

PENN Medicine



RIGHT FROM THE START

Penn Medicine's bold actions to eliminate racial disparities in maternal health are helping healthy families to grow.

Plus:

Celebrating the Nobel Prize: Penn Medicine's world-changing mRNA discoveries garner medicine's highest honor

Dementia treatments on the horizon after decades of discovery



AN INDESCRIBABLE SURPRISE

John Pryor, Jr., a sophomore at Temple University and a member of the Naval Reserve Officers Training Corps (NROTC), had no idea when he volunteered for Color Guard duty at an event this fall that the occasion was a Navy ball for Penn trauma providers celebrating a groundbreaking partnership in which Navy clinicians embed with teams at Penn Medicine. His father, Maj. John P. Pryor, MD, had been the medical director of Penn's trauma program when he was killed in action on Christmas night in 2008, while serving as an Army combat surgeon in Iraq.

After "displaying the colors" and packing up to leave, John stayed to listen to the speakers, who mentioned his dad's name. He wasn't sure he'd heard it correctly until C. William Schwab, MD, took the podium. After the ceremony, John approached Schwab to say hello. It took a moment for Schwab, a former Navy surgeon, the founder of Penn's trauma program and a mentor of Pryor's, to realize whose hand he was shaking.

"He said, 'John!' and then hugged me tight for 30 seconds. When he pulled away, he was crying," Pryor, Jr. said.

A crowd formed around John and people asked to take pictures with him. For many in attendance, it was the first time they had seen "John John" since he was a small child. They were overjoyed to speak with the young man whose mannerisms were so similar to his father's.

"The rest of the night was indescribable—smiles, tears, emotion," said Schwab.



Top photo: C. William Schwab, MD, with John Pryor, Jr., and Niels D. Martin, MD, chief of the division of Traumatology, Surgical Critical Care and Emergency Surgery. Photo by Katie Burke.

Inset: Maj. John P. Pryor, MD, served two tours of duty as a combat surgeon for the U.S. Army in Iraq.

► **Read more about the emotional reunion, and about the unique Penn Trauma/U.S. Navy partnership, at PennMedicine.org/blog.**



12

DEPARTMENTS

- Left THE PREP**
An Indescribable Surprise
- 2 EDITOR'S NOTE**
Collaborations Changing the World
- 3 VITAL SIGNS**
Cancer Center's 50 Years, Surgical Care Access
- 42 DEVELOPMENT MATTERS**
Marvel of mRNA, Mountain Trek for Women in Immunotherapy, Diversity in Nursing
- 46 ALUMNI NEWS**
Alumni and Faculty Obituaries
- 48 FUTURE PROGNOSIS**
Where Future Leaders of Health Equity Innovation Take the Reins

STAFF

- Rachel Ewing
Editor
- Meredith Mann
Assistant Editor
- Graham P. Perry/NCS Studios
Design/Art Direction
- Peggy Peterson
Contributing Photographer
- ADMINISTRATION
Patrick Norton
Vice President for Public Affairs
- Holly Auer, MBE
Associate Vice President,
Communications

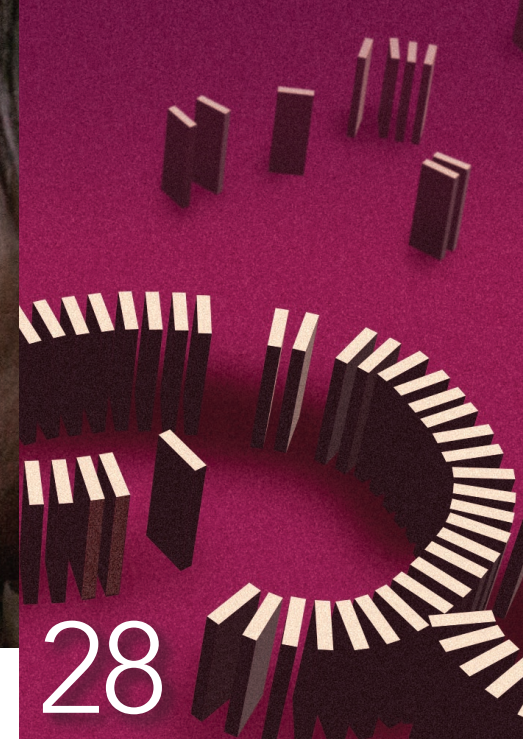
PENN MEDICINE IS AVAILABLE ONLINE AND VIA EMAIL!

You can read and share the stories from this issue and recent past issues of *Penn Medicine*, browse related links, and enjoy extra photos online. Visit: PennMedicine.org/magazine

Subscribe to the magazine's email edition: PennMedicine.org/news/subscribe



16



28

PENN MEDICINE

FALL WINTER 2023 / VOLUME XXXIV NUMBER 2

12 The World Cheers mRNA

Bringing an end to the COVID-19 pandemic was only the beginning. The 2023 Nobel Prize in Physiology or Medicine celebrated Penn Medicine research breakthroughs using mRNA that led to the first successful vaccines using this technology.

16 Right from the Start

By Christina Hernandez Sherwood

For Black families to grow and thrive, the U.S. health care system must reverse the trend of serious harm and death before, during, and after childbirth. Penn Medicine is taking bold action to improve maternal health and eliminate disparities.

28 Changing the Picture for Dementia

By Queen Muse

The domino chain of discovery is finally creating a path to a cure for Alzheimer's and related diseases of the brain. Foundational discoveries at Penn were crucial to arriving at this moment after decades of promising ideas failed to translate to drugs that slow and reverse the symptoms of these devastating conditions.

Penn Medicine is published for the alumni and friends of Penn Medicine by the Office of Public Affairs. © 2023 by the Trustees of the University of Pennsylvania. All rights reserved. For alumni address updates, visit quakernet.alumni.upenn.edu or contact medalum@dev.upenn.edu. Address all other correspondence to *Penn Medicine Magazine*, Department of Communications, 3600 Civic Center Boulevard, 5th Floor Suite 500, Philadelphia, PA 19104-4310, or call 215-662-2560, or email penntimedinecommunications@uphs.upenn.edu.

Collaborations Changing the World

It's time to put the trope of the solitary genius scientist to rest, once and for all. Today and tomorrow, the scientists and medical leaders who are changing the world for the better are made more powerful, and making more possible, through collaboration. And, as this issue's stories show, many of the collaborations that exemplify this spirit are happening right here at Penn Medicine.

Let's start with medicine's highest prize: The 2023 Nobel Prize in Physiology or Medicine was awarded to a pair of scientists, Katalin Karikó, PhD, and Drew Weissman, MD, PhD. The duo began collaborating at Penn Medicine in the late 1990s, and it was through the combined expertise they both brought to the partnership—Karikó's in the chemistry of RNA, Weissman's in the body's immune response to infectious disease—that they achieved breakthrough discoveries in the early 2000s that made mRNA vaccines for COVID-19 possible decades later. Today, the newly launched Penn Institute for RNA Innovation, directed by Weissman, has collaborations with more than 250 labs across the country and world, with a goal to double that number in the next year. The team assembled there aims to change the world with an astonishing array of new vaccines and therapies for diseases as diverse as Lyme disease, sickle cell anemia, and heart disease. (See more coverage of both the Nobel Prize win and the future of mRNA on page 12.)

Another powerful pair of researchers, Virginia M.-Y. Lee, PhD, MBA, and the late John Trojanowski, MD, PhD, likewise formed the gravitational core for many more scientists at Penn Medicine and worldwide who have begun to change the bleak picture for individuals and families struggling with neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, and more. Lee and Trojanowski were a married couple in the early stages of separate careers before they chose to combine their complementary expertise to solve a pressing problem. Neurodegeneration was the right one for them, using Lee's experience in biochemistry and Trojanowski's skill as both a neuropathologist and a connector with other physicians treating patients. Now, after decades of slow and stalled progress, research and clinical teams tackling Alzheimer's disease and other neurodegenerative disease finally appear to be on the cusp of tangible hope to slow and reverse the effects of cognitive decline. (See the full collection of stories detailing how we got to this moment and what happens next, beginning on page 28.)

Solving the most pressing challenges in medicine may require an even deeper degree of collaboration. Many of most intractable problems are a type that can't be solved with a flash of insight or a single new type of medication.



And they may require multiple solutions working together all at once. This is the case with the distressing racial disparity in maternal health. In Philadelphia, Black women are four times more likely to die of a pregnancy-related cause than white women, and nationally, the United States has the worst outcomes in maternal health of any developed country. Our cover story on page 16 details how Penn Medicine has built a coordinated, multidisciplinary effort over the last several years to reverse that trend. While Elizabeth Howell, MD, MPP, chair of Obstetrics and Gynecology, led the effort along with Sindhu Srinivas, MD, MSCE, the push has been system-wide, involving personnel from every Penn Medicine birthing hospital, and every department that touches the care of a birthing parent from prenatal care through to their ongoing health care after giving birth.

Collaboration is also how it's possible to do more than any one person, team, or organization can achieve alone. When it comes to maternal health disparities, numerous Penn teams are collaborating with insurers, public health officials, other hospitals, tech companies, and more, to ensure the successful practices that save lives and prevent complications for patients at Penn Medicine, reach expectant and new parents in more places, regardless of where they receive their care.

Changing the world isn't any one person's job at Penn Medicine. It is everyone's, working together.

RE

Rachel.Ewing@penmedicine.upenn.edu



The Abramson Cancer Center at the University of Pennsylvania marks its 50th anniversary year in 2023.

Since the discovery of the Philadelphia chromosome in 1960 by Peter Nowell, MD, who would go on to become the first director of the Abramson Cancer Center (ACC), the ACC has made tremendous strides in cancer research, care, and prevention.

Founded in 1973, the ACC celebrated its 50th anniversary this year—a half century of clinicians and researchers working together, across disciplines, sharing knowledge in pursuit of high-risk, high-reward concepts to improve the landscape of cancer for patients and families.

In the mid-1970s, the five-year survival rate for patients with breast cancer was about 75 percent, which has improved to over 90 percent now, according to the latest data from the National Cancer Institute.

Kate Korson is one of those success stories. Korson was living on a ranch in Colorado when she found a lump in her breast in January 2023. Before she even had a biopsy, she decided: If it was cancer, she was going to Penn Medicine, where her own mother had been successfully treated in a clinical trial for colorectal cancer nearly 20 years earlier. Her diagnosis of triple-negative breast cancer was confirmed a week later on her 34th birthday, and the next day Korson began planning her move to Philadelphia. After a few months receiving an experimental chemotherapy she received as part of a clinical trial at Penn Medicine, her tumor shrank significantly, and she underwent surgery after a much shorter course of chemotherapy than usual. By October, Korson was sharing her story alongside her oncologist and surgeon as an inspiration for other patients on *Good Morning America* on ABC.

Thanks to progress in cancer prevention, early detection and drug development, survival rates have greatly improved for patients with many other cancer types in recent decades, too.

“What we're seeing now is new hope for a patient hearing the words, ‘You have cancer,’” said Robert Vonderheide, MD, DPhil, director of the ACC. “Fifty years ago, we had very limited resources to treat those patients. That's different now. As we look ahead to the next 50 years, our team is working together with a singular focus to bring discoveries from the lab to patients as quickly as possible through clinical trials. In the future, we want to produce not only more cures for cancer, but methods to intercept it so that the cancer never develops in the first place.”



Breast cancer patient Kate Korson (center) was joined by two of her physicians, oncologist Hayley Knollman, MD, and breast surgeon Lola Fayanju, MD, on *Good Morning America* in October.

► Read more about Kate Korson's story at [PennMedicine.org/Blog](https://www.pennmedicine.org/blog), and about the Abramson Cancer Center at [PennMedicine.org/cancer](https://www.pennmedicine.org/cancer)

NARCAN BOOTCAMP, THEN THE WHITE COAT

First-year medical students learn lifesaving skills on day one.



Photo by Avi Steinhardt

Imagine walking into a public restroom and finding a person unconscious on the floor, with no obvious injuries. It could be an overdose. Would you know how to respond?

First-year medical students at the University of Pennsylvania's Perelman School of Medicine (PSOM) now do, thanks to the instruction they received during medical bootcamp, a training session held on their first day of orientation.

Cindy Christian, MD, assistant dean for Community Engagement at PSOM and leader of orientation events, explained that each year, incoming students learn and practice how to handle two different medical emergencies during their first week of medical school. This year's first session focused on using naloxone (Narcan®), an over-the-counter nasal spray, to reverse an opioid overdose. (The second session was about Stop the Bleed techniques, including tourniquets and wound packing, with volunteers playing the role of trauma patients.)

A Critical Skill

Students worked long and hard to get into medical school, but Christian noted that their initial classes focus more on learning basic sciences, with limited patient experience. They will begin working with actual patients on a daily basis in their second year. Narcan training provides a confidence-boosting skill, with practical application, on their very first day of medical school.

"One of the goals we have in introducing them to the opioid crisis and how to use Narcan is to give them some

simple, hands-on exposure to things that can make a difference and potentially save a life," Christian said.

The need and opportunity to help is immense. According to the Philadelphia Department of Public Health, there were 1,276 unintentional drug overdose deaths in 2021—the highest ever reported in Philadelphia. Of those, 82% involved fentanyl, a synthetic opioid that is 50-100 times stronger than morphine. Nationally, the most recent Centers for Disease Control and Prevention (CDC) reports show that overdose deaths involving opioids increased by more than 15 percent from 2020 to 2021 and those involving synthetic opioids other than methadone, such as fentanyl, increased over 22 percent.

For student Setareh Gooshvar, of Florida, who learned to use Narcan as an undergraduate, the session served as a valuable refresher course and a way to stay informed about the state of the opioid epidemic in Philadelphia and the surrounding regions. "I appreciated the training being early on in our time in medical school, as it provided context to the importance of Narcan availability," Gooshvar said.

Bonnie Milas, MD, a professor of Clinical Anesthesiology and Critical Care Medicine at PSOM, was the keynote speaker at this year's event and provided the mannequins and Narcan used at the bootcamp.

Milas lost two sons to accidental opioid overdoses and devotes her personal time to educating the public and lawmakers about overdose prevention. She has advocated for expanded access to Narcan and, earlier this year, testified before the

U.S. Food and Drug Administration (FDA), which helped result in a new law making the treatment available without a prescription.

She said the medical students were receptive to Narcan training as young people who are socially aware and engaged in their local communities. They are also in the age group (25-35 years) in which the overdose rate is the highest, and they could conceivably encounter someone who is overdosing.

"It could be another medical student, somebody at the Philadelphia Eagles game, or their nephew or cousin when they go home and visit for Thanksgiving," Milas said.

Hands-On Instruction

During bootcamp, the instructors talked to the students about opioid use and taught them how to recognize, assess, and respond to a drug overdose. There was a panel discussion featuring substance use and recovery specialists with lived experiences, and a Q&A opportunity. Students asked a range of questions, from what to do after giving someone Narcan to how to talk to a patient after they regain consciousness.

Gabrielle Scales, a student from North Carolina, said, "One of my biggest concerns surrounding Narcan was that I could injure someone by administering it when it may not

have been necessary—but the trainers assured me the drug was of no harm to an individual if they didn't end up needing it."

Students formed small groups and practiced their new skills on medical mannequins dressed and positioned to simulate real-life patients. After, each was given a two-dose supply of Narcan to carry with them in case of emergency.

Milas noted that physicians are often held to a higher ethical standard than the average person and that she hoped with the knowledge and medication they now had, the students would be willing to help a stranger.

"Whether they're disheveled or a smartly dressed businessperson, that stranger is someone's sibling or spouse or child," she said.

Scales said, "My biggest takeaway from the training was to not be a passive bystander. Becoming equipped with the tools to help, if there is a situation that necessitates it, makes me more confident in my ability to step in."

— Abby Alten Schwartz

To watch Milas speak about her experience and learn how to order free fentanyl test strips and Narcan in Philadelphia, view this article online at [PennMedicine.org/magazine](https://www.pennmedicine.org/magazine).



