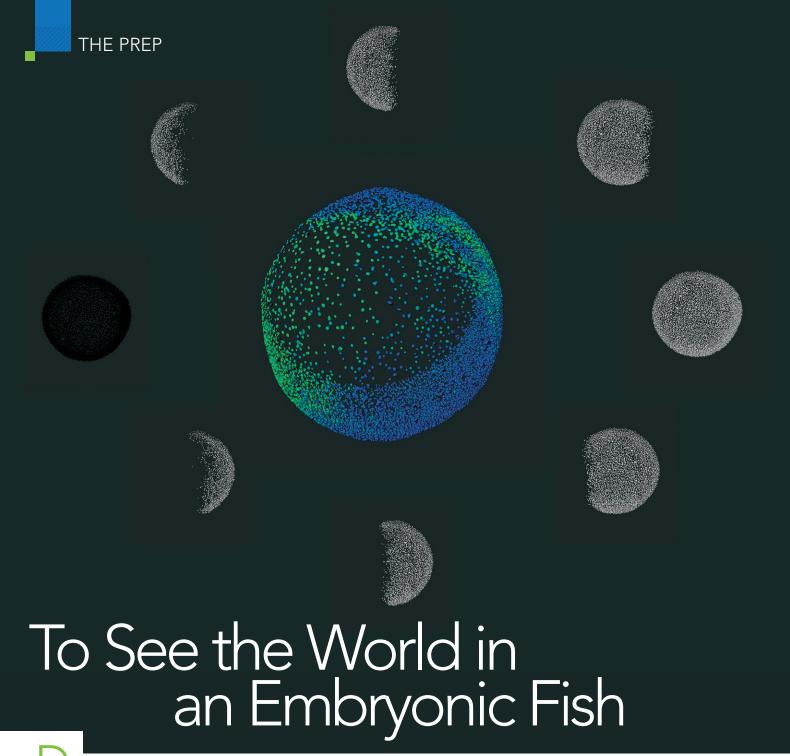


Medicine ONE INTEGRATED HEALTH SYSTEM

The Science of Suicide

Uterus Transplant: Unlocking Mysteries of Human Pregnancy

A Chinese Plastic Surgery Pioneer's Connection to Penn



espite their celestial appearance, all of the orbs in this image are zebrafish embryos. Each pinprick spot, whether white in the moon-like images or blue or green in the Earth-like one, represents a single cell that is bustling with a specific type of growth factor signaling. "In the Mullins lab, the zebrafish (our model organism) is our world," said Francesca Tuazon, who created this winning image in the graduate student category of the 2018 Perelman School of Medicine "Art of Science" competition.

A doctoral candidate in the lab of Mary Mullins, PhD, a professor of Cell and Developmental Biology, Tuazon uses a variety of methods to visualize and quantify the process called BMP signaling. The BMP signaling pathway is an important biochemical mechanism by which individual cells in a growing embryo differentiate top from bottom, from back. In a zebrafish, that differentiation happens fast—in a window of time between 4 and 12 hours after fertilization. Visually capturing the dynamics of that shift is Tuazon's challenge—and inspiration.

Read more about Tuazon's winning image and see the other winners of the 2018 Perelman School of Medicine Art in Science competition on the Penn Medicine News Blog at PennMedicine.org/magazine/art2018



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10 25 Years of Integration, Innovation, and Ideals

By Steve Graff and Rachel Ewing

A quarter century after the University of Pennsylvania Health System was established as one of the first fully integrated academic medical centers, its progress would undoubtedly make the institution's founder, Benjamin Franklin, proud.

Wonder within Wonder | By Queen Muse

Penn Medicine's uterus transplant trial offers hope for a rare form of infertility—and at the same time, has the potential to unlock a deeper understanding of human pregnancy.

The Name of Song Ruyao | By S.I. Rosenbaum

A pioneer of plastic surgery in China, Song Ruyao (1914-2003) was known for his achievements aiding others who suffered; few at Penn knew what he endured in his own life.

36 Tangling with the Science of Suicide

By Carole Bernstein

Maria A. Oquendo, MD, PhD, is probing the human mind and brain to prevent more lives from being lost to the tenth leading cause of death in the United States.

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Painting with Light in the Darkness

t was pitch dark in the photographer's studio, and the shoot was officially over. The subject, Maria Oquendo, MD, PhD, had returned to work. Usually, as the magazine editor, if I go to a photo shoot, I arrive early to see the space and the setting, and sometimes to stand in as the subject to help our photographer and art director make decisions about lighting. But this time was different. For one thing, the lighting decision was obvious, yet radically unusual: complete darkness. And this time, I stayed late and made my own mark on a couple of real photos, not just the preliminary test shots.

Waving a pen light in the darkness while photographer Peggy Peterson shot a 15-second exposure, I drew a series of curly "C" shapes with tails—backwards question marks. You can see them (from the photographer's vantage point, facing the right way) as part of the composite image on page 39. The technique is called "painting with light," and it produces an image that shows every bit of illumination, every movement of the light, during the long exposure when the camera's aperture is held open. It is a kind of miniature retrospective, or summation, of those 15 seconds—the whole sequence of motion collapsed into a single still frame.

The technique was something our designer and art director, Graham Perry, chose to use for our profile of Oquendo, Penn Medicine's chair of Psychiatry, because it works as a symbolic way of displaying how her research on suicide brings light to the darkest corners of the human psyche. The method itself in action, though, represents other aspects of Oquendo's work, and of the stories in other pages of this issue.

When you paint with light, you have to have a vision for what you're creating, some idea of the final picture. Yet that picture only emerges at the end of a span of work; it's not truly visible while you're creating it. You create in darkness, then see the picture of your light.

That description could fairly describe most research endeavors—and Penn Medicine's uterus transplant trial, perhaps more than most. Led by Paige Porrett, MD, PhD, and Kate O'Neill, MD, MTR, with a broad, multidisciplinary team of co-investigators, the trial featured in our story on p. 22 is not only a remarkably sophisticated and new way of helping women with a rare form of infertility. It's also a way of holding light up to the darkness of the great unknowns of human pregnancy—questions about the immunology of pregnancy, of the root causes of common complications, and much more, that can't readily be studied in human subjects under typical circumstances.

Like a "painting with light" photo, our cover story (p. 10) is a snapshot of the actions of a span of time—in this case, 25 years. A quarter century ago, leaders at Penn Medicine set out to establish the University of Pennsylvania Health System as one of the nation's first fully integrated academic health centers, and over the years the health system



emerged through troubled times and grew to thrive as one of the preeminent academic medical centers in the world. There was a vision, an enormous amount of challenging work during the long exposure before the picture was completed—and now tens of thousands of patients, researchers worldwide, and generations of physicians trained here, can see the result.

Painting with light is a neat little photographic technique. It makes a pretty picture. But it's also a lesson, and a reminder that even if you might not see the progress of your work as you're making it—you're making it still. Picture what you want to create. Hold up your light in the darkness. Draw your question. Create the picture you envisioned. Make something great. And enjoy the issue. □



rachel.ewing@uphs.upenn.edu @PennMedMag



Penn Medicine Racks Up Top Rankings

Penn Medicine was named #2 on *Forbes* magazine's first-ever "America's Best Employers for Women" list, which ranks employers across the nation.

Forbes partnered with market research firm Statista to identify the companies who are the most successful at supporting and growing their female workforce. Statista surveyed 40,000 Americans, including 25,000 women, working for businesses with at least 1,000 employees. The survey included questions related to working conditions, diversity and how likely they would be to recommend their employer to others.

"People created opportunities for me to be exposed to different parts of the organization and higher levels of leadership," Regina Cunningham, PhD, CEO of the Hospital of the University of Pennsylvania (HUP), told *Forbes*. "I have worked at a number of hospitals—three other health care systems—and Penn Medicine has, by far, the best hospital culture."

Penn Medicine was also named #6 among large employers on *Forbes* magazine's annual "Best Employers in America" list, up from #7 in 2017.

On both lists, Penn Medicine was the highest ranking employer in Pennsylvania and in the health care industry overall.

Not only is Penn Medicine receiving recognition as a great place to work, but accolades also continue to accrue for the work happening within the institution: Penn Medicine hospitals were ranked among the top hospitals in the nation by U.S. News & World Report for the 12th consecutive year, achieving Honor Roll status and top rankings in 12 clinical specialties. The combined enterprise of HUP and Penn Presbyterian Medical Center was named to the prestigious Honor Roll list, and ranked as the top hospital in Pennsylvania, in the 2018-2019 annual survey by the magazine. Out of nearly 5,000 hospitals analyzed nationwide, Penn Medicine is among only 20 institutions to be named to the publication's 2018-2019 Honor Roll. According to the magazine's editors, Honor Roll hospitals each perform near the top of the rankings in at least half a dozen specialty areas.

Preventable Hospital Readmissions Cut by More Than 25 Percent Under Innovative Contract



After the first year of an innovative, five-year contract between the University of Pennsylvania Health System and Independence Blue Cross (Independence), the health system reported a more than 25 percent cut in hospital

readmissions—the largest readmission reduction in both organizations' history. As part of the first collaboration of its kind in the United States between a health system and a health insurer, the two organizations have launched a new slate of innovations to reduce the number of patients who return to the hospital within a month of going home. The contract provided that Independence wouldn't pay for the resulting hospitalization in those cases.

The new contract, which took effect July 1, 2017, marked Penn Medicine's entry into a new way of working with Independence that is designed to encourage collaborative

efforts by the insurer and health systems to improve quality of care and reduce health care costs for Independence members.

The efforts that led to this improvement included leveraging electronic health records to stratify patients by risk of readmission; improving coordination between the inpatient clinical team and outpatient follow-up and home health care; implementing more robust home care services for disease management and medication teaching after discharge; monitoring high-risk patients remotely after leaving the hospital; and reviewing patient data daily and having a care coordinator reach out to the patient if indicators are trending toward trouble.

"To see such a drastic improvement just one year into our partnership with Independence serves as a great motivator to continue finding ways to bend the curve of rising health care costs," said Ralph W. Muller, CEO of the University of Pennsylvania Health System. "That can only happen if we work together to keep patients healthier, and in the first year of our new model, we're proud to have shown that we can achieve both goals."

Abramson Cancer Center Researchers Propel Drugs to Approval



Penn-Developed CAR T Cell Therapy Moves Ahead in Europe

- Personalized cellular therapy Kymriah (tisagenlecleucel, formerly CTL019) approved by the European Commission (EC)
- First chimeric antigen receptor (CAR) T cell therapy permitted for use in the European Union in two distinct indications: treatment of relapsed or refractory B-cell acute lymphoblastic leukemia (ALL) in patients up to age 25, and relapsed or refractory diffuse large B-cell lymphoma (DLBCL) in patients over 18
- Developed at Penn's Abramson Cancer Center in collaboration with Children's Hospital of Philadelphia and Novartis
- Decision follows approval from the U.S. Food and Drug Administration (FDA) for Kymriah in B-cell ALL and DLBCL in the United States

"This approval demonstrates the global impact of the therapies we developed in Philadelphia, and the far-reaching potential of these therapies to change the way cancer is treated across the world."

Carl June, MD, Richard W. Vague Professor in Immunotherapy & Director, Center for Cellular Immunotherapies, Abramson Cancer Center "This is a true breakthrough. Until today, there were no anti-tumor therapies available for patients with these tumors who were not candidates for surgery."

Study Principal Investigator Daniel A. Pryma, MD, Associate Professor, Radiology and Radiation Oncology, Chief, Nuclear Medicine and Clinical Molecular Imaging

First Nonsurgical Treatment for Rare Neuroendocrine Tumors Approved

- Targeted radiotherapy AZEDRA (iobenguane I131) approved by the FDA for nonsurgical treatment of neuroendocrine cancers
- First ever nonsurgical treatment for the rare neuroendocrine cancers pheochromocytoma and paraganglioma approved by the FDA
- Approval was based on a multi-center trial led by researchers in the Abramson Cancer Center and was granted to Progenics Pharmaceuticals



Penn Partnership to Improve Health Care Education and Quality of Care in Southeast Asia



In an effort to improve health care and to create new undergraduate and graduate medical training programs in Vietnam, Penn Medicine and Penn Nursing have launched a formal alliance with the Vingroup—an enterprise that encompasses a newly formed private not-for-profit university project, VinUni, as well as the largest and leading private health service provider in Vietnam, Vinmec.

The partnership will focus initially on the establishment of medical and nursing schools within VinUni, and on the enhancement of graduate medical education and health care programs within the Vinmec Health Care System. Penn will also support the Vinmec Health Care System to enhance the quality of care and clinical training, initially at the International Hospital in Times City, Hanoi. The ultimate goal is to build a new VinUni/Vinmec teaching hospital in Hanoi, along with future plans to create medical residency training programs and a robust clinical research portfolio focused on translational medicine.

