source of truth in the cloud," Van Wert says.

The company facilitates a reduction in unwanted hospitalizations and intensive care utilization — reducing the stress on health care providers and improving patients' quality of care. "We're helping families and clinicians to go through the very complicated process of reflecting on values and then developing goals of care that fit within certain clinical contexts," says Van Wert.





▲ From left: KRISTIN BARKLUND, KIMYA STIDUM, MARGARET WEI, PERMSUK LAMPRASITIPON, ANTHONY DUONG, AMANDA PECORARO, LOTO REED, ELSIE WANG.

Primary Care and Population Health: The SCOPE of Compassion

Loto Reed, associate coordinator in the division of primary care and population health, went into her annual review armed with an idea: a staff community service program to build motivation and togetherness in the division. Probably no one, including her, could have imagined how quickly and successfully the program would come together.

Her division chief, Sang-ick Chang, MD, MPH, clinical professor of primary care and population health, was very receptive to the idea. And when Chang brought it up at the next division staff meeting, a handful of staff members were immediately interested. By February 2018 Stanford Community Outreach Partnership Efforts (SCOPE) had begun, and in March the group hosted its first event at an East Palo Alto homeless shelter, ProjectWEHOPE, with 10 volunteers including Chang and Jonathan Shaw, MD, clinical assistant professor of primary care and population health.

Chang has already noticed how SCOPE has affected his staff. Since the group started, he says, “There’s a palpable sense of shared mission, fun and pride, with more interaction and support among the staff.”

A LOCAL EFFORT

The group is well-organized: 10 core members rotate responsibilities, and each month a different member is responsible for choosing a volunteer organization and coordinating the effort. Events are often in the evenings, to accommodate staff work schedules.

SCOPE has also partnered with three core organizations: ProjectWEHOPE in East Palo Alto, Hope’s Corner in Mountain View, and HealthTrust in San Jose. Events are varied, ranging from packing lunches at a homeless shelter to preparing boxes and helping clean the kitchen at San Jose Health Trust.

Reed says that these partnerships are about making a difference where you live. “As a team, we decided to focus on building a strong relationship with our community partners so we can have an impact, and we wanted to keep it as local as possible,” she explains. “We have communities right in our backyard that can really use the support. There’s so much we can do to help our community,” she adds. “It’s just nice for our neighbors to know that Stanford cares.”

The partnerships also allow for progress over time. “We’re hoping to show volunteers how their efforts are improving the lives of the less fortunate,” Reed explains. “And it’s really helping everyone — not just the people that receive the help, but also our volunteers in SCOPE, because they get a real idea of what’s going on in our communities.”

Faculty are getting involved as well. “Everyone’s so excited and it’s actually increased the interest for the faculty to do some collaborative work with the staff. These events have really built a bridge between the faculty and staff,” Reed states.

Chang agrees: “People, both faculty and staff, come to Stanford to be part of a noble cause, and that nobility extends not just to academic and clinical contribution, but to social and community contribution as well.”

One of their major efforts this year was a supplies drive for the Ravenswood after-school program in East Palo Alto. SCOPE members Amanda Pecoraro, administrative associate for primary care and population health, and Tayler Kiss-Lane, fellowship program coordinator for primary care and population health, created an Amazon wish list based on Ravenswood’s needs. Faculty and staff went online and picked items to donate, which enabled SCOPE to collect over \$2,000 worth of supplies.

A VISION FOR THE FUTURE

SCOPE members also wanted a concrete way of tracking their contributions. They set a goal of 200 volunteer hours for 2018, and as of September, they had already completed 167 hours. The group ran events through the end of 2018, including a winter care package drive with packages of clothing and other necessities to help keep the less fortunate warm during the winter season as well as “an uplifting message to keep their hearts warm,” according to Reed.

2019 will be a year for strategic planning to determine what the group will look like moving forward. Monthly lunch meetings help everyone prioritize. The majority of the volunteers are from primary care and population health, although they have also worked side by side with staff from other divisions. “We’re hoping this can spark interest for other staff members to collaborate and share ideas and events so that we as a Department of Medicine community can come together and give support where it’s most needed,” Reed says.

Chang shares her sense of purpose: “My hope is that SCOPE will add weight to long-standing community partnership efforts around the campus,” he says, “to tip the scales for Stanford Medicine to become known in our local community not just as an international scientific entity, but one that truly cares about the health and well-being of our local community.”

SCOPE and other staff-led initiatives like it are a new way of looking at wellness: By helping others, we also help ourselves.



▲ From left: **DANI ZIONTS, AMANDA PECORARO, LOTO REED, TAYLER KISS-LANE, ANTHONY DUONG, NADIA SAFAEINILI, AMIR SHAGHAFI, MAE VERANO.**

▼ From left: **ANTHONY DUONG, LOTO REED, KIRSTI WENG, ELSIE WANG.**



COMPASSION INTO ACTION

Team members of the primary care and population health division are passionate about SCOPE and the values that led them to community service in the first place. They’ve adopted the motto “Putting Compassion into Action.” Here’s what they have to say:

Margaret Wei, finance manager, calls the SCOPE events “very uplifting,” adding that they give her “a sense of joy, hope, optimism, faith and relief.”

Taylor Kiss-Lane, fellowship program coordinator, called volunteering for SCOPE “extremely rewarding and fulfilling, in addition to being incredibly important.” She adds, “I believe it’s our social responsibility to help our neighbors and fellow human beings in need.”

Kimya Stidum, education program coordinator, calls service “a core value.” “If I profess to love my neighbors yet do not offer what I can to support them when they find themselves in need of support, then my values and actions are not in alignment and that is a problem for me,” she states.

Amanda Pecoraro, administrative associate, grew up with grandparents who did charitable works and encouraged their grandchildren to do the same. “I guess they rubbed off on me,” she concludes. “I’ve always tried to volunteer around the holidays or at different events. I currently sit on a board in my neighborhood that fosters opportunities for our low-income residents. So when Loto asked if it was something I would be interested in, there was no question about it.”

Anthony Duong, program coordinator, appreciates the sense of power and community that SCOPE brings: “I love how we empower other faculty and staff members to make them realize they have the capacity to make a difference in people’s lives.”

Nadia Safaeinili, qualitative researcher and project manager, says SCOPE “gives the division the opportunity to practice our mission in a very personal and real way.” She adds, “SCOPE could not exist as it does without Loto’s thoughtful leadership, organization and warmth. She cares so deeply about serving others and that makes our group shine!”

Sang-ick Chang, MD, PhD, clinical professor in primary care and population health, is deeply impressed by the work SCOPE has done: “The competence, diligence, and idealism with which the participants approached this project is a window into how high-performing and idealistic our staff really are,” he says. “I have been truly impressed with their passion and successes, and it makes me realize how lucky we are to have such a talented team.”