A MAP TO OUR CHANGING WORLD

Penn Medicine’s strategic plan envisions ways to meet the moment—and beyond.



“For a vision to become real, it has to happen on the ground.”

Penn Medicine’s new strategic plan for 2023-2028, “Serving a Changing World,” lays out a lofty set of goals for the University of Pennsylvania Health System and Perelman School of Medicine, from centering equity and access in patient care, to embracing new technologies and ideas for educating the next generation of caregivers, to making Penn Medicine the country’s most environmentally friendly health care system.

But these goals are firmly grounded in the amazing work that takes place across the organization every day. The plan’s five pillars reflect the diversity of people who make up Penn Medicine—and the determination they share for making their communities, and the world, a healthier, safer, greener, fairer, and more dynamic one, with “breathtaking discoveries” and “great accomplishment.”

► To learn more about the plan, and watch the *Serving a Changing World* video introducing it, visit PennMedicine.org/Strategic-Plan

LESS PAPERWORK, MORE ‘PEOPLEWORK’

Penn Medicine’s goal is to be, and be seen as, the most clinician-friendly health system.

From an “ambient listening” project that automatically transcribes what’s said during a clinical encounter—meaning physicians spend less time facing their computer screens entering notes—to a pilot program bringing delivery robots to the floors of Lancaster General Hospital, to modernizing antiquated systems of faxing patient records, there are countless ways Penn Medicine is working to help physicians and other staff focus more on patients, and less on busywork.

“Penn is really focused on thinking about efficiency for health care workers across every spectrum,” said Raina Merchant, MD, MSHP, vice president and chief transformation officer of the University of Pennsylvania Health System (at right in photo). “We’re trying to reduce repetitive tasks to make the work that employees are doing meaningful, allowing them to operate at the top of their license.”

► Read more at PennMedicine.org/Blog



SETTING A PATH FOR THE FUTURE

A new leader aims to keep building on Penn’s uniquely powerful track record in research in Pathology and Laboratory Medicine, from cancer immunotherapies to the pathology of Alzheimer’s.



Molecular Diagnostics at Johns Hopkins Hospital in Baltimore for five years. Though he speaks highly of those workplaces, Netto said coming to Penn was “a no brainer.”

“The institution is a huge attraction, and the department has a great reputation,” he said. That reputation includes spearheading the development of CAR T cell therapy, an immunotherapy to treat cancer.

He is excited to lead the department during this pivotal time for the field. “This is an era that is very critical for pathology as a discipline,” he said, citing advances in bioinformatics, data sciences, genomics, and more as a source of transformational change.

“The impact of these advances has been most appreciated in oncology, immunotherapy, cellular therapeutics, and genetic diseases, but the irreversible tide is expected to revolutionize our entire discipline” he said.

Precision Pathology

Netto’s ultimate goal is to make Penn Medicine a leader in the pathology of the future—what he calls “precision pathology.” This, he explains, is the practice of providing the most precise personalized diagnoses and predictions of how a disease will respond to therapy, tailored to each patient based on their blood or tissue analysis, combined with information about their genetics and their disease course and symptoms.

“This department has a lot of strengths that we can capitalize on,” Netto said. They comprise Penn Medicine’s bench science and research in pathology, as well as its emphasis on translational medicine, leading in areas from brain degenerative disease to immunology, he noted.

“There are huge opportunities on the clinical side to develop more harmonization and ‘systemness’ among the entities that Penn Medicine represents,” he said. New technology such as digitalization, including artificial intelligence, machine learning, and bioinformatics will help address logistical and infrastructure issues, he adds.

Specifically, Netto looks to harmonize the laboratory information system and seamlessly share data electronically among Penn Medicine entities. He also aims to provide all Penn Medicine patients with the same quality of pathology and lab services, regardless of where they seek care, and to assure that clinicians have equal access to service across the system.

“Pathology is a field where you’re part clinician and part scientist,” he said. “So it’s a perfect discipline.”

— Abbey J. Porter

George J. Netto, MD, the new chair of the Department of Pathology and Laboratory Medicine at the Perelman School of Medicine, is not “the old image of a pathologist.” In other words, he said, he doesn’t hunch over a microscope alone in his basement, and he is not a shy introvert. Far from it.

“I’m definitely a ‘people person,’” said Netto, who started at Penn Medicine on August 1. “I don’t stay in my office.” Rather, he likes to get out and talk to residents and other department members, and he keeps an open-door policy. Helping his new department to shape the future of precision pathology is a major goal, but he’ll also take time to discuss his passion for soccer—honed during his upbringing in Brazil (his parents were Syrian immigrants there)—or tips of where to find the best cheesesteaks as a new Philadelphian.

Those “people person” skills also come into play with one of Netto’s key priorities in his new role. “It’s building teams and supporting growing talents and helping junior faculty grow in their own careers,” he said—all part of developing “a team of leaders.”

A Critical Moment

A specialist in genitourinary and molecular genetic pathology, Netto comes to Penn Medicine from The University of Alabama at Birmingham, where he was the endowed chair of the Department of Pathology from 2016 until this year. Previously, he served as director of Surgical Pathology

UNWAVERING FOCUS

The Perelman School of Medicine’s group centering women’s health research and career advancement continues to innovate with new initiatives on intersectionality, biomedical research, and salary equity.



The first in-person conference of FOCUS on Health & Leadership for Women at Penn Medicine since the COVID-19 pandemic was not your typical medical meeting, with a parade of lecturers, poster sessions, and PowerPoint presentations. In part, it was a workshop for women faculty to focus on their own health and well-being and to take charge of their own personal and professional needs—while also reflecting on important issues driving gender equity in research.

This year’s event included on-the-spot opportunities to schedule primary care visits and mammograms, as well as an active, hands-on session focused on personal wellness action plans.

FOCUS, based in the Perelman School of Medicine for over 25 years, is dedicated to supporting the careers of women faculty and staff, and to leading the charge for research and education in women’s health. For conference attendees, who included residents, faculty, and researchers, the gathering also provided an opportunity to catch up with the latest offerings from FOCUS, which continue to adapt and evolve to meet the needs of women in academic medicine.

Mentors and Sponsors

Underrepresented minority women faculty at Penn have new ways of connecting with a career advocate thanks to a one-year-old FOCUS program, URSponsored, which encourages career advancement while addressing intersectionality in academic medicine. A partnership with the Alliance of Minority Physicians, it won a 2023 Excellence Through Diversity Fund grant to create a video that features its 26 protégé/sponsor pairs, set up focus groups, and conduct professional development sessions.

Gender Representation in Science

Sometimes drugs have different effects in men compared to women—a point raised at the FOCUS fall conference in the leadoff presentation by Janine Clayton, MD, the National Institute of Health’s associate director for Women’s Health. Therefore, it is critically important to conduct medical research that reflects the real gender and sex diversity of the populations who may be treated.

At Penn Medicine, FOCUS has a new partnership with another University center, Penn PROMOTES Research on Sex and Gender in Health, to incorporate the analysis of sex and gender differences into Penn biomedical research programs while also advancing gender equity in the workforce. In its first year, this program, RAising the Investment in Sex and Gender Evidence (RAISE) awarded three \$20,000 pilot grants to junior researchers working to incorporate sex as a biological variable into their research, such as a study that examines how sex hormones and inflammatory biomarkers present in females who have sickle cell disease. A second round of grantmaking is now underway.

From Advancement to Outcomes

Helping faculty connect with one another—whether through a conference, a mentoring or sponsorship relationship, or through a research directory developed through RAISE—provides networking opportunities for these faculty to advance in their careers and improves their well-being.

The FOCUS team recognizes that compensation matters, too. At the 2022 FOCUS fall conference, held virtually, a leading expert on salary equity in academic medicine was an invited speaker. Carrying that work forward, Courtney A. Schreiber, MD, MPH, the executive director of FOCUS and a professor of Obstetrics and Gynecology, has worked with other FOCUS leaders and school leaders to advance the evaluation and action toward making faculty compensation more equitable by gender. Gender equity has been included as a core principle of updated compensation principles affecting faculty of the Perelman School of Medicine.

In parallel, FOCUS has also highlighted the trailblazing work of Drs. Lisa Bellini, senior vice dean for academic affairs, and Deborah Driscoll, senior vice president for the Clinical Practices of the University of Pennsylvania, to advance gender-inclusive policies, such as one that adjusts clinical schedules to support staff who need lactation breaks.

“The connection between supporting women in academic medicine and better outcomes for patients and the public health is crystal clear,” said Schreiber. “We need to advocate for a diverse clinical and scientific workforce—our health depends upon it.”

— Meredith Mann

HOW THE HOSPITAL SHARES THE HARVEST

Penn Medicine is addressing unmet social needs that can impact patients’ health.



Penn Farm, in the shadow of the Hospital of the University of Pennsylvania (HUP) Pavilion, is one of several sources of fresh produce supplying HUP Harvest with nutritious food for patients in need. HUP Harvest, previously called the HUP Food Pantry, is also a member of Philabundance, the city’s largest food relief agency, which supplies a minimum of 500 pounds of dry and frozen food each week.



Bilikisu Abdulazeez shopped at the pantry this spring and summer after her prenatal visits to HUP. She said it was a relief on a tight budget and a tight schedule with four sons at home and a fifth then on the way, born in September.



“It’s not just a good deed,” said Sofia Carreno, MSN, RN, HUP Community Engagement Manager. “It’s providing human-centered, relationship-centered health care.”

Photo courtesy Sofia Carreno

► View the photo essay at CommunityImpact.PennMedicine.org.

PUTTING SURGICAL CARE WITHIN REACH

Serving a growing number of patients who would otherwise struggle to access surgery before it became a life-threatening emergency, Penn Medicine’s Center for Surgical Health is recruiting new volunteers and expanding to meet ambitious goals.

Carrie Morales, MD, was a second-year medical student at the Perelman School of Medicine (PSOM) when she and then-general surgery resident Matthew Goldshore, MD, PhD, MPH, noticed a serious disparity in patients’ ability to access surgical care. Patients without insurance, for example, had limited ability to see surgeons for treatable problems until their condition became urgent or life-threatening. As a result, they made frequent visits to the emergency department, or lived with debilitating pain.

Together with their mentor, gastrointestinal surgeon Jon Morris, MD, Morales and Goldshore launched the Center for Surgical Health (CSH) at Penn Medicine with a mission of “improving the surgical health of vulnerable individuals and under-resourced communities.” At the time of the launch in 2020, they set a goal of serving 60 patients in their first year.

Instead, they helped 180 patients get access to care that would otherwise be out of reach.

Three years later, Morales is a plastic and reconstructive surgery resident at Penn Medicine, and Goldshore is a pediatric surgery fellow at Children’s Hospital of Philadelphia, and the program they started has grown from a volunteer project

to a nonprofit organization with three full-time employees. CSH served its 900th patient this fall.

Helping Patients Overcome Obstacles

CSH isn’t a clinic, but instead pairs patients with trained volunteer “Personal Patient Navigators” to help them address the barriers preventing them from getting surgery, like applying for insurance, scheduling appointments, and securing transportation to the hospital. Additionally, volunteers screen patients for emotional distress, public benefits, and immigration needs and refer them to partner organizations like the Penn Law Immigrant’s Rights Project and HIAS Pennsylvania. “The perioperative period is a high-stress, high-vulnerability window in people’s lives,” Morales said. “We are honored to have our patients’ trust during that time and try to maximize benefit—connecting them to world class surgical care and resources for stable housing, nutritious food, primary care, legal services, and more.”

Morales recalled one patient who was visiting the emergency department weekly due to TMJ pain so severe that it was preventing him from eating. Because his condition was not



immediately life-threatening, he was always sent home with a recommendation to follow up with an outpatient visit—something he was unable to do, both logistically and financially, as a Spanish-speaking, undocumented immigrant without insurance. An emergency medicine resident eventually connected him with CSH.

CSH paired him with a Spanish-speaking Personal Patient Navigator who helped him apply for Emergency Medicaid based on his inability to eat. They helped him get an appointment with a Penn oral and maxillofacial surgeon and accompanied him to the appointment. The surgeon quickly solved the problem with a procedure called a joint arthroscopy with removal of scar tissue and injection of steroids.

This patient was “a perfect example of someone who was completely debilitated by a surgical condition that for someone with insurance could be quite minor,” Morales said. “He was back to normal within two weeks.”

Major Grant Fuels Growth

Program manager Lauren Rossi said that having a full-time staff has allowed CSH to formalize and streamline their programs, increase their capacity, and reduce the time it takes to get patients seen by providers. In the last two years, the center has also expanded its network to include more surgical subspecialties and began partnering with advanced practice providers who consult on cases.

CSH has also grown its base of volunteers, attracting many from the medical school. More than a third of first-year medical students at PSOM have applied to be Personal Patient Navigators each year since 2021.

And the center recently received a major boost to support its expansion, with a \$310,000 grant from the Independence Blue Cross Foundation. The funds will be used to expand CSH’s network of referring doctors and clinics in the Penn Medicine network and regional community health centers, hire an additional employee, improve data collection and reporting, create a formal certification program for Personal Patient Navigators, and ultimately increase the number of patients being served, with a goal of connecting 3,000 patients to care by January 2025.

“Disparities in surgical care are among the greatest barriers to health equity,” noted Lorina Marshall-Blake, president of the Independence Blue Cross Foundation. “The Center for Surgical Health is poised to set a standard in surgical care for vulnerable populations, create a new paradigm for preventive surgery, and present a community health and training model that could be extended to other fields of practice.”

Ambitious Goals for the Future

Sarah Hamimi, a second-year medical student at PSOM, signed up to volunteer, not just to give back, but also to gain frontline experience in working with patients. In one memorable case, a patient she was assisting sought care because of irregular menstrual periods. In the process of treating her, surgeons found and removed a malignancy that otherwise wouldn’t have been detected.

“It’s such a privilege for patients to trust us with their care,” Hamimi said. “We’re seeing not just how much impact it has on their lives now, but potentially years down the line as well.”

Morales notes that many in the community can serve as a Personal Patient Navigator, not just medical students. “Our biggest need now is volunteers,” she said. “In order to meet our expansion goals and care for all the patients we know need us, we need more volunteers.” Eligible volunteers include any Penn Medicine staff, Penn graduate students, third- and fourth-year undergraduates at the University of Pennsylvania, as well as allied health students and health care professionals at area medical institutions. All applicants are screened on an individual basis and, if selected, volunteers undergo an onboarding process, daylong training, and weekly check-in meetings.

And the team is thinking even bigger. Long term, the center is working on formalizing and documenting its processes so its model can be replicated elsewhere. Staff have received interest from academic hospitals throughout Pennsylvania and across the U.S., Rossi said.

“While our early success has been phenomenal and excited everybody, it’s also just the tip of the iceberg,” she said. “There’s still so many more people to help.”

— Ilima Loomis

To learn more about the Center for Surgical Health, view this story online at PennMedicine.org/magazine. People interested in volunteering with CSH can email CSH@pennmedicine.upenn.edu for an application.



THE WORLD CHEERS mRNA

Photos by Daniel Burke

Bringing an end to the COVID-19 pandemic was only the beginning. The 2023 Nobel Prize in Physiology or Medicine celebrated Penn Medicine research breakthroughs using mRNA that led to the first successful vaccines using this technology.



FEATURE

From Celebration to Inspiration

On Oct. 2, the day unfolded with the world's eyes on Penn, as Weissman and Karikó spoke to media from across the globe after they were announced the winners at 5:45 a.m., Philadelphia local time. Before leaving for a press conference and celebrations at Penn, Weissman called his parents to break the big news to them. Their response was ecstatic: "I don't know what to say, I'm ready to fall on the floor!" exclaimed his mother. A Penn Medicine video of the sweet phone call quickly went viral.

"Here at Penn Medicine, we're making breathtaking discoveries and we're putting them to work," said J. Larry Jameson, MD, PhD, executive vice president of the University of Pennsylvania for the Health System and dean of the Perelman School of Medicine, during a press conference streamed to reporters worldwide. He called the pair's Nobel win "a testament to the transformative power of science."

