MEDICINE

WINTER 2024

FIGHT OF HIS LIFE

IU BASKETBALL LEGEND TED KITCHEL TAKES ON PARKINSON'S DISEASE

FINDING THE HOLY GRAIL OF ALZHEIMER'S DISEASE

ADDRESSING BURNOUT IN EMERGENCY MEDICINE

REIMAGINING CARDIOVASCULAR RESEARCH

Ted Kitchel teams up with IU School of Medicine to advance Parkinson's disease research

TOUGH & DETERMINED

Dear Alumni and Friends,

Ted Kitchel knows all about toughness.

Growing up as a farm kid in Galveston, Indiana, Kitchel cultivated the toughness he would need to play for Indiana men's basketball coach Bobby Knight. That toughness came in handy as Kitchel helped the Hoosiers win the NCAA championship in 1981.

And now, he's harnessing that toughness again as he battles Parkinson's disease. Not one to sit on the sidelines, Kitchel is fighting back against his diagnosis—both in therapeutic boxing and fundraising for research.

Kitchel's determination to make a difference in the face of adversity is the same force that drives us here at IU School of Medicine. His story, told in this issue of IU MEDICINE, is one example of our persistence.

Across many disciplines, our researchers are doing the work to answer medicine's toughest questions.

In our research on Alzheimer's, we're looking at the earliest stages of the disease. Doctors Donna Wilcock and Jeff Dage are helping to create pathways for early intervention with their work investigating biomarkers. And through her research on early-onset Alzheimer's, Dr. Liana Apostolova is on a quest to understand why the disease strikes some people before the age of 65.

That determination extends into our cancer research as well. Our focus on accelerating discoveries at the School of Medicine was on display earlier this summer at the Indianapolis Motor Speedway. IndyCar driver Marcus Armstrong, racing for legendary owner Chip Ganassi, ran in the Gallagher Grand Prix in a car decked out with an IU Simon Comprehensive Cancer Center paint scheme–a gift from a donor.

We also have our sights set on curing multiple myeloma. We've created a registry of 1,000 diverse patients to help in that mission–harnessing data that will help us understand the genetic differences in myeloma patients and diversify our clinical trials.

All of this is hard work. Burnout rates for doctors are at an all-time high in the wake of the COVID-19 pandemic. While all specialties face their own difficulties, emergency medicine doctors face perhaps the most challenges. As applications for the specialty have decreased, we're looking at ways to change that trend.

Like Ted Kitchel, our clinicians and researchers are built tough. That toughness is bolstered by the continued support of our IU School of Medicine community. Thank you for helping make our work possible.

With gratitude,

Jay L. Hess, MD, PhD, MHSA

Executive Vice President for University Clinical Affairs
Dean of the School of Medicine
Walter J. Daly Professor
Indiana University

FIGHT OF HIS LIFE

Ted Kitchel, IU researchers take on Parkinson's disease

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This publication is produced by the Office of Gift Development and Alumni Relations to keep alumni and donors informed about the power of philanthropy. To comment, contact Bobby King at 317-278-1986 or bk16@iu.edu.

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THE DIFFERENCE MAKERS

BY BOBBY KING

Whether they work in small towns or urban settings, in the lab or in the clinic, Indiana University School of Medicine alumni make a difference each day in the lives of the patients they serve. Our alumni award winners for 2023 and 2024 are sterling examples of the ways the school and its alumni improve health care for the people in their communities and around the world.

GEORGE W. SORRELLS, JR., MD, COMMUNITY PHYSICIAN

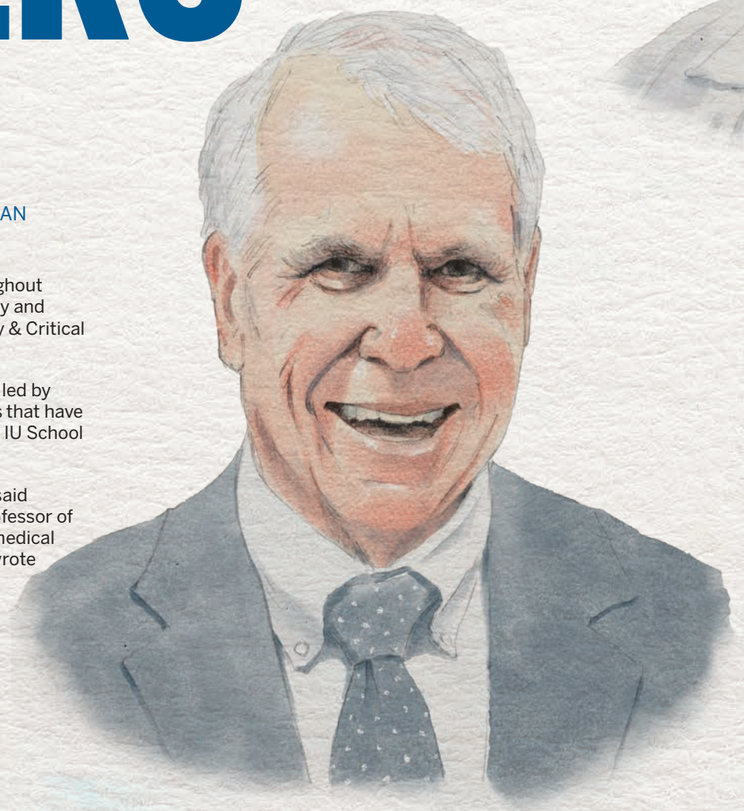
SHARON SINGLETON, MD, '00

Sharon Singleton, MD, became CMO of Neighborhood Health, a Federally Qualified Health Center in Fort Wayne, in January 2020. As COVID-19 struck, she spearheaded the clinical response, guiding the consolidation of services from two clinics into one that prioritized high-risk patients, including the insured, underinsured, and uninsured.

Facing the crisis head-on, she rapidly revamped clinic entrances, enforced strict screenings, and ensured everyone had masks and essential PPE. Recognizing patient concerns about hospitals, she championed the establishment of a "Sick Clinic" at a second location for in-person evaluations. As soon as it was possible, they expanded to offer COVID-19 testing and vaccinations, receiving enthusiastic support.

Today, the organization operates at full capacity with safety measures in place across medical, dental, optometry, chiropractic, behavioral health, pharmacy, and lab services. Singleton is helping to plan for a third clinic in 2025 reflecting her strong commitment to community health.

That commitment extends beyond the clinic, as she has held leadership roles on the Indiana University School of Medicine Dean's Council, Fort Wayne Medical Society and Foundation, and on the IU School of Medicine Alumni Board. She has also served as an adjunct clinical faculty member at IU School of Medicine.



GEORGE W. SORRELLS, JR., MD, COMMUNITY PHYSICIAN

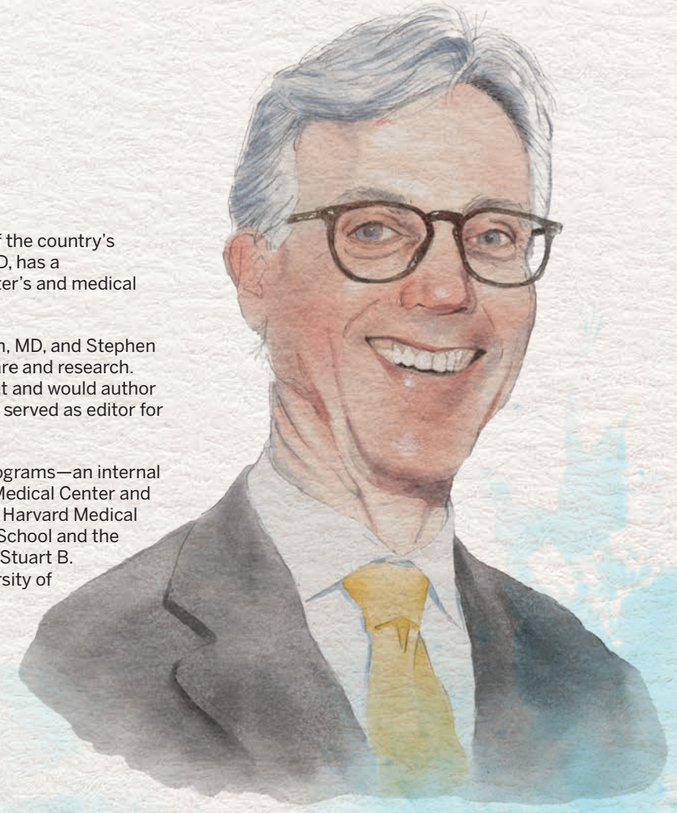
MASON GOODMAN, MD, '73

A dedicated physician and model community leader throughout his career, Mason Goodman, MD, specializes in immunology and pulmonary critical care for IU Health Physicians Pulmonary & Critical Care Medicine in Indianapolis.

William Silvers, MD, who nominated Goodman, said he has led by example in patient care as well as entrepreneurial interests that have benefited society, including encouraging others to support IU School of Medicine.

Goodman has provided care to many illustrious Hoosiers, said Lawrence H. Einhorn, MD, the Livestrong Distinguished Professor of Medicine at IU. But he provides the same compassionate medical expertise to patients at all socioeconomic levels, Einhorn wrote in a letter supporting Goodman's nomination.

Goodman completed his undergraduate and medical school at Indiana University. He was trained in internal medicine at University of Texas Southwestern, followed by two of the premier allergy/immunology and pulmonary critical care fellowships in the country: the National Jewish Hospital and University of Colorado in Denver. With plenty of offers in hand, Goodman chose to return to Indiana.



DISTINGUISHED MEDICAL ALUMNUS

DANIEL F. HAYES, MD '79

Recognized as a global expert on breast cancer and one of the country's leading authorities on tumor biomarkers, Daniel Hayes, MD, has a distinguished career that began with undergraduate, master's and medical degrees from Indiana University.

Hayes credits the influence of IU oncologists Larry Einhorn, MD, and Stephen Williams, MD, for his desire to pursue a career in cancer care and research. He began publishing research articles as a medical student and would author nearly 450 peer-reviewed publications. Over his career, he served as editor for eight books.