Cancedda to Helm Botswana-UPenn Partnership

Corrado A. Cancedda, MD, PhD, joined Penn as director of the Botswana-UPenn Partnership (BUP) in July. Based in Gabarone, Botswana, Cancedda will spearhead a new phase of BUP's development. Cancedda has an extensive global health background leading teams throughout sub-Saharan Africa. He served for four years as Partners in Health's (PIH) director of training and medical education in Rwanda. He also served as executive director of the PIH Ebola response in Sierra Leone, and most recently as the principal investigator of the Resilient and Responsive Health System Initiative in Liberia. Cancedda served on the faculty at Harvard Medical School prior to joining Penn.



Corrado Cancedda with Lesego Sethole, BUP Human Resources Manager



New Class Begins Journey into Medical Profession

After receiving their short white coats and stethoscopes at the annual White Coat Ceremony in August, 152 incoming first-year medical school students at the Perelman School of Medicine recited the Declaration of Geneva, a modern version of the Hippocratic Oath, pledging to treat the ill to the best of their abilities, preserve each patient's privacy, and to teach the secrets of medicine to the next generation. They were surrounded by friends, family, and faculty.

ENTERING CLASS FAST FACTS

9

4/% male

152 students 53% female

From 23 states

20% underrepresented minorities in medicine

Honors & Awards

AAMC Awards for Excellence

Three faculty members in the Perelman School of Medicine received awards from the Association of American Medical Colleges (AAMC), the professional organization of all 151 accredited U.S. medical schools and nearly 400 major teaching hospitals and health systems nationwide.



Robert Wood Johnson Foundation David E. Rogers Award: David A. Asch, MD, MBA'89, GME'87

John Morgan Professor of Medicine and Medical Ethics and Health Policy and Professor of Health Care Management at Wharton, and Executive Director, Penn Medicine Center for Health Care Innovation

The AAMC confers the award for "major contributions to improving the health and health care of the American people."



Alpha Omega Alpha Robert J. Glaser Distinguished Teacher Award: Gail Morrison, MD'71, GME'76

Executive Director, Innovation Center for Online Medical Education, Special Advisor to EVP/Dean, and former Senior Vice Dean for Medical Education

Morrison was one of four recipients of the award recognizing outstanding contributions to medical education.



Award for Distinguished Research in the Biomedical Sciences: Stanley Plotkin, MD

Emeritus Professor of Pediatrics

The award honors outstanding medical research related to health and disease having a positive impact on medicine and on the health of patients and populations.

Sleep Research Society Distinguished Scientist Award: David F. Dinges, PhD

Professor and Chief, Sleep and Chronobiology

This award honors a single individual of prominence for contributions over an entire career and is the society's highest honor.

Elected to the Italian Academy of Science and the German National Academy of Sciences: Garret FitzGerald, MD

Professor, Systems Pharmacology and Translational Therapeutics, Director, Institute for Translational Medicine and Therapeutics

The German National Academy (Leopoldina), is the oldest continuously existing academy of medicine and the natural sciences in the world, and the Italian Accademia Nazionale dei Lincei (Lincean Academy) is the oldest national academy of science; each awarded FitzGerald for his scientific achievements.

American Society for Mass Spectrometry Biemann Medal: Benjamin A. Garcia, PhD

Presidential Professor of Biochemistry and Biophysics

The early-career award recognizes significant achievement in basic or applied mass spectrometry, a technique for detecting the components of a sample by their mass and charge.

António Champalimaud Vision Award

Three Penn Medicine researchers were recognized for their revolutionary work leading to the first successful gene therapy to cure an inherited cause of childhood blindness, among the seven total awardees sharing the 1 million Euro prize.



L to R: Maguire, Bennett, and Jacobson

Jean Bennett, MD, PhDF.M. Kirby Professor of Ophthalmology

Samuel G. Jacobson, MD, PhD
Professor of Ophthalmology

Albert M. Maguire, MD *Professor of Ophthalmology*

Albany Medical Center Prize in Medicine and Biomedical Research: Carl June, MD

Richard W. Vague Professor in Immunotherapy in Pathology and Laboratory Medicine, Director, Center for Cellular Immunotherapy in the Abramson Cancer Center, and Director, Parker Institute for Cancer Immunotherapy

Albany Medical Center has given out the \$500,000 award annually since 2001 to those "who have altered the course of medical research." It is one of the largest prizes in medicine and science in the United States, according to the organization.

President of the American Society for the Surgery of the Hand: L. Scott Levin, MD

Paul B. Magnuson Professor of Bone and Joint Surgery, Chair, Orthopedic Surgery, and Professor, Plastic Surgery

The Society includes more than 3,800 orthopedic, plastic and general surgeons from around the world.

American Society for Bioethics and Humanities Lifetime Achievement Award: Jonathan D. Moreno, PhD

David and Lyn Silfen University Professor, Penn Integrates Knowledge (PIK) Professor, Professor of Medical Ethics and Health Policy, of History and Sociology of Science, and of Philosophy

The award is the Society's highest honor, recognizing excellence in bioethics, given in recognition of longstanding achievement. The Society cited Moreno as "one of the world's foremost experts in bioethics and politics and bioethics in national security."

Marfan Foundation Hero with Heart Award: Reed Pyeritz, MD, PhD

William Smilow Professor in Division of Translational Medicine and Human Genetics

The award pays tribute to Pyeritz's four decades of dedication to improving heart health in the 200,000 people in the U.S. living with Marfan syndrome and related disorders.

International Atherosclerosis Society Gotto Prize: Daniel Rader, MD

Seymour Gray Professor of Molecular Medicine and Chair, Genetics

The prize, which is given once every three years, recognizes outstanding scientific or medical advancement in understanding the causes and reducing the development of atherosclerosis.

Alzheimer's Association's Khalid Iqbal Lifetime Achievement Award in Alzheimer's Research: John Q. Trojanowski, MD, PhD

William Maul Measey-Truman G. Schnabel, Jr., M.D. Professor of Geriatric Medicine and Gerontology

The leading nonprofit funder of Alzheimer's research worldwide honored Trojanowski for his decades-long record of ground-breaking discoveries on neurodegenerative disease.

Elected Members, National Academy of Medicine

Four new Penn Medicine faculty members are among 75 new U.S. and 10 international members elected by their peers for accomplishments and contributions to the advancement of the medical sciences, health care, and public health—one of the nation's highest honors in biomedicine.



Susan M. Domchek, MD Basser Professor in Oncology and Executive Director, Basser Center for BRCA



Daniel E. Polsky, PhD Professor of Medicine, Director, Leonard Davis Institute for Health Economics, and Robert D. Eilers Professor of Health Care Management at Wharton



M. Celeste Simon, PhD Arthur H. Rubenstein, MBBCh Professor in Cell and Developmental Biology and Scientific Director, Abramson Family Cancer Research Institute



Rachel M. Werner, MD'98, PhD'04 Professor of Medicine and of Health Care Management at Wharton

Perelman School of Medicine Welcomes New Academic Leaders



Benjamin Sun: Chair of Emergency Medicine

Benjamin Sun, MD, MPP, FACEP, joined Penn Medicine as chair of the Department of Emergency Medicine in September. Sun is an emergency physician and federally funded health services researcher who is nationally recognized for his expertise in the areas of safety, quality, and cost-effectiveness in health care. He joined Penn Medicine from Oregon Health & Science University (OHSU) in Portland.

Sun has served as the principal investigator on 15 grants from the National Institutes of Health, the Department of Veterans Affairs, the Agency for Healthcare Research and Quality, and private foundations with total funding of \$11 million. His research has resulted in a substantial body of scholarly work in journals including *Circulation*, *JAMA Internal Medicine*, and *Annals of Emergency Medicine*.



Lisa Walke: Chief of Geriatric Medicine

Lisa M. Walke, MD, MSHA joined Penn Medicine in July as chief of the Division of Geriatric Medicine in the Department of Medicine. Walke is nationally recognized as an outstanding leader in geriatrics who has pioneered innovative practice models directed to caring for the elderly. Walke joined Penn from the Yale University School of Medicine and its nationally recognized program in geriatrics, where she most recently served as an associate professor of Medicine and associate chief for clinical affairs of the Yale Geriatrics Section and was the project director for Yale's federally funded Geriatric Workforce Enhancement Program.

Among her many accomplishments, Walke established a comprehensive service line focused on improved patient experiences, lower

cost, and improved population health for older adults in the greater New Haven Area. She also developed a hospital consultation service, a comanagement program with Geriatric Psychiatry for their hospitalized patients, a senior-friendly emergency department, and a home visit program for homebound seniors.

Walke's scholarship is directed toward implementation science and focuses on developing innovative educational and care delivery models that improve health outcomes for older adults. In 2013, Walke was appointed as a Harvard Macy Institute Scholar and a AAMC Mid-Career Women Professional Development Scholar. Walke is also recognized as an outstanding teacher and innovator in geriatric medicine who has held leadership roles in education in geriatrics.



E. John Wherry: Chair of Pharmacology

E. John Wherry, PhD, was appointed the new chair of the department of Systems Pharmacology and Translational Therapeutics in July. Wherry is the Richard and Barbara Schiffrin President's Distinguished Professor in the department of Microbiology and an international leader in the study of T cell exhaustion, which prevents optimal control of infections and can hamper anti-tumor immune responses.

He is currently director of the Institute for Immunology, co-leader of the Abramson Cancer Center's Immunobiology Program, and co-director of the Parker Institute for Cancer Immunotherapy at Penn. In each of these leadership roles, he has fostered cross-disciplinary collaborations to accelerate discoveries and apply findings within the basic sciences to clinically translatable approaches.

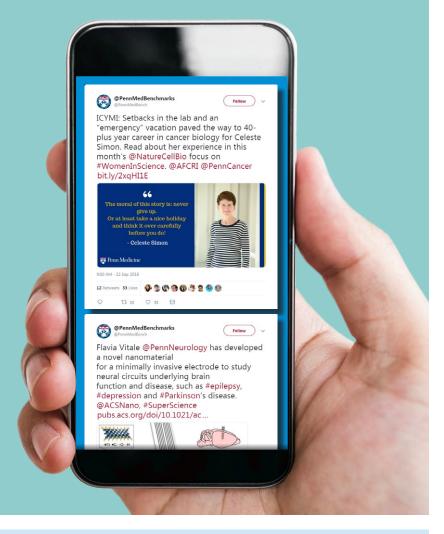
The department of Systems Pharmacology and Translational Therapeutics ranks first in the nation among pharmacology departments for NIH funding. The department is closely involved with the Institute for Translational Medicine and Therapeutics (ITMAT), home to the Clinical and Translational Science Award (CTSA) and in the leadership of the Penn Genomics Institute. Wherry's appointment will create further bridges to many departments and centers by focusing on inflammation, leading to new high impact research in pharmacology and experimental therapeutics.

Basic and Translational Research in 280 Characters or Less

The new Benchmarks Twitter account (@PennMedBench) aims to amplify basic and translational research efforts and to create a diverse, interconnected network of Penn Medicine faculty and students, researchers and journal editors across institutions and disciplines, and other stakeholders, all while "looking at life in the dish, through the microscope, and in the cloud."

Whether profiling the brilliant minds leading the charge on scientific discovery, offering a glimpse of the behind-the-scenes process, celebrating milestones, sharing media coverage, or live-tweeting conferences and events, Benchmarks skips the jargon, unpacks the technical elements, and makes basic science research approachable and understandable.

Follow the Benchmarks account online at twitter.com/PennMedBench.



Read Vital Signs online at PennMedicine.org/magazine/fw18vs

LETTERS



Bioethics Perspective Vital in Dental Medicine, Too

I read with interest the "20 at 20" article on recipients of Penn's Master's of Bioethics (MBE) degree, having received my MBE in 2004. It was nice to see many faces of fellow classmates with whom I studied. I continue to be very proud of my degree and the fact that I was the first dentist to receive it. However, I was disappointed with the fact that you did not include a dentist in your list of twenty. Penn's School of Dental Medicine continues to offer a double degree with the MBE program and there have been a number of degree recipients over the past twenty years. It is important to emphasize the need for a new generation of dentists to achieve the skills imparted in the program and apply them to the current ethical issues of dental healthcare.

I commend you and Penn Medicine Magazine for highlighting a wonderful MBE program. It is amazing that twenty years have passed.

Jeffrey G. Garber, DMD, MBE'04

Assistant Professor of Restorative Dentistry, Nova Southeastern University College of Dental Medicine Former Clinical Associate Professor of Oral Medicine, University of Pennsylvania School of Dental Medicine



This year, 2018, marks 25 years since the University of Pennsylvania Health System (UPHS) was first established—a milestone that would undoubtedly make the institution's founder, Benjamin Franklin, proud.

fter 25 years, the combined mission of patient care, medical education, and research that define Penn Medicine is a proven principle. As Penn Medicine's model has evolved over this quarter century, it continually demonstrates itself to be visionary, collaborative, resilient, and pioneering, all while maintaining Franklin's core, altruistic values of serving the greater good and advancing knowledge.