Shortly before 1 p.m., a crowd began to gather in the lobby of the Smilow Center for Translational Research, normally a fluid space: people coming and going from appointments and meetings, patients and staff grabbing a bite to eat from the nearby café as they pass by the backdrop of a colorful mural displaying the history of vaccine development in Philadelphia. Ultimately, the space swelled with hundreds of students, staff, and faculty who came to hear from the Nobel laureates in person and snap some selfies as mementoes.

Seeing so many well-wishers gathered in one place, Karikó confessed to being moved. "A tear came to my eye here," she remarked. Karikó advised the many young scientists in the crowd to persevere and follow their dreams, but also to "enjoy what you're doing and have fun!"

"I look out at this group and I see researchers, collaborators, and people from my lab ... you guys are deserving of this award as much as me," observed Weissman. "You are the heart of Penn Medicine, you'll be developing new things from mRNA. We need to celebrate all of you!"

It isn't every day that hundreds of cheering strangers mob a pair of scientists in hopes of getting a selfie. But on the University of Pennsylvania campus, Oct. 2, 2023 was far from an ordinary day. Early that morning, Penn Medicine researchers whose years of scientific partnership unlocked understanding of how to modify mRNA to make it an effective therapeutic, learned that they were named winners of the 2023 Nobel Prize in Physiology or Medicine. Katalin Karikó, PhD, an adjunct professor of Neurosurgery in Penn's Perelman School of Medicine, and Drew Weissman, MD, PhD, the Roberts Family Professor of Vaccine Research in the Perelman School of Medicine, are the 28th and 29th Nobel laureates affiliated with Penn, joining nine previous Nobel laureates with ties to the University of Pennsylvania who have won the Nobel Prize in Medicine.

After a chance meeting in the late 1990s while photocopying research papers, Karikó and Weissman began investigating mRNA as a potential therapeutic. In 2005, they published a key discovery: mRNA could be altered and delivered effectively into the body without activating inflammation to induce cells to produce large amounts of encoded protein that could activate the body's protective immune system. The mRNA-based vaccines elicited a robust immune response, including high levels of antibodies that attack a specific infectious disease that has not previously been encountered. Unlike other vaccines, a live or attenuated virus is not required at any point.

When the COVID-19 pandemic struck, the true value of the pair's lab work was revealed in the most timely of ways, as companies worked to quickly develop and deploy vaccines to protect people from the virus. Both Pfizer/BioNTech and Moderna utilized Karikó and Weissman's technology to build their highly effective vaccines to protect against severe illness and death from the virus. In the United States alone, mRNA vaccines make up more than 655 million total doses of SARS-CoV-2 vaccines that have been administered since they became available in December 2020.



NOW mRNA IS CHANGING THE WORLD

Vaccines against SARS-CoV-2 were the first time that mRNA technology was used to address a worldwide health challenge. Next come all the rest.

The mRNA discoveries made at Penn nearly two decades ago, and whose pioneers were recently awarded the Nobel Prize, represent a multi-use tool, not just a treatment for a single disease. The technology's potential is virtually unlimited; if researchers know the sequence of a particular protein they want to create or replace, it should be possible to target a specific disease. Through the Penn Institute for RNA Innovation led by Weissman, researchers are working to ensure this limitless potential meets the world's most challenging and important needs.

Infectious Diseases and Beyond

Just consider some of the many projects Weissman's lab is partnering in: "We're working on malaria with people across the U.S. and in Africa," Weissman said. "We're working on leptospirosis with people in Southeast Asia. We're working on vaccines for peanut allergies. We're working

on vaccines for autoimmunity. And all of this is through collaboration."

Clinical trials are underway for the new malaria vaccine, as well as for a Penn-developed mRNA vaccine for genital herpes and one that aims to protect against all varieties of coronaviruses. Trials should begin soon for vaccines for norovirus and the bacterium *C. difficile*.

Single-Injection Gene Therapies for Sickle Cell and Heart Disease

The Weissman lab is working to deploy mRNA technology as an accessible gene therapy for sickle cell anemia, a devastating and painful genetic disease that affects about 20 million people around the world. About 300,000 babies are born each year with the condition, mainly in sub-Saharan Africa.

Weissman's team has developed technology to efficiently deliver modified mRNA to bone marrow stem cells, instructing red blood cells to produce normal hemoglobin instead of the malformed "sickle" version that causes the illness. Conventional gene therapies are complex and expensive treatments, but the mRNA gene therapy could be a simple, one-time intravenous injection to cure the disease. Such a treatment would have applications to many other congenital gene defects in blood and stem cells.

In another new program, Penn researchers have found a way to target the muscle cells of the heart. This gene therapy method developed by Weissman's team, together with Vlad Muzykantov, MD, PhD, the Founders Professor in Nanoparticle Research, could potentially repair the heart or increase blood flow to the heart, noninvasively, after a heart attack or to correct a genetic deficiency in the heart. "That is important because heart disease is the number one killer in the U.S. and in the world," Weissman said. "Drugs for heart disease aren't specific for the heart. And when you're trying to treat a myocardial infarction or cardiomyopathy or other genetic deficiencies in the heart, it's very difficult, because you can't deliver to the heart."

Weissman's team also is partnering on programs for neurodevelopmental diseases and neurodegenerative diseases, to replace genes or deliver therapeutic proteins that will treat and potentially cure these diseases.

"The potential is unbelievable," Weissman said. "We haven't thought of everything that can be done."

Global Access to Lifesaving mRNA Therapies

Crucially, mRNA technology is simple enough that it should be possible to make these future treatments for sickle cell and other diseases available around the world, at low cost, even in places with few resources. And this is a priority for Weissman and for Penn. "It's just an IV injection," Weissman explained. "You can do that anywhere. You don't need fancy equipment, a fancy medical center. You give somebody an IV injection, and you're done."

To date, Weissman has partnered in building 18 mRNA-capable Good Manufacturing Practice (GMP) sites across the world, a type of specialized production facility that can make drugs and vaccines for human use. All of these sites are beginning with manufacturing vaccines, Weissman said, but all are interested in developing therapeutics and gene therapies. "I think, in the next few years, we're going to see more and more of these GMP sites and research infrastructure sites across the world developing new and novel treatments."

Collaboration is key for the global reach of Penn's mRNA research. "It would be impossible for the members of my lab to have to learn and set up new model systems for every disease we wanted to follow," Weissman said. "We find the best people in the world and ask them, 'Do you want to collaborate on making this vaccine or therapeutic?' And to me, that's the most important thing that makes research work, and that allows research to move forward." □

► Explore more about the future of mRNA discoveries at PennMedicine.org/mrna

Right From the Start

By Christina Hernandez Sherwood

For Black families to grow and thrive, the U.S. health care system must reverse the trend of serious harm and death before, during, and after childbirth. Penn Medicine is taking bold action to improve maternal health and eliminate disparities.



Photo by Megan Tidmore

After an exhausting pregnancy punctuated by hospital visits for severe nausea and vomiting, Talicia Williams, 25, was at the finish line. Late on a muggy July night in 2021, Williams vaginally delivered her second child, her first baby girl, at the Hospital of the University of Pennsylvania. It was finally time to rest.

Then Williams' mother noticed the blood clots.

New and expectant mothers in the United States are more likely to die than those in any other developed country in the world. In 2021, the year Williams' daughter, Zahiri, was born, the U.S. maternal mortality rate was nearly 33 deaths per 100,000 live births, according to the Centers for Disease Control and Prevention. For Black women in Philadelphia like Williams, the risk of death is four times that of their white counterparts. Perhaps the most heartbreaking: More than 80 percent of these deaths are preventable.

As blood soaked her hospital bed, Williams was perilously close to becoming a statistic.

But within moments, about a dozen Penn Medicine doctors and nurses flooded her hospital room, bringing a cart loaded with supplies to treat the hemorrhage. A doctor massaged Williams' uterus while reaching inside her to remove remaining blood clots. Another team member used an ultrasound to check for placenta fragments. A third started an intravenous line for fluids. A nurse told Williams: "We're not going to let you die."

Williams, who survived the hemorrhage, fully recovered and is back home as a mother of two in West Philadelphia, later learned that her life-saving care on the night of Zahiri's birth wasn't an anomaly. The standardized postpartum hemorrhage treatment she received, which included the availability of hemorrhage carts, enhanced safety protocols and training for labor floor nurses to rapidly transfuse blood, was part of a comprehensive, system-wide, multi-year initiative by Penn Medicine to improve maternal health outcomes and reduce racial and ethnic disparities.

The approach to maternal health equity at Penn Medicine encompasses a unified effort from across the University of Pennsylvania Health System, endorsed and supported as a system goal by its executive leaders, with participation from any and all departments that could potentially make an impact.

This comprehensive undertaking involves not only a broad array of quality improvements and innovations in patient

care, but also faculty research and community engagement. Some of the core principles underlying the efforts include standardizing patient care during key moments in pregnancy and childbirth to reduce opportunities for racial bias, and centering equity as a goal by targeting specific maternal health programs to historically underserved populations. More than just focusing on pregnancy and childbirth, the initiative aims to connect with pregnant people during this unique time of intensive medical care as a bridge across the continuum—aiming to keep them and their entire families connected to a lifetime of quality health care. And wielding a broader influence with these innovations is a primary goal, so not only Penn patients benefit, but also new parents and families across the city of Philadelphia, the region, and the U.S. as a whole.

“We’re doing everything we can to intervene so we can have a healthy mom and a healthy baby, and then have that translated to a healthy family and healthy community,” said Elizabeth Howell, MD, MPP, chair of the Department of Obstetrics and Gynecology in the Perelman School of Medicine and the Harrison McCrea Dickson, MD President’s Distinguished Professor, who is spearheading the initiative along with Sindhu Srinivas, MD, MSCE, a professor and vice chair for quality and safety in the department.

“The ripple effect is huge,” Howell said.

The new system-wide standard procedure for postpartum hemorrhage care is just one aspect of the maternal health equity initiative. Starting in 2020, Howell and Srinivas led an outreach process that went wide and deep to connect with faculty and front-line staff at all five birthing hospitals in Penn Medicine’s system, building consensus and connections. The system-wide team goal gave a framework for each person involved in the care of a birthing parent or infant to see their role in patients’ experiences—and to contribute to both discrete and collaborative efforts to reduce the harmful inequities for Black birthing parents.

The results speak for themselves. Maternal morbidity—that is, health problems resulting from pregnancy and childbirth—dropped nearly 30 percent at Penn Medicine hospitals after the first year of implementing the system-wide effort to address disparities.

Today, Philadelphia’s postpartum hemorrhage death rate is lower than the national average. That is partly due to Penn Medicine’s influence in the city—Penn hospitals account for roughly half of all baby deliveries in Philadelphia. But it also stems from the hospital system’s commitment to sharing its successes with maternity care providers throughout the city and beyond, helping to improve care for even more new and expectant mothers. “Penn is not proprietary with [its innovation],” said Aasta Mehta, MD, MPP, medical officer of women’s health at the Philadelphia Department of Public Health and an obstetrician-gynecologist at Pennsylvania

Hospital. “There’s a sense of collaboration and community and improving the health of all.”

At Penn Medicine, the motivation behind this massive effort runs deep. The death of a mother—from postpartum hemorrhage, a cardiovascular complication, an infection, suicide, substance use disorder or any other cause—has intergenerational effects, said Howell, who knows from personal experience. “My dad lost his mother from a preventable cause when he was 10 years old,” she said. “He was always so worried that he or my mom might pass away and that [his children] would have to live with the pain he lived with. I grew up with this story.

“He’s 80-something now and he’ll still come to tears when he thinks about his mother,” Howell added. “It’s that profound impact that women and birthing people play in families. They are the cornerstone, not only of families, but of communities.”

Banishing Bias

Until 2021, anemia in pregnancy was diagnosed differently based on a patient’s race. The thinking had been that because Black women are more likely to be anemic (lacking a sufficient number of healthy red blood cells), pregnant Black patients needed to reach a lower red blood cell count than patients of other races to be diagnosed with and treated for anemia, said Rebecca Feldman Hamm, MD, MSCE, an assistant professor of Obstetrics and Gynecology at the Perelman School of Medicine and a Penn Medicine attending physician.

The race-based criteria were standardized by the American College of Obstetricians and Gynecologists (ACOG), and Penn Medicine followed that national guideline—until a Penn team’s research findings overturned it.

The race-based criteria for diagnosing anemia meant that Black patients were treated as though they were healthier than they actually were, Hamm said. By analyzing data from more than 1,000 pregnancies, Hamm found that pregnant Black patients at the Hospital of the University of Pennsylvania were much more likely to come to delivery with low hemoglobin, a protein contained in red blood cells. “People with lower hemoglobin are more likely to get a blood transfusion, which is associated with other morbidities like fatigue and postpartum depression,” Hamm said. “Likely this different definition of anemia was propagating disparities for Black women.”

In response to Hamm’s data—and as part of the maternal health overhaul—Penn Medicine stopped using ACOG’s race-based anemia guideline in 2020. Hamm and her team presented their data at a national maternal-fetal medicine conference in 2021, prompting ACOG to scrap its race-based criteria. “Now, anemia is defined nationally the same for everyone,” she said. Hamm’s team is currently working on a study with the health insurer Independence Blue Cross to determine how the guideline change has impacted Black women across Pennsylvania.



“We’re doing everything we can to intervene so we can have a healthy mom and a healthy baby, and then have that translated to a healthy family and healthy community,” said Elizabeth Howell, MD, MPP, chair of the department of Obstetrics and Gynecology.

Not all biases are as explicit as the race-based anemia guideline. In fact, more prevalent are unconscious biases, the stereotypes we form about certain people or groups without our own awareness. These are more difficult to change on a personal level, Hamm said, but standardizing certain practices can minimize their impact. “We can allow for all women to be managed the same,” she said, “improving outcomes for everyone and, specifically, reducing disparities.”

Standardizing Care

One potential contributor to the disparity in maternal health outcomes: Black women are more likely than any other group to deliver by Cesarean section (C-section), a major abdominal surgery with significant risks of complications, including infection and blood loss. Labor induction, the process of stimulating the body to begin or continue the

labor process, has been associated with lower C-section rates. But at Penn Medicine, labor induction was extremely variable across hospitals and even providers, Hamm said, depending more on where a doctor trained or their past experience, than a standard set of guidelines.

In 2020, Hamm, along with Lisa Levine, MD, MSCE, and other Penn researchers published the results of a prospective cohort study of more than 800 women undergoing labor induction. Black women who were managed with a standardized protocol, rather than at the provider’s discretion, had a significant reduction in C-section delivery rates. Standardized labor induction has since been implemented as a quality improvement change at the Hospital of the University of Pennsylvania and Pennsylvania Hospital. In related work, Hamm and others found that standardizing C-section risk counseling with labor induction increased Black patients’ satisfaction with the birth process.

Standardizing the best-in-class approaches can likewise help address pregnancy-related deaths that stem from cardiovascular conditions. Heart failure and other heart conditions



Photo by Peggy Peterson

Abike James, MD, MPH, is lead physician at Penn OBGYN Associates and vice chair for diversity, equity and inclusion in Obstetrics and Gynecology. She emphasizes the importance of rebuilding and strengthening patients' trust in the health care system to reduce disparities.

account for nearly half of these fatalities in Philadelphia, and Black women have up to quadruple the risk of non-Black women. Another Penn research team led by Levine along with Abike James, MD, MPH, is now studying how to most effectively deploy a standardized cardiovascular risk assessment that was developed several years ago by a maternal care collaborative in California. The algorithm uses a combination of vital signs, risk factors, medical history, and symptoms to determine whether a patient is at risk for a cardiovascular complication. Retrospective analyses of patients who experienced fatal complications showed that, if used correctly, the algorithm could have predicted up to 90 percent of these deaths before they happened.

Yet a study in New York found that only about 30 percent of patients received follow-up testing after the algorithm flagged them as at-risk.