A Project to Reduce Rape of Young Kenyans

The topic is daunting, even unbelievable in our world, and the complexities that surround it are hard to grasp. How do you teach girls aged 12 to 14 to fight off a sexual assault — in Kenya — in slums where regular meals and clean water are not assured? Moreover, almost as important, how can you know whether the lessons actually worked?

Reliable survey data indicate that as many as 46 percent of Kenyan women experience sexual assault as children. For the most part, these girls do not report rapes or assaults, even to their parents, as the risks are too great.

The nonprofit group No Means No Worldwide, founded by Lee Paiva from San Francisco, has been working to reduce the incidence of rape in young girls and women in Kenya since 2010. Anecdotal reports about the prevention program have been positive, with the girls being inspired by an educational intervention that increases their self-esteem and teaches them defensive tactics.



The reports of the girls successfully avoiding attempted rapes and sexual assaults have been rewarding to those involved in the program. But objective data had been missing, leaving them to wonder if the time and money being spent are having the desired result. To gather those data, Stanford researchers, led by Michael Baiocchi, PhD, tackled the challenging job of designing a randomized controlled trial that compares the rate of rape in trained girls with that in untrained girls.

THE INTERVENTION

The intervention is taught in school by local women and introduces four pathways to preventing sexual assault. The girls are introduced to situational awareness, where they learn to recognize dangerous situations and to look around for who or what can help them. They are taught that their own thoughts and feelings are valued and thus they learn to be empowered to make themselves heard in dangerous situations. They learn what to say — to shout — in such a situation. And they learn physical skills for defending themselves. Not only do they learn to fight off an attack, often by family members or boyfriends, but they also learn how to report those attacks so the situation can be improved.

CHALLENGES OF RANDOMIZATION

The team decided that the most ethical way to learn the relative effectiveness of the intervention and, critically, to collect objective data on outcomes is to use a delayed-treatment study design. Girls would be randomized into two groups: one taught the intervention immediately, the other taught the intervention later. The two groups complete surveys at three time points, measuring the difference in the number of rapes in both groups of girls over two years.

Baiocchi, assistant professor of medicine in the Stanford Prevention Research Center, is the principal investigator of the trial. Although randomized controlled trials are considered the gold standard for measuring differences between two groups, as a statistician Baiocchi immediately recognized issues that might compromise the results of the trial and devised ways to either avoid or account for them.

PROBLEMS AND SOLUTIONS

Having learned about some specific problems from their earlier, smaller study of girls in 28 schools, Baiocchi and his colleagues — statistics PhD students Rina Friedberg and Evan Rosenman — created statistical tools that would let them avoid a false-negative result. A study with a false-negative result, which would incorrectly show no benefit from an intervention that really does work, can be devastating as it can cripple an otherwise valuable line of research.

◀ MICHAEL BAIOCCHI, PHD



Photo by Nichole Sobbecki

▲ Stanford researchers **CLEA SARNQUIST** and **MICHAEL BAIOCCHI, PHD** (center left and right), work with Kenyan researchers and data collectors to refine their latest survey.

The first statistical problem was spillover, which is a major problem for behavioral interventions. In Nairobi the schools the girls attended were close enough to one another that girls who were taught the intervention might share what they learned with friends who were in the delayed intervention group. After several months of such sharing, the trial could have 500 trained girls in the intervention group, another 100 trained girls in the supposedly ‘untrained’ group, and only 400 truly untrained girls. This spillover between trained and untrained groups could jeopardize the result. “Even if your intervention is working and it’s doing a really good job,” explains Baiocchi, “if it spills over in ways that you’re not anticipating you get a fake null result.”

The fix for this problem, says Baiocchi, was to develop a framework for “weighted-design randomized trials where you can either create a lot of spillover or no spillover at all. For interventions that have a social component, such as the Kenyan girls playing together, the framework is useful for defining indirect effects.”

The second problem was imbalances between the arms of randomized trials. Statistically, a randomized trial with 5,000 flips of a coin is very likely to have groups that are similar, whereas a trial with 28 flips of a coin is quite likely to have imbalances. In their initial trial of 28 schools, imbalance hit the study hard. One of the two groups had a rape rate of 11 percent at baseline while the other had a rape rate of 7 percent; such an imbalance at baseline can challenge drawing strong results from the trial. “To overcome this,” says Baiocchi, “we developed a sensitivity analysis that asks how imbalanced arms of the trial have to be before your conclusions are suspect. Our framework helps researchers who use cluster-randomized trials understand how much imbalance is too much imbalance. This framework is a win for public health randomized trials.”

ADAPTING THE NEW TRIAL

The current trial includes girls in 94 schools: Girls in 48 of the schools receive the training immediately while 46 schools will have the intervention at a later date. The researchers have been careful to put schools with tight social bonds in the same cohort, therefore avoiding having the intervention spill over from trained to untrained girls. Friedberg explains that “just dividing everyone geographically might result in two populations that are materially different, and then you have another problem.”

Baiocchi adds that to avoid both the spillover and imbalance problems “we selected schools that were far enough apart that we didn’t believe the girls would form friendship bonds but close enough that the schools looked very similar.”

AN UNEXPECTED STUDY

Baiocchi and his graduate students have an opportunity to measure the impact of their training in a completely unanticipated study. Rosenman describes a new project with political beginnings. “Because of Kenya’s disputed presidential election in 2017 and the wave of violence that ensued, our data collection was disrupted for months. That gave us the opportunity to think about how political violence relates to sexual violence, and so we are comparing two cohorts, one from before the election and one after.”

Baiocchi further explains how this study will help them: “We would expect to see an uptick of violence against vulnerable populations during this period. Now we have a chance to learn whether our intervention performed better or worse during those months.” This project may provide useful, empirical evidence for developing interventions to reduce rates of sexual assault in active conflict zones — the topic of the 2018 Nobel Peace Prize.

Committee That Advises Medicare on Service Prices Is Biased — but Bias Has Its Benefits

Physicians on a committee that recommends prices for health care services under Medicare are biased toward their own specialties, resulting in proposals that could generate more income for their own practices, according to research by Stanford Health Policy's David Chan, MD, PhD.

Yet Chan also finds that involving physicians in setting prices improves the quality of information used in the process — a significant benefit for Medicare and patients alike.

“Communication is good because information benefits everyone,” says Chan, an assistant professor of medicine at the School of Medicine and investigator at the Department of Veterans Affairs. “Sometimes you need some bias to allow communication to happen. This is often why we have intermediaries, and in the case of the committee, it appears to be an example of this.”

Chan and his colleague, Michael Dickstein from New York University, published their independent analysis in a working paper released by the National Bureau of Economic Research.

Medicare, the federal health insurance program for elderly Americans, pays about \$70 billion a year to the physicians who provide health care services to its participants.

The prices for those services are set by a committee of physicians convened by the American Medical Association, known as the Relative Value Scale Update Committee (RUC).