Hayes trained in some of the nation's most prestigious programs—an internal medicine residency at the University of Texas Southwest Medical Center and an oncology fellowship at Dana-Farber Cancer Center and Harvard Medical School. He later served on the faculty at Harvard Medical School and the Georgetown University School of Medicine and is now the Stuart B. Padnos Professor of Breast Cancer Research at the University of Michigan Rogel Cancer Center.

Hayes is a past president of the American Society of Clinical Oncology, a position which made him one of the most influential leaders in the world of cancer. He has written opinion pieces for *The New York Times* and *The New England Journal of Medicine*. He has won several awards for his research, mentoring, and clinical care.

DISTINGUISHED MEDICAL ALUMNA

ALLISON BRASHEAR, MD ’87

A groundbreaking researcher in neurology, a skilled academic administrator, and a champion for women in medicine, Allison Brashear, MD, has been described as a shining star in both science and leadership.

As a researcher at IU, Brashear reported the first case of the very rare neurological disorder known as rapid-onset dystonia Parkinsonism (RDP), characterized by involuntary muscle contractions. She is now recognized as an international expert in rare neurologic disorders, and her work has fundamentally transformed their treatment. Her leadership in clinical trials has led to three FDA-approved medications for treating spasticity and cervical dystonia, enhancing care for millions of patients.

She was lead investigator for a trial published in the New England Journal of Medicine that first demonstrated that botulinum toxin successfully treated wrist and finger spasticity in stroke victims.

Brashear, a 1987 IU School of Medicine graduate who completed a neurology residency here in 1991, has had a successful career in leadership. She has served as dean of two medical schools—at the University of California-Davis School of Medicine and currently at the Jacobs School of Medicine and Biomedical Sciences at the University at Buffalo. Previously, she served for 15 years as chair of neurology at Wake Forest University School of Medicine.

Brashear has been an advocate for promoting diverse leaders in medicine, and she was instrumental in creating one of the first national leadership programs in neurology for women. She is a frequent lecturer on the importance of diversity in medicine and a lifelong champion of advancing women’s leadership in the field.

GLENN W. IRWIN JR., MD, DISTINGUISHED FACULTY AWARD

RICHARD RINK, MD, ’78

Described as one of the preeminent surgeons in the world today, Richard Rink, MD, is internationally recognized as the foremost authority on reconstructive surgery in pediatric urology.

Now Emeritus Professor of Pediatric Urology at Riley Hospital for Children and IU School of Medicine, he served as chief of pediatric urology for 25 years. He aimed to “provide world-class pediatric urology care to the children of Indiana.”

A talented technical surgeon, Rink has trained many of the most prominent urologists in the world and innovated surgical techniques and training, leaving a lasting influence on the field. He has 320 published articles, 53 book chapters, and three textbooks, making him a sought-after lecturer. One advocate for Rink wrote that “one would be hard-pressed to find an individual who has contributed more in forwarding the clinical care of children with pediatric urology needs.”

For these and other achievements, he was awarded the Pediatric Urology Medal from the Academy of Pediatrics in 2022—the highest honor given to pediatric urologists.

EARLY CAREER ACHIEVEMENT

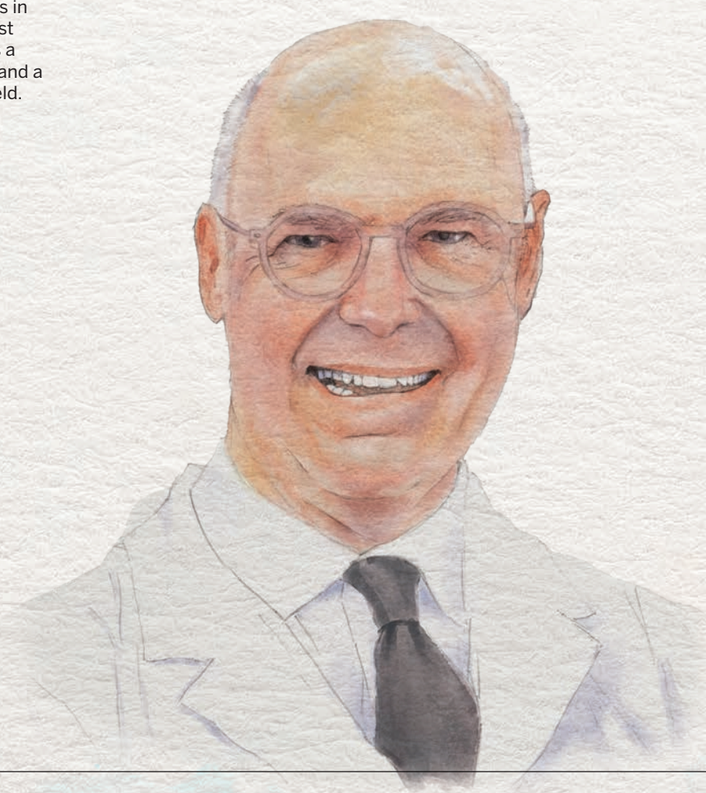
BRANDON BROWN, MD’08

A pediatric radiologist at Riley Hospital for Children, Brandon Brown, MD, has built an impressive early career focused on three goals: improving prenatal diagnosis and perinatal care; clinical research on advanced MRI techniques in fetal imaging; and leading discussions and education on ethics and professionalism in radiology.

At Riley, Brown is the director of fetal and perinatal imaging. MRI technology is increasingly being used in the diagnosis of prenatal anomalies. As one of the founding members of Indiana’s first destination fetal center, Brown has significantly advanced its use as part of the new maternity and newborn health initiatives at Riley, even building a clinical research program. He has created an integrated and consultative service for radiology to interpret advanced prenatal imaging and to counsel families with complicated pregnancies.

Brown has participated in NIH-funded research on the effects on the fetal and neonatal brain in pregnancies exposed to drug abuse. Other research interests include studies on the use of MRI to detect and characterize abnormal placentas and the correlation of placental and brain development in cases of complex fetal abnormalities.

In addition to being a mentor to more than four dozen medical students and residents, Brown is the winner of the IU Trustees Teaching Award, the exemplar of Professionalism Award, and was the chair of professionalism for the largest radiology medical society. He teaches medical ethics and professionalism in the medical school and the school of liberal arts.



ON THE RISE

BY BOBBY KING

New research and education building begins to take shape.

IU School of Medicine's new home in Indianapolis—an 11-story medical education and research building—is beginning to rise above the city's near northside.

The three-story education portion of the building—the "academic base"—is taking shape and should be substantially complete by the end of 2024. By summer 2025, it should be furnished, equipped and ready for occupancy.

These academic floors, oriented around a three-story atrium, will boast a diverse array of classroom sizes, innovative learning labs and 12 learning communities to provide students with the support they need to thrive.

Construction of the research tower—rising eight floors above the base—is expected to begin next summer and be completed by the end of 2025.

The research tower will add 35,532 gross square feet of new research laboratories, along with lab support spaces—room enough for 18 to 20 principal investigators. Much of that space will be devoted to cancer and neuroscience research.

All told, the structure will provide 323,000 square feet of new space, making it the largest project in the school's history. More importantly, future generations of physicians and scientists will train here and make discoveries that will change medicine.

FOLLOW THE PROJECT:

Get a bird's eye view of the new medical education and research building and get inspired by the future of medicine and innovation at IU. To learn how you can support future physicians and leave an enduring legacy, contact Sam Kinder at 317-278-5635 or kindersm@iu.edu.

Fly through a 3D rendering
go.iu.edu/MERB-fly

Watch a time-lapse video of the construction
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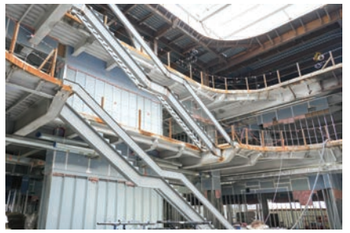


The Medical Education and Research Building will be completed by the end of 2025.

PRACTICE | UNDERSTANDING CANCER

Tracing the Story of Myeloma

BY MATTHEW HARRIS

The Indiana Myeloma Registry charts new variables of the disease in pursuit of more effective therapies.

MULTIPLE MYELOMA ISN'T DEFINED BY ITS SPEED.

This cancer of plasma cells, which makes up less than 2 percent of all new cancer cases, unfurls slowly. It begins with mutations that produce abnormal white blood cells in bone marrow. The process often halts there, and those warped cells remain a minority.

But for 20 percent of patients, cancer steadily crowds out healthy cells. Here, oncologists apply an evocative label: smoldering multiple myeloma. For an unfortunate minority, their grim trajectory ends with cancer hijacking marrow, causing painful lesions that result in bone fractures.

So, if we know the plot, how can researchers halt the narrative?

Indiana University School of Medicine has a tool to help them sketch an outline for each patient: the Indiana Myeloma Registry. Launched in 2018, the registry has steadily amassed a repository of tissue samples, along with a rich trove of medical backgrounds and treatment histories. Soon, it will reach a pivotal milestone: a statewide enrollment of 1,000 patients.

"It is our mechanism for writing the history of each patient," said Mohammed Abu Zaid, MD, who helped launch the registry at the IU Melvin and Bren Simon Comprehensive Cancer Center.

Biobanks aren't a revolutionary concept. Yet IU's registry—funded through the university's Grand Challenges program—wanted to go beyond physical samples. Rapid advances in therapy mean myeloma patients are living longer, and some researchers envision a future where treatments more closely resemble those for a chronic condition.

That progress makes it vital to follow patients over a prolonged period and trace the progression of their disease. That outlook–and the data required–make IU's registry distinct. Along the way, the setup should help clear another persistent hurdle in cancer research: lack of diversity.

Each patient in the registry supplies a saliva sample, which can be done remotely through a mailed kit, along with their medical history. Researchers use the physical sample to generate a genetic profile.

The sample also allows Brian Walker, PhD, a medical and molecular genetics professor, to deploy next generation sequencing to uncover the mechanics that slowly drive myeloma. Cells used in this research typically come from patients with highly aggressive cancer. Using the registry offers Walker's lab the opportunity to explore whether mutations vary based on severity.