The Penn team quickly determined why follow-up testing rates were so low, said Levine, the Michael T. Mennuti, M.D., Associate Professor in Reproductive Health and director of the Pregnancy and Heart Disease Program, who is leading the effort. Patients did not understand the severity of their risk or the importance of follow-up care, she said, or they

faced logistical barriers, such as lack of time and not knowing where to get testing.

Through a multi-million dollar grant from the American Heart Association, the Penn Medicine team crafted patient education materials, including an animated video and a website, and hired a patient navigator to help streamline the follow-up process. They are first implementing the algorithm at Penn Medicine hospitals and will then work to implement the algorithm at all hospitals across Philadelphia. "The causes of maternal morbidity or mortality and disparities are so multifaceted," Levine said. "To make a dent in the problem, you have to address it from all different angles."

Rebuilding Trust in the Medical System

Bolstering patients' trust in clinicians and the health care system is an important element in reversing health care disparities. "When patients don't feel heard by their providers, that leads to mistrust, which means they might not come in, which means they might delay care," said James, lead physician at Penn OBGYN Associates, vice chair for diversity, equity and inclusion, and associate professor of Clinical

Obstetrics and Gynecology. "That's how it spirals into disparity. We need to better ensure that patients aren't left with negative feelings that will make them not come back."

Equity-focused engagement efforts, both with individual patients and community-based groups, go a long way toward building trust, James said.

In one such project, researchers at Penn Medicine, in partnership with CocoLife, a Philadelphia community organization supporting Black maternal health, are working together to better connect doulas with hospital deliveries. Pregnant and postpartum women who were supported by doulas—professionally-trained, non-medical support people for birthing parents—have been shown to have better child-birth outcomes, such as lower rates of C-section. In low-income communities in particular, doula support improved the likelihood that new mothers would succeed with breastfeeding.

But there is no standardized, proven approach to best integrating doulas into hospital-based maternal care—and the Penn team hopes to create one.

The doula initiative is one of two research efforts out of the March of Dimes Research Center for Advancing Maternal Health Equity, a first-of-its-kind collaboration for maternal health equity research and racial disparity solutions that is housed at the University of Pennsylvania and led by Howell. In another project, Penn Medicine researchers are testing whether bringing postpartum care to the neonatal intensive care unit at the Hospital of the University of Pennsylvania will help reduce disparities.

Mehta shared a story that exemplified the need for regaining a patient's trust in health care during pregnancy, and the risks from damaging it: In 2021, a Philadelphia woman with substance use disorder became pregnant, which motivated her to improve her health. The woman attended her prenatal appointments and made an effort to stop using drugs,



Principles of the Push for Maternal Health Equity at Penn Medicine

Penn Medicine adopted a system-wide goal in 2020 to reduce racial and ethnic disparities in maternal morbidity and mortality. Tackling this challenge from multiple angles and at all Penn Medicine locations where birthing parents receive care, the system's approach has a few core principles of success:

STANDARDIZING CARE

Implementing known best practices for maternal health at key moments in pregnancy, childbirth, and postpartum consistently for all patients

CENTERING EQUITY

Reaching out specifically to Black and other historically disadvantaged populations to ensure that efforts address inequities

CONTINUUM OF CARE

Recognizing pregnancy and childbirth as a chance to engage birthing parents and their families in lifelong health care

INFLUENCE AND IMPACT

Sharing successes throughout Philadelphia and beyond

but reported that staff members at a drug treatment facility called her “fat” and treated her poorly. Two years after safely delivering her baby, the woman died of an opioid overdose, a death Mehta sees as a failure of maternal health care.

“There were so many opportunities in that pregnancy where we could have helped change the trajectory of what happened to this woman,” she said. “When people are pregnant, they’re meeting you halfway. You can’t re-create that motivation any other time in people’s lives. Let’s regain their trust in that time period, so they continue to stay engaged. That impacts not just their health, but their family’s health.”

Navigating Care from the Hospital to Home

New mothers and their babies typically leave the cocoon-like environment of the hospital maternity floor within a few days of delivery. Their discharge marks the end of a particularly intense nine months of medical support: from the monthly, then biweekly, then weekly obstetric exams during pregnancy to the 24/7 access to nurses in the hospital. Once they return home after giving birth, most new parents will not be seen by a medical professional for the next month and a half, until the typical six-week postpartum appointment with their obstetrician.

In those first six weeks, the elation of new motherhood is often mixed with a great deal of stress. New mothers are still recovering from childbirth, dealing with pain and soreness, heavy vaginal bleeding and urinary incontinence. Those who had C-sections are bracing their incision site with a pillow during every laugh or sneeze to prevent the stitches from reopening. As many new mothers struggle with breastfeeding, their newborns wail for milk every two to three hours. Faced with what can feel like an endless day of round-the-clock feedings and diaper changes, punctuated by precious little sleep, a whopping 80 percent of new parents report experiencing “baby blues” during the first few weeks postpartum.

“If you talk to moms, you’ll hear there are a lot of symptoms in the two-to-three weeks [postpartum] that they assume is the price they paid for having a child,” said Mario DeMarco, MD, an associate professor of Clinical Family Medicine and Community Health and director of Family Medicine Obstetrics. Many new parents struggle alone, finding that, by the time of their six-week appointment, the issues have either resolved on their own (as is typical of postpartum bleeding and baby blues) or they’ve given up (as often happens with breastfeeding). That might explain why as many as 40 percent of women nationally never attend a postpartum visit. “We weren’t delivering care in a time-sensitive way,” DeMarco said.

But for the unlucky few, early postpartum problems can quickly develop into much more serious complications. Of the approximately 1,000 childbirth-related deaths in the United States each year, about one in every five occurs between one week and six weeks postpartum. “It’s not a complicated delivery or somebody who is very sick,” DeMarco said. “It’s someone who gets discharged from the hospital and experiences some sort of symptom. It could be cardiomyopathy or preeclampsia or stroke. It could be suicide, homicide or a drug overdose. For them, a six-week visit wouldn’t have been helpful.”

ACOG agreed, and in 2018 recommended that new mothers are seen sooner, specifically within three weeks of giving birth.

As part of a Penn Family Care program focused on “the fourth trimester,” or the first three months post-delivery, these practices set a goal for all patients to have a postpartum visit within three weeks of delivery—either in person or via telehealth—in addition to their baby’s regular checkups. Since implementing the program in 2021, the proportion of Penn Family Care patients with a postpartum visit within the first three weeks more than quadrupled to 64 percent from 15 percent. Though the findings were consistent in Black and non-Black patients, the option of telehealth postpartum care during the COVID-19 pandemic decreased racial disparities in visit attendance.

But, DeMarco said, while Penn Family Care hopes to lead others to adopt the three-week postpartum visit through their example, the six-week visit remains the typical standard in most health systems. To bridge the gap in these crucial early weeks, Penn Medicine rolled out several initiatives that leverage technology to make it easier for patients to access postpartum care.

Texting Buddies for Triage

Healing at Home is a text messaging program for low-risk postpartum patients who delivered at the Hospital of the University of Pennsylvania. It covers the period from hospital discharge to the six-week postpartum visit, keeping patients engaged in their health through interactions with “Penny,” an AI-augmented conversational agent. Penny sends personalized messages with anticipatory guidance, such as “your baby’s umbilical stump will fall off soon,” and can also answer most patient questions on breastfeeding, constipation and more.

“I see Healing at Home as a triage for which patients need extra support,” said Kirstin Leitner, MD, an assistant professor of Clinical Obstetrics and Gynecology and the Penn Medicine physician who created the program. “It offers [providers]

the potential to say, ‘This patient keeps asking questions, or is screening high on her postpartum depression screening or is still having elevated blood pressures. She might be a patient worth bringing in for a [two-week] visit versus a patient who has had her third baby and is smooth sailing.’”

Text messaging is more accessible to people with fewer resources, Leitner said, such as those who don’t have internet at home, since most have a cell phone plan with unlimited text messaging. Since its launch in March 2020, Healing at Home has had more than 1,800 participants. Of the top 10 percent of highest-engagement users—that is, participants who asked a lot of questions, followed up with Penny and used emojis and pleasantries with the chatbot—90 percent were Black women. Patients who are breastfeeding their baby and patients having their first baby are more likely to engage in the platform. Not only is engagement higher, but there are some improved outcomes such as high rates of contraceptive acceptance and higher rates of exclusive breastfeeding at one week of life. “There probably is a

group of Black, breastfeeding first-time moms who are more likely to engage with Penny than reach out to their provider through traditional communications,” Leitner said. “They’re using this as a tool to reach out. And sometimes, that’s the first step.”

Penn Medicine’s system-wide commitment to reducing maternal morbidity and mortality for Black women has been important to Healing at Home’s success. “I can’t tell you how many times I’ve written in a paper or proposal on the awful rates of maternal mortality in the U.S. compared to other countries,” Leitner said. “To have leadership emphasize this [problem] has been hugely helpful to allow us to bring solutions to people.”

Because of efforts at the Hospital of the University of Pennsylvania to boost hypertension screening during preg-

Photo by Peggy Peterson



Black women are more likely to experience preeclampsia, a serious condition in pregnancy and postpartum characterized by high blood pressure. Penn Medicine’s Heart Safe Motherhood program helps parents stay on top of their blood pressure monitoring at home, reducing disparities. The program’s reach now includes all Penn Medicine birthing hospitals and two of the other three birthing hospitals in Philadelphia.



Photo by Peggy Peterson

It's easy for new parents to skip taking care of their own health. For that reason, at Penn Family Care, Mario DeMarco, MD, regularly screens parents for common health concerns at a baby's well visit, too. At Elijah Miller's six-month appointment, DeMarco was able to help Nicole Miller with her then-undiagnosed postpartum depression.

nancy, most patients enrolled in Healing at Home already own and use a blood pressure cuff. With hypertension a concern for many postpartum women, even those without a previous diagnosis, Leitner added regular self blood pressure checks to Healing at Home in 2021; this has helped connect patients with additional support and intervene sooner. A patient who screens severely high once or mildly high twice is

enrolled in a program that is one of Penn Medicine's longest-established and widest-reaching success stories in using text messaging technology to save lives: Heart Safe Motherhood.

Heart Safe Motherhood, a text-based, remote blood pressure monitoring program, was established in 2014 in response to poor attendance rates at a postpartum blood pressure clinic for high-risk new mothers, said co-founder Adi Hirshberg, MD, director of obstetrical services at the Hospital of the University of Pennsylvania and an associate professor of Clinical Obstetrics and Gynecology. Black patients reported

significant barriers to accessing in-person health care, including transportation, childcare and cost. But they were also the group who needed this postpartum health monitoring the most: Black women are more likely to suffer from preeclampsia, a serious condition in pregnancy and postpartum characterized by high blood pressure.

Heart Safe Motherhood provides patients with a blood pressure cuff and educates them on how to use it. Once discharged from the hospital, postpartum patients receive text-message reminders to conduct twice-daily blood pressure readings at home, for 10 days, and report the readings to their providers via reply message. A 2019 study of the program found that vastly more patients—more than 90 percent overall—submitted blood pressure readings via text, versus the number of patients not in the program who attended the in-person clinic. The effect for Black patients in particular was most dramatic, rising to 93 percent submitting readings via text vs. only 33 percent who were checked in person. (By comparison, among non-Black patients, 70 percent had their blood pressure checked in person.)

Penn Medicine's focus on maternal health disparities has positive benefits for all pregnant and postpartum patients, Howell said. "The lessons learned are shared for all of our populations," she said. "Our approach to maternal health, our standards, everything we're doing is being elevated from this effort. We're targeting the disparity, but it's going to improve health for all."

Heart Safe Motherhood is now available for patients at all five Penn Medicine birthing hospitals—the Hospital of the University of Pennsylvania and Pennsylvania Hospital in Philadelphia, and at Penn's regional hospitals in Chester County, Lancaster, and Princeton—as well as two of the three other Philadelphia birthing hospitals that are not part of the Penn system. The model has also been adopted at an academic hospital in the Midwest, a health care institution in California and a large birthing hospital in the South. The program is enrolling an average of 72 patients every month. As of November 2023, Heart Safe Motherhood had collected more than 252,000 blood pressure readings from nearly 19,000 Penn Medicine patients.

In 2023, a longitudinal study of more than 1,000 patients, completed in collaboration with Independence Blue Cross, found that patients enrolled in Heart Safe Motherhood had fewer adverse events, including seizure and stroke, postpartum emergency department visits and hospital readmissions than those who weren't enrolled. These benefits were seen up to six months after delivery. The program also resulted in per-member cost savings for the insurer.

"This program is a great example of how a technology-based program can engage patients and reduce severe maternal morbidity and health inequities in the particularly vulnerable time right after birth when people go home," said Srinivas, who co-founded Heart Safe Motherhood with Hirshberg.

A Bridge to Lifelong Health after Pregnancy

At the end of Elijah Miller's six-month checkup at Penn Family Care in late 2020, DeMarco, a physician there, turned to the infant's mother and asked how she was handling life as a first-time mom. That's when the floodgates opened.

Nicole Miller, then 35, of Delaware County, had given birth to Elijah at the Hospital of the University of Pennsylvania between two events that defined 2020: the March COVID-19 lockdown and the May murder of George Floyd, a Black man in Minneapolis, by police. But it wasn't until Miller returned to work a few months after Elijah's birth that her mental health began to suffer. Miller, who identifies as African American and Italian, found her ongoing anxiety heightened not only by the typical concerns of new motherhood, like managing a breastmilk pumping schedule, but also by a deadly pandemic and waves of protests against the police brutality of Black citizens. By the time she was in DeMarco's office that fall, Miller's knees were aching under the 50 pounds she had recently gained from stress-induced binge eating.

With DeMarco's gentle questioning, Miller realized she was struggling with postpartum depression. "If nobody would ask me about [my feelings], I don't think I would share them with anybody," she said. "I would try to figure them out on my own. And I don't think I would figure them out in a healthy way."

Like so many new mothers, Miller never missed a checkup for her baby—at least five pediatrician appointments in the first six months of life. When time and resources are limited, as they often are for new parents, most mothers put their children's health needs ahead of their own. Data from more than 170,000 well-child visits at 35 practices across 10 states showed that, in the first two years of a baby's life, the birth mother was present for 94 percent of those appointments.



Photo by Peggy Peterson

“It’s not that women don’t engage with care,” DeMarco said. “It’s that they don’t engage with care for themselves.”

In 2016, Penn Family Care implemented a unique model known as “interconception care”: Its doctors provide health care for mothers during each well-child visit from 0 to 24 months. Mothers who are present at Penn Family Care well-child visits in the first two years are screened for tobacco use, depression, contraceptive needs, and multivitamin use. Sometimes, the screenings reveal a mom in crisis. “At that point, it is no longer a well-child visit,” DeMarco said. “It is a mom visit, because that’s what that family needs. They don’t need to talk about which Stage One baby foods to eat. They need Mom to get help.”

When Miller shared her struggles, DeMarco responded quickly. He ensured Miller was taking her anti-anxiety medication, emphasized the importance of a visit with her primary care provider, and connected her with a counselor. “Even though Elijah was his patient, he was making sure that my mental health was good,” she said. “If my mental health wasn’t good, how can I be a mom to Elijah?”

All told, DeMarco screened Miller at Elijah’s checkups about 10 times during her first two years postpartum. New mothers without major medical problems are likely to only have a few routine doctor visits during that same period. Some, DeMarco said, receive no care from the moment they are discharged from the hospital after delivery until they become pregnant again.

But receiving health care between pregnancies can help reduce future complications. In 2020, DeMarco was lead author on a study that found that counseling mothers on multivitamin use at their children’s pediatric appointments increased the likelihood the women would take multivitamins. “We can use primary care as an opportunity to help somebody have a healthy subsequent pregnancy,” he said, “or prevent that pregnancy if they’re not looking to become pregnant again.”

Nicole Miller has found her footing as a mother. Last summer, she took 3-year-old Elijah to the beach for the first time (he prefers the pool) and by the fall she was preparing his Buzz Lightyear costume for a local Halloween celebration. “Me and Elijah, we try to do everything together,” Miller said. “We’re just living life through a 3-year-old’s eyes.”