The committee is composed of 25 physician specialty society representatives; 21 of these members occupy permanent seats, while the remaining four rotate. During their three meetings each year, 200 to 300 physician services typically are up for review.

The committee meets behind closed doors. Few know how the physicians — most of whom are specialists and not primary care doctors — reach their recommendations for the health care service prices, which Medicare then typically adopts.

But health policy and Medicare analysts do know the committee carries great clout.



▲ DAVID CHAN, MD, PHD

Their recommendations not only influence Medicare's direct expenditures, but also indirectly shape pricing in the overall market for physician services, which are valued at \$480 billion per year or 2.7 percent of the U.S. gross domestic product. The prices of medical procedures can also drive larger changes in physicians' procedural choices and the specialty career decisions of future physicians.

Chan, who is also a faculty fellow at the Stanford Institute for Economic Policy Research, spent four years investigating the practices of the committee and whether the prices recommended by the physicians are biased toward their own specialties. He and Dickstein gained access to 4,423 fee proposals that were reviewed by the committee from 1992 to 2013.

They found that increasing a measure of affiliation between the committee and proposers by one standard deviation increases prices by 10 percent — a consequence that could support critics who claim there is conflict of interest among the committee members.

But Chan and Dickstein believe that bias is not the only thing that matters when evaluating the committee. Unbiased pricing recommendations may still lead to poor pricing suggestions if they are imprecise and have no relationship to the truth.

They examined the quality of the pricing process by looking at the underlying data used in pricing proposals, as well as whether private insurers follow Medicare pricing decisions more when the underlying proposals come from affiliated specialties. Overall, they found that pricing decisions from affiliated proposals may be of higher quality, as private insurance tends to follow these decisions more closely.

“Our findings suggest Medicare faces a balancing act in setting prices,” the authors wrote. “Inviting input from the RUC may introduce bias in prices, but it may also improve the information extracted from specialties.”



▲ MICHELE BARRY, MD (right), discusses effects of climate change with KARI NADEAU, MD, PHD (left and below at Global Climate Action Summit).

Crossing Divisions to Solve Global Climate Change

“Global climate change has direct effects on our health, and in my field one direct effect is allergy,” says Kari Nadeau, MD, PhD, professor of medicine and pediatrics (and, by courtesy, otolaryngology).

“Increased carbon dioxide changes the pH level in the air, which causes longer seasons of pollen emissions and adversely affects those with asthma and allergies,” says Nadeau, the section chief of asthma and allergy in the division of pulmonary and critical care medicine and director of the Sean N. Parker Center for Allergy and Asthma Research.

Nadeau joined forces with Michele Barry, MD, professor of medicine and senior associate dean for global health, to talk about children’s health at a September 2018 Global Climate Action Summit in San Francisco.

The goal of the four-day event was to help state and local governments, businesses, universities, and individuals find solutions to problems caused by climate change. The summit was a call to create a practical plan and encourage citizens to think about how to mitigate climate change to improve our health.

Barry and Nadeau exemplify team science. They worked on the summit jointly as well as with others in the School of Medicine, across Stanford, at other universities, and in the Office of the Governor of California. The two Stanford professors collaborated with former Environmental Protection Agency administrator Gina McCarthy, who now co-directs C-CHANGE (Center for Climate, Health and the Global Environment) at Harvard, on a “Kids and Climate” panel symposium during the summit.

“Children bear the brunt of this,” says Barry, who directs the Center for Innovation in Global Health (CIGH). “Eighty-eight percent of the global burden of disease attributable to climate change falls on children under 5.

And we can’t think about just us or just our kids — we live in a globalized world.”

She cited a 2015 statement from the American Academy of Pediatrics that linked global warming and the health of children. “While climate change poses a threat to all human health and safety, children are uniquely vulnerable,” the statement said.

“Because children breathe more air and drink more fluid per body weight, they are exposed to more toxic air pollutants while their immune systems are still developing — and as anyone who’s spent time with a toddler knows, they put all kinds of things in their mouths — and thus are extremely vulnerable to ground pollutants,” Barry adds.

“We can all be instruments of change,” Nadeau says, explaining how a community she works with in Fresno recognized that the school buses their children rode each day were contributing to a high incidence of asthma. Together, community members and the school district worked to switch technologies in the buses to reduce diesel emissions. The result? A dramatic decrease in the incidence of asthma in their kids.

The Global Climate Action Summit is just one example of how Barry and Nadeau collaborate.

They teach alongside one another in Barry’s Planetary Health and Women’s Global Leadership class. Under Nadeau’s direction, the Sean N. Parker Center for Allergy and Asthma Research has awarded seed grants to several members of the CIGH. One grant was awarded in 2018 to CIGH member Gary Darmstadt, MD, for research involving treatment of gut and skin problems in children in Bangladesh.

A Push for Biomedical Innovation: **Three Chan Zuckerberg Biohub Stories**

The Chan Zuckerberg Biohub Initiative springs from a basic goal: “to make fundamental discoveries and develop new technologies that will enable doctors to cure, prevent, or manage all diseases during our children’s lifetime.” To that end, the Initiative awards money to scientists from three institutions — UC–San Francisco, UC–Berkeley, and Stanford — for leading biomedical research projects. Stanford is always well-represented; Catherine Blish, Euan Ashley, and David Relman are among recent recipients.

Catherine Blish *The Diversity of Immune Responses*

Catherine Blish, MD, PhD, is an associate professor of infectious diseases with a research background in immunology. Her project explores how the innate immune system copes with the diversity of viruses it encounters. As she explains, many people study the diversity of the adaptive host-immune response, but there’s also an “underappreciated” diversity within the viruses that infect us.

“So the question is, how does an immune cell recognize a bunch of different viruses?” Blish asks. “And what features of that recognition are common among viruses? If we know that, we can figure out how to target the responses that will best fight the viruses.”

Blish is looking at the innate immune system (specifically the natural killer cells and the monocytes) and how it recognizes patterns and diverse strains. She aims to figure out how those common recognition patterns

can be used to “come up with new, more broadly reactive approaches to vaccination.”

This research, which Blish calls “high risk, high reward,” has an ultimate goal of creating designer vaccines. One major goal is a universal vaccine that protects against all strains of the flu for several years.

The high reward part is clear, but why exactly is this high risk? Blish explains: “We’re studying cells of the innate immune system that one normally doesn’t try to generate vaccines from, so we have a lot of underlying biology to understand before we can actually bring this to the clinic.” She adds, “But that’s also what makes it more fun; it’s a new approach.”

Her Biohub award is a five-year conceptually oriented grant. Since the award was presented in 2017, Blish has made significant progress. Her team is working on three viruses: HIV, influenza, and dengue. As she puts it, “We’re getting close to understanding the specific receptors on natural killer cells that are required for recognizing HIV-infected cells.” They’ve also “identified a number of mechanisms by which natural killer (or NK) cells recognize influenza-infected cells.” She adds, “Some pathways are similar between the two viruses and some are different. So that’s been exciting.”