Recently, the lab showed that some of these white blood cells lack a gene that acts as a copy editor, preventing transcription errors or misplaced bits of genomic code. As precursor conditions trudge toward full-blown cancer, those mistakes pile up.

A patient's medical history, age, and demographics are another set of variables the lab can use to distinguish how cancer behaves. It's a level of granular detail that's often lacking. "You're not inferring relationships," said Walker, the Daniel and Lori Efroymson Professor of Oncology. "You can see exactly what the changes are, how the cells behave, and what the biology is."

Eventually, researchers could find pressing answers to vexing questions. Why do only one percent of patients with precursor conditions progress to myeloma? If we understood those mechanics, could we prevent the cancer?

"If nothing else, understanding those genetic differences would let us create subtypes and stratify patients more effectively," said Kelvin Lee, MD, director of the IU Simon Comprehensive Cancer Center, H.H. Gregg Professor of Oncology, and a myeloma researcher.

When patients enroll in IU's registry, they consent to provide occasional blood and bone marrow samples and access to their medical records. Those tissue samples, which are stored in Indianapolis, serve as time-series events. Paired with a treatment history, the registry crafts a real-time account of how myeloma behaves.

Researchers can learn how people respond to therapy, what changes are happening in cancer cells, and why some don't respond. "Even now, we are able to provide better tools to determine their prognosis," said Rafat Abonour, MD, the Harry and Edith Gladstein Professor of Cancer Research.

Those insights are coming at a crucial moment.

Since 2012, drugmakers brought a handful of new treatments to market, including several improved proteasome inhibitors. In myeloma cells, proteasomes are a garbage disposal to remove misfolded and poorly functioning proteins. Usually, these inhibitors, and another drug, halt that clean-up process. As the waste piles up, myeloma eventually dies. These second-generation drugs offered renewed hope for patients who saw traditional regimens fail.

Yet results in the real world haven't mimicked those posted during clinical trials. Instead of paving a path to long-term remission, some patients see their myeloma return within two years. IU's registry might help physicians and pharmaceutical companies understand why.

"Clinical trials are not always representative of the patients we see," said Abonour, who also leads IU's multiple myeloma program. "It's why I'm really excited about the registry. The more data we have from that, the better we can understand how these therapies are working in the clinic. We could come up with better tools and better classifications."

It's also a tool that drugmakers are keen to utilize.

Abu Zaid already said Genentech inked a partnership with the School of Medicine to use the registry as a pool to match patients with clinical trials. The benefits are easy to tease out. Minority patients, with incidence rates three times higher than other groups, could have easier access to the latest therapies. Meanwhile, patients whose myeloma isn't responding to existing treatment could have renewed hope.

And those insights are invaluable as oncologists try to adapt their care, Walker said. There's no sense in administering a drug when research shows that the genetic underpinnings of a patient's cancer probably make it futile.

"There's little point in treating a patient with a therapy that's likely not going to work," he said. "They could move on to more promising options."

Researchers at IU School of Medicine explore every facet of multiple myeloma–from the lab bench to the clinic. To support work that enhances care, contact Amber Kleopfer Senseny at 317-278-4510 or akelopfe@iu.edu.

"I'm really excited about the registry. The more data we have from that, the better we can understand how these therapies are working in the clinic. We could come up with better tools and better classifications." RAFAT ABONOUR, MD

RETURNING TO THE FOREFRONT OF CARDIOVASCULAR RESEARCH

BY BOBBY KING

For decades, cardiovascular research at Indiana University School of Medicine, under the banner of the Krannert Institute, blazed new trails in echocardiology and cardiac arrhythmias, just to name a few areas. Over time, though, the school's leadership in cardiovascular research began to fade.

In 2021, the institute was refocused and rechristened as the Krannert Cardiovascular Research Center. And that change could mean paradigm-shifting innovations in care for patients.

Researchers are embracing the newest tools in cardiac imaging to uncover secrets about the flow of blood through the heart's smallest vessels. They're looking at ways to stop the heart muscle damage that can continue even after blockages are reopened. They are exploring how to assess a patient's risk for cardiovascular problems based—not on an invasive procedure—but through nerve activity in the skin. And they are aiming to reduce troubling disparities in who gets heart transplants by improving the process by which such decisions are made.

"We wanted to reimagine, reinvigorate and put our name on the map," said Rohan Dharmakumar, PhD, who became the Center's first director as it was rechristened in 2021.

The results, in just two short years, have been impressive.

- Krannert researchers have been awarded 29 NIH research grants, which amounts to $22.7 million in 2023. Two years earlier, they had just two grants totaling $1.2 million.
- To carry out its ambitious mission, Krannert has expanded its research staff (faculty, staff and trainees) by more than 70 people.
- Plans are underway to build a state-of-the-art cardiovascular imaging center that would be the first of its kind in Indiana and the most advanced facility in the Midwest.
- Krannert has recruited six engineering graduate students from Purdue University to focus on developing new imaging techniques and building cardiovascular devices.

Part of Krannert's reimagining involved new partnerships with industry and with other scientists around IU School of Medicine, including radiologists, nephrologists, cell biologists, microbiologists, physiologists and experts in genomics whose work in areas beyond the cardiovascular system has implications for understanding the heart.

"The heart is not sitting alone. The heart is connected to so many other organs. Having a whole understanding and developing a systems-level biology is something that really benefits. When you start to collaborate, then you get new ideas." ROHAN DHARMAKUMAR, PHD

RESEARCH SNAPSHOTS

Rohan Dharmakumar, PhD

Executive Director of the Krannert Cardiovascular Research Center

Charles Fisch Professor of Cardiology

Some of the most exciting research coming out of Krannert is headed by Dharmakumar himself. A year ago, his lab launched a clinical trial to determine the effectiveness of a new treatment for patients who've suffered heart attacks. That trial is now expanding to include patients in India and the United Kingdom.

About half of the people who have heart attacks develop bleeding within the heart muscle. Iron from the bleeding drives the formation of fatty tissue in the heart, which replaces damaged heart muscle. Eventually, it can lead to heart failure.

Dharmakumar's lab is testing whether deferiprone, an FDA-approved drug previously approved to treat blood disorders, can remove the residual iron in the heart, leading to better outcomes for patients. If it proves successful, it could have a dramatic impact on the care of heart attack patients.

A related area of his work is focused on the early identification of blockages in the heart using a blood marker, rather than magnetic resonance imaging.

Thomas H. Everett, IV, PhD

Associate Professor of Medicine

Bursts of nerve activity can raise the heart rate and increase the risk of dangerous arrhythmias. Scientists have known that much for a while.

But IU School of Medicine's Thomas Everett, PhD is looking at whether that nerve activity—measured by sensors on the skin—can be used to gauge when patients are at risk for heart problems, whether it can provide an early warning for those problems, and whether nerve stimulation can be used to treat conditions such as abnormal heart rhythms.

With training in biomedical and electrical engineering, Everett is comfortable in the realm of electrophysiology. And he's found collaborators among Purdue University's biomedical engineering faculty. They are investigating how spinal cord injury increases sympathetic nerve activity and can lead to problems in the heart. Another Purdue partnership is looking at how vagal nerve stimulation affects the heart.

Everett's work on how nerve activity affects the heart is being applied to patients with COVID, both acute episodes that lead to intensive care and long COVID, which can be affected by changes in their vagal nerve activity caused by the disease. He's also looking at whether patients with atrial fibrillation who get cardiac ablation therapy can be risk stratified on whether they will need a repeat of the procedure.

One of the challenges of his work is developing portable tools to record the signals of nerve activity over long periods of time.

Khadijah Breathett, MD

Advanced heart failure and transplant cardiologist

Associate Professor of Medicine

Cardiovascular disease is the No. 1 cause of death for every population group, but risk varies by demographic. Non-Hispanic Black patients have the highest risk of dying from cardiovascular disease. The risk of developing different forms of cardiovascular disease is often higher for minoritized racial and ethnic groups than for white patients. Women have greater risk of cardiovascular disease as they age.

The reasons are multifaceted but include the fact that minoritized racial and ethnic groups and women are less likely to be given appropriate life-saving therapies.

These disparities—and their real-world implications for patients—are the focus of research for Khadijah Breathett, MD, who has the ambitious goal of making cardiovascular care more equitable.

"Most people want to do the right thing—and try to do the right thing," Breathett said. "But health care teams, physicians, clinicians and nurses are just like the rest of the U.S. They are still vulnerable to navigating social determinants of health, bias, and structural racism."

Breathett's national studies found that health care team members treat patients differently based upon their race and gender, despite best intentions. In multiple studies, health care team members viewed Black patients as less trustworthy and less likely to adhere to recommendations; white patients were given the benefit of the doubt and trusted, despite patients of both races having identical clinical histories. Women were viewed as less financially stable. These viewpoints contributed to the decision to recommend life-saving therapies based upon patient race and gender. In a separate multi-site study, strong health care team dynamics—those that challenge groupthink, promote critical opinion sharing, and feedback, among other traits—versus poor team dynamics were linked to offering life-saving therapies to women.

Making a difference in the way cardiovascular care is delivered is why Breathett chose the field. But she acknowledges the challenge of the task. "We're trying to do the impossible—change our system, change our behaviors," she said. "It's one of the most difficult things to do, but there is rigorous science to support methods to implement lasting changes.

Ankit Desai, MD

Cardiologist

Associate Professor of Medicine

The various research pursuits of Ankit Desai, MD, may appear to have little rhyme or reason but there's a good case to be made for the diversity of subjects he explores.

Desai is a cardiologist. He's also trained in basic, cellular and molecular biology. He's published on the genomics and the genetics of heart and lung diseases. So, he feels well-suited to diverse pursuits. When he gets the question, 'should you try to maybe focus on one thing?' he has a simple answer: "We go where science takes us. If we find something interesting, we have to follow it."