Penn Medicine's reach and impact would impress the lifelong teacher and inventor as well. One of the first integrated academic health systems in the nation, UPHS grew from a medical school with one owned teaching hospital

and a network of physician practices in the early years to a sprawling \$8 billion enterprise with six acute-care hospitals and hundreds of outpatient practices that serves a diverse group of patients across the continuum of care and across the region, from Center City Philadelphia to central New Jersey to the western reaches of Lancaster County, Pa. Alongside its clinical care, Penn Medicine—as it is known today, encompassing both UPHS and the Perelman School of Medicine—boasts one of the nation's top-regarded education and training programs for 21st century physicians within mere steps of a small city of cutting-edge research facilities



producing translational discoveries that have elevated the institution into the higher levels of advanced medicine.

"We serve the region with the most advanced medical procedures as well as convenient and geographically distributed primary care," said Ralph W. Muller, chief executive officer of UPHS. "Our innovations in patient care are models for the nation, as we both anticipate and shape what patients need."

In the early 1990s, under then-CEO and Dean William N. Kelley, MD, transforming Penn's traditional academic center—a teaching hospital, medical school, and research facilities—into an integrated system was viewed as a bold but necessary move. Penn's medical leaders saw integration as a path to greater patient reach in a changing health care market. Combining that with stronger cultural integration among the pillars of the academic center and heavy investments in research infrastructure, Penn could leverage its integration to cement its place as a national leader in medicine.

But there were bumps in the road. A few years after its establishment, UPHS was one of many health care organizations in a precarious financial situation in the late 1990s. While some academic centers questioned holding onto their hospital counterparts, Penn ultimately managed itself

out of its difficulties through governance and financial restructuring, heightened integration with the University, and fresh leadership, which put it on a more sustainable and successful path. Staff loyalty persisted, and patient care, research, and education all flourished.

Today, Penn Medicine employs over 40,000 people and serves millions of patients, from primary to the most complex care. Its medical school graduates some of the brightest minds and leaders in medicine. Its research endeavors have led to five U.S. Food and Drug Administration drug approvals within the last year alone.

And, through it all, integration—across missions, across disciplines, and across geography—has been key to success.

"Being on this campus, with the Wharton School, School of Engineering, Arts and Sciences, Nursing, Dental, Vet has a big impact day in and day out on what happens here and what happens elsewhere," said J. Larry Jameson, MD, PhD, dean of the Perelman School of Medicine and executive vice president of the University for the Health System. "I think the combination of integration within Penn Medicine and the integration within the University has created an environment where we really have very few peers." □



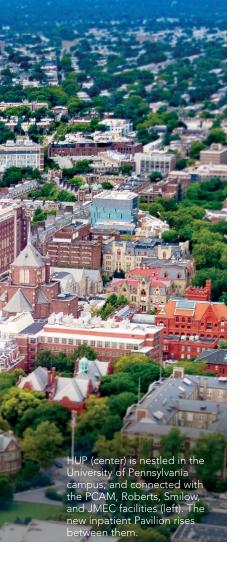
The driving force behind the birth of the health system and its continued growth hasn't changed in 25 years: high-quality care for patients throughout the region, and beyond.

he University of Pennsylvania Health System started as an inner-city hospital linked with Penn's medical school and a network of regional primary care and specialty physicians, called Clinical Care Associates, that continues today. From there, its boundaries swelled, as the Hospital of the University of Pennsylvania (HUP) was formally joined by two Philadelphia hospitals, each with a longer history of partnering with Penn as teaching sites, and the number of primary and specialty outpatient facilities also grew, with additions stretching across the map.

By the mid-2000s, Penn Medicine began its unprecedented growth spurt, starting with the construction of HUP's inter-

connected clinical-research-education hub, with the outpatient Perelman Center for Advanced Medicine (PCAM), a "one-stop shopping" facility for patients requiring complex multispecialty care, and Roberts Proton Therapy Center; Smilow Center for Translational Research; and Jordan Medical Education Center (JMEC). Over the last five years, three more hospitals from central Pennsylvania to central New Jersey joined the health system—Chester County Hospital, Lancaster General Health, and Princeton Health.

A decade ago, Penn Medicine saw 1.4 million outpatient visits and 40,000 inpatient admissions per year. That reach has soared as the system grew: Penn Medicine now cares





We have placed a system-wide emphasis on what we call the "Penn Medicine Experience." As a result of a culture campaign, educational programs, patient ambassadors, and other coordinated efforts, patient satisfaction has soared. Today, patients say they are likely to recommend Penn Medicine practices at rates among the highest seen anywhere in the country.

> Beth Johnston, Executive Director, Clinical Practices of the University of Pennsylvania

for patients who visit over five million times per year in both its inpatient and outpatient facilities. Both the Perelman Center and many regional sites offer one-stop convenience for multiple outpatient specialty appointments; and for patients with serious or chronic illnesses, Penn Medicine's home care services have substantially grown.

"It went from a well-regarded mid-Atlantic, rather HUP-centric system, to a national powerhouse academic health system," said Peter D. Quinn, DMD, MD, senior vice president for the Clinical Practices of the University of Pennsylvania and the newly developed Penn Medicine Medical Group, an umbrella organization to support physicians



across the entire system. "The three downtown hospitals are almost functioning as one big medical campus. We've merged with other hospitals...and we're coordinating a geographic distribution of practices, which allows our patients access to care closer to home and work. The game changer that will take Penn to the next level stratosphere is the \$1.5 billion Pavilion—the hospital of the future." \Box



The decision to unite into an integrated system was only a first step in the recipe for Penn Medicine's success. "If you look at the top hospitals in the country today, most are part of integrated systems," said UPHS CEO Ralph W. Muller. "But integration alone is not what makes us great." Muller and other Penn Medicine leaders point to a few key ingredients that have made the organization successful.



UNITING AROUND QUALITY

Penn Medicine's growth in clinical care has been intimately linked to its strategic emphasis on continuously improving the quality and safety of that care. In the mid-2000s, under the leadership of Chief Medical Officer Patrick J. Brennan, MD, that effort coalesced into Penn Medicine's first "Blueprint for Quality and Patient Safety," as a guide, a roadmap, and a shared language for all of Penn Medicine's clinicians and other staff to focus on system-wide priority areas of quality improvement. Reducing healthcare-acquired infections was one early priority, and other initiatives have attacked ventilator-associated and aspiration pneumonias. Co-led by both the chief medical officers and chief nursing officers from across Penn Medicine's entities, the Blueprint is revised every four years to adapt to changing needs. An emphasis on reducing readmissions has included an innovative partnership with the region's largest private insurer, Independence Blue Cross (IBC). Launched in 2017 with IBC and Penn Medicine's new five-year contract, the effort has been a key driver of an unprecedented 7 percent reduction in 30-day preventable readmissions. Among patients insured by IBC, preventable readmissions dropped more than 25 percent, with improvements for key patient groups such as those with cancer and heart failure.



BUILDING FOR THE FUTURE

Penn Medicine's growth from a single owned teaching hospital to a region-wide system of six acute-care hospitals and numerous outpatient sites is self-evident. Less evident is the strategic investment in strengthening each facility to flex unique strengths as part of a larger whole. Penn Presbyterian Medical Center (PPMC) is one case in point: "When I took over as CEO, Presbyterian needed a rebirth," said Michele Volpe, who has led PPMC for 18 years. PPMC first recruited Penn-trained physicians, then over a span of years built up clinical strengths in Medicine, Radiology, Anesthesiology,



Michele Volpe

Surgery, and other departments. "The next, very large change, was just three years ago: the transition of our Level One Trauma Center from HUP to Presby and then the Pavilion for Advanced Care," Volpe said. "I can honestly say, and I think most people in the system will say this, the journey has just been magical. It has absolutely changed the perception of Presby, within and outside the health system." Pennsylvania Hospital similarly transformed into a mighty force in cancer care, orthopaedics, and neurosciences, among other areas—and Penn Medicine has made significant investments in the growth of its newer regional hospitals including Chester County Hospital and Lancaster General Health while building on unique strengths to deliver care close to patients' homes.



STRENGTHENING FINANCES

In the late 1990s, Penn's health system was in financial turmoil, as the system's income failed to keep pace with the expenses incurred by its burgeoning research enterprise and its purchases of independent outpatient practices. The multiyear turnaround effort culminated in an innovative fiscal model implemented under CEO Ralph W. Muller, called "Funds Flow." The model channels resources from successful areas of the clinical enterprise to support Penn Medicine's holistic success across its research



Keith Kasper

and education missions, as well as in underfunded areas of clinical practice. Under the leadership of UPHS Chief Financial Officer Keith Kasper and Beth Johnston, executive director of the Clinical Practices of the University of Pennsylvania, the model decentralizes decision making and rewards clinical units for building up their own financial strength. "One noteworthy aspect of Funds Flow," Muller said, "is that in addition to driving patient satisfaction, it incentivizes cost control at a time when there is a growing need across the health care world to keep costs down." The financial stability that Funds Flow engendered has been essential to investments in Penn Medicine's sustainable growth in this century.



INVESTING IN PEOPLE

"Penn Medicine Academy is the differentiator between having great strategies and being able to successfully implement those strategies for the outcomes we all desire," Muller said. As the learning and change management arm of the health system, PMA's core mission is to sustain an agile environment by investing in people, developing strong leaders, building a skilled workforce, igniting engaged teams, and managing change. In the last year, PMA facilitated over 57,000 learning hours for over 7,700 participants with topics focused on developing leadership, customer service, project management, and other essential skills. It has built libraries of just-in-time online, mobile-friendly learning modules that VP for Learning and Organization Development Cindy Morgan calls "a friendly booster shot of new skills" for staff at all levels, from the front line of care to the executive suite. Since its establishment more than a decade ago under former VP for Organization Development and Human Resources Judy Schueler, PMA's imprint on the health system has continually grown and strengthened the organization's agility in the face of change. PMA has orchestrated the use of simulation and stakeholder engagement that substantially reshaped the design of Penn Medicine's new inpatient Pavilion in addition to supporting hundreds of other change initiatives.



INTEGRATING SERVICES

"People don't get sick and come to a pathology department or a radiology department," said Peter D. Quinn, DMD, MD, senior vice president for the Clinical Practices of the University of Pennsylvania. "They just get sick, so there needs to be coordinated and integrated care among all the departments, or physician groups in our community-based settings, to properly treat the patient." Penn Medicine delivers that complex care to patients through a model of integrated disease-based service lines. Multidisciplinary



Philip A. Okala

teams focus collaboratively on services for cancer, heart and vascular disease, neurological and neurosurgical conditions, musculoskeletal issues, women's health, transplant, metabolic conditions, digestive diseases, and others. "We also know that costs are very concentrated in a small proportion of the patient population: Five percent of patients account for 50 percent of health care spending," said Phil Okala, chief operating officer of UPHS. "The service-line approach helps our clinicians to work in teams that address these high-acuity and chronic-care needs with care that is coordinated across inpatient, ambulatory, and post-acute settings, all connected through a single electronic health record across our region. Ultimately this leads to better patient outcomes and lower costs."



"You need a culture that embraces diversity of thought and encourages people to be bold, collaborate, and cross disciplinary boundaries," said J. Larry Jameson, MD, PhD, dean of the Perelman School of Medicine. "The many centers and institutes that we have created are terrific catalysts for that kind of collaboration." And that collaboration has been a vital part of the formula for success at Penn Medicine.

Larry Jameson believes answers to seemingly intractable problems can appear with the help of a fresh set of eyes and perspectives. That's why he's so keen on having cancer researchers rub elbows with neuroscientists studying aging, ophthalmologists work alongside veterinarians, and people with engineering backgrounds camp out in operating rooms.

"Partnering with others with different perspectives can spark ideas of how to build a biomedical device in a different way," Jameson said.

It's the kind of thinking that now permeates many corners of Penn Medicine, where faculty and staff from dozens of institutes, centers, and departments work in multidisciplinary teams across all of Penn's 12 schools pursuing the toughest questions in medicine and health care.

"There are two major differences that separate Penn Medicine from others," Jameson said. "The first is we are a fully integrated organization...meaning the health system, the faculty practice plan, research, and the medical school

are part of one organization. The second major difference is that we are fully integrated within the university, not only by governance but also geography."

Having all of those minds in one place, in a spirit of collaboration, for decades, has yielded dividends.

Leaning In

The health system's highly integrated approach was devised early on, in part, to contend with the increasingly complex problems facing society.