She’s optimistic about the results of her work. “We’re learning about fundamental immunologic mechanisms,” she says. “That will help in the future as we think about therapeutics and vaccines.”



◀ CATHERINE BLISH, MD

EUAN ASHLEY, MBCHB, DPHIL ▶



Euan Ashley

Genes and Genetic Variants in the Heart

Euan Ashley, MBChB, DPhil, professor of cardiovascular medicine and genetics, came to Stanford from the United Kingdom 14 years ago. He's excited by the possibilities of his Biohub award, which he calls "a really fantastic opportunity" for better understanding the heart. His grant's ultimate goal is to "understand at a much deeper level how genes and genetic variants interact in heart development, health, and disease." This understanding, he believes, will "allow us to target disease more precisely."

Ashley's grant proposal began as a collaborative effort. He and colleagues like James Priest, MD, assistant professor of pediatric cardiology at Stanford (as well as other investigators at Stanford, UCSF, and UC-Berkeley), tried to figure out "where we could really make an advance that wouldn't have been possible without this award." They ended with the goal of better understanding the heart at multiple levels, and in particular how this understanding could be "elevated by the use of new approaches such as artificial intelligence."

The group, then, will focus on three investigations: The team at UCSF will work together with the Stanford group on deep learning, which is a form of artificial intelligence particularly suitable for interpreting images and videos. It can be trained to recognize areas of the heart from ultrasound and MRI scans and identify abnormalities, some of which might not be visible to the human eye.

The UC-Berkeley team will be studying genetic variants. Ashley explains that in the past researchers usually had to confine themselves to studying a single variant at a time, but that "doesn't get close to understanding the complexity of a biological system" in which potentially thousands of variants interact. The UC-Berkeley team will attempt to "model combinations of genetic variants" and get closer to understanding the complexity of the genetic control of the heart.

Finally, Ashley's team at Stanford will be looking at the smaller picture: single cells. Their aim is to "look at and characterize

individual single cells: measure their size, their shape, their distensibility, and then connect that to the genetic changes that we noted in the first and second parts of the grant."

Ashley plans to take full advantage of the Biohub community and its resources, including sequencing resources and a community of investigators regularly presenting their work to one another. As he puts it, "I love collaboration and I love the interdisciplinary nature of the Biohub."

David Relman

The Interaction of Microbial Communities

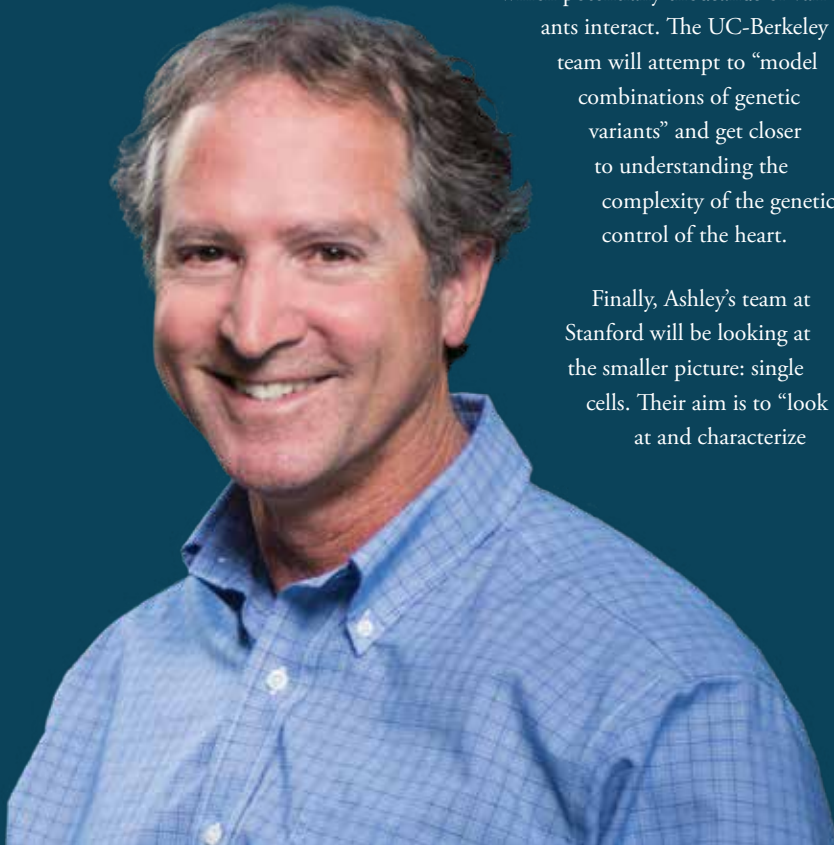
David Relman, MD, Thomas C. and Joan M. Merigan Professor of Medicine and professor of microbiology and immunology, has been working for two decades on the microbiome. He adds, "What I love about my work is the discovery of unrecognized diversity and function in the microbial world (where the vast majority of biological diversity has arisen) and unraveling the interwoven relationships between microbes and humans."

When Relman applied to the Chan Zuckerberg Biohub Initiative, leaders created a Microbiome Initiative with several faculty at Stanford, UCSF, and UC-Berkeley, in addition to Relman. The point of the initiative — and Relman's work — is to bring investigators together to better understand the "key properties of native microbial communities in the human body" and how they "confer and support health." Relman and his collaborators hope this will allow doctors and scientists to someday create synthetic communities in the lab that can be used therapeutically.

To that end, over at least three years, Relman and his collaborators — Michael Fischbach (bioengineering), KC Kuang (bioengineering), and Justin Sonnenburg (microbiology and immunology) at Stanford, as well as colleagues at UC-Berkeley and UCSF — plan to use robotics, anaerobic microbial cultivation technology, mass spectrometry, and ecological theory to explore the microbial communities of humans.

An important feature of these microbial communities is how community members interact with each other and with their host. These interactions will be "a major focus" of the teams' research. Relman in particular will, as he explains, "lend expertise in studying stability and resilience, explore the use of new technology to study the human small intestine, and apply some of our findings from and to human subjects and patients."

Relman appreciates the Biohub's "emphasis on group efforts, shared skills, and transdisciplinary thinking," adding, "This approach in some ways mirrors the workings of the microbial communities that we study: cooperation, shared resources and products, and diversity. We're hoping that we can produce benefits for our community (of humans) that match even a small portion of the benefits that our microbial communities provide to us!"



GI's Move to Redwood City: Creating Multiple Opportunities

Not long ago, new patients at the gastroenterology and hepatology (GI) division would sometimes wait for months for a non-urgent appointment. They were well cared for once they got in, but the clinic space in Palo Alto was small, the huge enterprise was overwhelming and intimidating, and parking was nightmarish. Then someone suggested the possibility of moving five miles away to Redwood City, where an existing building could be redesigned to meet their needs. The division's leadership decided to do it.