A few of his interests include:

SICKLE CELL DISEASE. When Desai became a cardiologist in 2010, there were few studies on the causes of sudden death in people with sickle cell disease, a disorder primarily affecting Black people. The conventional wisdom was that it was unrelated to the heart. But his lab found a protein, at higher levels in patients with sickle cell disease, that may be the cause of deadly arrhythmias—and a potential way to stop them.

PULMONARY ARTERIAL HYPERTENSION. He's zeroing in on a way to treat the genetic deficiency that leads to pulmonary arterial hypertension—sometimes likened to a cancer of the blood vessels in the lungs—that progressively restricts blood flow in the lungs, causing the right side of the heart to fail. Women are affected by the disease at a rate three to four times higher than men.

ANGIOGENESIS AND MYOCARDIAL INFARCTION. Blockages of blood vessels in the heart can be deadly. His lab found a way to spur new blood vessel growth in the heart—angiogenesis—a discovery with the potential to save patients dying from heart attacks by creating new pathways for blood supply. He's awaiting a patent on the discovery and the private investment needed to move it forward. "Ultimately, you want to do something for these patients," he said. "I know we have something potentially novel."

To help IU School of Medicine find new ways to prevent, detect, and treat heart disease, contact Kathryn Red at 317-274-3685 or kred@iu.edu

ALZHEIMER'S HOLY GRAIL

A BLOOD-BASED BIOMARKER TO AID DIAGNOSIS AND IMPROVE TREATMENT

BY MATTHEW HARRIS

FOR MOST OF the past decade, Jeff Dage, PhD, has focused on pursuing a "holy grail" in medicine—one long coveted by his former employer, Eli Lilly and Company, and its peers in the pharmaceutical industry: a blood-based biomarker to aid in the diagnosis of Alzheimer's disease.

By 2014, Big Pharma had poured billions into developing drugs to break down the hallmark of the disease—plaques and tangles in the brain. The hunt for accessible biomarkers—indicators in the body that Alzheimer's pathology is present—unfolded in parallel. And while less public, searching for biomarkers has been just as essential.

Discovering a biomarker associated with Alzheimer's, a neurodegenerative disorder afflicting 6.5 million older Americans, would serve two aims. It would allow companies like Lilly to run more efficient clinical trials to verify that their drugs are effective. And as new medicines achieve approval, blood-based biomarkers would serve as easy-to-use screening tools for identifying patients for treatment.

In 2018, Dage and collaborators from the Mayo Clinic Study of Aging delivered the first reliable example that this was possible. They used PET scan images to measure a protein in the brain, phosphorylated tau, that is associated with Alzheimer's disease.

Staining on a pathology slide reveals a tau tangle, a hallmark of Alzheimer's disease, and the basis for a test to detect the condition.

They made improvements the following year. And, in 2020, Dage and his collaborators published landmark papers establishing that they had, in fact, identified a useful blood-based test for Alzheimer's. Their results showed the test was 96 percent accurate in determining whether a patient had pathological evidence of disease—better than an MRI, on par with a PET scan. The group estimated the test might be commercially available within three years.

That it emerged so quickly is remarkable.

"Five years ago, if you had asked me if I thought we'd have a blood test for Alzheimer's, I'd have said you're dreaming," said Donna Wilcock, PhD, director of the Center for Neurodegenerative Disorders at Indiana University School of Medicine and the Barbara and Larry Sharpf Professor of Alzheimer's Disease Research.

Time is of the essence. By 2050, according to a report by the American Alzheimer's Association, the number of Americans diagnosed with the memory-robbing disease is expected to double. Yet Dage and Wilcock underscore the same point. "We're still at the very beginning," said Dage, now a senior research professor of neurology at IU.

Finding those answers lured Wilcock and Dage to IU School of Medicine. Their arrival added even more depth to an abundant bench of talented researchers in neurodegenerative disorders. Advances in diagnosing and treating Alzheimer's have taken time, but that progress is rapid compared to work in vascular dementia, Lewy body disease, and Parkinson's disease.

"That's what I was brought here for," said Wilcock, who earlier this year uprooted her lab from the University of Kentucky's Sanders-Brown Center on Aging. "I want us finding and validating biomarkers for all the other dementia-causing pathologies."

For Dage, the journey to IU was much shorter, barely a mile from Lilly's corporate and research hub. Despite the proximity, Dage admitted he "didn't really have a full appreciation for the nature of the work that's going on" at IU.

Clarity came when he needed samples for a project related to rare neurodegenerative disorders known as frontotemporal dementia. Dage reached out to an NIH-backed repository at IU, the nation's largest biobank for dementia. During Dage's conversations with Tatiana Foroud, PhD, who oversees the facility, talk turned to the possibility of Dage helping set up a biomarker lab.

Lilly agreed to cover 10 percent of his time to work on the project, but Dage quickly realized it was far too small. To pursue the project and innovative work would mean leaving the pharmaceutical giant, which he did in 2021. Moving to the School of Medicine "was an opportunity to blaze a new path for myself," he said.

"FIVE YEARS AGO, IF YOU HAD ASKED ME IF I THOUGHT WE'D HAVE A BLOOD TEST FOR ALZHEIMER'S, I'D HAVE SAID YOU'RE DREAMING."

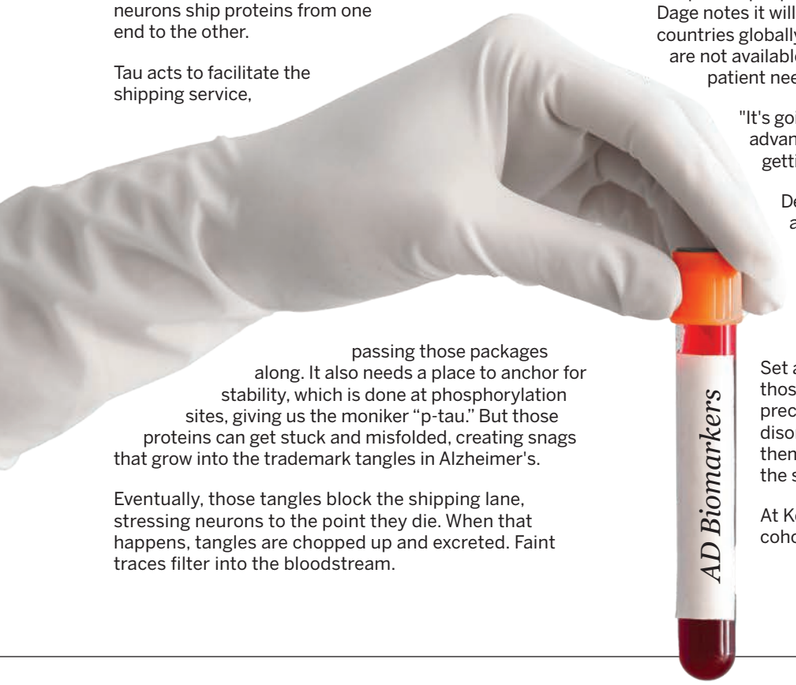
DONNA WILCOCK, PHD

THE BLOOD TEST Dage helped design might serve as a template for discovering biomarkers for other diseases.

But in 2014, his idea to look in blood for a biomarker of a disease occurring in the brain was met with skepticism. Then, Dage's team at Lilly needed biomarkers to test the potential of drugs to act on a target. That search led them to an intriguing protein: phosphorylated tau.

Set aside all the syllables and think of tau this way: cargo transport. Neurons in our brain have cell bodies, a long axon, and synapses at the end. Those synapses—and the signals they fire off—regulate our memory, motor skills, and behavior. To keep that network online, neurons ship proteins from one end to the other.

Tau acts to facilitate the shipping service, passing those packages along. It also needs a place to anchor for stability, which is done at phosphorylation sites, giving us the moniker "p-tau." But those proteins can get stuck and misfolded, creating snags that grow into the trademark tangles in Alzheimer's.



Eventually, those tangles block the shipping lane, stressing neurons to the point they die. When that happens, tangles are chopped up and excreted. Faint traces filter into the bloodstream.

So, what makes Dage's version unique? The antibodies it uses don't occur naturally: They were designed for this specific purpose. "We really spent a lot of time engineering those tools to make the test what it is," Dage said. To test its performance, the drug company partnered with several academic institutions around the world, led by the Mayo Clinic in Rochester, Minnesota, Lund University in Sweden and University of California, San Francisco.

It's hard to understate the potential importance of this discovery. Instead of ordering expensive scans or subjecting patients to spinal taps, a physician would need only perform a blood draw and send the vial for a low-cost analysis. Expanding the pool of people screened will matter everywhere, but Dage notes it will be incredibly impactful in less advantaged countries globally or rural areas in the U.S., where specialists are not available and primary care is essential to meeting patient needs.

"It's going to give people who have no access to advanced techniques the possibility of one day getting tested at their local clinic or CVS," he said.

Developing drugs and biomarkers in tandem is also likely to be a staple in the future. "That's why it felt so quick with Alzheimer's," Wilcock noted. "Everything just converged at the same point."

EXPANDING THE GRID to find new markers is where Wilcock comes in.

Set aside drug development for a moment. Without those markers, researchers still struggle to precisely articulate how some neurodegenerative disorders unfold and what mechanisms power them. Even when they have candidates, verifying the scope of their role is vexing.

At Kentucky, Wilcock's lab relied on an autopsy cohort—individuals who agreed to donate their brains, tissue samples, and medical histories—to vet candidates. Sometimes, translational research isn't linear.

A prime example is discovering a potential marker for vascular dementia, where regions of the brain are deprived of oxygen and critical nutrients. To cope, the brain tries to grow new vessels to boost its supply, a process that uses specific proteins. So, Wilcock's lab used stored samples of patients' spinal fluid to see which of these growth factors the brain relies on.

The results showed a potentially odd culprit: placental growth factor. Usually, that protein is found in the umbilical cord, where large blood vessels support a developing child. It's also present in other tissues but at very low levels. "What in the world is that protein doing in the brain?" Wilcock said.

"Not only was there more of that protein around, but higher amounts were associated with white matter changes in a patient's brain. "Nobody had ever considered it in the context of brain disease."