"It was this emergence of centers and institutes in the 1990s and the sense that to be a successful research enterprise we were going to need to be more interdisciplinary. We had to work across the campus," said Deborah Driscoll, MD, chair of the department of Obstetrics and Gynecology, and director of Penn's Center for Research on Reproduction & Women's Health. "We started thinking about women's health more broadly, bringing in members from other de-

Penn has acknowledged that just as health care has become a team-based activity, research is also team-based. And those teams increasingly need to cross different disciplines. We need the basic, clinical, and translational research done at places like Penn to be tightly aligned with the private industry that will then take newly developed drugs and treatment technologies to market. Neither alone is sufficient, both are necessary.

Darrell G. Kirch, MD, President and CEO, Association of American Medical Colleges (AAMC)

partments, from the vet school, Nursing, Children's Hospital of Philadelphia to help us solve global health problems like preterm birth. Penn emerged as a national leader and this transdisciplinary approach to research has contributed to our success."

The push for integration ramped up further at the turn of the century under former University President Judith Rodin, PhD, and intensified with current President Amy Gutmann,

PhD. Gutmann has championed greater interdisciplinary collaborations since she first arrived, most notably with Penn Integrates Knowledge (PIK), an initiative that supports professorships for faculty whose work draws from two or more disciplines housed in different Penn schools. Out of 22 PIK professors today, 12 have appointments in the medical school.



Amy Gutmann

The program was emblematic of a number of shifts that enabled a longstanding perceived division between the health system and the University to finally fade away.

"The thought was the medical school and health system was something across Spruce Street, but when I was there, I tried to make that idea disappear...and that worked," said Arthur Rubenstein MBBCh, who served as executive vice president of the University for the Health System and the medical school's dean from 2001 to 2011. "When opportunities happened, with the dental school or vet school, I was there in the deliberations, and I felt empowered to go out and implement President Gutmann's agenda or add to it—and make the medical school and the other schools partner."

"They viewed the medical center as an integral part of the university for the first time," he added. "It was a two-way thing. We felt like connected parts of a whole."

Paying it Forward

Integration with both the University and within Penn Medicine continued under Rubenstein's tenure, and only strengthened as new leaders joined, including Ralph Muller, CEO of UPHS, in 2003, and then Rubenstein's successor, Jameson, in 2011, all of whom helped fuel many newer multidisciplinary initiatives on campus and beyond.

"Penn Medicine today propels the most groundbreaking, interdisciplinary research and clinical care in the world,"

Gutmann said. "Our strategy for delivering breakthrough medicine to hundreds of thousands of patients has keenly focused on connecting the highest quality medical education and clinical care with innovation powerfully driven by teams working across traditional boundaries on Penn's campus and beyond. Connectivity and creativity come together to make our academic health system an inspiring anchor for the entire Penn community. The ripple effect is vast: This work is mapping the future of medicine for the whole world." Today, 25 free-standing interdisciplinary centers and institutes and countless basic science and clinical departmental centers exist: from the Leonard Davis Institute of Health Economics to the Center for Sleep and Circadian Neurobiology to the Penn Epigenetics Institute.

"I have really enjoyed the integration with the rest of the university," said David Asch, MD, MBA'89, GME'87, a professor of Medicine and Medical Ethics and Health Policy, who has also taught an undergraduate course for 20 years. "Intellectually, I feel like I'm a citizen of Wharton and the medical school and connected to many of the other schools. This is something that literally no other university can pull off."

Asch is also executive director of the Penn Medicine Center for Health Care Innovation (PCHI). The center was created in part to leverage behavioral economics and technology to address patients' health needs during the "other 5,000 hours" when they are not at a clinical appointment. It not only drives innovation within Penn Medicine but exemplifies the organization's push to transform the health system—and everything outside of it.

"I think PCHI is a leading center... because we have been pretty deliberate about educating the rest of the world about what we are doing," Asch said. "In the end, if it's important for Penn Medicine to be doing it, then we should be teaching it."

"Many health systems have innovation centers," said Roy Rosin, MBA, Penn Medicine's chief innovation officer. "What makes ours unique is the breadth of activities embedded throughout the system to improve processes for everybody. We're lucky to have the support and team able to craft novel care delivery models that have started to become national best practices." □

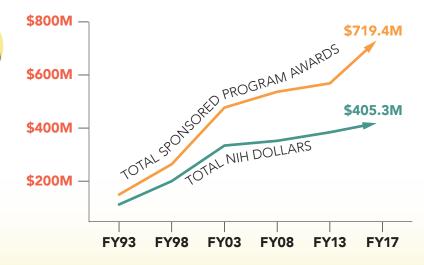
Penn Medicine has done a better job than any other institution in the country sharing the risk between the clinical and academic enterprises which has paid significant dividends to both the institution and the broader community. By balancing risk and the flow of funding and investments strategically, Penn's leadership has been able to grow the knowledge base and push out innovations in both research and patient care in a way that few others can match.



RESEARCH ENGINE REVS UP

Benjamin Franklin famously said, "diligence is the mother of good luck." And indeed decades of hard work and significant institutional investment underlie the good luck Penn Medicine has celebrated in recent months. Since last year, the Food and Drug Administration has approved multiple new therapies developed at Penn Medicine—including cellular and gene therapies that were the first of their kind—to treat cancer, reverse blindness, and more. Penn Medicine's leaders say that this translation of breakthrough discoveries into new treatments and improved health is only accelerating.

As a physician scientist, I always felt supported at Penn.
There has been significant investment in our research infrastructure. One of the biggest growth areas has been in clinical research and trials.
Today, clinical research is integrated into clinical care and one of the reasons patients seek care at Penn Medicine is the availability of such a wide range of clinical trials and the opportunity to try new and more effective treatments."



Deborah Driscoll, MD, Chair, Obstetrics and Gynecology

PHILANTHROPIC SPARK

Philanthropic support from donors at every level has been a vital element undergirding Penn Medicine's growth and achievements of the past 25 years. The number of donors has increased by almost 200 percent since the health system's founding in 1993. The giving rate for Penn's medical alumni in 2018 is 26 percent, one of the highest rates among peer instututions.

The largest gift in Penn's history (\$225 million) was from Raymond G. Perelman (front) and his late wife, Ruth, in 2011, renaming the school the Raymond and Ruth Perelman School of Medicine at the University of Pennsylvania. Philanthropy large and small has been a vital component of Penn Medicine's growth and success over the last 25 years, under the leadership of (L-R) CEO Ralph Muller, President Amy Gutmann, and Executive Vice President and Dean J. Larry Jameson.







I think we're just beginning what will ultimately be a wave of activity with biotech, in particular, but other kinds of technologies, digital technologies, beginning to set up their activities in the greater Philadelphia area...

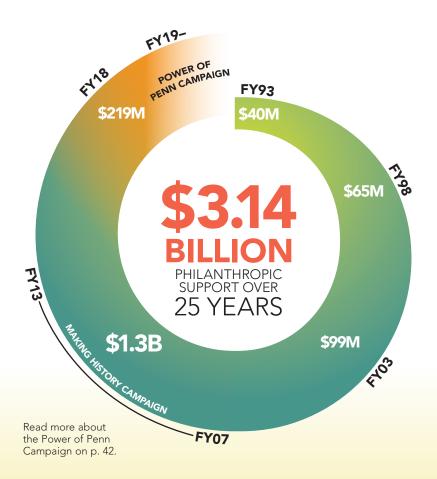
As I've watched this over the last seven years, the growth of this activity is nonlinear. It's picking up very fast and I think that will continue.

J. Larry Jameson, MD, PhD

ACTIVE CLINICAL RESEARCH STUDIES IN 2018



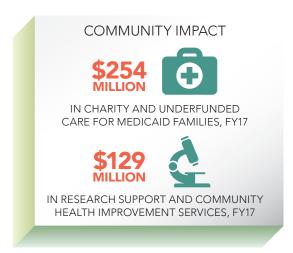
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Gifts have grown to over \$200 million this past year. Success has been accelerating year after year. And I would say it's dependent on these philosophies: integrating with a great university, making the alumni proud of us, showing our financial strengths, and building up great programs. People have had a lot of confidence in us, like the Perelmans, the Smilows and the Abramsons...They saw things were going to be great here, and they wanted to be a part of it. And they have been role models encouraging a broader base of philanthropic support.

Arthur H. Rubenstein, MBBCh, 2001-2011 Executive Vice President of the University of Pennsylvania and Dean of the Perelman School of Medicine

ECONOMIC FORCE



Academic health systems treat millions of patients, educate the medical workforce, and conduct groundbreaking research, but they're also vital economic anchors for their communities. In fact, they contribute more than \$562 billion in gross domestic product (GDP)—which translates to about 3.1 percent of the total U.S. GDP, on par with the transportation and food services industries—and support over 6.3 million jobs.

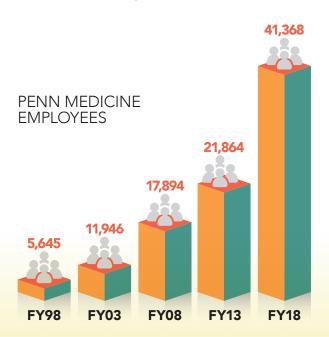
As the largest private employer in Philadelphia along with the University, Penn Medicine has had a profound and growing economic impact around the city and throughout Pennsylvania and New Jersey. The system generates a spectrum of jobs, attracts new businesses, and causes a ripple effect of dollars spent in the surrounding communities. In fiscal year 2017, Penn Medicine provided \$500 million to benefit the community.

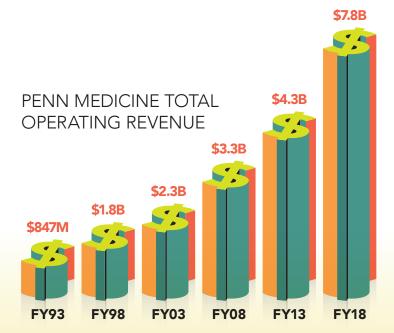
"We've contributed to the economic vitalization in Philly," said Ralph Muller, CEO of UPHS. "We recruit and hire great people, who become part of the workforce and intellectual life of the city and buy houses, go to restaurants, art centers and museums. We have built billions of dollars of buildings, which is a major source of construction jobs, as well as the anchors of redeveloping neighborhoods. It's a powerful combination of forces that cause us to be great place for medical care, and Philly a great place to live."

Penn has built an international reputation as a catalyst for innovation across many disciplines. We've amplified our faculty members' bold ideas and visionary research through a series of fruitful industry partnerships and more recently, through investments in promising technologies that are cementing Philadelphia's growing reputation as an innovation incubator and destination for cutting-edge tech jobs. From cellular therapy to nanotechnology, we're a magnet for top talent in these emerging fields, and we've leveraged our position to incentivize companies to get their start in Philadelphia and create new jobs in our region.



Kevin Mahoney, Executive Vice President and Chief Administrative Officer, UPHS







Atlantic Media. "At the University of Chicago and at Penn, Ralph awoke these dormant enterprises and fashioned them into shining models of what health care can be in this country. Ralph is the most uncommon talent in academic medicine."

Muller has overseen \$6 billion in investments on outpatient and inpatient facilities.

"I always remember him telling us you are never going to improve your bottom line by just cutting costs, you have to grow. And grow Penn did," said Deborah Driscoll, MD, chair of the department of Obstetrics and Gynecology.

Today, people within a 100-mile radius of Philadelphia

CEO Ralph W. Muller announced this year that he will retire in June 2019 after leading UPHS for 17 years of its 25-year history. He's eager to acknowledge the staff who make Penn Medicine great and to share his game plan for success.

Ralph Muller has a penchant for sports metaphors when talking shop. So it's fitting he slipped one in talking about the quarter-century milestone moment for UPHS.

"You start winning some ball games, and all of the sudden people believe you are going to start winning some more," he said. "We improved patient care, emphasized nursing, and markedly improved our finances."

The metaphor not only captures the momentum the health system experienced during his tenure, but also the man behind so much of it.

"Penn is one of the great health systems in the country, if not the world," said William Ferniany, PhD, CEO of the University of Alabama at Birmingham Health System who was the chief administrative officer at UPHS from 1992 to 2006. "Ralph has done a fabulous job there, leading it. Penn is strong as it can be. It supports a strong research mission. You don't find much better than Penn. It has come an enormous way since 1992."

When Muller arrived in 2003, Penn Medicine was in need of strong leadership to continue navigating the turnaround from its late-1990s financial downturn. Arthur H. Rubenstein, MBBCh, had been executive vice president of the University and dean of the medical school for two years and knew that his onetime University of Chicago colleague Muller, a former social scientist who led that university's health system for 16 years, had the diverse set of health policy, economic, and executive skills that Penn needed to excel.

Muller emphasized fiscal discipline and smart investment as he guided the health system through its financial turnaround. But Muller's transformative efforts also focused on staff training and smartly growing the system, implementing a fiscal innovation called "Funds Flow" for the sharing of resources across the enterprise; after 12 years, this has become a national model of strategic program building.