And those normal travails of family life—the joys and the typical tantrums and tensions between mother and child—are exactly what all parents of every racial and ethnic group



Photo by Graham Perry

should get to focus on. It’s the motivation behind Penn Medicine’s efforts to shepherd patients safely from pregnancy and childbirth to the early postpartum period and beyond: to give every new parent a chance to grow and thrive as part of a healthy family and community.

For Talicia Williams, the West Philadelphia mother who survived a life-threatening postpartum hemorrhage in 2021, the fears from the night of baby Zahiri’s birth have given way to the everyday joys of motherhood. Williams and 2-year-old “Zay-Zay” share a special bond. Big brother Tayale recently turned 5 and attends a half-day preschool program. Zahiri loves to chase him when he’s home—and to playact some ideas she has picked up about mothering from Williams, the mother she so easily could have lost in those crucial moments after her birth. “My niece was crying and Zahiri ran out and shushed her,” Williams said, laughing at her toddler pretending to be her cousin’s mom. “I’m like, ‘Girl, you’re the same age!’” ☐

▶ **To learn more about maternal health visit**
CommunityImpact.PennMedicine.org/
maternal-health-equity

Changing the Picture for Dementia

By Queen Muse
Photos by Peggy Peterson

The domino chain of discovery is finally creating a path to a cure for Alzheimer's and related diseases of the brain. Foundational discoveries at Penn were crucial to arriving at this moment after decades of promising ideas failed to translate to drugs that slow and reverse the symptoms of these devastating conditions.

Imagine the journey of medical innovation as a stretch of dominoes winding along a branching, curving path. Each domino is a crucial step in the process from fundamental biological discoveries to the introduction of new medications and treatments. At the very beginning of this intricate chain, clusters of dominoes symbolize discoveries in basic research. When first set on an empty plane, these tiles may look modest, but each one represents a crucial scientific revelation—a biochemical pathway that describes a disease mechanism, or a molecule that a future drug might be designed to target. And each is filled with potential energy, waiting to set a next line of dominoes in motion. The field is ready for new branches to be added for preclinical and clinical testing of new drugs—some that turn out to be dead-end paths, and others that continue to stretch on toward the promise of better treatments and cures.

In the realm of neurodegenerative diseases, the foundational work of scientists like Virginia M.-Y. Lee, PhD, MBA, and the late John Q. Trojanowski, MD, PhD at the University of Pennsylvania's Perelman School of Medicine, formed crucial early placements in the scientific framework. Their discoveries set the field on the path toward advancements in the development of new medicines for Parkinson's disease, Alzheimer's disease, and other memory- and aging-related conditions.

Lee and Trojanowski, research partners who were also partners in life as a married couple, entered the field four decades ago when researchers had only recently developed standardized methods for diagnosing neurodegenerative conditions and neuropathologists were still in the beginning stages of understanding how these conditions progress through changes in the brain. Few treatments existed for diseases like Parkinson's and epilepsy; other conditions like amyotrophic lateral sclerosis (ALS) and Alzheimer's had none.

Fast forward to 2023, and it appears that a major cascade of dominoes is finally in motion. Seen from above, the result is a picture of hope for patients with these diseases—particularly Alzheimer's. In July, the Food and Drug Administration (FDA) granted full approval to Leqembi (lecanemab), a biologic drug developed by Japanese pharmaceutical company Eisai and Massachusetts-based biotech company Biogen. Leqembi has shown promise in removing amyloid plaque in the brain—one of the known primary causes of Alzheimer's disease—slowing cognitive decline in early Alzheimer's patients. It is the first and only fully approved anti-amyloid drug. Indiana-based pharmaceutical company Eli Lilly is on the verge of introducing another.

Researchers have undergone decades of flawed hypotheses, mismeasurements, and failed clinical trials—dominos toppled, realigned, and reset, to arrive at what some are calling a historic moment.

Connecting the Dots

When Trojanowski came to Penn in 1981, Alzheimer's disease research centers didn't exist, researchers had yet to launch a single clinical trial for an Alzheimer's drug, and the pathophysiology of the disease was still largely unknown. In the years that followed, the field saw its first burst of important discoveries. In 1984, biochemists George Glenner, MD, and Caine Wong, PhD, of the University of California San Diego, identified a key component of the plaques that form in the brains of patients living with Alzheimer's, a protein now known as beta-amyloid. In 1985, Trojanowski established the Penn Medicine Brain Bank, where families could donate specimens from patients who died with dementia to inform future research. And in 1987, the National Institute on Aging (NIA) and Warner-Lambert Pharmaceutical Company (now Pfizer) launched a clinical trial for tacrine, the first drug created to specifically target Alzheimer's disease symptoms.

It was amid this momentum that Lee joined the Penn faculty and began partnering with Trojanowski on research focused on Alzheimer's and Parkinson's disease, ALS, frontotemporal degeneration, and other related disorders. Together, Lee and Trojanowski set out to understand these disorders from multiple angles with Lee, the biochemist, using her extensive knowledge of basic science, and Trojanowski, the neuropathologist, tapping into his unique access to brain samples from patients with Alzheimer's disease.

Lee and Trojanowski made their first major discovery in 1991, when they determined that neurofibrillary tangles in Alzheimer's brains are made up of tau, a protein that causes the structure of nerve cells to collapse. Until then, the makeup of these tangles was unknown. This critical finding was the first clue that the tau protein would be equally important to amyloid in Alzheimer's disease research. A year later, the duo launched the Center for Neurodegenerative Disease Research (CNDR) at Penn. It was one of the region's first centers dedicated exclusively to investigating the causes and mechanisms of neurodegenerative diseases and, according to Edward B. Lee, MD, PhD, a scientific hub that demanded innovation.

"I think the most important thing they [Lee and Trojanowski] did was create a space and environment where people were expected to be excellent. They provided all the resources you needed to achieve that," said Edward Lee (no relation to Virginia), who was once a graduate student and then post-doc fellow in the CNDR and is now an associate professor of Pathology and Laboratory Medicine and the leader of Penn's Brain Bank. "We never felt like we weren't able to do an experiment or pursue something, because all

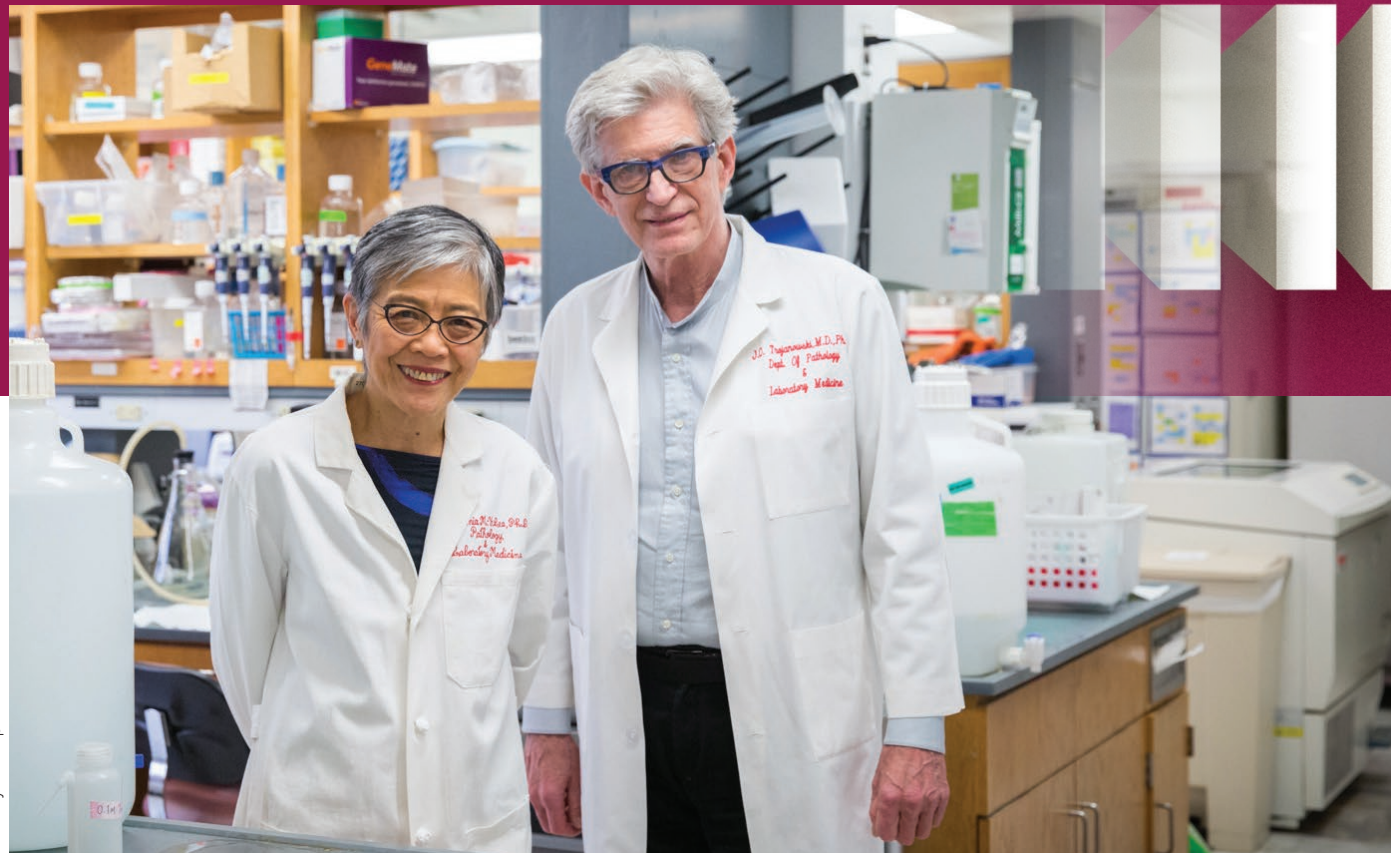


Photo by Scott Spitzer

Virginia M.-Y. Lee, PhD, and the late John Trojanowski, MD, PhD, worked together for decades and helped fundamentally define the mechanisms of multiple neurodegenerative diseases. They also set the tone of excellence for other researchers in the field and at Penn.

the resources were there. They were very rigorous about [their work].”

In the following years, Virginia Lee and Trojanowski’s work extended beyond Alzheimer’s disease. Lee and Trojanowski identified the abnormal protein alpha-synuclein, accumulating in areas of the brain known as Lewy bodies, as the primary contributor to Parkinson’s disease; and were the first to discover that the abnormal folding of a protein known as TDP-43 causes what is now recognized as frontotemporal dementia, a rare neurodegenerative disorder that primarily affects the lobes of the brain responsible for personality, behavior, language, and decision-making. Lee’s research further demonstrated that cell-to-cell transmission of these pathological proteins explains how each disease progresses.

These discoveries were groundbreaking, not only because they provided a better understanding of the underlying mechanisms of these diseases, but also because they offered potential targets for drug development.

Setting Up & Toppling Down

Watching research discoveries unfold for neurodegenerative diseases can be an emotional roller coaster for families of patients, researchers, and clinicians alike. As early scientific discoveries and biomarkers have moved into clinical trials over the last few decades, there has been a shared sense of hope and anticipation, a belief that these promising treatments might finally result in a cure.

But more than a few of those trials have failed. The pipeline of once-promising treatments for Alzheimer’s disease exemplifies the ebb and flow from progress and failure. These moments of setback, however, are often the very thing that keep researchers going—because understanding why a treatment fails can ultimately pave the way for more effective therapies in the future.

Attempts to develop anti-amyloid treatments for Alzheimer’s, such as Eli Lilly’s semagacestat, often encountered challenges in clinical trials that led to failure after years of testing. Similarly, trials of Merck’s experimental drug verubecestat were discontinued due to inefficacy. Biogen and Eisai’s aducanumab, designed to reduce amyloid beta buildup, also faced setbacks, with Phase 3 trials halted in 2019. In 2021, the FDA granted aducanumab (now known as Aduhelm) accelerated approval, which means the company will be required to submit further proof of the drug’s clinical benefit before full approval can be granted. The decision was controversial, as the FDA granted accelerated approval against the advice of an advisory panel whose 10 out of 11 members voted against it.

These failures show just how difficult it is to develop effective treatments for diseases that plague our brains, even when those treatments are based on ever-growing knowledge of how the disease develops. Years spent at the bench, followed by decades of clinical testing, can still end with hopes dashed. Yet at long last, researchers now believe drug discovery for neurodegenerative disease has reached a tipping point: the critical moment when a crucial, well-placed domino initiates a chain reaction that causes a whole new picture to emerge.

The FDA’s July 2023 approval of Leqembi can be seen as that first domino push along a new branch. Although the monoclonal antibody treatment requires biweekly infusions, Leqembi has spurred the development of multiple complementary treatments, including oral pills. These new medications aim to work alongside Leqembi or to be used in individuals with mild cognitive impairment, or even before people have any symptoms, to prevent the progression to dementia. There are also new treatment breakthroughs for ALS. In April, the FDA approved tofersen, a medication designed to treat ALS in adults with a SOD1 gene mutation, further expanding treatment options for ALS patients.

Time, Virginia Lee says, will be the truest determining factor for whether the new treatments being introduced will become long-term cures.

“The state of the art right now is to treat and then follow [the patient] for two to three years to see if beta-amyloid goes up or down,” she said. “Now we want to see whether five or 10 years from now they’re still cognitively fine, that they haven’t declined or that they’ve declined much more slowly.”

The Domino Chain of Discovery

Penn Medicine continues to be a hotbed of neurodegenerative disease research advances. Virginia Lee and Trojanowski’s discoveries were foundational, but equally so is the impact they have had on a community of research activity on Penn’s campus and far beyond, with a whole new generation of researchers now committed to standing up the next critical dominoes in the chain building toward faster diagnoses and better cures.

A groundbreaking test, unveiled in April 2023 at Penn, promises to detect Parkinson’s disease before symptoms even manifest. Penn Medicine researchers, in collaboration with the Parkinson’s Progression Markers Initiative and the Michael J. Fox Foundation, confirmed the accuracy of the alpha-synuclein seed amplification assay in identifying individuals with Parkinson’s disease and categorizing them according to genetic and clinical indicators. This early detection could potentially be a game-changer in managing the disease and developing interventions at an earlier stage.

Another discovery in July 2023 pinpointed a new protein as a promising target for Alzheimer’s treatment. Penn researchers discovered that the gene responsible for encoding tripartite motif protein 11 (TRIM11), a protein linked to tau production, effectively inhibits degeneration in small animal models of neurodegenerative disorders similar to Alzheimer’s disease. Their findings identified TRIM11 as a pivotal player in the removal of the protein tangles responsible for multiple neurodegenerative conditions.

The direct impact of Virginia Lee and Trojanowski’s mentorship can also be seen in the success stories of their mentees, like Alice Chen-Plotkin, MD, who, in addition to making significant contributions to our understanding of Parkinson’s disease and ALS, today leads the first-of-its-kind Molecular Integration in Neurological Diagnosis (MIND) Initiative in the Perelman School of Medicine at Penn. The MIND Initiative collects medical data and blood samples from Parkinson’s patients to analyze their genetic makeup, aiming to categorize patients based on genetic and biomarker contributions, improve diagnosis, and eventually develop more effective treatments for the disease.

Another of Virginia Lee and Trojanowski’s mentees, Daniel Skovronsky MD, PhD, currently serves as the executive vice president and chief scientific and medical officer for Eli Lilly and Company. As a graduate student at Penn, Skovronsky worked under Lee throughout his residency training in pathology. Skovronsky went on to found a company called Avid Radiopharmaceuticals, which developed the first FDA-approved agent for brain imaging of amyloid plaques in patients with cognitive impairment. Now as CSO of Lilly, Skovronsky is overseeing the development of donanemab, which soon may become the second FDA-approved anti-amyloid drug for the treatment of Alzheimer’s disease. The company unveiled data from a late-stage clinical trial of the drug in July, showing it slowed cognitive decline in patients in the early stages of the illness. It’s anticipated that Lilly might secure FDA approval for the drug by the close of 2023 or in early 2024.