Those findings served as the basis for a grant from the National Institutes of Health, a portion of which Wilcock transferred to IU. The experience reinforces an integral lesson. "People assume translation goes from a test tube to animal models to a human," she said. "But there's also the ability to work backward."

Wilcock knows it's not enough to find a thread to pull on from individuals who have already died from their condition. "We don't know which symptom was the first to appear and when clinical symptoms began to appear," she said. "Which one tipped them over the edge to start having severe cognitive problems?"

Dage and Wilcock are still settling into their respective roles at IU, but they fill a long-sought niche. Aside from its biorepository, IU is home to three NIH-supported centers focused on Alzheimer's. One, led by Bruce Lamb, PhD, develops new mouse models. Lamb partnered with Alan Palkowitz, PhD, to oversee the TREAT-AD center, which vets previously unexplored drug targets. The third is the Indiana Alzheimer's Disease Research Center, led by Andrew Saykin, PsyD, which focuses on studying the disease in human participants. Liana Apostolova, MD, also spearheads work in early-onset Alzheimer's.

What's impressed Dage is the degree to which those disciplines blend through the Stark Neuroscience Research Institute. "IU is in a class of its own with their camaraderie and collaboration." It will also come in handy as Dage expands his scope into other neurodegenerative disorders.

Wooing Dage is also an obvious coup, Wilcock said. "Jeff is a critical piece, and if we could clone him twice, that would be awesome," she added.

Next comes recruiting other talented researchers—and her pitch line is straightforward. "We want this to become a destination for precision health in dementia," she said.

"IT'S GOING TO GIVE PEOPLE WHO HAVE NO ACCESS TO ADVANCED TECHNIQUES THE POSSIBILITY OF ONE DAY GETTING TESTED AT THEIR LOCAL CLINIC OR CVS."

JEFF DAGE, PHD

Your support helps world-class researchers speed up the search for ways to detect neurodegenerative diseases. To learn how you can help, contact Andrea Spahn-McGraw at 317-278-2124 or anspahn@iu.edu

BY LAURA GATES

An IU-led landmark study of early-onset Alzheimer's disease is now in year 5.

Liana Apostolova, MD, has been on a 5-year quest to better understand a form of Alzheimer's disease that strikes people early—before age 65. Her lab's first-of-its-kind Longitudinal Early-onset Alzheimer's Study (LEADS) now has 700 participants. The research is producing valuable insights—and even more questions.

"There is so much more we can learn," said Apostolova, the associate dean of Alzheimer's disease research and the Barbara and Peer Baekgaard Professor of Alzheimer's Disease Research at Indiana University School of Medicine. "Unraveling the mysteries of early onset Alzheimer's disease is very uplifting and motivating."

More than 6 million Americans are living with Alzheimer's. Just 6 percent of them are under the age of 65. In this younger subset, the disease progresses nearly five times faster than it does in people with late-onset disease.

Early-onset Alzheimer's was a largely neglected population for research until Apostolova and her team launched LEADS. Now LEADS has IU's largest grant, with nearly $80 million in total funding primarily from the National Institute on Aging. That grant is up for renewal next year.

"A large effort like this was much needed so we can make large-scale discoveries and have the power to unravel new genetic signals and new therapeutic avenues," Apostolova said.

Since the early 2000s, Apostolova has delved into developing imaging techniques and genetic biomarkers for Alzheimer's disease, becoming a leading national expert. She is a frequent speaker at national and international conferences and has co-authored hundreds of publications.

Alzheimer's & Dementia, the journal of the Alzheimer's Association, recently published a special issue devoted entirely to LEADS—a validation of their work's impact.

"We're really proving to the world how enormously prolific we are," Apostolova said.

When LEADS launched in 2018, Apostolova's team at IU consisted of 10 people. Since then, her team has tripled.

The number of U.S. data collection sites has increased from 14 to 18, and five international sites have been added—Buenos Aires, Barcelona, London, Amsterdam and Lund (Sweden). Apostolova's co-principal investigators on the project include Gil Rabinovici, MD, University of California–San Francisco; Brad Dickerson, MD, Massachusetts General Hospital and Harvard Medical School; and Maria Carrillo, PhD, of the Alzheimer's Association.

"This is all launching from IU," Apostolova said proudly. "It's very exciting. We're launching much more in-depth analysis of the genetic data with a larger scale of samples assembled around the world."

Apostolova has the daunting task of directing it all. She insists it isn't "work"—it's a fulfilling vocation that brings her joy.

"I'm in awe of how hard she works to keep the LEADS study running smoothly, and how she finds the time and energy to constantly try to build and expand on it, not just to advance research, but also to provide more services and benefits to study participants and their families," said Kelly Nudelman, PhD, a geneticist working on LEADS and an assistant professor of medical and molecular genetics at IU School of Medicine.

The progress can't be measured merely in numbers. Apostolova is reminded of that each week as she meets with real people living with this memory-robbing disease.

All of them enrolled in LEADS knowing their contributions likely wouldn't be able to help them but could help provide solutions for future sufferers of early-onset Alzheimer's.

For a few of them, however, there is some hope now.

In July, the FDA gave full approval to the first drug shown to slow cognitive decline in Alzheimer's patients in the early stages of disease. Lecanemab (marketed as Leqembi), from drugmakers Eisai and Biogen, is an anti-amyloid drug that helps clear the plaques in the brain associated with Alzheimer's. Apostolova presented positive findings from the Phase 3 clinical trial for a similarly working drug from Eli Lilly (donanemab) at the 2023 Alzheimer's Association International Conference in Amsterdam in July.

"It's a dream come true for us to be able to do something to help our patients," Apostolova said.

It's unknown whether this type of drug will benefit early-onset patients as much as the larger population of Alzheimer's patients over age 65. That's something LEADS will be evaluating in patients who qualify for a clinical trial.

Since the underlying pathology for each Alzheimer's patient is unique, personalized medicine is key.

> ***"Unraveling the mysteries of early onset Alzheimer's disease is very uplifting and motivating."***
>
> LIANA APOSTOLOVA, MD

One surprising finding from LEADS has been the low rate of early-onset Alzheimer's caused by an inherited genetic mutation, previously thought to be the main cause of Alzheimer's disease in people younger than age 65. Among LEADS participants, just one percent have gene mutations causing the autosomal dominant form of the disease.

"We have learned early-onset Alzheimer's disease is most often sporadic," Apostolova said.

Because Alzheimer's disease is more prevalent in Black and Hispanic populations, the LEADS team has actively focused on recruiting diverse participants with supplemental funding from the Alzheimer's Association.

There is still much to learn and a long way to go before medical science can predict and prevent Alzheimer's from developing in those at risk. What Apostolova knows is that the disease looks and behaves differently in people who develop symptoms before age 65.

"I believe our unique cohort will be of great interest to pharmaceutical companies," she said. "These individuals hold unknown facts and potential hints for finding cures for Alzheimer's."

Liana Apostolova and her peers have made IU School of Medicine a leader in Alzheimer's disease research. To learn how you can support their critical work, contact Andrea Spahn-McGraw at 317-278-2124 or anspahn@iu.edu.

State of EMERGENCY

BY MATTHEW HARRIS

IU School of Medicine strives to address burnout, mental health stressors and gender inequities faced by emergency medicine physicians.

Matt Rutz, MD, walks between units in the ER at Sidney & Lois Eskenazi Hospital.

INSIDE A RADIO DISPATCH ROOM, MATT RUTZ, MD, SAT PATIENTLY AS GENTLE STATIC FILLED THE AIR.

AN EMERGENCY physician, he was waiting for a voice telling him if a 62-year-old woman who had taken a volatile mixture of narcotics and alcohol would be coming to see him at Sidney & Lois Eskenazi Hospital.

Finally, the crackling voice of a paramedic piped up. "She's made multiple suicidal comments to her son," the medic said. “She wanted to die, and she wanted him to come over and hold her." Yet, the woman's heart rate, blood pressure, and oxygen levels were normal. And the medic relayed this: She doesn’t want to be trucked to the ER.

Rutz's eyes grew wide. He shook his head in slight exasperation. While disconcerting, the woman's behavior and condition didn’t clear the bar for Indianapolis police to force her to go to the hospital. "I need you to talk to her and make sure she understands the implications of not going to the hospital," the medic said.

Rutz stood up and walked briskly back to the desk at the front of the unit where patients in severe condition receive care. He met Natalie Moore, MD, a second-year resident, with her head tilted and a walkie-talkie pressed to her ear. Only two months into the most brutal stretch of her training, Moore must try to sway a patient she cannot see.

"I hate these," Moore said.

"You carry no risk," Rutz said. "Just try to do your best for the patient."

She pressed a button on the walkie-talkie and spoke slowly. "Can the patient hear me?" Fifteen seconds of silence. Then, the medic gave her a garbled go-ahead. "I would encourage you to come to the hospital so we can take care of the thoughts you're having of harming yourself," Moore said. For 30 seconds, more silence.

Finally, the medic reported: "She's tired and wants to go to bed."

With the call over, Rutz summoned Moore for a quick sidebar. "We're not on scene to evaluate the situation," he says. "We have to hope they're doing what's right."

Together, on this Sunday overnight shift in October, Rutz and Moore saw more than 25 patients—three from minor car accidents, two with complications from going off dialysis and one man who was faking alcohol withdrawal, tremors and all.

Even the night's highest drama—a man who showed up with a gunshot wound—unfolded calmly. After he was stripped in a shock room, trauma surgeons delivered the good news: the bullet had passed harmlessly through fat tissue in his belly.

"So, I'm good?" he asked.

By 3 a.m., the tide of patients ebbed, enabling Rutz and Moore to quietly update their charts, enter orders, parse CT scans, and leave concise notes for colleagues. At 4:30, Rutz tossed out a question. "Does it feel slow?" he said.

WORKING IN AN emergency room has always been hectic. Stress and burnout are not new. Finding a work-life balance is not easy, said Peter Pang, MD, who chairs the Department of Emergency Medicine at IU School of Medicine. But even among those who know the territory, the past couple of years ratcheted up the strain.