"In my opinion, as to force of intellect—clear, linear, rigorous, brilliant thought—Ralph Muller is unsurpassed in American health care," said David Bradley, who specialized in academic medical centers as the founder and longtime owner of the Advisory Board Company, and who is now chairman of the

can access Penn Medicine facilities close to home. Muller also championed leadership development, and the Penn Medicine Academy today is the lynchpin of the organization's emphasis on learning and managing change.

Muller has also been described as a visionary leader with a knack for interacting with people, from the C-suite down.

"It goes beyond just the doctors," said Peter Quinn, DMD, MD, senior vice president for the Clinical Practices of the University of Pennsylvania. "He knows the person at the information desk. He knows the environmental services people. He has great people skills, and I think that is part of his success."

And he has a "tremendous intuition on what to do at the right time," Rubenstein noted.

Those instincts have paid off. Penn Medicine has consistently earned rankings among the nation's top honor roll hospitals by *U.S. News & World Report*, and this year, was named the top health care employer in the nation and the #6 employer overall by *Forbes* magazine, as well as the #2 employer for women.

"We are now seeing the most successful health system in the country, and I am proud of the fact I've helped be a part of that," Muller said. "It comes down to great patient care and staff, who I feel privileged to work with and who do a great job."

Many will also remember his strong civic engagement, having led the creation of the Penn Medicine High School Pipeline and CAREs grant programs—two initiatives that underscore the institution's founding mission of public service.

"Ralph's leadership of the health system has been in keeping with what has always made Penn great," said J. Larry Jameson, MD, PhD, dean of the Perelman School of Medicine and executive vice president of the University for the Health System. "He recognizes that, when you work together, everybody is better off. Now we are 40,000 strong, working together to promote the good of society. It's where Ben Franklin started and it is where we are today." □

Read this story online with related links at PennMedicine.org/magazine/pennmed25

Wonder within Wonder Wonder

By Queen Muse
Illustrations by Graham Perry



Penn Medicine's uterus transplant trial offers hope for a rare form of infertility—and at the same time, has the potential to unlock a deeper understanding of the complex biology of human pregnancy.

n the beginning, she had no idea anything was wrong. But after six months of negative pregnancy tests, Kathleen O'Neill, MD, GME'15. MTR'15 soon found herself in the same situation she was already counseling many patients through. O'Neill was at that time a fellow in reproductive endocrinology and infertility at the Hospital of the University of Pennsylvania (HUP), and she was ready to start a family, just as she has helped many other women start theirs. Like many of her patients, O'Neill would be able to have children but not the way that most women do. O'Neill now hopes the same will be true for a select few patients she sees in a groundbreaking clinical trial of a relatively new technique: uterus transplant.

O'Neill, today an assistant professor of Obstetrics and Gynecology at Penn Medicine, serves alongside Paige Porrett, MD, GME'12, PhD'08, an assistant professor of Transplant Surgery at Penn Medicine, as a principal investigator of the trial. Their study is particularly remarkable because it not only

offers hope to women unable to give birth because they lack a functioning uterus. It also nestles wonder within wonder: transplanting a functioning organ into a place where one is in many cases missing altogether, then applying a separate feat of medical science to coax new life into the world from that organ. And in an area where numerous fundamental mysteries remain—because highly intensive human study is so rarely practical—it also shows promise of delivering a world of new discoveries about how the body achieves pregnancy and birth, through a deep look at the biological basis of human reproduction.

Infertility Options

In the months that followed O'Neill's diagnosis of unexplained infertility, she went through two cycles of in vitro fertilization (IVF). In a typical IVF cycle, multiple eggs retrieved from a woman's ovaries are combined with sperm in a laboratory to create embryos. The embryos will grow for several days in the lab before being transferred to the woman's uterus.

As many as 1 million babies have been born in the U.S. since 1981 with the help of fertility treatments like IVF, but success rates vary. Depending on her health and age, a woman may have to undergo several cycles of IVF before becoming pregnant. O'Neill's first cycle of IVF ended in miscarriage; the second led to the healthy birth of her now four-year-old son.

"I was seeing patients who were going through IVF and miscarrying, and at the same time I was going through it myself. It was very surreal," O'Neill recalled of the events of 2013. "But eventually I thought, maybe this is good; maybe this is going to make me a more empathetic doctor and I'll understand more about what these patients are going through. And I think, in a lot of ways, it did."





Kathleen O'Neill, MD, MTR, and Paige Porrett, MD, PhD.

When counseling women about their options in her current role in Penn's Fertility Care practice in Philadelphia, O'Neill now draws from her own experience to offer patients words of encouragement and reassurance: "We might not be able to help you have a baby the way you initially planned to, but we can help you build a family." She has performed hundreds of reproductive surgeries and IVF procedures.

For women with uterine factor infertility (UFI), the options currently available to achieve parenthood are adoption and IVF in combination with surrogacy. Women living with UFI are unable to birth a child either because they

Birth of a New Procedure

A uterus transplant is a surgical procedure that involves a healthy uterus (usually donated by a living donor) being transplanted to a woman who has UFI. In 2017, O'Neill, Porrett and co-investigators including Eileen Wang, MD, and Nawar Latif, MD, MPH, launched the Penn Uterus transplantation for Uterine Factor infertility (UNTIL) Trial. The multi-year trial will offer women with UFI their only chance to carry a pregnancy.

There are many differences between traditional organ transplantation and uterus transplantation. While kidney, heart and other organ transplants are

Penn's uterus transplant trial is particularly unique for its intensive focus on research. Porrett, O'Neill, and their colleagues are not only joining the ranks of the pioneers of this surgical technique in hopes of establishing it as a safe and effective option for more patients; they are pairing that effort with a comprehensive, multidisciplinary effort to better understand how the body handles pregnancy.

have been born without a uterus, have had a uterus surgically removed, or have a uterus that does not function—conditions that affect 1.5 million women worldwide.

While she's grateful to have options to offer women who have UFI, O'Neill says adoption and surrogacy have their limitations: IVF and surrogacy can often cost from \$90,000 to \$150,000, a price that many women simply can't afford. Adoption costs can likewise run into the tens of thousands of dollars and may not be an option for all would-be parents. O'Neill also notes that neither adoption nor surrogacy offer what many of her patients seek. "Many of the women I talk to, they want to experience a pregnancy; they want to know what that feels like," she said. "So, I was really excited when uterus transplantation came along as another option."

permanent procedures used as life-saving measures for individuals with terminal diseases who are often older, uterus transplants are not a medical necessity. They are temporary and are typically performed in young, healthy women who do not have a lot of other medical problems. The goal of a uterus transplant is to achieve pregnancy and birth. After a successful birth, the woman undergoes a second surgery to have the donated uterus removed.

Successful organ transplantation requires the use of immunosuppression medications to allow the body to tolerate the donor tissue by preventing their immune system from fighting it off as a foreign invader. Traditional organ transplant patients are required to take immunosuppression drugs for the rest of their lives. In uterus transplantation, because the organ is eventually removed,



The Cost and Choice Conundrum

The UNTIL trial shows great promise both for the participants and for future research of women's health issues. But the concept of uterus transplantation is still relatively new, and thus has its detractors. Criticisms include health risks women must face (two years of tests and high-risk surgeries) and the financial burdens they might experience in the future if the procedure is brought out of trials and approved for regular clinical use (projected costs in the range of \$200,000-300,000).

At its core, uterus transplantation has reignited an age-old debate over a woman's right to choose what she wants to do with her body, and it has reopened political discussion about whether insurers should cover the costs associated with treatment of infertility—a condition that until recently was not even recognized as a disease by the American Medical Association.

Despite criticism, O'Neill and Porrett believe uterus transplants should be offered in addition to other fertility options, not in place of them; and that the woman should be the one who ultimately chooses what lengths she is willing to go to bear a child.

"It's all about introducing more options, and not saying one of these options is perfect for all women, but saying let's make as many options as possible available for women and let's not judge them based on which option they want to use," O'Neill said.

"Cost is going to be an issue with any new medical procedure," Porrett added. "But if we focus on finding ways to standardize and improve the process, as we get better at it, we may be able to make it widely available to potentially thousands and thousands of women who want this as an option."

patients will take these drugs for only a finite amount of time—typically two to five years.

Studies of uterus transplants date back to the early 1960s, when doctors first tested the procedure in animal models. This work would eventually lead to the first successful live birth in a mouse model in 2003. In 1999, doctors at Sahlgrenska University Hospital in Gothenburg in Sweden began preliminary research of living donor uterus transplants in humans. More than a decade later, in 2012, news of the Swedish team's first successful transplant caught the attention of many in the medical community, including O'Neill and Porrett, who viewed the procedure as a promising, new option for some women living with infertility. Two years later, in 2014, the Swedish team achieved its first successful live birth from a uterus transplant patient. Since then, uterus transplants have been attempted in humans at least 40 times. A total of 12 babies have been born to women with uterus transplants worldwide; the majority of them in Sweden and, recently, two in the United States. But excitement has been tempered by many failed transplants. O'Neill, Porrett, and their team are out to accelerate progress in the field.

A living friend or family member donated the uterus that was transplanted for all of the successful post-uterus-transplant births reported in Sweden and U.S. to date. In the Penn trial, however, O'Neill and Porrett's team may perform uterus transplants from either deceased donors or living donors, depending on availability and the preference of the individual woman receiving the transplanted uterus.

Penn's trial is particularly unique for its intensive focus on research. Porrett, O'Neill, and their colleagues are not only joining the ranks of the pioneers of this surgical technique in hopes of establishing it as a safe and effective option for more patients; they are pairing that effort with a comprehensive, multidisciplinary effort to better understand how the body handles pregnancy—whether or not that pregnancy

results from a uterus transplant or more established infertility treatment, and whether or not the pregnancy is healthy.

No matter what they achieve, clinically or in research, the process won't be easy.

Biological Mystery

No pregnancy is ever simple. Nearly 4 million babies are born in the U.S. each year, yet there is still so much that remains unknown about what happens in a woman's body during and after pregnancy. Beyond the more commonly understood physical changes like stretchmarks and newly formed breast tissue, an unknown number of biologic and immunologic transformations occur in a woman's body during pregnancy.

During pregnancy, a woman's body accommodates a number of complex changes; her heart pumps more blood; partially of its father's genome, making it biologically different from the mother's body, the mother's immune system should identify the fetus as a foreign invader and expel it. During pregnancy, however, a woman's immune system somehow tolerates the fetus despite its "foreign" status. How this occurs exactly remains unknown.

Much of Porrett's training has focused on the phenomenon of immunological tolerance during pregnancy and other biologic consequences of pregnancy—though, as a transplant surgeon, women of childbearing age don't make up a large share of the patients that she treats. After earning her medical degree from Northwestern University in Chicago, Porrett came to Penn for a doctorate in Immunology (completed in 2008) and residency in surgery (2010), followed by a fellowship in transplantation surgery (2012). Porrett has long been intrigued to learn

It is still unclear how many of the physiologic changes of pregnancy may persist into postpartum life. The tremendous changes that occur to a woman's immune system may alter her body's functions forever.

her body changes how it metabolizes food; her uterus expands to roughly 500 times its normal size; her joints soften; her sense of smell improves; and then, in almost miraculous fashion, when the baby is born the body naturally returns to its pre-pregnancy state.

However, it is still unclear how many of the physiologic changes of pregnancy may persist into postpartum life. And the tremendous changes that occur to a woman's immune system may alter her body's functions forever.

The immune system's changes during pregnancy are their own special mystery. The primary function of the human immune system is to identify foreign cells and tissues (invaders) in the body and launch an attack to remove them. Because a fetus is made up

whether and why women who have been pregnant in the past experience worse kidney transplant outcomes. Porrett is actively investigating whether the immunologic mechanisms that permit tolerance of a fetus during pregnancy are remembered by a woman's immune system in later life. Now, in studying uterus transplantation, her challenge is to understand an unusually complex pregnancy scenario where the woman's immune system must tolerate the immunological differences of both the organ donor and the fetus.

Porrett is also a mom, and she says her journey to motherhood helped drive her interest in leading the trial.

"I came to be a mom relatively late in life; I did not want to have a baby for a long time and then later, I changed my mind. I'm so glad that I did because it's one of the greatest things that ever happened to me," she said. "Having that personal experience, understanding that desire to have a child, and now learning more about the struggles women with infertility face, it just makes me that much more motivated to help them."

The Quantified Pregnancy

A successful uterus transplant and birth is a massive undertaking.

The UNTIL trial will pool the expertise of a 50+ member team of doctors, surgeons, psychologists, social workers, pharmacists, nutritionists, nurses, and bioethicists who will help guide transplant recipients through as many as 150 medical procedures ranging from urine and blood analyses to ultrasounds, cervical biopsies, and surgeries.