The continued success of their mentees, and the continued trail of scientific discoveries, not only reaffirm the importance of Virginia Lee and Trojanowski’s early work but also represent a significant leap forward in the quest for a cure.

“Within my lifetime we may actually prevent people from having bona fide dementia. I don’t think I would have been able to say that 10 years ago,” said Lee, who, at 77, has no plans to ever retire from science. “We know these new treatments can prevent decline. In the next three years or so, we’ll be able to see if it can last longer. I’m optimistic that it will.” ◻

A Legacy of Love and Learning

Virginia M.-Y. Lee's life in science together with her late partner, John Trojanowski, is a testament to her dedication to understanding the brain.

The plan for Virginia M.-Y. Lee's life was simple. She would attend the Royal Academy of Music in England, study for two or three years, then she would get married and teach kids how to play piano.

This wasn't a vision she'd concocted herself, but she longed to leave her small hometown in Hong Kong and travel the world. "My mother thought that would be a good trajectory for me," Lee recalled.

So, after high school, she trekked to the heart of London and began learning the intricate compositions of Rachmaninov and Beethoven. But after two years at the Academy, Lee knew she was destined for a different path.

"I was pretty good at it [piano], but it wasn't really for me." She convinced her mother to let her refocus her studies on science instead. It's a good thing she had the courage to go her own way.

Over the past 40 years, Virginia M.-Y. Lee, PhD, MBA, has become one of the most decorated researchers in the world and a prominent leader in research at Penn Medicine. Lee is best known for her deep exploration of the misfolded proteins that contribute to the advancement of conditions such as Alzheimer's disease, frontotemporal degeneration (FTD), Parkinson's disease, and amyotrophic lateral sclerosis (ALS). Lee's groundbreaking discoveries have garnered numerous accolades, including the prestigious Breakthrough Prize in Life Sciences, and bolstered the development of new treatments for neurodegenerative diseases that were once believed to have no hope for effective therapies or cures in our lifetimes.

It's a career made possible through sheer dedication, a passion for unraveling the mysteries of neurodegenerative diseases, and a partnership that both challenged and motivated Lee to aspire to the highest levels of achievement.

A Profound Personal and Professional Partnership

In 1976, Lee found herself at a bar in Boston. She was by then two years into a postdoctoral fellowship in Neuropathology at Boston Children's Hospital at Harvard Medical School. She didn't drink, but she'd been invited out that evening by her neighbor who wouldn't take no for an answer. Lee was sipping a Coke when she saw a very tall, skinny guy come walking through the door. She recognized him as the "very handsome man" she'd seen a few times before; once at a seminar at Harvard, another time, out walking with a woman. They'd always exchanged glances but never spoke. That day, however, Lee felt compelled to finally strike up a conversation.

"Have I met you someplace before?" she asked the man, not realizing she was using probably one of the most common pick-up lines ever uttered. The man smiled. His name was John Q. Trojanowski, and he was then a student finishing up his combined MD/PhD degree at Tufts University. They talked for hours that night, realizing they'd crossed or nearly crossed paths multiple times.



Virginia M.-Y. Lee, PhD, MBA



Lee, Trojanowski, and other Penn researchers made major discoveries about the causes of neurodegeneration using brain specimens donated by patients to the Penn Medicine Brain Bank. Read more about the brain bank on p. 36.

“We really hit it off,” Lee recalled with a smile. “And from that day on, we’ve been together.”

The couple moved to Philadelphia in 1980. Lee initially took a job with industry, then pursued an MBA at Wharton, but found herself missing laboratory science. Lee joined Trojanowski a few years later at Penn Medicine, where their partnership extended beyond the personal into the professional realm. They joined forces to tackle some of the most pressing questions in neuroscience.

“We decided we should work together. We had different expertise, but we thought, if we put them together, maybe we could do something important,” Lee said.

Important is an understatement for what Lee and Trojanowski went on to discover.

They discovered tau, alpha-synuclein, and TDP-43 proteins, and were first to define the crucial roles these proteins play in the progression of Alzheimer’s disease, Parkinson’s disease, and other neurodegenerative disorders. Over the next four decades, the duo founded the Center for Neurodegenerative

Disease Research (CNDR) at Penn, authored numerous seminal papers, and co-led research teams that made significant strides in the field of neuroscience. Their collective research paved the way for the development of new therapeutic strategies and drug candidates aimed at combating neurodegenerative diseases.

“I didn’t realize this until we were successful, that it’s very unusual for anyone to be able to accomplish what we did,” Lee said.

Unfiltered Collaboration

Colleagues often marveled at Lee and Trojanowski’s synergy, describing their relationship as a model of collaboration and dedication ... but also, a forum for no-holds-barred arguments and debates.

Edward B. Lee, MD, PhD, now co-director of Penn’s Institute on Aging, first met Virginia Lee (no relation) and Trojanowski in 1996 as a graduate student when their lab was located in the basement of the Maloney building at the Hospital of the University of Pennsylvania. He remembers the couple having full-blown arguments over the intercom system for all to hear.

“It was amusing. That’s just how they interacted with each other,” he said. “It wasn’t malicious, they just didn’t have a filter with each other. If they were thinking something or if they felt a certain emotion, they would just let it show.”

Bickering aside, the passion they had for their work and each other was undeniable.

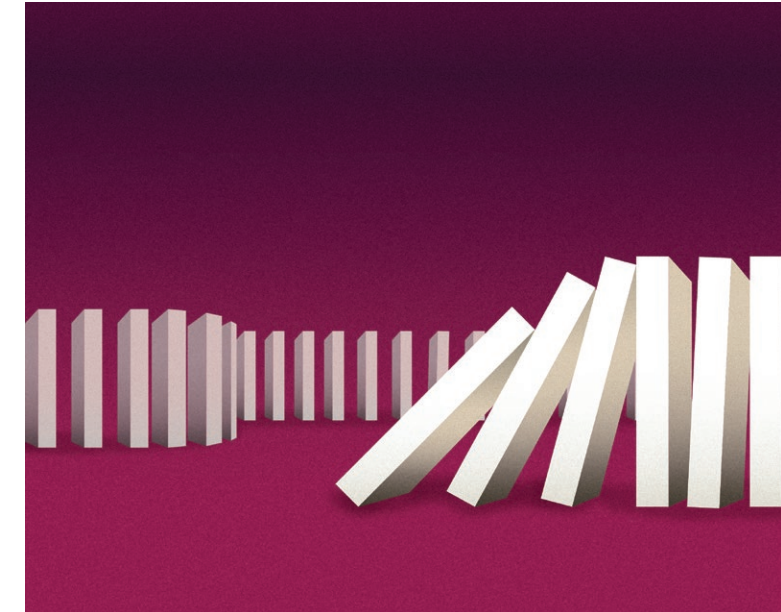
“Sometimes people didn’t know what to think when we were at work and we’d sometimes argue in front of everybody,” Virginia Lee said, with a laugh. “During our 40-plus years’ relationship, I don’t think we’ve gone more than 24 hours without making up and speaking to each other. We were very close.”

Loss and Legacy

Trojanowski passed away on Feb. 8, 2022, at the age of 75. Lee returned to work shortly after his funeral. It was the one thing she says helped her cope with the loss of her lifelong companion and friend.

“That following Monday, I went back to work. It was the best thing I could think to do so I wouldn’t sit around being miserable and feeling sorry for myself,” Lee said. “I miss him but I think that, you know, we’ve worked together for so many years, so the work really has kept me going.”

Colleagues from around the world expressed in tributes the profound impact Trojanowski had on their lives and on the field as one of the most highly respected and most



frequently cited neuroscientists in the world. His partner remains committed to carrying her part of that work forward.

Virginia Lee’s legacy as a scientist, collaborator, and mentor continues to inspire future generations of researchers. Her work not only continues to deepen understanding of neurodegenerative diseases, but also exemplifies the power of collaboration and unwavering dedication to scientific inquiry.

“I don’t count my medals. I’m actually amazed,” she said with a laugh. “If you would’ve asked me when I was 15 years old what I would be doing now, I would be blown away by what I have accomplished. I never knew that I’d have the ability to do what I’ve done.”

Reflecting on what has kept her going all these years, fighting to make her mark in neuroscience where so few women and minorities have stood, she credits the strength of one support in particular: “My husband, John. He always believed in me.”

Before Trojanowski’s passing, the duo agreed they would continue their research for as long as they were physically able. Lee says she plans to make good on her promise.

“We decided that we were not going to retire, and that was a good decision,” she said. “To be very honest, if I stopped working, I wouldn’t know what to do with myself.” ☺

The Gift of Knowledge

The fundamental answers to the core questions of neurodegenerative diseases—how and why these diseases develop—are found within the brain itself.

The Penn Medicine Brain Bank, established in 1985 by John Q. Trojanowski, MD, PhD, then an early-career faculty member in Pathology and Laboratory Medicine, has been crucial to discoveries over the past four decades. More than 2,000 families have donated specimens from deceased loved ones with dementia, in hopes of finding answers that will help others with these devastating diseases.

Edward Lee, MD, PhD, the co-director of Penn's Institute on Aging and leader of the brain bank, discussed how the brain bank helps families and researchers to meaningfully support discovery and the drive toward better treatments for neurodegenerative diseases.

How and where do you get specimens for the brain bank?

We collaborate with investigators in the departments of Neurology, Medicine, Psychiatry, and others who treat and do clinical research with patients with a variety of neurodegenerative diseases including Alzheimer's disease, Parkinson's

disease, frontotemporal degeneration (FTD), amyotrophic lateral sclerosis (ALS), and others. These patients are highly phenotyped, meaning that research-quality data including neuroimaging, neuropsychologic, genetic, biofluid, and other measures are obtained over the patient's disease course.

These patients are offered a research brain autopsy, which is important because sometimes a patient's symptoms can be caused by one of several different underlying molecular processes. For example, we have found that for individuals with Alzheimer's disease, less than a third only have Alzheimer's disease neuropathologic change (meaning beta-amyloid plaques and neurofibrillary tangles). Other neurodegenerative disease changes, such as protein aggregates made of alpha-synuclein or TDP-43, and cerebrovascular disease are also extremely common. Understanding this heterogeneity is probably very important for future therapy development and clinical trial design.



What are the goals of the brain bank?

An important outcome is providing families and caregivers a comprehensive and final diagnosis for the neurodegenerative disease that affected their loved ones. Because some neurologic disease syndromes can be associated with a variety of underlying disease processes or pathologies, the only way to know for certain what is causing some of these syndromes is to do a brain autopsy. This knowledge may have implications for family members, as different neurodegenerative diseases are associated with variable genetic risk.

It also provides patients, families, and caregivers the knowledge that their brain donation is contributing to our fundamental understanding of these devastating diseases. On the research side, these brain examinations are linked to deep clinical phenotyping. Being able to link data collected during life with the final autopsy diagnosis is helping us develop better biomarkers for disease. These tissues are also used for basic biochemical and molecular analyses to better understand the fundamental mechanisms that cause neurodegeneration.

How have these brain samples helped researchers to better understand neurodegenerative disease?

In 1991, using samples from the brain bank, Virginia M.-Y. Lee purified the protein tau and identified it as the source of neurofibrillary tangles in the brain, and in 2006 the research team purified and identified TDP-43 as the protein that aggregates in ALS and frontotemporal lobar degeneration. Tissue from this brain bank was also used to demonstrate that alpha-synuclein is the protein that comprises inclusions in Parkinson's disease and Lewy body disease.

The demonstration that tau is the protein that comprises neurofibrillary tangles, and that TDP-43 is the protein that comprises inclusions in frontotemporal lobar degeneration and amyotrophic lateral sclerosis, were both watershed moments. These two proteins are still considered some of the most important targets if we are going to treat the underlying causes of Alzheimer's disease and related dementias.

Additional discoveries include the phenomenon of cell-to-cell transmission of neurodegenerative disease pathologies. It turns out that proteins such as tau, TDP-43, alpha-synuclein, and others seem to spread through the brain's connections (the neural connectome). This suggests that blocking this spread can be a therapy. This work, done by Trojanowski and Lee with colleagues such as Penn pathologists Kelvin Luk, PhD, and Silvia Porta, PhD, is heavily dependent on using brain bank tissues as a source of protein aggregates (or "seeds") which are used and analyzed in various experimental models and assays.

The brain bank has been important in recent work done in my laboratory where we have identified a novel form of neurodegenerative disease called vacuolar tauopathy. Together with my Pathology colleague Vivianna Van Deerlin, MD, PhD, we found that vacuolar tauopathy was caused by a mutation in a gene called VCP. We are now trying to target VCP for the treatment of Alzheimer's disease and related dementias.

The focus of our brain bank on study across diverse neurodegenerative diseases including dementias, movement disorders, and other rare neurodegenerative disease conditions, has required an immense amount of coordination with collaborators who span different divisions and departments. One of Trojanowski's greatest feats was his ability to bring these diverse stakeholders together which has led to the realization that these different neurodegenerative diseases share a lot of common features with each other. For example, at the outset, it was not clearly recognized that diseases such as Parkinson's disease and ALS affected cognitive function. These were thought to be purely motor or movement disorders. However, astute Penn clinicians were recognizing that these patients were having cognitive issues, and this was solidified when we were able to examine brain bank tissues and show that the spread of disease is much wider than originally appreciated.

— Interview by Meredith Mann



The Connection to Care

With innovative memory disorder drugs on the horizon, Penn Medicine is working to address the challenges patients and families still face, from diagnosis, to treatment, to supportive care.

There is no cure for any neurodegenerative disease—not Alzheimer’s disease, or Parkinson’s, or Huntington’s, or amyotrophic lateral sclerosis (ALS), or any of the numerous other diseases that, slowly or quickly, erode away at a person’s ability to think, remember, or control their body movements. People who live with these conditions are forced to navigate a bewildering journey through the labyrinth of cognitive decline. As their condition progresses, memories fade, words slip away, and daily tasks become elusive puzzles, casting a shadow over both their personal lives and cherished relationships. Caregivers—family and close friends who support those living with cognitive impairment—grapple with significant losses, both financial and emotional, as they navigate the journey alongside their loved ones.

So it’s an especially hopeful time for families when new treatments for neurodegenerative diseases arrive. While it may not cure a loved one’s condition, a new treatment can help manage symptoms or slow the progression of the disease, potentially giving families more time to enjoy life as they’ve always known it.

The Food and Drug Administration’s (FDA’s) recent approval of Leqembi is one of those hopeful moments. The anti-amyloid treatment promises to slow decline in patients with early-stage Alzheimer’s disease. It’s the first in a new class of medicines that target amyloid plaque in the brain, a suspected culprit of several cognitive conditions. But the time and distance between a new treatment being approved by the FDA and being delivered to the patients who need it, are often fraught with challenges.

And now growing numbers of patients with Alzheimer’s disease and their families, while energized with new hope, are navigating these challenges as an added uphill climb. At Penn Medicine, a determined coalition of interdisciplinary clinicians, physicians, and researchers is working to dismantle the barriers hindering patients’ access to vital care.

Ready or Not?

New treatments for neurodegenerative diseases don’t come along often. The FDA approved Radicava in 2017, making this drug, which reduces oxidative stress in cells, the first new treatment designed specifically for ALS in 22 years. Leqembi is the first new Alzheimer’s disease therapy to receive full FDA approval in over 20 years. Leqembi is also generating a lot of excitement in the industry because it represents a new class of drugs, monoclonal antibodies that attack plaques in the brain to slow cognitive decline by directly acting on molecules associated with the disease. There are others like it in the making, including Aduhelm and donanemab, both of which are in various stages of the journey toward proving efficacy and gaining full FDA approval. But as a first, Leqembi is both an exciting and challenging new offering for patients and health care centers.