Preparations for the move were exhaustively detailed. Consultants were brought in and, says W. Ray Kim, MD, chief of the division, "They literally counted the steps that patients take, that staff take, that physicians

take. Then they came in with Lego-like building blocks, and they had us arrange them. Then they mocked it up with cardboard boxes and we went through a day in the clinic with that mockup, then fixed things the best we could. They analyzed our workflow and talked with us about optimizing it. And then they built a physical space that would support the clinic space we wanted."

The building's redesign incorporated all the changes faculty sought to accommodate patients on the long appointment waiting list. It also gave them the opportunity to build to meet their future needs.

"As we were planning for the move," says Uri Ladabaum, MD, senior vice chief of the division and medical director of the Digestive Health Center, "we stepped back to see how we wanted to practice in the future. The changes we wanted revolved around having patients taken care of by teams of people — physicians, nurses, patient care coordinators, medical assistants — who are now grouped into team cells. Every patient has one individual key contact person or navigator on their team cell. The physical space, the hardware, was designed around our new practice model, the software."

Clinical spaces — including imaging and pharmacy on the first floor, the clinic on the second floor, and endoscopy on the third floor — occupy Pavilion D while administrative and clinical research areas are across a 30-foot-long bridge in Pavilion C. "The co-location of the clinic activity with clinical research and administrative space is really a huge thing for us," says Ladabaum. Kim agrees: "It's fantastic."

THE CLINIC

Patients access the examination rooms in the clinic through one door, and members of the team cell through another. Behind the second door is a large area where all members of team cells work together. Ladabaum describes the clinic as "a very efficient space, very pleasant, calming. People have a good feeling being here, first and foremost the patients and their families, who are always the focus of the design, but then also the staff and faculty who work here."

The clinic space lends itself to housing several multidisciplinary clinics, which especially pleases Linda Nguyen, MD, head of the clinic. "We have a pelvic health program where colorectal surgery, GI, urology, and urogynecology all see patients in the same area. We also have a multidisciplinary esophageal program, where both a gastroenterologist who specializes in esophageal disorders and a foregut surgeon can take care of patients with GI motility disorders like gastroparesis."

"Because we're working together, we're easily able to talk to each other about mutual patients, and we meet to discuss those patients both informally and formally and come up with a comprehensive plan. In this way,



▲ URI LAUDABAUM, MD, listens to a patient.

▼ RAY KIM, MD (left), works with a team cell member.





▲ LINDA NGUYEN, MD (right), performs a procedure.

patients with complex problems, irrespective of which one of us they see, have a group of physicians who are on top of their case,” Nguyen adds.

One administrative change that directly benefits patients is moving procedure scheduling under the supervision of the clinic. Now when patients are seen in the clinic and are found to need procedures, those procedures are scheduled before they leave the clinic.

THE ENDOSCOPY SUITE

One floor up from the GI clinic is the endoscopy suite. Its design also reflects thoughtful attention to detail: All medical equipment is suspended from the ceiling or walls, freeing the floor for ready reconfiguration of rooms for different procedures. There are nine rooms for endoscopy procedures, and each has a pre-procedure area immediately outside. Rather than wait in a common waiting room, patients occupy the pre-procedure area outside their endoscopy suite and then are taken just a few feet for their procedure. Afterward they are taken to a central recovery room.

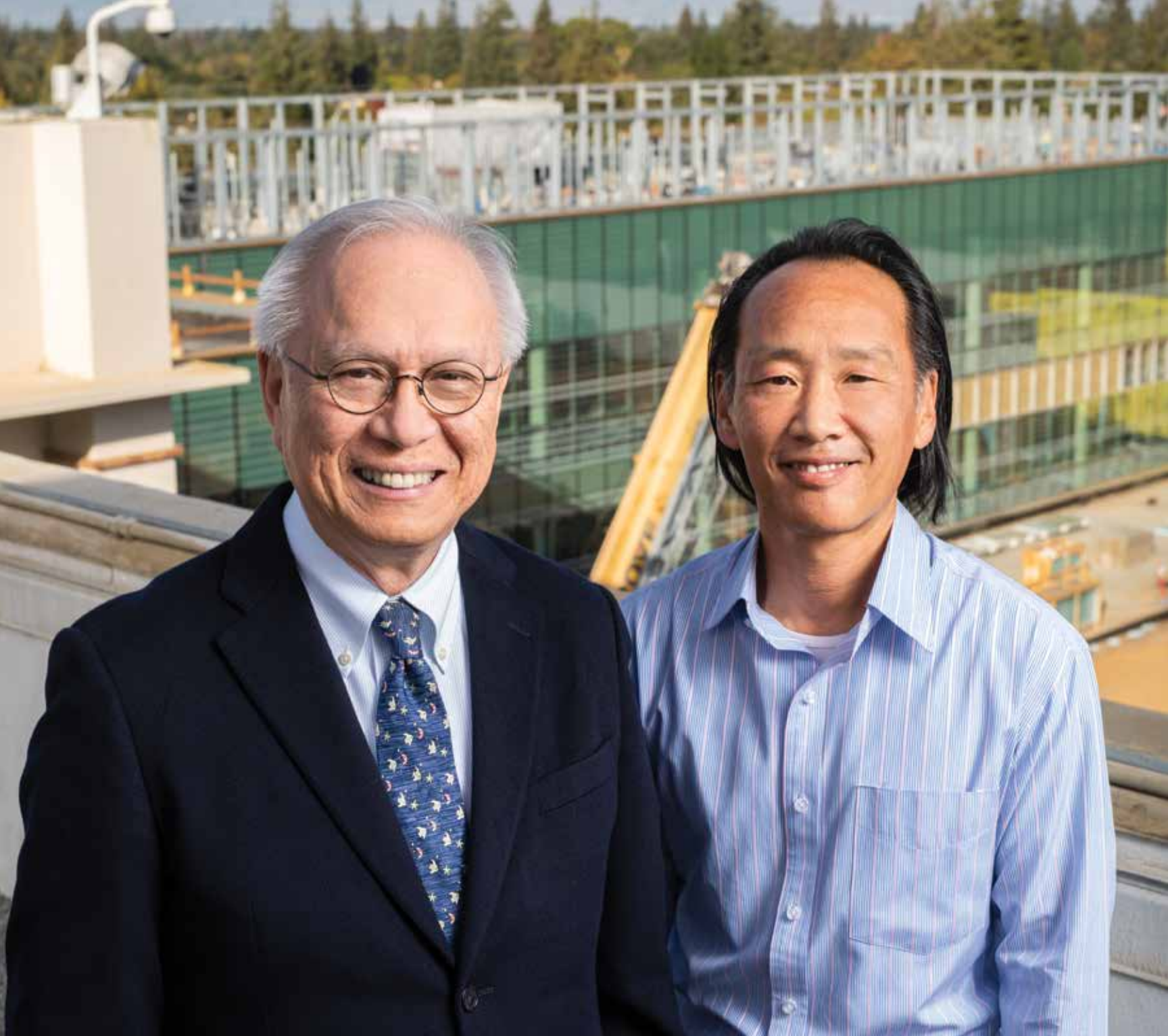
Back in Palo Alto, a second endoscopy suite is maintained at Stanford Hospital. Ladabaum explains the reasoning behind this decision: “That suite is focused on more advanced, complicated cases: inpatients who are

sicker, and certain types of procedures that need fluoroscopy or complicated equipment. By focusing on just those types of patients, that unit is developing efficiencies in more challenging scenarios.”