While there are many medical visits in the course of a typical healthy pregnancy—roughly 15 times over 40 weeks, encompassing seven or more prenatal check-ups and screenings women participating in the UNTIL trial will be monitored far more intensely before, during, and after pregnancy. They will have weekly visits for at least two years, and will submit more than 100 blood samples, over 30 urine samples, and undergo more than two dozen cervical biopsies over that two years. From pre-transplant evaluation to final follow-up after up to two births, a uterus transplant patient's course can take anywhere from 16 to 24 months. This intensive prenatal screening schedule will help ensure the safety of mom and baby throughout transplant, pregnancy, and delivery. The detailed surveillance also gives doctors the unique opportunity to gather data for future research that may help improve other infertility treatments.

Candidates for the UNTIL trial must be women with UFI between the ages of 21 and 40 who don't smoke and are in general good health. Potential candidates are required to complete an initial questionnaire and undergo an extensive health screening through which researchers will assess everything from physical health to social support systems. Experience is an equally important component for success in uterus transplantation. Penn is one of only three centers in the U.S. that currently offer uterus transplants to women with UFI.

O'Neill is an expert in reproductive endocrinology and infertility. A graduate of the University of Michigan Medical School, her training includes a residency in obstetrics and gynecology at Barnes-Jewish Hospital of Washington University in St. Louis, a fellowship in reproductive endocrinology and infertility at HUP, and a master's degree in translational research from the Perelman School of Medicine at Penn.

Her expertise is an ideal complement

to Porrett's background in transplant surgery and immunology.

Deep Biology of Pregnancy

Together, and with the rest of their collaborators, O'Neill and Porrett are well positioned to take the many measurements of a quantified pregnancy and translate that into a wide range of advances in understanding of how pregnancy occurs, how it changes women's bodies, and how to treat many rare and common complications.

As their co-investigator Nawar Latif, an instructor in Gynecologic Oncology noted, "We're going to gain tremendous knowledge from this trial about

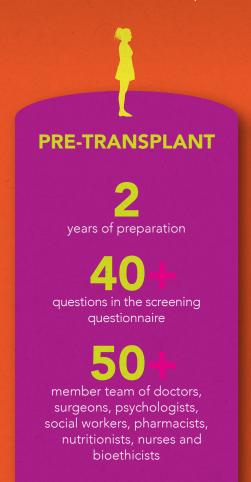
anatomy, surgery, perfusion of the uterus and other organs. Obstetricians will also learn a lot about transplant and pregnancy, and how we can better manage those situations. It's uncharted territory."

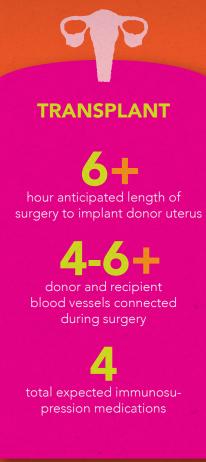
Consider the placenta. This fascinating organ temporarily grows in a woman's uterus and is expelled after pregnancy. In addition to providing nutrients and oxygen to the fetus and removing fetal waste through the umbilical cord, the placenta transfers antibodies from the mother that provide immune protection for the fetus.

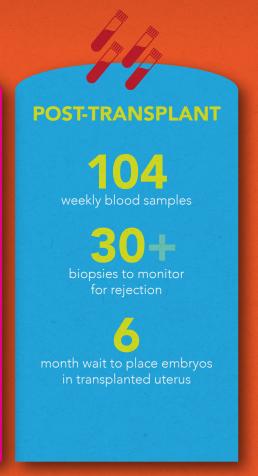
As Porrett explains, the placenta comes into contact with various tissues

Uterus Transplant Trial: By the Numbers

Women who participate in the uterus transplant trial commit to a lengthy, multifaceted process that requires a tremendous amount of effort both by the women who undergo the procedures and the medical team that performs them.







in the uterine wall, including immune system cells which would normally come from the mother, but in the setting of a uterus transplant, these cells are derived from the donor. As the placenta matures while the fetus grows, the fetal immune system is also developing and growing, but researchers still do not know exactly when some of the earliest immune precursors occur in the fetal blood.

"We know the fetus is having an effect on mom and that mom is also having an effect on the fetus," Porrett said, "but how much of this comes from the local uterine environment and therefore might be influenced by the donor is still unknown."

As the surgical director of the Living Donor Kidney Program in Penn's Transplant Institute, Porrett also sees the trial as an opportunity to apply her years of organ transplantation knowledge to a completely new patient population.

In the field of transplantation, immune rejection of the donor's organ by the recipient is prevented through the use of medications which restrain the immune system. Porrett refers to these immunosuppressive drugs as "highly effective but not specific," because immunosuppression drugs limit all of the body's immune responses—not just those that might damage an organ, but also immune cells that are harmless to it and may be required to respond to other threats to the body, such as bacterial or viral infection. But perhaps, Porrett theorizes, research on the immunology of pregnancy could help doctors make immune suppression far more specific. Essentially, she hopes to someday trick the immune system into responding to any donor organ—lung, liver, or kidney—in the same way that it responds to a newly developed fetus during a normal pregnancy. Transplant patients could be spared all the complications that come with immunosuppressive drugs—notably the constant vigilance to avoid exposure to infection because even a common cold could be life-threatening in the face of their bodies' weakened defenses.

"Nature has solved our problem; the body achieves immune tolerance in

pregnancy every single time," she said. "But we still don't fully understand how. Better understanding of the biologic mechanisms of fetal maternal tolerance could completely revolutionize the way we immune manage our patients because the body is capable of doing this. We just have to figure out how to influence it to do so."

The UNTIL trial will give researchers unprecedented access to observe and screen multiple women during these early stages of pregnancy, possibly allowing them to uncover new information about when and how the fetal immune system is formed.

The trial may also help improve understanding of some of the most common complications that occur during pregnancy and transplantation.

Thrombosis (blood clotting) and preeclampsia (high blood pressure during pregnancy) are two of the more common complications that occur in pregnancy as well as in uterus transplantation, but doctors do not yet know much about why either occurs even though these conditions can be life-threatening to both mother and baby. Porrett estimates thrombosis occurs in roughly 30-40 percent of uterus transplants. According to the Preeclampsia Foundation, approximately 5 to 8 percent of pregnancies are affected by preeclampsia, a disease thought to occur because not enough blood flow reaches the placenta, thereby limiting the amount of oxygen and food that reaches the fetus. This ultimately results in low birth weight.

Obstetricians see preeclampsia and eclampsia in women from all over the world but do not yet understand the biologic basis for it. It's an area of research that trial co-investigator Eileen Wang is excited about exploring through the trial.

"Our field has been plagued by the complications of pregnancy; one is

preterm birth and the other big category in terms of number and frequency is hypertensive disease in pregnancy or preeclampsia," explained Wang, the director of Obstetrical Ultrasound in Penn Medicine's Maternal Fetal Medicine Program. "I think it's a big arena to explore because right now we don't have a lot of good answers."

As Wang explains, women who enter pregnancy with vascular conditions such as hypertension, long-term diabetes, or lupus have a much higher risk of preeclampsia. Through the trial, researchers will be able to observe healthy women as a comparison. By monitoring blood flow to the uterus multiple times throughout the trial, researchers may learn how to improve the blood flow to that organ and reduce the risk of preeclampsia.

Porrett says knowledge gained from the trial will be crucial to helping researchers address these and other complications to make uterus transplantation safer and more accessible, as high thrombosis and preeclampsia rates are major barriers to offering uterus transplant therapy more broadly. She's also hopeful that the trial will help change the way women's health issues are viewed and treated for years to come.

"Ultimately, these women are enabling us to study something that is very abnormal so that we can understand something more about what is normal," Porrett said. "I'm thrilled to participate in something that may, to some extent, help raise awareness of infertility and hopefully revolutionize the care of women's health issues across the board."

□

Read this story online with related links at PennMedicine.org/magazine/utx

At the time this article published, more than 100 women from more than 25 states have entered the screening process for enrollment in the Penn trial. The UNTIL trial is still enrolling patients. For more information, visit http://www.whcrc.upenn.edu/uterine-transplantation.



A pioneer of plastic surgery in China, Song Ruyao (1914-2003) was known for his achievements aiding others who suffered; few at Penn knew what he endured in his own life.

very morning, he would arrive at Penn Tower—a blocky former hotel, converted to medical offices across the street from the Hospital of the University of Pennsylvania—and take the elevator to the tenth floor.

Penn medical students and residents in the plastic surgery division were aware that Dr. Song was something of a legend: a man who had studied at Penn in the 1940s and gone on to become a pioneer of plastic surgery in China. Warm and dignified, he was also a resource for young doctors, a living link with history.

"Just having that presence was a good thing," recalled Linton Whitaker, MD, at the time the chief of the division. "Residents could stop by and talk with him, fellows and post-graduates in training could talk to him."

But few knew what he'd endured. His younger second wife, Chen Nanping, was popular and much-loved by staff and students alike, but Song did not speak of the fate that had befallen his first wife, or what obstacles he'd faced in the process of establishing plastic surgery as a Chinese discipline.

"He'd been through a tremendous amount," Whitaker said. Now Song had returned after half a century to the campus that had given him his education, where all he wanted to do was write his memoirs. Whitaker had given him a desk in an alcove on the tenth floor. Each day Song would settle in, open a notebook, and begin to write, in long columns of Chinese characters, the story of his long and tumultuous life.

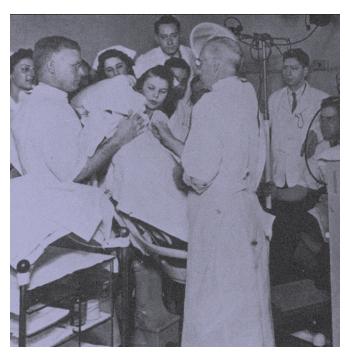
Sites of Suffering

Everywhere else, the war would be called World War II. But China would remember it as the Anti-Japanese War. And it was marked by the horror of the survivors' injuries.

Many soldiers shipped home from the front were horrifically maimed: noses blown off, jaws torn open. Song Ruyao was a young dental surgeon in Chengdu, and he never forgot the helplessness he felt. "Everyone just stared blankly at these anti-Japanese soldiers with malformed faces, unable to speak, unable to eat, suffering psychological and biological agony," he recalled many years later.

It was not the first time Song had seen extreme human suffering. When he was 12 years old, refugees from a famine had huddled outside the gates of his city, Haicheng, in Liaoning province. Many were sick with typhoid fever and officials refused to let them in. But Song's father, a practitioner of traditional medicine, went out to treat the sick. Song watched his father die of typhoid not long after.

After that, life was difficult for Song. While his widowed mother struggled to save pennies, he excelled at the local school—until it was closed after the Japanese occupied the area in 1931. Song was 16. He traveled to Jinan as a student



Robert Ivy, MD, DDS, was one of the best known and revered plastic surgeons in the United States and the first professor of Plastic Surgery at Penn.

exile and enrolled in medical school there with only his high school degree, then transferred the next year to a dental university in Chengdu, where the cost of living was lower. Even so, he could hardly afford pencils and paper. Once, he recalled years later, he broke a pen while studying, and had to tie it back together since he couldn't afford another one.

But he persevered and practiced making careful drawings to aid his education. This artwork so impressed one fellow dental student, Wang Qiaozhang, that she married him. After graduation, Song became a surgeon and teacher at Huxai University, where he was much admired for the careful sketches and watercolors he still made of each operation, which he hung up in his office.

Soon, Song found himself promoted to chair of Surgery. Yet despite being at the top of his field, he was powerless to help the wounded soldiers lying in agony before him. Some had gunshot wounds to the face, others terrible burns. There was no known surgical treatment in China that could repair such damage.

As the war continued, however, something happened that would change Song's life—and ultimately bring plastic surgery to China.

An elderly patient arrived at the hospital for dental surgery. The operation was complex: Song had to extract seven rotten teeth, flatten out the man's deformed alveolar bone, and suture the whole thing up—but the procedure went smoothly, "clean and neat" as Song recalled later.

As it turned out, the patient was no ordinary old man; as Song had guessed on sight, he was Chen Bulei, national political leader Chiang Kai-Shek's personal assistant, speech-

writer and policy-drafter, recently appointed deputy secretary general of the Supreme National Defense Council, the top organ of wartime China. A few days after the surgery, Chen's wife came to the hospital to seek out Song. Chen, she told him, had suffered so long from his rotten teeth that he'd tried to pull a tooth himself and only succeeded in passing out. Chairman Chiang himself had finally insisted that he take time off and get surgery. But now, Chen's wife told Song, Chen "didn't feel any discomfort at all."

"You are a promising young person who should be trained," she said. "He is willing to send you to the United States for further study."

Song and Ivy

In 1943, Song arrived in New York. Traveling by air, land and sea—and avoiding the theaters of war—the journey had taken him more than a month and 7,500 miles. When he'd left China, he wrote later in his memoir, it was late summer. But here, it was already snowing.

"No one was wearing a thin shirt and shorts like me. The first thing I had to do was to buy a pair of warm clothes," he wrote. "The first time I put on a beautiful new suit made in the United States, I felt a little inconvenient. I didn't know where to put my hands."