First, there was a pandemic. Waves of gravely ill patients, some of whom couldn’t be saved. Even as it has receded, patient visits increased, with physicians seeing even more patients than before the pandemic. By 2022, 60 percent of emergency physicians reported feeling burned out, a 17-percentage point spike over the previous year.

The vocation instills an unyielding mantra: The sickest patient is in the waiting room, the one yet to be seen. A physician must quickly pivot from running a code in a shock room to treating a patient with a minor cut on their head. There's scant time to take a beat, refocus, and process what they've witnessed.

"How do you tell a parent their 3-year-old is dead? That's not a normal thing to do," Pang said. “You're also expected to give the next patient your very best. And rightfully so, they deserve our best."

A SMOOTH-FUNCTIONING emergency department is a marvel of close team coordination among physicians, nurses, techs, specialty consultants, and hospitalists. But national staffing shortages have been felt locally as the demand for patient beds has increased. Teams supporting physicians manage overflow care and wait times tick up.

"They're being asked to do more with less," said Heather Kelker, MD, who practices at Riley Hospital for Children and is an assistant professor of clinical emergency medicine at the School of Medicine. "If we're used to a certain way of running something that's now strained, it doesn't feel too good."

While physicians draw six-figure salaries and enjoy a particular esteem, they're not immune to economic pressures. In one study, 70 percent of ER physicians agreed that "corporatization of medicine" strongly impacted job satisfaction.

Charting, for example, can be a flash point. It's no longer just a tool to share clinically significant information. It now folds in billing, coding, and litigation protection. To keep up, some physicians spend hours charting at home after a shift ends. "Those day-to-day stresses of how an ER functions add up and impact us over time," Kelker said.

UNDER PANG, the department has moved to try to reverse trends gnawing at its faculty and the next generation of physicians they train.

Faculty like Julie Welch, MD, ramped up research to understand the mechanisms that drive burnout, erode work-life balance, and create gender inequity. Others study the impact of peer-support programs and policy changes. That requires investment—dollars Pang deems well spent.

"My sense is we've done more than most, and it has to stay that way," Pang said.

The School of Medicine, IU Health, and Eskenazi Health worked to support their teams during the pandemic. IU Health and the School of Medicine were already striving to improve wellness and that work intensified during the pandemic. In emergency medicine, wellness was embedded into the incident command structure, demonstrating its importance.

Both groups spent the past year amassing information. IU Health's group found emergency physicians believe they lack the tools—mostly staffing—to work efficiently. The school's group joined similar committees from peer institutions working toward the same end. "Wellness is a vague term," said Kelker, who serves on both committees. "We need tools that can help us define it."

Pang's department has already rolled out tangible policy changes.

During the first and third trimesters of pregnancy, residents can opt out of night shifts. When the child is born, the resident gets six additional weeks of flexible scheduling. There's now financial support for wireless equipment for lactating mothers, and bereavement leave: the department foots the cost when a resident picks up a shift for a grieving colleague. A peer support group for physicians facing malpractice claims has also been created.

"Our approach to wellness is to have a learner's heart. We don't have all the answers, but this work matters. We're going to work toward solutions."
PETER PANG, MD

Some research shows that working at an academic medical center provides a buffer. Physicians at medical schools like IU devote more work hours to non-clinical duties like teaching and research, which can boost feelings of personal accomplishment. Some studies—albeit with small sample sizes—also report lower burnout rates.

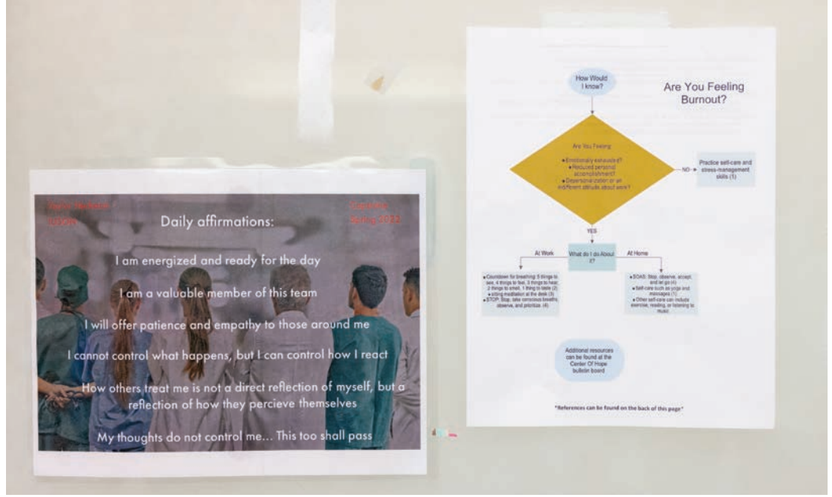
It's not without tradeoffs.

Academic faculty make less money than physicians in a community practice. Yet they experience a shared commitment to training physicians, scholarship, and innovation.

A GLIMPSE of this dynamic is visible at Eskenazi, where the ER handles more than 100,000 patient visits a year–a new patient every five minutes. Many are uninsured. They might be dealing with the acute consequences of a chronic condition. Or the results of street violence.

Two years ago, Eskenazi felt the tug of the trends pulling on emergency medicine. Nurses were fed up with the abuse from patients. Managers told them to jot down incidents on a form and drop them in a box. Eventually, those reports made their way to Marla Doehring, MD, who practices at Eskenazi and serves as one of the leaders of committee for residency safety. "The incidents didn't shock me," said Doehring, an associate professor of clinical emergency medicine. "The sheer volume did. I thought we needed to do something."

The result: a study on workplace violence. It found offenders were often men who came to the ER voluntarily.



Signage in the ER is a small way Eskenazi helps staff with burnout.

Usually, an incident—most often reported by nurses—involved swearing or threats of legal action. But sometimes the lack of civility extended well beyond vulgarity and threats. Despite that, most healers default to their ethical code.

Esknazi took the data to heart. It increased security, tweaked no-tolerance policies to include non-violent harassment, and posted QR codes to streamline incident reporting. Even so, those efforts can't erase lousy behavior.

That was true when Rutz encountered a patient writhing on a bed. Paramedics brought him to Eskenazi after an aide at a long-term care facility found him on the floor of his room and agitated. He looked to be in his late 50s. He had a patchy white beard and wore only his underwear.

Moore, two nurses, and a paramedic surrounded him, each trying to hold him in place. His words were slurred. A medic said the patient had suffered a stroke two months earlier. Rutz moved to the foot of the bed, placed his hands just above the left knee, and pressed.

The patient muttered at Rutz: "I will f—- you up."

"Just relax, dude," the medic said slowly.

But the man didn't heed the advice, wriggling onto his side. Moore called for a dose of droperidol, a sedative used when a patient is aggressive. Rutz asked the medic about the man's condition when they found him. Details were scant. A nursing aid suspected he'd been down for an hour before she discovered him.

"I'm gonna sue all of you," the patient yelled.

"Seems fair," Rutz quipped.

Good humor embodies Rutz's approach to the stresses of his profession. When overseeing the unit, he keeps the vibe breezy. Any small favor—like a nurse handing him a chart—is met with a pleasant "Grazie." But when he steps into a patient's room, he sounds like a man catching up with a neighbor as they're knocking out some yard work.

What sustains his affable bearing? "The patients," said Rutz. "A lot of folks are grateful for any care they can receive. Sometimes, it's as simple as giving them meds for high blood pressure or info on how they can get transportation to another clinic."

IN SOME WAYS, Rutz personifies a cultural shift in his field. He finished residency in 2015, coming up in an environment that emphasized the grind: no breaks, no running to the restroom, and, crucially, not vocalizing stress.

Now, those topics are atop the docket when new residents arrive.

Kyra Reed, MD, an assistant professor of clinical emergency medicine and an assistant program director, hosts a retreat at her home where future ER doctors learn about the department's policies and programs. When they open their Outlook calendar, a session with a counselor is already booked. They also complete a psychological needs assessment.

"We want to remove any barrier or stigma," Reed said. "That all conveys just how crucial their mental health and well-being is to us."

Throughout their intern year, lectures return to topics around burnout. The department also uses peer support for residents working ICU shifts—often a young physician's first exposure to caring for very sick patients. During those sessions, a resident leader sits down with the intern to discuss any issues.

Older residents, though, have different needs. For those in their second year, their workload ramps up dramatically. Almost half their shifts are in high-acuity areas, leading resuscitations in shock rooms.

"You're making high-level decisions and you're newly on your own," Reed said. "That's a lot of weight."

Two months into her second year, Moore feels every ounce of it pressing down. "It's very overwhelming," she said. "I pretty much feel all the time like I'm missing something or doing something wrong."