While Medicare has agreed to cover the cost of Leqembi (an estimated \$26,500 per year), the tests and scans required to qualify for the drug are not covered by many insurance plans. Felicia Greenfield, MSW, LCSW, executive director of the Penn Memory Center (PMC), estimates the positron emission tomography (PET) scan required to confirm the presence of amyloid in the brain costs around \$9,000. Medicare only recently announced that it will cover these scans. In the meantime, patients who can’t afford a PET scan will have to undergo a spinal tap instead. The procedure, which requires local anesthesia and uses a needle to collect cerebrospinal fluid from the space surrounding the spinal cord in the lower back, is more likely to be covered by private insurance plans but is also mildly uncomfortable relative to a PET scan.

Before even reaching this point in an evaluation, patients and their families must go through a gamut of systemic challenges. It begins with a race against time. Neurons, the brain cells responsible for memory, cognition, and information processing, are the linchpin of our mental faculties. Cognitive decline is irreversible. Once neurons are damaged or lost, they typically cannot be replaced or repaired.



But the reality is that most people grappling with the initial signs of cognitive decline fail to seek professional help until symptoms worsen, often explaining away symptoms as normal signs of aging. Those who voice concerns about their cognition to their primary care physician (PCP) often find themselves at a crossroads.

“PCPs are not necessarily trained or equipped to diagnose specific diseases that cause dementia, and that can be a barrier for enrolling in research, receiving appropriate care, or medication,” Greenfield said.

Many PCPs, constrained by time and training, may refer patients to geriatricians, neurologists, geriatric psychiatrists, and neuropsychologists instead, but, Greenfield explains, these specialists are in woefully short supply, especially in rural areas.

Patients who specifically hope to receive Leqembi first must consider the drug’s risks, which include the potential for brain bleeds, hypersensitivity reactions, headaches, and more. Patients and their families also have to consider the logistical challenges of frequent hospital visits for a lengthy qualification process. It begins with a clinician assessment to determine if the person experiencing symptoms of cognitive decline has mild cognitive impairment (MCI) or mild-stage dementia. MCI affected 13 million Americans last year alone. It’s predicted that number will reach 21 million by the year 2060, representing a vast number of people who might be eligible to receive the drug. However, if a patient transitions to moderate dementia, as all patients eventually will with the progression of the disease, the journey ends there. They no longer qualify for Leqembi.

If the patient does have MCI or mild-stage dementia, they move on through a series of additional evaluations including magnetic resonance imaging (MRI) scan, blood tests, and genetic testing to rule out the potential for brain bleeds and other adverse effects; followed by either the PET scan or a lumbar puncture to confirm the presence of beta-amyloid in the brain. The journey requires time, patience, and—depending on a patient’s insurance coverage—a lot of out-of-pocket fees. It also requires access to an expert who can provide careful interpretation of this complex set of evaluations and test results—a level of expertise that most clinicians do not currently have.

Care Systems Rising to the Challenge

To ensure a patient can even go through this process to qualify for Leqembi, a health care center must possess significant resources. In an optimal scenario, a cohesive network of clinicians, including primary care physicians, geriatrics specialists, Alzheimer’s specialists, genetic counselors, radiologists, and infusion teams, would operate within the same network. This synergy would facilitate a more efficient process for scheduling procedures and seamless

referrals between practitioners. And, of course, those specialists would have the capacity to accommodate new patients alongside their existing caseload.

Comprehensive centers that are designated as Alzheimer's Disease Research Centers by the National Institute on Aging, including the Penn Memory Center, play a pivotal role in providing reliable diagnoses, treatment options, and access to clinical trials for patients who live in proximity to academic institutions with such centers. However, the PMC too is grappling with the challenge of trying to serve an increasing number of patients seeking evaluations with a limited pool of available providers to meet this demand.

"With the majority of our providers dedicating their time to research, we have a limited capacity to accept new patients into our clinical practice," said Greenfield, who added that the center has taken steps to increase its clinical capacity and reduce evaluation wait times.

"For years we have worked on development of the tools to detect and monitor patients with Alzheimer's disease," said David Wolk, MD, co-director of the PMC and a professor of Neurology in the Perelman School of Medicine, "and we are now faced with the exciting, but daunting, task of moving these tools into clinical practice."

The arrival of new anti-amyloid treatments has driven a need for what Lee Leibowitz, Penn Medicine's associate vice president of Clinical Strategy, described as the convergence of "research-level resources for a clinical endeavor," a commitment that few health care centers are currently willing or equipped to undertake.

"Penn is somewhat unique because we have all of this expertise in one place," Leibowitz said. "Not just here [in Pennsylvania] but around the country, this may be the first time—for a clinical reason, not a research reason—that centers are bringing this all together."

Leibowitz manages the protocols for new clinical services and programs at Penn Medicine. He has seen novel categories of treatments arrive before. When targeted gene therapies were first introduced in 2017, cancer centers had to adapt by establishing new infrastructure to support personalized medicine. It required a similar process of shifting interdisciplinary teams and resources from a research to a clinical effort, and advocating for coverage of the many new treatments

that entered the market. This was a massive undertaking; it's the same kind of effort that will be needed to accommodate care for patients as more advanced therapies for neurodegenerative diseases move toward the clinic.

As these new treatments emerge, Penn Medicine clinical leaders are working to control the things they can: increasing clinical capacity, shortening evaluation waitlists, and streamlining the qualification process for anti-amyloid treatments like Leqembi.

For matters beyond Penn Medicine's control, like determining which treatments are covered by various insurance companies or payers, they advocate. Leibowitz is working with several insurance companies who have yet to support coverage of Leqembi. The goal, he says, is to assure payers that with proper administration, the drug will only be given to the patients who truly need it.

"Our advocacy, to help them understand the rigor that we're bringing to the patient selection process, is important," Leibowitz said. "It's not about getting lots of patients on the therapy; it's about getting the right patients on therapy. So, we want to partner, and we want to advocate and help the payers understand it's really important to provide this drug to the right patients."

With its vast network of providers and clinical resources, Penn Medicine is uniquely positioned to serve as a model for health care centers nationwide on how to screen for and administer anti-amyloid treatments effectively and efficiently.

Supporting More Than Medical Treatment

For families facing the difficulties of cognitive decline, access to medical treatment is just one piece of the puzzle. As Greenfield explains, many families also need help navigating resources in their communities, or social or emotional support, or help finding an alternative living arrangement for their loved one; or they may need to learn specific techniques for managing challenging behaviors that dementia and other neurodegenerative diseases may cause.

The PMC offers several of these supports, including caregiver education and coaching; short-term psychotherapy for caregivers of people in mild stages of dementia; support groups; and a variety of programs such as Cognitive Comedy, grief yoga, mindfulness meditation, and memory cafes. Many of these services, however, are funded solely through philanthropy and community-based grants.

"If the support goes away, we run the risk of not being able to offer this care to our families," Greenfield said.

Medicare's coverage limitations present another critical challenge. Currently, Medicare does not cover the cost of in-home respite care or expenses associated with assisted



Felicia Greenfield, MSW, LCSW, executive director, and co-directors David Wolk, MD, and Jason Karlawish, MD, lead the Penn Memory Center, an Alzheimer's Disease Research Center that offers a number of supports for patients and caregivers navigating Alzheimer's disease and other dementias.

living or memory care facilities. According to Greenfield, the average cost for in-home respite care in Philadelphia is \$25 per hour with a 3-hour minimum, and the cost of a memory care facility is on average \$7,000 to \$10,000 per month.

"This is out of reach of the majority of people who need care," she said, adding she believes this Medicare policy should be changed to alleviate the financial burden on families struggling to afford necessary care.

One positive development that PMC Co-director Jason Karlawish, MD, believes will be critical to helping families is The Center for Medicare and Medicaid Services (CMS)'s introduction of the GUIDE model. The voluntary, nationwide model is designed to ensure standardized dementia care, including caregiver training, education, and support services. When implemented, GUIDE can help dementia patients stay in their homes longer, delaying nursing home placement and enhancing their quality of life. The model also offers reimbursement for caregiver support services and a \$2,500 annual allowance for respite or long-term care.

It's the first time Medicare has ever been positioned to support this kind of care.

"Medicare's default has been that it doesn't pay for long-term care services and supports because, as the statute was originally written, those things weren't considered medical care," explained Karlawish, a professor of Medicine, Neurology, and Medical Ethics and Health Policy in the Perelman School of Medicine. "GUIDE will allow a participating health care system to deliver caregiver services and supports to people with dementia. That's huge."

Greenfield anticipates Penn Medicine and other health care centers nationwide will soon adopt GUIDE to improve access to these services; and Karlawish is optimistic that GUIDE will also help promote health equity by ensuring underserved communities have equal access to its interventions.

While the hurdles ahead are many, Karlawish says he and his colleagues are looking optimistically at how far the field of neurodegenerative disease care has advanced and the impact the work they are doing now will have on families for years to come.

"It's a very exciting time to be in the field. We're very optimistic and very hopeful," he said. "We recognize there will be some bumps and challenges along the way but we're living in a revolution that's going to improve the quality of life for thousands of families. To that, I say, it's about time." □

DONORS CHAMPION THE MARVELS OF MRNA

Does any other story make the importance of novel medical research and the need to support those who conduct it so clear?

As they so often do for significant Philadelphia causes, the Roberts family has taken a leadership role in supporting both today's mRNA researchers and the explorations of the future. In 2021, they established the Roberts Family Professorship in Vaccine Research for Drew Weissman, MD, PhD, to help his team realize the promise of mRNA to fight a multitude of diseases. The Roberts family also created the Katalin Karikó Fellowship to provide support for early-career scientists in the field of immunology. Currently, the Karikó fellowship is jointly held by Norbert Pardi, PhD, and Michela Locci, PhD, both assistant professors of Microbiology. The two are close collaborators in the Weissman lab's program to develop universal influenza vaccines. The chair and fellowship exist in perpetuity and will be passed on to researchers who will make the discoveries of tomorrow.

This fall, winning the world's best-known donor-sponsored prize has shone a very bright light on the achievements of Weismann and Karikó. From research support to fellowships to funding for international partnerships, donors are finding many ways to support the future of mRNA and novel science at Penn.

Taking Aim at Every Infectious Disease, Cancer, and Genetic Disorders

The mRNA delivery system can activate the immune system against not just the coronavirus, but all manner of devastating diseases. Read more about the projects underway on pages 14-15 in this issue.



Aileen and Brian Roberts: "It is our family's privilege to support the life-changing research conducted at Penn and we are eager to see how the next generation of scientists and physicians work to accelerate the development of the advanced therapies of the future."



Fellowships for Junior Faculty and International Scholars

Many exploratory studies are run by less experienced researchers who often fail to attract conventional funding and who are most vulnerable when budget cuts are needed.

In addition, educating young minds from both the United States and around the world is essential to scaling up mRNA research and production. People everywhere can only benefit from the new protections of mRNA when knowledgeable scientists can assist in distribution and treatment across the world. The cost of such education is difficult for less affluent nations to afford. Weissman's lab already trains scientists from nations including Argentina, Brazil, and Thailand, but more outreach is needed.

Worldwide Access

Penn Medicine is collaborating with world governments to expand access by establishing production sites and training local scientists. For instance, Weissman's lab is working with local partners in Thailand to create a COVID-19 vaccine to be used in middle- and low-income countries throughout the region.

▶ To find your way to a part of this breakthrough for the ages, please visit PennMedicine.org/mrna



JOIN THE CLIMB!

A Mountain Trek to Benefit Women in Immunotherapy Research at Penn

Kristen Hege, MD, and her husband Gib Biddle are hiking the Pacific Crest Trail to raise funds for early-career women scientists at Penn's Center for Cellular Immunotherapies (CCI). The couple seeks to raise \$500,000 through the Penn Giving Page that Hege created.

Clearly, these two enjoy daunting challenges. The Pacific Crest Trail is 2,658 miles long and reaches its highest elevation at 13,180 feet. Only 14 percent of hikers who undertake it finish the entire trail.

Likewise, curing cancer might be an intimidating goal for some. Hege, however, has just recently retired from a noteworthy career treating cancer patients and leading cancer research and drug development. She frequently worked with Penn Medicine's Carl June, MD, the Richard W. Vague Professor in Immunotherapy and Director of the CCI, and Bruce Levine, MD, the Barbara and Edward Netter Professor in Cancer Gene Therapy, whom she considers the "true pioneers of the breakthrough field of cellular immunotherapy."

Hege believes this area of research will soon scale a series of very high pinnacles. She writes, "After 25 years of dedicated and iterative research, the field of cellular immunotherapy is now at the tipping point, with potential applications across a spectrum of serious human diseases, well beyond cancer."

Based on her career-long observations, Hege believes it is essential to support female scientists. "While women enter medical and scientific fields at equal numbers to men," she

writes, "women are still underrepresented in leadership roles across academia and the biopharma industry. Women need opportunities, financial and emotional support, and mentorship to embark on, persist in, and thrive in science and medicine."

In some ways, this trek brings Hege full circle. As a first-year medical student, she coped with the recent deaths of both her parents by biking down the Pacific Coast. "The solitude, natural beauty, and physical challenge was a tonic for my soul, allowing me to heal and move beyond the pain and loss as I embarked on my medical education and future profession," she writes. "Now, as I enter retirement and reflect on my career in science and medicine, it seems fitting to turn around and walk back along the crest of the western mountains from Mexico to Canada and reflect on the progress we have made in cancer immunotherapy research and the great opportunities ahead."

As of mid-November, Hege's Giving Page has raised nearly \$300,000. Major \$100,000 gifts came from her former employer Bristol Myers Squibb and Bill Haney, CEO and co-founder of Dragonfly Therapeutics, a developer of immunology therapies. More than 125 additional donors have kicked in so far.

▶ You can learn more and make a donation to Hege's Giving Page online. Visit this story at PennMedicine.org/ magazine for the link.

DONOR-SPONSORED ASPIRE PROGRAM AIMS TO BOLSTER DIVERSITY IN NURSING

Program's focus is to build a diverse workforce from the local community



Students from Philadelphia are now seizing a new chance to learn about and start careers in nursing. In January 2023, the Howley Foundation, La Salle University, and Penn Medicine launched the ASPIRE Program at the Hospital of the University of Pennsylvania (HUP) to offer these students financial and educational support, as well as an enthusiastic welcome to the profession.

According to high school junior SirNira, the ASPIRE program is proving to be inspiring:

“My first year in the ASPIRE Program was awesome. I loved how I got to learn so much and feel at home. I never

was upset about not hanging out with friends or doing anything else on Saturdays because I was able to be with my ASPIRE family, who wanted to help me reach my goal of becoming a nurse. I loved the shadowing opportunities, being on Penn’s campus, meeting like-minded people, and generally learning about how broad the field of nursing is and that there is truly something for everyone. I constantly talk about being an ASPIRE Scholar and how fortunate I am to wear our shirts and my badge.”

The program is funded by the \$7.5 million commitment of the Howley Foundation. Since 2001, this organization has



sponsored scholarship and education programs leading to work for students from low socioeconomic backgrounds in Cleveland and Philadelphia.

At HUP, the program is led by ASPIRE Program Manager Gabrielle Mariotti, MSW, LSW and Nursing Professional Development Specialist Diana Rodenbaugh, MSN, RN, CMSRN, WCC. With the strong endorsements of leadership from both the University of Pennsylvania Health System and LaSalle, the program has made a quick start. Twenty-five high school students have been selected in a highly competitive

process and are exploring the nursing profession as ASPIRE scholars.

In their junior and senior years, high school students in the program participate in enrichment sessions led by HUP nurses. ASPIRE scholars are introduced to topics such as the history of nursing and various nursing specialties. They also gain CPR certification, observe bedside care in clinical units, and practice a range of nursing skills. Most of all, they become part of a community that is dedicated to and excited for their success.

After completing each year of enrichment sessions, students receive a \$500 stipend. Seniors who qualify are given the option to attend La Salle University to earn a BS in nursing. They are offered part-time employment at HUP to supplement their academic experience with peer support, mentorship, and hands-on career experience. The Philadelphia program is modeled on the successful ASPIRE program that the Howley Foundation sponsors at the Cleveland Clinic.