For the first year, he worked as a resident at Rochester University Hospital. But the dental and oral surgeons had been called to the front, and Song wound up as an assistant

Song Ruyao and Penn surgeon Robert Ivy were in some ways kindred souls: dental surgeons with ties to China who cared for soldiers after disfiguring war wounds.

to a brain surgeon instead of training in his own specialty. So in 1944 he traveled to Philadelphia to meet with a surgeon who taught at the University of Pennsylvania: Robert Ivy, MD (1905), DDS (1902). Recognizing Song's talent—and facing a shortage of plastic surgery trainees—Ivy invited him to stay at Penn and "make himself useful in the surgery room," as Ivy wrote later.

The two were in some ways kindred souls. Ivy had more than a passing familiarity with Chinese culture—he had spent part of his childhood and two years of his young adulthood in Shanghai, where his father, a British dentist, practiced for many years. And, like Song, Ivy had begun as

a dentist whose wartime experiences had led him toward surgery. A commissioned captain during World War I, he was posted to the office of the Surgeon General in Washington, D.C. to help plan for the care of soldiers injured in the jaw and face.

The problem before Ivy in the U.S. in 1917 was much the same one that faced Song in China in 1942: Organizing care for the incoming wounded was difficult, Ivy wrote later in his memoir, because "at that time there was no recognition of plastic surgery as a specialty and very few men were known to be proficient or specially interested in this field." In one way, however, Ivy was more fortunate than Song would be a generation later: The armies with which Ivy served had already developed some techniques through necessity in the previous years of war. Before they were deployed in the field, Ivy and his fellow surgeons were sent to train briefly at hospitals in France and England. "Thus, the Americans had the advantage of profiting from the experience of their French and British colleagues who had had to start from scratch," Ivy wrote.

Today, World War I is acknowledged by scholars as the origin of modern plastic surgery—as well as cosmetic surgery. It didn't take long for the public to realize, as plastic surgeon Max Thorek put it, "If soldiers whose faces had been torn away by bursting shell on the battlefield could come back into an almost normal life with new faces created by the wizardry of the new science of plastic surgery, why couldn't women whose faces had been ravaged by nothing more explosive than the hand of the years find again the firm clear contours of youth?"

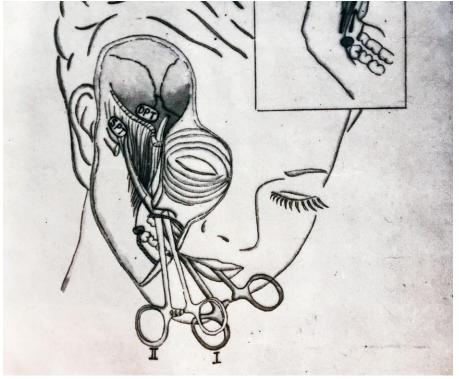
Ivy rejected cosmetic surgery as less essential than reconstructive surgery and would not practice it, but Song eager to learn everything he could—studied the nose job and other cosmetic techniques with other surgeons while he was at Penn.

Whether or not Ivy endorsed this line of study, he was impressed by Song. "Ronald Sung," as Ivy knew him, was "one of the most remarkable students" to attend Penn's Graduate School of Medicine, Ivy wrote many years later in his memoirs. Just as he had as a student in Chengdu, Song kept an exacting notebook of every operation, illustrated by watercolor diagrams and cross-sections, and this notebook would eventually become a master's thesis.

To help support Song while he studied, Ivy arranged for him to work as a teaching assistant in the department of anatomy. Between this job, his surgical residency, and his thesis, Song was extremely busy, often working late into the night.

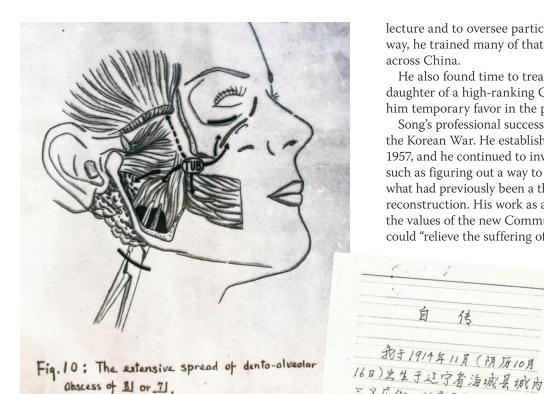
In 1946, Song's wife Wang—who would go on to be a dental pioneer in her own right—came to the U.S. on her own program of study. She was stationed first in Boston and then in New York, but they must have found time to visit: In 1948, Wang gave birth to their second child, a daughter.

In the same year, Song earned his Master of Medical Science degree from Penn and received a prestigious job offer from the university in Chengdu. It was not an easy decision for Song and Wang. The Sino-Japanese war that had sent Song to the U.S. was over, but the Communist revolution was fully underway. Their daughter was an American citizen by birth, and many of their friends at Penn advised them to stay in the U.S.





During his studies, Song kept an exacting notebook of every operation, illustrated by watercolor diagrams and cross-sections, and this notebook would eventually become a master's thesis.



At Penn in the 1940s, Song studied surgery and drew careful images of what he learned (above). In the 1990s, he returned to write his memoir (right).

abscess of 81 or 71

Nonetheless, Song decided to return. As he wrote many years later, he believed he could be useful to his country. "China needs to build," he reasoned. "The people need plastic surgery."

After Song left Philadelphia, Ivy thought often of his former student—one of Song's watercolors had pride of place in Ivy's dining room.

Decades of Turmoil

When Song returned in 1948, China was entering what would be decades of turmoil. A year later, the Communist Party took over the country, including the operations of Chengdu hospital; two years after that, the Korean War began, pitting Chinese and North Korean soldiers against South Koreans backed by the U.S. Once again, Song's skills were needed to treat the wounded. But the weapons of war were different than those used in World War II: The U.S. forces had napalm. No known treatments for the resulting severe burns existed, so Song was forced adapt extensive skin grafting techniques to save the victims' lives. There were so many wounded, and so few plastic surgeons available, that he rotated from surgery to surgery—finishing one operation, changing clothes, then immediately starting another—sometimes for twelve hours at a time. When he wasn't operating, he was training military surgeons in Changchun and Beijing, and traveling across the country to lecture and to oversee particularly difficult cases. In this way, he trained many of that generation's plastic surgeons across China.

He also found time to treat civilians—including the daughter of a high-ranking Communist leader, securing him temporary favor in the party.

Song's professional success continued in the decade after the Korean War. He established a plastic surgery hospital in 1957, and he continued to invent new surgical innovations such as figuring out a way to accomplish in a single surgery what had previously been a three-stage procedure for nasal reconstruction. His work as a surgeon seemed to align with the values of the new Communist regime: a discipline that could "relieve the suffering of the working people," Song

wrote later. He even developed a procedure to reconstruct the crushed and deformed bound feet of rural women, allowing them to walk without pain.

But the very meaning of plastic surgery was changing around him. Increasingly, under the influence of Communism, plastic surgery was being connected to bourgeois Western notions of vanity.

Song's work reconstructing the injured faces of Korean War soldiers had been seen as legitimate—as long as he did not focus too much

on aesthetic concerns. Over time, the government began to apply the concept of class struggle to plastic surgery more and more. "Emphasizing form is a capitalist style of treatment; a proletarian ought to emphasize the recovery of function," he recalled being told.

For a time just after the Korean War's end, Song had weathered a political campaign that had targeted him and other prominent doctors. His youth and his background of poverty had shielded him from attacks that were linked to the suicide deaths of some of his colleagues then.

But in the mid-1960s the Cultural Revolution began, and Song and his family would not be spared.

Song's plastic surgery hospital was condemned as a "bourgeois beauty salon" and shut down. Song himself was convicted of crimes, his home was ransacked, and his wife, Wang, was imprisoned. Song would say later that she never really recovered from her time in prison, where her back was broken. For the rest of her life she walked with a stoop, and she suffered from depression until her death in 1988.

三义庙街。父亲是个自学的莲生

据说,医术不错。在我儿类那年

山东大紫菀。紫瓦纷纷行"关东

逃生,其中有一部分受民在到达

Song himself was sent to one of the notorious "May 7th" re-education schools, where he and other intellectuals were made to study Chairman Mao's writing and do hard physical labor. Though he rarely discussed this part of his life, he later told one interviewer that he had once been forced to write his own name in the dirt, and then rub it out until all that was left was dust.

Reconnecting East and West

Song had managed to write to Robert Ivy back at Penn just once during the Communist era in China, but after the Cultural Revolution began there were no more letters. Ivy had never forgotten his friend, however. As an old man, he still talked about Song with younger colleagues, including Linton Whitaker.

When Whitaker got to know Ivy, the latter had become a "legend" at Penn. Whitaker was tasked as a young faculty



Linton Whitaker with Song Ruyao in the operating room in the 1990s.

member with chauffeuring the retired Ivy to medical conferences. "I was assigned to go get the old man," he said. "And we'd talk a lot on these car trips."

Whitaker heard the name of Song Ruyao again in the 1980s, when China began to open to the West.

Song had been reprieved from his re-education in the countryside by a moderate leader in the Communist Party. He had re-established his plastic surgery teaching hospital; the rebuilt hospital, Badachu, had 400 beds. And as China opened itself to the West, he once again began attending international conferences. On one trip to California, he visited Mann's Chinese Theater and saw the famous sidewalk where movie stars had signed their names in cement. He remembered being forced to write his name in the dirt and erase it. But upon seeing Greta Garbo's name, he wrote, his thought was, "Hey, the famous movie stars also wrote their names in the dirt with their fingers!"

He also began hosting plastic surgery conferences, inviting distinguished doctors from East and West to "learn

from each other's strengths, and jointly improve the level of plastic surgery."

As the Western doctors were escorted into the lecture hall at Badachu Hospital at the first conference in 1981, a band played "Jingle Bells"—the only Western song they knew. But Western surgeons who attended later noted they were impressed by what Song had accomplished there. Peter Randall, MD (1923-2014), then the chief of Plastic Surgery at Penn, was among them.

One night during that first conference there was a banquet for the visiting surgeons. Song, who usually wore a "Mao suit"—the Communist uniform of political correctness—came to the banquet in a double-breasted Western-style blue serge suit. It fit him perfectly. "You look very sartorial," Joseph McCarthy, MD, a plastic surgeon from New York University, complimented him. Song thanked him, adding, "I bought it in Philadelphia when I was with Dr. Ivy."

Ivy had passed away in 1974, but by inviting Randall to China, Song had made a new point of contact at the school where his mentor had worked. "The connection was re-established," said Whitaker, who in 1987 succeeded Randall as chief and today remains a professor and chief emeritus.

Song befriended both Randall and McCarthy in the 1980s, and later, when they helped found Smile Train, a charity helping children with cleft palates, Song worked closely with the organization to establish the pilot program in China.

And then, in 1992, Whitaker received a letter from Song, asking to return to Penn. "He looked at it as his beginnings and his inspiration for being a plastic surgeon," Whitaker said. "He contacted me wanting to come back to his origins."

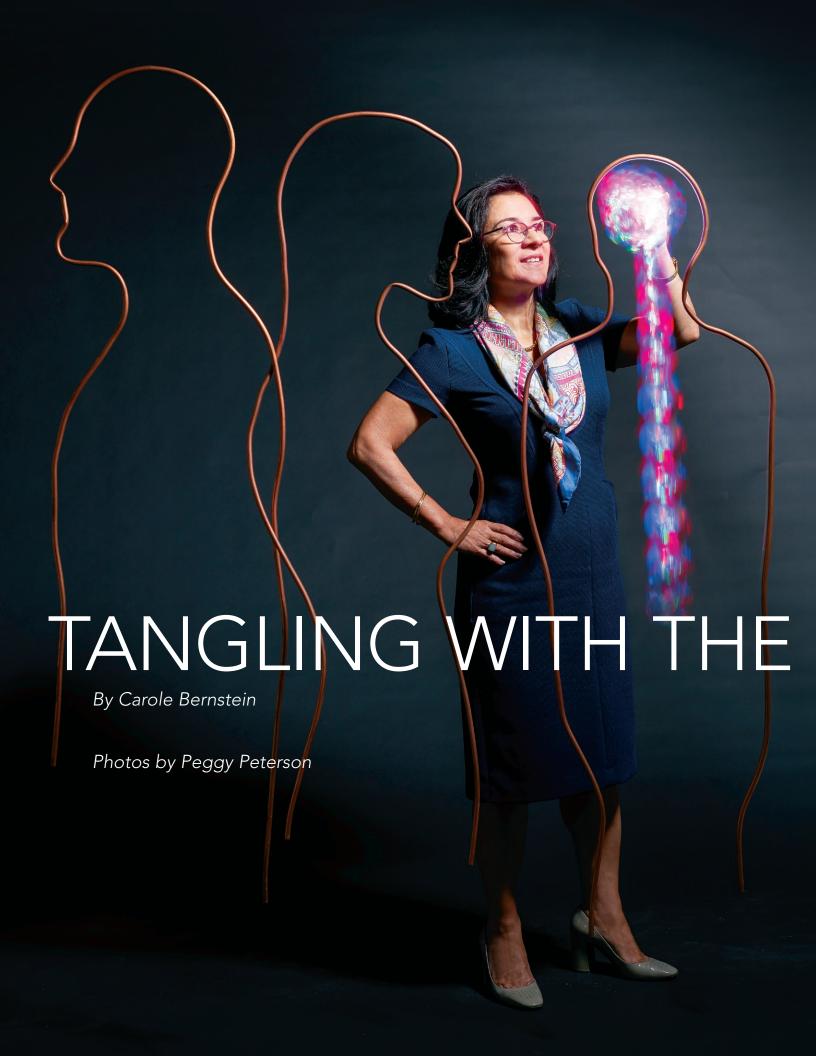
Song arrived on the Penn campus in 1993, accompanied by his second wife, Chen Nanping. Philadelphia was "a city full of memories," Chen said. Her husband visited the Graduate Hospital and the anatomy laboratory where he had worked, and reread his thesis in the library, she said.