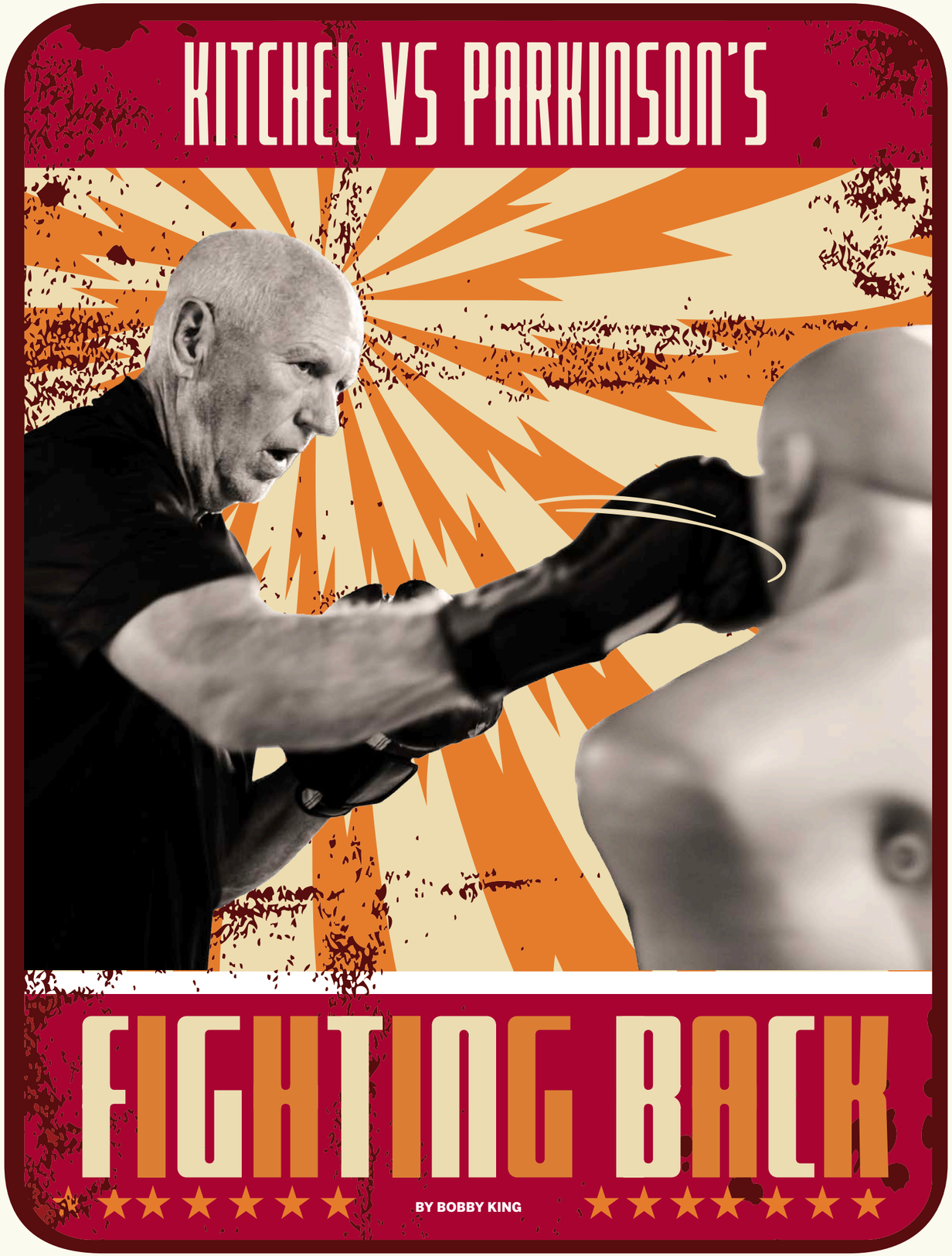
That sensation is normal. Second-year residents might receive a lecture focused on efficient charting, coping with exhaustion, and maintaining work-life balance. By the third year, content shifts to maintaining empathy and workplace safety.

To cope, Moore thinks only of the next step for each patient in her care. She knows the volume she sees at IU—sometimes six patients an hour—surpasses other programs. Stress now means competence later.

Rutz said Moore's experience is unfolding normally. "She's getting her butt kicked," he said. Soon, though, her baseline will reset. Once that acclimation ends, Rutz said his attention would turn to building confidence.

Rutz paused and looked up. Moore had stepped into a room and started chatting with a patient. He grinned. "She's so good," Rutz said. "She just doesn't know it. There's a little bit of imposter syndrome. We need to work through that, but she's got what it takes."

IU School of Medicine trains many of the state's emergency physicians. To help us offer a stellar training environment, contact Ken Scheer at 317-278-2122 or kescheer@iu.edu.



TED KITCHEL,

the former Indiana University basketball star who won a championship under the late, legendary coach Bobby Knight, straps on some boxing gloves and takes position across from a silent, straight-jawed figure who, by coincidence, is also named Bob.

Bob has flesh made of rubber, a skeleton of metal, and a face that is imminently punchable. He is, after all, a boxing dummy built to take a beating. And Ted, now 64, is about to give him one.

Ten blows to Bob's face. Ten to the chest. Ten to the gut. And the dummy looks dazed. With Bob dispatched, Ted moves over to a 50-pound bag of dead weight hanging from a chain like a side of beef. He unleashes a torrent of blows, first with his left hand, then the right, then in combinations. Between 2½-minute bursts, Ted takes 30-second breaks. The bag seems to appreciate it.

The workout continues. There's more punching, some kickboxing, some toe-tapping exercises and several minutes of jumping rope, which Ted describes as a "killer," although he looks like he could go for more. Finally, Ted grabs a baseball bat off a rack and begins beating the tar out of a truck tire. It's a violent display. By the time he's done, the tire is properly tenderized and the smooth dome of Ted's head is covered in large beads of sweat. "I'm pretty worn out," he says flatly.

Even in this gym, the competitor in Ted Kitchel comes out. A guy in his class once made a display of unloading 66 punches on one of the boxing apparatuses—an impressive showing.

Ted stepped up and hit the machine 100 times. The classmate returned and hit it 101. Tired of trifling, Ted unleashed a furry of 210 blows, and it was game over. "Most people who know me know that I'm a little competitive," Ted said. "I couldn't let somebody beat me."

That seems to include his real opponent these days, the toughest adversary Ted has ever faced, the foe trying to rob him of his balance and make his right hand—his shooting hand—shake in ways it never did even in the closest games. The adversary he's trying to defeat—with exercise and fundraisers to support research at IU School of Medicine—is Parkinson's disease.

★★★★★★★★★★★★★★★★

"MOST PEOPLE WHO KNOW ME KNOW THAT I'M A LITTLE COMPETITIVE." TED KITCHEL

"ONE. TWO. THREE. FIGHT BACK!"

Ted Kitchel is, in some ways, the quintessential Hoosier. He grew up on a farm in a small town—Galveston, Indiana—where his family grew corn and soybeans. He worked on his jump shot on a hoop in the barn. He led tiny Lewis Cass High School to its first sectional championship back in the days when big schools and small ones competed for the same title—the way he prefers it. At IU, he took his share of abuse from Knight—"He was always on my ass," Ted says. "He knew I could handle it." He met his future wife Kristi—a diver turned cheerleader—at IU. He helped lead the Hoosiers to three Big Ten titles and was a key cog on the team that won IU a national championship in 1981.

Yet Ted's Hoosier story took an unexpected turn. In 2015, he developed a tremor in his right hand. At first, he thought it was a side effect of the medications he was taking for blood clots. But the tremors persisted and one of his colleagues at FootJoy, the sports gear company where Ted worked in sales, urged him to see a neurologist in Boston. He went and, in less than 20 minutes, Ted received both a diagnosis and a second opinion: It's Parkinson's. That's how clear the symptoms were.

At the time, all Ted knew of Parkinson's was its impact on Michael J. Fox, the actor whose tremors were by then visible for the world to see. Fox's case was much more advanced, the doctor said. And Ted found some reassurance learning that, while not curable, Parkinson's is a disease patients can live reasonably well with for a long time. Still, Ted said, in a low-key assessment of this pivotal moment in his life: "It kind of scares you."

Once back in Indiana, after Ted delivered the news to Kristi and their children, he was connected to doctors at IU, which has been named a Center of Excellence by the Parkinson's Foundation for its high-quality care. Eventually, he came under the care of S. Elizabeth Zauber, MD, the center's director and an associate professor of clinical neurology at IU School of Medicine.

In most people, Zauber said, the causes of Parkinson's disease are not clear. Exposure to certain pesticides and other toxins is believed to be one culprit. For many patients, the suspect seems rooted in genetic factors.

IU School of Medicine is conducting Parkinson's disease research in several areas.

Zauber's research includes clinical trials of new medicines aimed at treating the symptoms of the disease as well as drugs to slow its course, along with studies of the impact of Deep Brain Stimulation and focused ultrasound as treatment for motor symptoms.

Tatiana Foroud, PhD, a professor in the Department of Medical and Molecular Genetics and the school's executive associate dean for research affairs has support from the Michael J. Fox Foundation and the NIH to maintain a biorepository of blood, tissue and other samples. They were collected as part of ongoing research studies seeking to chart the biological and clinical changes across the spectrum of the disease—and to identify early signals of the disease and points where treatments should be directed.

Foroud and Zauber are both part of an ongoing research study funded by the Parkinson Foundation that provides free genetic testing and counseling for people with Parkinson's disease—a service that tells them if they have inherited genetic variants associated with Parkinson's disease.

While there are medications that alleviate the symptoms, there are no treatments proven to slow the course of the disease over time—except maybe one. Exercise hasn't yet been proven to slow Parkinson's, but there are some indications that it may do so. Zauber says there even seems to be a dose-dependent effect in reducing the symptoms—the more intense the exercise regimen, the greater the benefit.

This is the idea that draws Ted twice weekly to the Social of Greenwood, a center for seniors near his home. It's where he faces off against Bob—and against Parkinson's.

As soon as they learned of their dad's diagnosis, Ted's kids—Tyler, Scott and Mackenzie—began scouring the web for information about the disease. They quickly noticed the part about the need to exercise. They also discovered Rock Steady Boxing.

Developed in Indianapolis by a patient with Parkinson's who received some training in boxing, Rock Steady Boxing groups have since spread across the United States and around the world. It employs an assortment of exercises—many boxing-oriented—that include cardiovascular work, balance exercises, stretching and strengthening.

Zauber is an enthusiastic believer in Rock Steady Boxing. She sits on the non-profit's board. And she's about to begin a research study that aims to find out precisely which aspects of exercises in the Rock Steady regimen are most effective for Parkinson's.

Wherever that leads, it's clear Rock Steady gives people like Ted a chance to literally fight back against this chronic illness. "When you are hitting the punching bag," Zauber said, "you are, in a way, hitting this disease and taking control of your health in a way that can be very empowering for people."

Ted Kitchel has plenty of stories to tell about his playing days—and of Knight. When he was sidelined with a pulled a groin muscle, Knight grew angry when Ted told him he'd be out of action for three or four days. "When I was (playing) at Ohio State," Ted recalls Knight yelling, "(John) Havlicek played with two pulled hamstrings." To which Ted quipped to teammate Phil Isenbarger that the great Havlicek, even on two bad legs, was still much preferable to Ohio State's sixth man back then—Bobby Knight.