Two other clinics remain in Palo Alto, explains Kim: “a liver transplant clinic where we need surgeons, nurse coordinators, and others located at the hospital helping us; and a collaborative clinic at the cancer center.”

ACCOMPLISHING THEIR MISSION

Academic medical centers pride themselves on attention to their tripartite mission: to care for patients, to conduct research, and to train the next generation of care providers. Ladabaum believes the new facility that gastroenterology and hepatology occupies in Redwood City helps the division accomplish those goals. He says, “The idea is to fulfill our mission as an academic division. First, we want to provide outstanding patient care in a very friendly environment, and now we have what’s necessary to do that. Second, we need to integrate clinical research, and the personnel to do that are right here with us. Third, we need to train fellows, residents, and medical students, and the space really is conducive to that, too.”



▲ LAWRENCE LEUNG, MD (left), and PHILIP TSAO, PHD

A Database of a Million Veterans

The goal is simple but ambitious: collect samples and medical data from a million American veterans to create an enormous database of medical information. For Philip Tsao, PhD, research professor of cardiovascular medicine, and Lawrence Leung, MD, Maureen Lyles D'Ambrogio Professor of Medicine and senior associate dean for Veteran Affairs, the Million Veterans Program, or MVP, is a way to enhance both veterans' health and the medical field in general.

Tsao and Leung have been collaborators for years, and when Leung started work as chief of staff at the Palo Alto VA, he invited Tsao to join him. Leung believed that the VA — a nationally integrated hospital system with records that went back decades, and in fact the first adopter of what is now the EHR or electronic health record—was an ideal place for genomics research.

So seven years ago Tsao moved his lab to the VA, and they began their work. Both doctors thought the Palo Alto VA in particular was an excellent site for genomics research, with roughly 1,000,000 outpatient encounters per year and a close relationship with Stanford, where they'd be able to, as Tsao says, "leverage the local talent" in various departments, including medicine, genetics, and statistics. Tsao explains that the VA would provide "an opportunity to really quickly collect a large cohort."

THE BEGINNINGS OF MVP

Leung and Tsao's interest in genomics research led them to Washington, DC, where they hoped to pitch their project plans to national VA leaders. Ironically, that was when they found out about the MVP program, an effort much like theirs that was already in motion. That was 2011, and now over 50 VA sites across the country are recruiting individuals for MVP. The program has passed 700,000 participants, "well on the way to a million," Tsao says. Now they're thinking of surpassing a million.

MVP participants donate at least four sources of data: a blood sample, access to their electronic health record, a baseline lifestyle survey with demographic information, and a more extensive lifestyle survey with detailed dietary information as well as other medical statistics. All participants can opt out of any part of the voluntary program, but many do everything, including the longer lifestyle survey.

They're also asked to consent to be re-contacted once their data has been processed. For Tsao this is a crucial part of the project both for the veterans and the larger medical world: Their data can be revisited, their health resampled to "see how their biological signals are changing over time." And if researchers discover a correlation between, for example, genomic material and a particular disease, they can go back to individuals and study them in more detail, in what Tsao describes as "types of fine mapping studies" that will be crucial as the program goes forward.

Veterans proved to be ideal genomic study subjects for another reason: their patriotism. "They're very much interested in continuing to serve their country," Tsao says, adding that he's heard dozens of participants say that participating in MVP is "one way they can contribute, not only to their brothers in arms but also to their country. The research effort may not help them individually but it will help not only their brothers but also generations to come. Veterans are very interested in research that will pay forward."

TRANSLATING DATA INTO RESULTS

So far, so good. But the next step is both daunting and slightly ambiguous: What will they do with all the information they've collected? Seven years in, the data is being organized, and qualified researchers are beginning to access it. As Tsao states, "Some of our first papers are just coming out, and we're very excited about not only what has been done up to this point, but the potential of the study itself." For example, the team at Stanford/Palo Alto VA has recently published a study in *Nature Genetics* that greatly expands the number of genetic factors that contribute to lipid levels. (High levels of these blood fats are a major risk factor for heart disease.)

The possibilities raised by this type of data are exciting. "We know that certain risk factors such as blood pressure and your cholesterol level are

important for heart attacks, and we now can go back decades and get people's cholesterol levels over time. We can look at their maximum cholesterol level, we can look at the trajectory, and we can look at what the interaction with different drugs may have been."

The Palo Alto VA has also launched its own center: the VA Palo Alto Epidemiology Research and Information Center, or ERIC, to facilitate the analysis of MVP-gathered data. The center will take advantage of the proximity to Stanford and involve contributions from many Stanford-based programs in harvesting MVP's data for research. Collaborators include Tim Assimes, MD, PhD, associate professor of cardiology and epidemiology; Michael Snyder, MD, Stanford W. Ascherman Professor and chair of the department of genetics; Wing Wong, PhD, Stephen R. Pierce Family Goldman Sachs Professor in Science and Human Health and professor of biomedical data science; and Hua Tang, PhD, professor of genetics and statistics.

"There's a diverse and deep amount of talent at Stanford," Tsao says. This type of collaboration leads to novel methods to approach biology. Tsao, Leung, Snyder, and colleagues recently published a paper describing a new technique that harnesses the power of machine learning applied to genetic data and health records.

Tsao and Leung are currently co-directors of the Palo Alto MVP program, as well as co-directors of ERIC with Assimes. Tsao is one of the three principal investigators for the nationwide MVP program, and he's the principal investigator of one of the first approved studies to examine the MVP data: a study on cardiometabolic disease with Assimes and Jennifer Lee, MD, PhD, associate professor of endocrinology and epidemiology. Lee and Assimes are also involved in a study to incorporate some of the work of Nigam Shah, MBBS, PhD, associate professor of biomedical informatics, into the VA electronic health record to improve the phenotyping of individuals, which they will then apply to their genomics work.

THE FUTURE OF MVP

The far-reaching goals of MVP can overwhelm, Tsao says. "One of the fears would be that we make a lot of discoveries and then we inundate both patient and provider to a point where it becomes more harm than good," he explains. "Beyond the science there's a whole host of work that needs to be done to integrate this into health care."

But he's optimistic about its overarching hopes. "The ultimate goal would be to discover diagnostics, prognostics, and theranostics that could be eventually brought into the clinic. And of course understanding the basic underpinnings of disease and how we can apply those to identify individuals who are at risk, and then help in the management of both disease and health."