To learn more about how you can contribute to the ASPIRE program and other opportunities to build a more inclusive health care workforce, please scan the QR code and visit the ASPIRE Program website.

Progress Notes will resume with the next issue. Send your progress notes and photos to: Donor Relations Penn Medicine Development and Alumni Relations 3535 Market Street, Suite 750 Philadelphia, PA 19104-3309 medalum@dev.upenn.edu

1950s

John Charles Bucur, MD, MS'53, a neurosurgeon; Aug. 17. He began college at Ohio University in January 1943, and enlisted in the Army by the summer. He served in the European Theatre with the 17th Field Artillery Observation Battalion V Corps, entering the field in day two of Operation D-Day and later participating in the liberation of Buchenwald.

After the war, Bucur attended the University of Biarritz in France, eventually returning to Ohio University and graduating with degrees in zoology and mathematics. He then earned his medical degree from the University of Pittsburgh School of Medicine in 1951. In 1953, he received a master's degree in surgery from the University of Pennsylvania and completed his neurosurgery residency at the VA hospital in Long Beach, CA. He then served as staff neurosurgeon at the VA before relocating to Arlington, VA to establish his private practice in neurosurgery. Bucur played a crucial role in founding Fairfax Hospital (now INOVA).

Frederick E. Wawrose, MD'54, a psychiatrist; Oct. 1. Wawrose completed his medical internship at the Hospital of the University of Pennsylvania, where he eventually joined the clinical faculty. He moved to Vancouver, WA, serving in the U.S. Public Health Service, focusing on the distribution of the polio vaccine to local children. In 1956, he joined the U.S. Army Medical Corps. He spent six months as a ward officer in Neuropsychiatry in Fort, Campbell, KY, before being transferred to Okinawa, Japan,

where he served as a ward officer in Neuropsychiatry at the U.S. Army Hospital.

Wawrose was honorably discharged from his military service and returned to Philadelphia to complete his residency in psychiatry at the Institute of the Pennsylvania Hospital and undertake a fellowship in child psychiatry at the Child Study Center. He served as director of the Child Study Center from 1967 until 1970, when he moved his family to Huntingdon, PA and opened a psychiatric practice, serving as the county's only psychiatrist for many years. He was the sole psychiatrist at J.C. Blair Memorial Hospital for 25 years, also serving as chief of the Medical Staff. He was also the first psychiatrist to practice at Huntingdon's Community Mental Health Center, as well as the State Correctional Institutions. In addition, he served as a psychiatric and clinical director at Hollidaysburg State Hospital and as a staff psychiatrist at the Community Mental Health Center of Juniata Valley. Wawrose was board-certified in Adult and Child Psychiatry and was a member of many medical associations.

Barry Sorrel Savits, MD'59, a surgeon; July 2. Savits attended Princeton University and the University of Pennsylvania School of Medicine. A surgical residency followed at Mount Sinai Medical Center in New York. Subsequently, he spent a year in Cuenca, Ecuador with Project Hope in 1965 to successfully salvage a failing medical school and train its surgical staff. He also provided in-country medical care in Afghanistan and Kenya. Savits served his country as a commander in the U.S. Navy for two years during the latter part of the Vietnam War in Guam and Morocco. Following his service, he had a surgical career in Brooklyn for 40 years, serving as director of Surgery at St. Mary's Hospital and the Kingsbrook Jewish Medical Center, where he was involved in resident and student training as well as clinical research. He fostered the concept

of outreach through participation in neighborhood clinics and support for local family practitioners. The remainder of his career was spent in the private practice of surgery.

1960s



Edgar P. Nace, MD'65, a psychiatrist; Sept. 23. After graduating from medical school and training at the Institute of Pennsylvania Hospital, Nace served three years as a major in the Army as a research psychiatrist at Walter Reed. He established numerous substance abuse programs in both private and teaching hospitals.

Nace was a member of many medical associations, including the American Psychiatric Association.

Nace contributed extensive work with numerous nonprofit organizations to establish and advance mental health treatment programs for the homeless. He received numerous awards for his work and also engaged in mental health missionary work in Russia. He maintained a busy private practice of clinical, addiction, and forensic psychiatry, as well as being medical director for Integrated Psychotherapeutic Services, which provides psychiatric services for the homeless. He authored multiple publications on the diagnosis and treatment of substance use disorders, including his book *Achievement and Addiction*.

Guy A. Catone, MD, GME'66, an oral and maxillofacial surgeon; July 31. Catone graduated from Pennsylvania State University in architectural studies,

the University of Pittsburgh in chemistry and biology, the University of Pittsburgh School of Dental Medicine, and the University of Pennsylvania Graduate School of Medicine. He completed a residency in oral and maxillofacial surgery at Henry Ford Hospital in Detroit, MI, followed by a research fellowship at the University of Alabama Medical Center in Birmingham, AL.

Catone was on the medical staff at Allegheny General Hospital, Forbes Hospital, and Shadyside Hospital, in addition to his private practice and faculty appointments as an assistant professor at the University of Pittsburgh and an associate professor at Drexel College of Medicine. For decades, he was director of Oral and Maxillofacial Surgery at Allegheny General Hospital. He has made many contributions to medical literature, including the book *Laser Applications in Oral and Maxillofacial Surgery*. He was a member of numerous national and international professional societies and served on the advisory committee of the American Board of Oral and Maxillofacial Surgery.

1970s

William K. Sherwin, MD'75, GME'79, PhD'75, a dermatologist; July 19. Sherwin graduated from St. Joseph's College in phys-



ics in 1969. He earned medical and doctorate degrees in Immunology from the University of Pennsylvania School of Medicine in 1975, where he was the first student to be accepted into the combined MD/PhD program. He completed his internship at Lan-kenau Hospital in Wynnewood.

Returning to Penn for his dermatology residency, Sherwin joined a private practice in Bala Cynwyd where he practiced medicine for more than 40 years. He was a member of the American Medical Association, the American Academy of Dermatology, the Pennsylvania Medical Society and Montgomery County Medical Society, the Philadelphia Dermatological Society, and the Royal Society of Medicine. He was also a fellow of the College of Physicians of Philadelphia and a past president of the Pennsylvania Academy of Dermatology.

1980s

Francene Mason, MD, GME'83, an oncologist; June 12. Mason graduated from the University of Pittsburgh School of Medicine,



later completing her postgraduate medical internship, residency, and fellowship in hematology-oncology at the University of Pennsylvania. There, she also served as chief medical resident, the second woman to hold this position in 250 years, and eventually became an associate professor. She won many prestigious teaching awards and became a founding member and head of the oncology division at Penn Medicine at Radnor.

In 2000, Mason moved to Colorado. She pioneered a new field of cancer and exercise research, generating new scientific discoveries on the impact of fitness in both preventative- and prognoses-related cancer data, and authored a book called *The Force Program*. She was a member of the American Society

of Clinical Oncology, American Medical Athletic Association, and the American College of Sports Medicine.

Mason spent several years practicing in medically remote areas, including Alaska and Northern Idaho, and was the medical advisor of the nonprofit Live by Living, which sponsors outdoor fitness activities, retreats, and volunteer opportunities for cancer survivors and caretakers. Mason and her therapy dog, Wyn, volunteered with the Canine Corps of Boulder. She was the first volunteer to propose and implement the idea of taking a therapy dog into the psychiatric ward at the hospital and advocated therapy dog access for all.

FACULTY

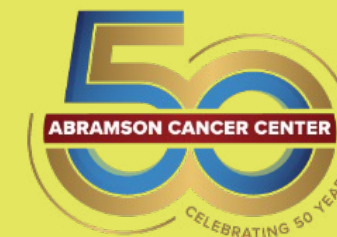
David Boettiger, PhD, a professor emeritus of Microbiology; Oct. 6. Boettiger was born in Baltimore MD, and attended Earlham, a Quaker College in Indiana, graduating in 1964. He was active in the civil rights movement and the peace movement, and joined the Peace Corps during the Vietnam War, where he served as a teacher in rural Ethiopia.

As a PhD student with Howard Temin at the University of Michigan, in 1970 he helped discover the protein reverse transcriptase, an enzyme that can turn RNA into DNA, a discovery which would earn Temin the Nobel Prize in 1975. The enzyme has become among the most widely used in molecular biology today, in analysis of gene expression by sequencing the DNA transcripts produced from RNA templates.

Boettiger worked as a professor of microbiology at the University of Pennsylvania from 1974-2014, then professor emeritus. He studied the molecular mechanisms of cell adhesion. Cell adhesion is critical for the integrity of tissues and organs, and for the infection of cells by microbes and viruses. In recognition of his contributions, he was made a Fellow of the American Association for the Advancement of Science.

Francene Mason, MD. See Class of 1983.

A Philanthropic Puzzle



Many Penn Medicine supporters have a clear vision, whether that is fostering the next generation of physicians through scholarships or helping patients in need of financial assistance.

However, Marlene Ferguson Brenner's philanthropic plans presented a puzzle for her survivors—and eventually Penn Medicine staff—to solve.

Brenner established a charitable remainder trust in her will that provided an income stream to her sister during her sister's life. After her sister's passing, the funds left in the trust (the "remainder") were designated to charitable causes.

"Supporting loved ones and making a lasting impact on causes we value are not mutually exclusive. Many people find that with just a little bit of planning, they can achieve both—and often do even more than they thought possible," said Robert Vosburgh, JD, Penn Medicine's Executive Director of Gift Planning. "That is exactly what Ms. Brenner achieved with a charitable remainder trust."

Brenner's charitable goal was to support medical research, but she did not name specific beneficiaries. Instead, she delegated this responsibility to her trustee. Working together with Kathleen P. Hertkorn, MA, the Abramson Cancer Center's (ACC) Senior Executive Director of Development & Chief Development Officer, her trustee identified the ACC's Discovery and Innovation Fund as the perfect way to honor Brenner's goals and her legacy of generosity.

The Discovery and Innovation Fund fuels groundbreaking research. The Fund and its community of donors' generous support have significantly expanded clinical trials and translational work, bolstered basic and population-level science, and catalyzed the growth of the ACC's extraordinary team. These approaches are powering the ACC to its 50th anniversary this year, with philanthropic gifts driving continued progress toward the world we all hope for: a world without cancer.

"This gift helps us to continue this legacy of excellence and innovation. We are so grateful for Ms. Brenner's generous and thoughtful gift and her trustee's assistance in making it possible," said Hertkorn.

Vosburgh added: "The collective power of our community can unveil unexpected ways to make a difference. Working with donors and their advisors together, Penn Medicine's development team can help tailor specific gift strategies to meet donors' goals at any point in their charitable journey."

What impact do you want to make on the world? Contact Robert at vosburgh@upenn.edu or 215.898.5341.



WHERE FUTURE LEADERS OF HEALTH EQUITY INNOVATION TAKE THE REINS

By Jonathan Waller

Penn Medicine’s Health Equity Advancement Lab (HEAL) works to channel research insights into concrete plans for a more equitable health care system while empowering its fellows to make transformational change.

Jaya Aysola, MD, MPH, wants to move health equity out of the so-called ivory tower and into the hands of people wearing white coats. “Most research into the overall state of health care equity has been framed in broad concepts like ‘structural bias’ or ‘structural inequality,’ or has taken a very niche approach, examining things like equity in randomized clinical trials,” said Aysola, the executive director of Penn Medicine’s Center for Health Equity Advancement (CHEA) and associate professor of Medicine in the Perelman School of Medicine. “But there’s this whole space in between where we’ve struggled to translate these concepts into concrete action.”

That space is where CHEA’s Health Equity Advancement Lab (HEAL) aims to make a difference.

HEAL is akin to a think tank but more hands-on, bringing together diverse experts in health equity and data informatics with community partners to build innovative programs and new ways of thinking to take on challenges in health equity.

The program also presents unique opportunities for up-and-coming scientists and clinicians committed to tackling health care disparities to access mentorship, resources, and support to build their own networks of like-minded collaborators.

The Anthropological Lens on Health Equity

As a research fellow in HEAL, Michelle Munyikwa, MD, PhD, has been involved in a number of initiatives, including a critical analysis of preclinical medical curricula, which cast light on the historically misguided use of race in medical education and advocated for a more comprehensive understanding of human diversity. This work, including a perspective piece in the *New England Journal of Medicine* that Munyikwa co-authored with Aysola and other collaborators, has shaped how race is perceived in medical practices and medical school curricula nationwide.

Munyikwa began this work while completing a joint MD/PhD program in anthropology at the Perelman School of Medicine and is now a resident in Internal Medicine and Pediatrics at Penn and Children’s Hospital of Philadelphia.

Training during the COVID-19 pandemic in Philadelphia, she was also an integral collaborator in developing Penn Medicine’s Social Needs Response Team (SNRT), an interdisciplinary initiative addressing the socio-economic challenges faced by underserved patient populations that were exacerbated by the pandemic.

“We would call patients and pose questions related to food insecurity, housing insecurity, and other struggles their communities were encountering. This really helped us to get a full picture of what these patients were up against,” Munyikwa said. “For instance, we advised a patient who tested COVID-positive about social distancing precautions, but realized, ‘Well, they can’t quarantine from their family because they live with 12 people in a two-bedroom house.’”

The team was set up to help patients in these situations find community resources—such as temporary housing in this patient’s case. Today, the social needs response team continues to expand to connect patients to resources for social needs after they are discharged from Penn Medicine hospitals.



Michelle Munyikwa, MD, PhD

Building Community Connections

Another CHEA program, evaluated by HEAL, Food Access Support Technology (FAST), is similarly designed to expedite patients’ access to food when they are experiencing food insecurity. Tyler Lian, now a third-year medical student in the Perelman School of Medicine, worked with Aysola and her team on the development and evaluation of FAST during his work as a HEAL fellow. FAST is a centralized digital platform designed to connect health systems, community-based organizations (CBOs), and small businesses in Philadelphia to optimize food delivery to underserved populations throughout the region. Using FAST, community members can place food requests on behalf of neighbors in need, which are reviewed and referred to eligible CBOs and small businesses, who then fulfill the requests with food boxes delivered right to an individual or family’s home.

Penn Medicine helped build the tool—but does not need to be the middle-person in facilitating access to food for those who need it.

“Through significant community input, health care organizations can better identify the gaps that exist in service delivery, more effectively support community-based organizations, and arrive at solutions that benefit everyone,” Lian said.

Amplifying Underrepresented Voices

HEAL continues to conceptualize and launch programs to advance health equity in workforce advancement, social needs, and social risks, working with 14 research fellows from groups traditionally underrepresented in medicine of varying professional levels.

“The last thing you want to do to improve upon health care disparities or health inequalities is to have the same players in the room trying to solve problems that, perhaps a lack of diversity has caused,” Aysola said. “To make real progress, you need to uplift underrepresented individuals and communities by giving them the space and opportunities to make a real difference.” □

► **Read more about HEAL and find links to more detailed stories about the FAST app for food insecurity and Social Needs Response Team, at PennMedicine.org/magazine.**

Department of Communications
3600 Civic Center Boulevard, 5th Floor Suite 500
Philadelphia, PA, 19104-4310

PAID

Phila., PA
Permit No. 2563

A SENDOFF TO STOCKHOLM

Winners of the 2023 Nobel Prize in Physiology or Medicine, Katalin Karikó, PhD, and Drew Weissman, MD, PhD, received a surprise gift during the dedication of the Penn Institute for RNA Innovation as a special sendoff before attending the prize ceremony in Sweden. J. Larry Jameson, MD, PhD, dean of the Perelman School of Medicine and executive vice president of the University of Pennsylvania for the Health System, presented the two scientists with a photoshopped, framed image commemorating the now-legendary moment when the pair first struck up a conversation by a photocopier. The resulting collaboration led to research breakthroughs in the use of mRNA for vaccines and therapies, including vaccines against COVID-19 developed to rapidly quell the pandemic.

► **Read more about the excitement and celebration of the Nobel Prize at Penn, and about the world-changing future of mRNA, on page 12.**

Photo by Eddy Marengo