The story was supposed to just be a laugh shared between teammates. But when IU won the championship and their celebration banquet was broadcast on local TV, Isenbarger took the microphone and shared Ted's quip in front of Knight and the world. Knight, Ted learned later, turned to someone and said: "Kitchel couldn't have thought of that. He ain't that f——— smart."

For all Knight's fire, Ted appreciated him as a great coach. But for instilling him with grit—and the resiliency he uses now to confront Parkinson's—Ted credits his own mother. "My mother is very, very tough, hard-nosed," he said. "That is the way she expected us to be."

Parkinson's disease is the second-most common neurodegenerative disorder after Alzheimer's. It can cause slowness of movement, balance problems, tremors and stiff muscles. It can also lead to trouble sleeping, mood changes, fatigue and other symptoms. By itself, Parkinson's isn't fatal. However, the complications it causes—from falls and trouble swallowing—can be.

IDEAS | FIGHTING PARKINSON'S

These days, sleeping doesn't easily come for Ted. He occasionally experiences episodes of vertigo and battles fatigue. And then there's the only visible sign of Parkinson's in Ted Kitchel—the tremors in his right hand. They appear when he's sitting and talking or when he lines up a shot on the golf course, the head of the club wobbling just a bit.

At the same time, Ted's workout routine could leave someone decades younger gasping for air. And he remains within 10 or 15 pounds of his college playing weight. Even with the tremors in his hand, he remains a good golfer, but one who grumbles that Parkinson's has added a couple of strokes to his scorecard.

His teammates, these days, are the members of his Rock Steady Boxing class, who, like him, have Parkinson's. Together, they break their huddle before workouts with the count, "One, two, three, fight back." At gatherings for the Rock Steady families, Kristi says the spouses of the other classmates tell her how much it means to have Ted in class. "I think at first Ted didn't realize it, but he encourages so many of them, and gets them to do more than they think they can." But Ted maintains a matter-of-fact way of looking at things.

"People need to understand that just because they have Parkinson's, it's not a death blow," he said. "You've got to keep focusing every day, whether it is Rock Steady Boxing, whether it be lifting weights or working out, riding a bicycle. Stay active. Don't sit on the couch and feel sorry for yourself."

Aside from boxing, Ted is also fighting back against Parkinson's by raising that kind of awareness—in public speaking and in media appearances.

His biggest push—with intense support from his family and close friends—has been an annual golf outing at Valle Vista Golf Club in Greenwood that raises money for Parkinson's research at IU School of Medicine. The latest golf outing, in August, drew 135 golfers and raised approximately $75,000. Over four years, the event has raised more than $230,000 for research.

He kicked off the event by welcoming the golfers and then camped out on the 11th hole, playing the Par 3 with each of the groups passing through. Most of the time, his ball was the best one off the tee.

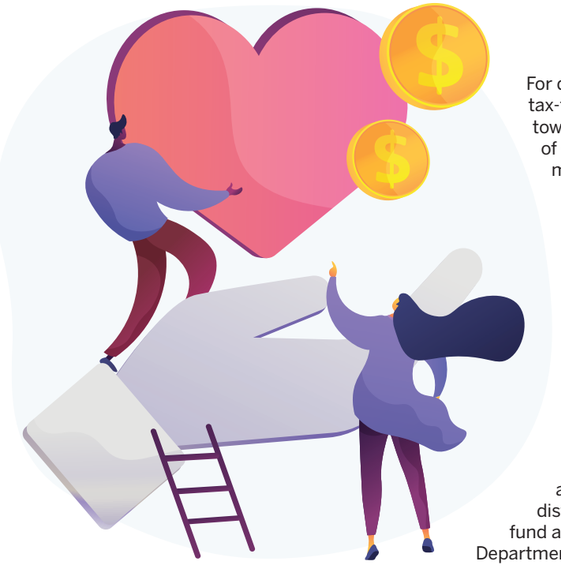
Ted and his family are hopeful the research at IU School of Medicine and other sites advances quickly enough to help him, but they also want it to benefit others. And maybe because of his mother's toughness, because of the thick skin he developed under Knight, and because of his Christian faith, Ted feels well-equipped to face his most formidable foe.

"The easiest thing to do is to say 'Why me? Why do I have the shaking?' The reason may be that I can handle it better than most people. The good Lord has put it on my shoulders to take care of it and **I'LL DO THE BEST I CAN.**"

TED KITCHEL

★ ★ ★ ★ ★ ★ ★ ★ ★ ★ ★

To support research aimed at understanding the biology of Parkinson's disease and easing its symptoms, contact Sam Kinder at 317-278-5635 or kindersm@iu.edu.



TAX-SMART CHARITABLE GIFTS FROM YOUR IRA

A retired Indiana University School of Medicine faculty member recently asked me to consider writing about how to make gifts from an Individual Retirement Account, or IRA. He understood that most of our alumni have an IRA—and that the charitable giving rules and tax implications can sometimes be tricky to navigate. In the limited space I have here, I will take on this requested task.

Before 2023, IRA owners over age 70½ had only one tax-smart option when making an outright, lifetime gift to charity direct from an IRA. Now, there are two.

MAKING AN OUTRIGHT GIFT

If you are over age 70½, you can make an outright, lifetime gift of up to $100,000 annually to a public charity directly from your IRA. This distribution to charity is not included in your taxable income and it could keep you from being pushed into a higher tax bracket.

For donors over age 73, this tax-free distribution also counts toward satisfying all or a portion of your annually required minimum distribution, or RMD. The IRS does not require you to begin taking your annual RMD until age 73, but at age 70½, you are allowed to make a tax-free distribution direct from your IRA to a public charity. Our alumni have been taking advantage of this tax-smart distribution to support IU School of Medicine.

For example, we have an alumna who makes annual $100,000 tax-free distributions from her IRA to fund a new professorship in the Department of Surgery. Another alumna is about to make her first tax-free distribution from her IRA so she can name a space inside our new medical education and research building now under construction in Indianapolis.

CREATING A CHARITABLE GIFT ANNUITY

For those over age 70½ there's a new provision in the law that allows you—just once—to make a tax-free distribution from your IRA to create a charitable gift annuity, or CGA, at your favorite public charity.

This new law specifies the IRA owner is allowed a one-time, tax-free distribution not to exceed $50,000 to create a CGA. The good news is that the distribution is not included as taxable income. The tax-free distribution also counts toward satisfying all or a portion of your annual RMD.

This new law has sparked many new conversations with donors and alumni asking about the mechanics and benefits of a CGA. For those not familiar, a CGA is gift vehicle involving a contract between a public charity and the IRA owner as donor. After making an irrevocable gift to a public charity, the charity pays the donor a fixed stream income for life. When the CGA terminates, the remaining assets are used for medical education or medical research, as the donor directs in writing. CGAs are rather easy to establish.

SOME ADDITIONAL THOUGHTS

The tax-free distributions I've discussed must be made to a qualified public charity. They cannot be made to donor advised funds, private foundations and supporting organizations.

The tax-free distribution direct from an IRA to a public charity does not generate a charitable income tax deduction.

END OF LIFE IRA CHARITABLE GIFTS

Under current tax law, your investment account receives a step-up in cost basis at the end of your life when the remaining assets are distributed to your loved ones. Utilizing this step-up in cost basis minimizes a loved one's income tax liability. Unlike an investment account, leaving your IRA at the end of your life to your loved ones actually exposes them to income taxes in a big way: Every distribution they receive from your unused IRA is included in their taxable income. Because an IRA is loaded with the deferred income tax liability, estate planning attorneys often tell philanthropic-minded IRA owners that there's a better way to pass assets to loved ones and to charity.

Because charities pay no income taxes on distributions received from an IRA, estate planning attorneys say it is tax-smart to leave at least a portion of your unused IRA to charity, and to leave your investment account to your loved ones. This enables more money to pass to the charity and minimizes a loved one's income tax liability.

LEARN MORE

If you have any questions about a charitable gift from your IRA, please contact Tim W. Ueber, IU School of Medicine's senior director of planned giving at 317-274-0187 or twueber@iu.edu.

Getting cancer research on track

BY BOBBY KING

At first glance, it might seem that auto racing and cancer research have little in common. But that's not how Kelvin Lee, MD, sees it.

"We are in the business of accelerating cancer research. And to beat cancer, you have to go fast, drive smart and have a great team," said Lee, director of the Indiana University Melvin and Bren Simon Comprehensive Cancer Center.

In that spirit, the two worlds of racing and research beautifully melded this summer on an IndyCar—specifically, Chip Ganassi Racing's No. 11 car, which sported the colors and logos of the cancer center at the Gallagher Grand Prix at the Indianapolis Motor Speedway.

The red and white livery, as the car exterior colors and logos in racing are known, was generously donated by the Jack, John and Jeff Schwarz family. The unique opportunity tied into the cancer center's Race to Beat Cancer public online education campaign, which focuses on cancer prevention and early detection. Specifically, it's aimed at breast, colon, lung and testicular cancers, as well as HPV-related cancers of the head and neck and cervix. As part of the campaign, experts from the cancer center provide easy-to-understand tips about prevention and early detection, signs and symptoms, screening guidelines, the latest research, and more.

The car, driven by New Zealander Marcus Armstrong, had a fast qualifying time, positioning it seventh in a 27-car field. Unfortunately, a first-lap crash knocked the car out of contention for a win. Still, Armstrong finished the race. And Lee, the cancer center director, said that's another thing racing and cancer share.

"All of us in cancer research had great empathy for Marcus. We know the feeling when you and your team plans everything so carefully and yet the unexpected happens—your experiment fails or your clinical trial results are far from what you expected," Lee said. "The important thing, though, is to do exactly what Marcus did: work together to get back on the track and keep moving toward the goal–curing cancer."

To speed up cancer research that saves lives, contact Amber Kleopfer Senseny at 317-278-4510 or akleopfe@iu.edu.

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