Both Leung and Tsao clearly believe in the enormous potential of this study. "MVP is the crown jewel of VA research," Leung says. "Palo Alto VA, in close partnership with the Stanford School of Medicine, will continue to play a leading role in the translation of this program in defining precision medicine."

Can AI Really Improve Care?

Arnold Milstein, MD, came to Stanford eight years ago with a simple assignment: Find out how to lower the national cost of producing great health care. Put another way, if we could find more affordable ways to deliver better care for conditions that consume the bulk of the country's health care spending, more monies would be available for other ways to improve human well-being — like education and social services.

Milstein was ideally suited to the task. He spent two decades working to improve health care value in the private sector, after which he served as an advisor to Congress and the White House. In 2011 he created Stanford's Clinical Excellence Research Center (CERC). It is the first university-based research center exclusively dedicated to discovering, testing, and disseminating cost-saving innovations in clinically excellent care.

One of CERC's areas of emphasis is discovering how artificial intelligence (AI) can prevent inadvertent and costly failures in intended care delivery. This focus began with a call from Professor Fei-Fei Li, PhD, director of the Artificial Intelligence Lab in the Stanford School of Engineering.

"Our subsequent conversations sparked a decision to create a unique cross-school Partnership in AI-assisted Healthcare, which we call PAC. We imagined a world in which AI improves the performance of a broad range of human services that affect health," Milstein says.

"We initially focused solely on health care in order to learn and make a difference before we expand our use of AI to improve performance across a broad range of health-affecting services," adds Milstein, who turns to a favorite initial target: lowering the incidence of hospital-acquired conditions or HACs.

"Every time a patient in a U.S. hospital acquires an infection that they didn't come in with, human misery and tens of thousands of dollars to the cost of a hospitalization follow," he explains.

"No clinician wants to impose hospital-acquired infections on their patients. But clinicians are busy. They're human. They're imperfect. So they don't always notice when they've just skipped a critical intended action step."

That led to thinking about how artificial intelligence could be used to help detect and correct — in real time — deviations in essential clinical actions, like maintaining hand hygiene, which is a primary way to prevent hospital-acquired infections.

In 2015 CERC researchers, alongside graduate students and faculty in the AI Lab, began developing a system that detects whether someone used the alcohol hand dispenser that sits on the wall next to every hospital room entrance. Their system relies on computer vision, a rapidly

progressing domain of artificial intelligence used in the automotive and other industries.

"If computer vision can detect when drivers initiate dangerous lane changes and safely control vehicular steering, can it similarly analyze motion to detect unintended deviations in important clinician behaviors or patient activities?" asked Milstein and Li's research team in a *New England Journal of Medicine* article.

AI systems that take advantage of computer vision are relatively inexpensive. By using them, the team has shown it can achieve greater than 95 percent accuracy in detecting inadvertent omissions in the use of the hand sanitizer before staff enter patient rooms.

The vision of making excellent care more effective and efficient also targets behaviors that affect lifelong health trajectories. In collaboration with Stanford researchers in child development and pediatrics, the team is testing how computer vision can let mothers know if their eyes inadvertently drift to their smartphone screen instead of responsively returning their infant's gaze.

The hope, Milstein says, is to unite technology and human care. "By mobilizing emerging science and technology from engineering, behavioral sciences, and medicine, Stanford can address a seemingly intractable national challenge to make affordable all forms of human caring that powerfully affect health."



CERC creator **ARNOLD MILSTEIN, MD** (right), collaborates with **FEI-FEI LI, PHD**, director of the Artificial Intelligence Lab. ►



▲ SONOO THADANEY, MBA (left), and ABRAHAM VERGHESE, MD

Humans *and* AI, Not Humans *versus* AI

“I hold out hope that artificial intelligence and machine-learning algorithms will transform our experience, particularly if natural-language processing and video technology allow us to capture what is actually said and done in the exam room,” writes Abraham Verghese, MD, professor of medicine and founding faculty director of the Stanford Presence Center.

“The physician focuses on the patient and family, and if there is a screen in the room, it is to summarize or to share images with the patient; by the end of the visit, the progress notes and billing are done. But AI applications will help us only if we vet all of them for their unintended consequences. Technology that is not subject to such scrutiny doesn’t deserve our trust, nor should we ever allow it to be deeply integrated into our work,” Verghese continues in a May 2018 article that appeared in *The New York Times Magazine*.

That sentiment is behind a key focus for Presence, a center that emphasizes the value of the human connection in the high-wire balancing act between high tech and high touch.

Presence aims to ensure that patients, clinicians, funders, legislators, and other stakeholders are at the table as equitable and inclusive AI solutions are created and deployed in health care.

To that end, Presence presented two symposia during 2018. In April, Jonathan Chen, MD, assistant professor of biomedical informatics, was a leader of the first symposium, “Human Intelligence and Artificial Intelligence in Medicine,” which addressed augmented intelligence of humans and machines for diagnostics. The 350 physicians, business leaders, policymakers, social and behavioral scientists, venture capitalists, and political activists in attendance were challenged to determine how to ensure that humans are augmented by AI in defining and delivering compassionate services.

On that subject Verghese says, “Pitting humans against machines is not the point. Rather, how best to relevantly engage both for the sum to be greater than the parts should be the focus.”

“Machines do many things very well, but they really can’t do the caring work, so how do we augment the two preemptively, proactively, and equitably for the outcome that we all seek?” he asks.

“Artificial Intelligence in Medicine: Inclusion and Equity” was the second symposium in August, which drew 275 attendees from around the world. Presence executive director Sonoo Thadaney, MBA, co-chair of the National Academy of Medicine’s Working Group on AI in Healthcare, was one of the symposium leaders. Acknowledging the potential unintended consequences of AI in medicine, she examined how to prevent and manage the possible exacerbation of inequity and exclusion in health care.

Thadaney speaks of a huge inequity that looms depending on an individual’s circumstances, saying: “We cannot have a world where technology creates greater inequity such that those of us with privilege have access to second opinions and concierge physicians, and the rest of the planet ends up with medicine that is meted out with the efficiency and emptiness of fast food. We cannot afford a health care apartheid.”

The Gordon and Betty Moore Foundation and the Robert Wood Johnson Foundation support Presence by funding the symposia as well as another innovative program that began at the end of 2018: the AI in Medicine Inclusion & Equity (AiMIE) 2018 Seed Grants Program. The AiMIE program provides initial funding for projects seeking equitable and inclusive frameworks for AI in medicine.

“Repositories of Horrible Stuff”

CEDAR to the Rescue

MAKING LARGE DATA EASILY AVAILABLE ONLINE

Several years ago, Mark Musen, MD, PhD, wrote: “The ultimate Big Data challenge lies not in the data, but in the metadata — the machine-readable descriptions that provide data about the data. It is not enough to simply put data online; data are not usable until they can be ‘explained’ in a manner that both humans and computers can process.”

Musen is a professor of biomedical informatics and director of the Stanford Center for Biomedical Informatics Research. He is also the head of CEDAR, the Center for Expanded Annotation and Retrieval, which helps researchers comply with requirements to archive their data so others can understand and use them. In a recent interview, Musen provided clarity about the problem of metadata.

WHY IS IT A PROBLEM FOR RESEARCHERS TO COMPLY WITH THE REQUIREMENT TO PUBLISH THEIR METADATA?

The greatest challenge of this whole enterprise is the problem of “What’s in it for me?” We reward scientists for authoring journal articles and for creating PDFs, but we don’t have a system that recognizes the data

contributions that scientists make. We need to change the culture so that when other investigators report secondary analyses of data, or when data sets are re-explored and then lead to new discoveries, there is a benefit to the original investigator other than being acknowledged in someone else’s paper. Currently, investigators don’t have the motivation to spend a lot of time making their experimental data easily available online, and they generally lack tools to enable them to do so in a standardized, reproducible fashion.

ARE THERE PROBLEMS WITH DATA CURRENTLY IN REPOSITORIES?

We’re starting to see an emphasis not just on putting the data into repositories but on actually doing a good job of it. The National Center for Biotechnology Information (NCBI) maintains most of the NIH repositories for experimental data, but it generally does no more than make sure that the forms are filled in. So NCBI databases contain lots of horrible stuff; for instance, some 25 percent of the metadata values that are supposed to be numeric don’t actually parse as numbers.

IS THIS WHERE CEDAR HAS A ROLE TO PLAY?

Precisely. The idea of CEDAR is to make it easier and more attractive for investigators to publish their data because more science is going to come out of it if they do. CEDAR has a whole library of templates that correspond to “minimal information models” for describing different classes of experiments. And we have technology that makes it easy to fill in one of these templates to describe your particular experiment when you are ready to upload your data sets to a repository. By filling in the template, you create standardized, searchable metadata that future investigators will use to locate the data and to make sense of what you have done. Using a cache of metadata that it already has stored, CEDAR can make suggestions as you’re filling out a template to accelerate the process of creating the metadata in the first place.

HOW IS CEDAR BEING USED TODAY?

CEDAR helps investigators put data sets online — with well-described metadata — that will allow future scientists to perform new analyses that may allow them to make new discoveries. Our collaborations with several large research consortia show that it’s not all that difficult for investigators to do a great job of annotating their data sets in a way that will benefit the entire scientific community. Immunologists in the Antibody Society use CEDAR to upload their data and metadata to repositories at the NIH. Scientists developing the Library of Integrated Network-Based Cellular Signatures use CEDAR in association with their own data coordinating and integration center. The Irish Health Research Board and the Dutch Clinical Funding Agency are evaluating using CEDAR to review proposed metadata before making funding decisions about new studies.



◀ MARK MUSEN, MD, PHD

Department of Medicine in Numbers

15 Divisions

606 Faculty
(107 University Tenured and Nontenured Line, 116 Medical Center Line, 330 Clinical Educators, 38 Instructors, 15 Emeritus)

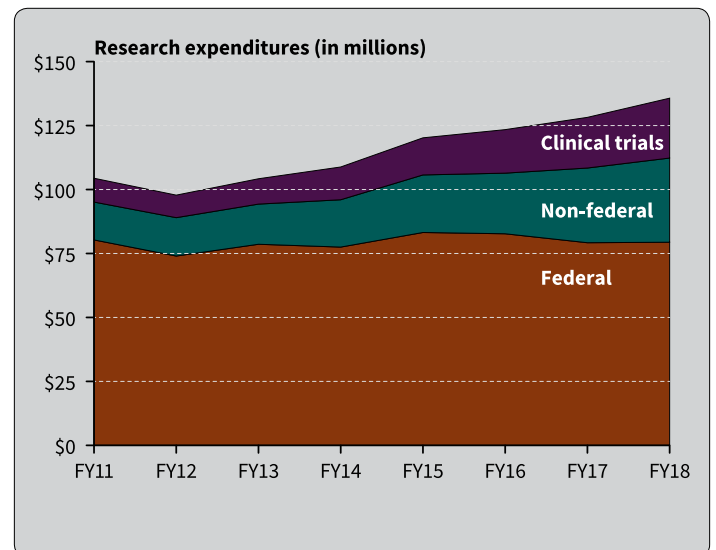
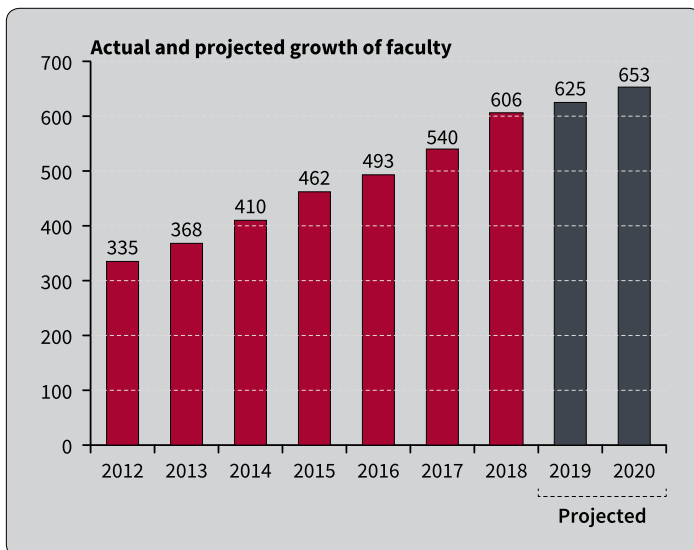
30 Endowed Professors

920 Staff & Research Associates
(586 Staff, 99 Research Associates, 235 Temporary Staff)

475 Trainees
(136 Residents, 160 MD Fellows, 179 Post-docs)

\$135.7M Sponsored Research
(\$79.4 million in federal grants, \$32.9 million in non-federal grants, \$23.4 million in clinical grants)

556 Grants
(4 Program Projects, 70 R-01s, 32 Ks, 21 Us, 14 Training, 36 other Federal Awards, 379 Non-Fed & Clinical Trials)



This is one of the great joys of being in an academic institution: discovery and mentorship all in one moment.



JUSTIN ANNES, MD, PHD



Pitting humans against machines is not the point. Rather, how best to relevantly engage both for the sum to be greater than the parts should be the focus.

ABRAHAM VERGHESE, MD

People, both faculty and staff, come to Stanford to be part of a noble cause, and that nobility extends not just to academic and clinical contribution, but to social and community contribution as well.



SANG-ICK CHANG, MD, MPH



I'm heartened that diversity and inclusion have come to the forefront of discussion at Stanford, and that Stanford is showing that these issues are important.

TAMARA DUNN, MD

At the end of this, there's a patient at the center of all of these discussions.



KATE LUENPRAKANSIT, MD