And every day, for two years, he wrote his life story.

When he returned to China, at 81 years old, he continued to work, both performing surgery and innovating new techniques. He authored textbooks detailing the procedures he had invented. And he adapted to a changing China: Where before he had been persecuted for practicing cosmetic surgery, now demand for cosmetic procedures was constant. In 1998, commissioned by the China Medical Foundation, he hosted the first "beauty medicine" conference in China.

Song died in 2003, having lived the adage a colleague attributed to him: "A scientific worker must live into old age, learn into old age, work into old age, survive and survive, never stop." \Box

Read this story online with related links at PennMedicine.org/magazine/songruyao



Maria Oquendo, MD, PhD, is probing the human mind and brain to prevent more lives from being lost to the tenth leading cause of death in the United States.

er speech is measured and considered, so her laugh takes the listener by surprise. It is loud, ringing, a little wild, and bursting with absolute enjoyment of life.

The laughter is just part of what is remarkable about talking with Maria A. Oquendo, MD, PhD. With some people all it takes is a question or two and it's like flipping a switch; they're happy to go on and on about whatever's on their mind. But Oquendo has a quality of really *listening*. She wants to figure out exactly what you want to know. She appears to choose her words, and her answers, very carefully. Everything she says seems to express, at its core, the importance of clarity. The quality of her attention is slightly unnerving.

Most days, though Oquendo's personality exudes cheerfulness, that focused attention nevertheless is directed on exploring the darkest, most troubling recesses of the human mind: suicide.

It's the tenth leading cause of death in the United States. And it's on the rise: The U.S. Centers for Disease Control and Prevention (CDC) reported in 2016 that the nation's

SCIENCE OF SUICIDE

If you or someone you know is experiencing suicidal thoughts, contact a mental health professional. The National Suicide Prevention Lifeline is confidential and available 24 hours per day, 7 days per week to provide support, information, and local resources. Call 1-800-273-TALK (8255). The crisis text line is also available for those in crisis to connect with a trained crisis counselor via text message at 741-741.

suicide rate hit a nearly 30-year high, and this June noted that rates continued rising in every state.

Oquendo, an internationally renowned expert on mood disorders with a special focus on suicidal behavior and global mental health, joined Penn last year as the department chair and Ruth Meltzer Professor of Psychiatry at the Perelman School of Medicine. Before that, she served as a professor of Psychiatry at Columbia University and research psychiatrist at the New York State Psychiatric Institute. In 2016-2017, she served as president of the American Psychiatric Association, the largest psychiatric association in the world with more than 37,000 physician members. She can boast (but generally doesn't boast) three decades' worth of awards and honors in her field. She began her career as a clinician, but since launching her research career 20 years ago has been continuously

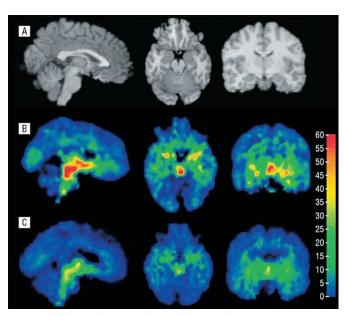
funded by the National Institute of Mental Health, has authored over 400 peer-reviewed publications, and became a member of the National Academy of Medicine.

No Easy Explanation

People who die by suicide are young and old, rich and poor. They are people's spouses, siblings, schoolmates, co-workers, babysitters, grandparents, neighbors. They have an obvious mental or physical illness or seem perfectly well. They appear to have lonely, isolated lives or fulfilling ones.

When they go, they may leave behind not just grief but guilt and questions. Those who knew them tend to speculate and try to explain why it happened. They may attribute it to a job loss, divorce, serious illness, or other hardship. I heard X's wife was unfaithful... Y's parents wouldn't pay to send her to college... It was probably because Z got fired...

But that's too simplistic, Oquendo says. The motivations for suicide are much more complex than people realize (and still not completely understood). "For many years, there's been a conceptualization of suicide as a catastrophic reaction



Oquendo's key studies have drawn on PET and MRI imaging to map brain abnormalities in mood disorders and suicidal behavior. Depressed Bipolar patients have much lower levels of Serotonin Transporter (bottom panel) than healthy volunteers (middle panel). Hotter colors (red and yellow) indicate higher binding compared to cooler colors (blue and green).

to something that goes awry in a person's life," she says. "But that doesn't really capture exactly what's happening."

She gets impatient with news accounts that implicate an external cause, like drought causing a spate of suicide deaths among farmers, and will occasionally pen a letter in response. "No, that's not why the farmers are committing suicide," she says. "I mean, okay, that doesn't help, but it's an interaction between some kind of psychiatric situation and the environmental stressor."

Oquendo's key studies have drawn on PET and MRI imaging to map brain abnormalities in mood disorders and suicidal behavior. One of the important things we now understand about suicide, she says, is that there's a biological, genetic component. Scientists are finding physical abnormalities in the brains of people who have died by their own hand. These differences have also been detected in the brains of individuals who have tried to harm themselves.

She cautions, though, that while researchers can see differences across groups of people, the findings aren't yet at the stage where a brain scan on a single individual can yield a diagnosis. So unfortunately you can't just bring someone in for medical imaging to find out if they're at risk.

Biomarkers to predict suicidal behavior, especially highly lethal behavior, are urgently needed in order to improve prevention efforts, Oquendo and her co-authors stated in a landmark 2016 brain-imaging study published in *JAMA Psychiatry*. In the paper, the researchers determined that individuals who have greater elevations in their serotonin 1A receptor are more likely to engage in more medically damaging suicidal behavior in the next two years.

The receptor is "a marker of serotonin 'tone,' if you will," she explains, likening the concept to "how active the system is in the brain." Significantly, the serotonin changes predicted how lethal the future suicidal behavior would be.

She notes, though, that just because someone has a genetic predisposition to suicide doesn't mean it will ever manifest itself. Some individuals with histories of suicidal behaviors in their families appear to be resilient to it. Oquendo also points out that treatments for conditions like depression or personality disorders can decrease suicide risk, even in individuals classified as high-risk. Therapeutic interventions matter.

Oquendo's research career is a trailblazing one, according to J. John Mann, MD, a professor of translational neuroscience in Psychiatry and Radiology at Columbia, and her mentor there. He says she is the kind of scientist who stays true to the data no matter how unpopular the findings might be. He recounts how in 2011 she published a study in the *American Journal of Psychiatry* which challenged the current thinking about lithium having certain anti-suicidal effects. "Instead of massaging the data—even though it flew in the face of all of the previous extremely promising but not as well-designed studies, and a lot of big names had lined up their opinions and reputations behind this idea—she went ahead and published." (How did the field react? "Stony silence," Mann says.)

Mann finds Oquendo's research accomplishments all the more remarkable because her path was not the traditional one. She had spent much of her career as a clinician before deciding to pursue research with his group. Mann says he had told her bluntly that her odds of success were low because she lacked sufficient background in statistics, brain biology, and imaging. "But I think that just made her more determined," he says. She tenaciously got herself up to speed, started running studies, and eventually began getting NIH grants, he says. "I don't know anybody [else] who had done that. She is amazing and inspiring."





Oquendo's professional interest is in a serious subject, but her joyful, ringing laughter is warm and welcoming to colleagues and trainees.

Defining Suicidal Behavior— Down to the Details

Oquendo calls the early 2000s "a really interesting time in suicide research" because of one particular high-profile controversy: Concerns arose among parents that prescribing antidepressants to children and teenagers might increase suicidal behavior. She notes, however, that there actually were no suicide deaths in any of the relevant studies. "Zero," she says. "But there was a lot of consternation; a lot of families were worried." But what exactly constituted suicidal behavior?

The FDA didn't have clear definitions. The agency commissioned Oquendo, then a researcher at Columbia University Medical Center, and colleagues Madelyn Gould, PhD, MPH, Barbara Stanley, PhD, and Kelly Posner, PhD, to investigate. The team created standards for defining suicidal behavior. Soon thereafter, the 2004 requirement for black box warnings—the highest level of FDA alert—was placed on all antidepressant medication labeling. The system was also endorsed by the CDC, and is now used worldwide. Oquendo and her colleagues even made it into the popular press, recognized as "Influentials" in the health arena by *New York* magazine.

In that classification system, a key refinement and extension of older such systems, the team identified sub-categories of suicidal behavior that had never been well described. One was "interrupted suicide attempt": For example, a person enters the room and knocks a gun out of the suicidal person's hand, saving their life. Another was "aborted suicide attempt," in which someone might pick up a deadly implement but then change their mind about using it. And "preparatory acts" refers to someone perhaps purchasing a deadly substance and writing a suicide note but going no further.

These subtleties are important to identify, says Oquendo, because they can be used to predict a person's future level of risk for taking their life. Columbia's John Mann agrees, and adds that, because people who engage in suicidal behavior are being found to have different patterns of suicidal ideation, different biology, and varying responses to stress, the one-treatment-fits-all approach seems increasingly inadequate. "One may need to think about different risk groups and have a strategy designed more specifically for them," he says.

Oquendo points out that psychiatrists and other therapists haven't traditionally asked their patients for a lot of details around suicidal behavior: "Clinicians often thought about suicidal behavior as a binary variable: yes or no, did they attempt to kill themselves or not." But she says the better we can describe the activities a patient has engaged in, the number of times they did them, and so forth, the better we can determine their degree of risk.

The Oquendo-Gould-Stanley-Posner classification system is not only useful for psychiatrists. The team tested a group of international experts and a group of pediatricians to see how they evaluated a set of case records. Once trained in the classifications, says Oquendo, the pediatricians were just as good as the international experts in distinguishing actual suicide attempts from non-attempts. As a result, a variety of providers can be involved in prevention efforts.

Oquendo says she's excited about a current research project to identify two new subtypes of suicidal behavior with different biological underpinnings. The subtypes are "planful" behavior in which the person methodically sketches out exactly what they're going to do, versus a person who appears to take their life on an impulse. The studies involve both brain scans and measurements of stress responsivity. Study participants are exposed to different stressors and their cortisol levels are measured. Oquendo's team has begun analyzing data; they plan to publish findings in the coming months.

Cultural (In)Sensitivity

While suicide is often viewed as the most extreme outcome of severe depression, it's important to understand that this isn't always the case, Oquendo says. She points out that suicide is seen in a variety of psychiatric conditions: Ten percent of people with alcoholism kill themselves, and 10 percent of people with schizophrenia. Eating disorders and anxiety disorders "also seem to predispose," she says.

In fact, Oquendo believes suicide should be classified as "its own thing" as opposed to a symptom of other mental illnesses. She was the first to propose that suicide be given its own diagnostic category, stating it would help psychiatrists more effectively track high-risk patients. She succeeded in getting it added to the DSM-5 in 2013, but only to the appendix: "What that tells you is there's a little bit of resistance to this concept."

She thinks the resistance may stem from a Western-centric view prevalent in the field. In Western culture, she says, one almost never sees suicide as a stand-alone phenomenon, separate from another psychiatric illness. But in India, China, and other cultures, many people who die by suicide are reported not to have an additional psychiatric condition. While acknowledging that differences in reporting may be a factor, she asserts that the way Western medicine classifies disease "doesn't necessarily have sensitivity to other cultural expressions of things." In addition to her other research, Oquendo studies mental health in countries outside the U.S. and Europe. With her former colleague Milton Wainberg, MD, a professor of clinical psychiatry and global mental health at Columbia, Oquendo is working on projects in sub-Saharan African countries including Mozambique, where there are a mere 13 psychiatrists serving a nation of 28 million people. The joint Penn-Columbia team is trying to figure out the most efficient, cost-effective ways to serve people's mental health needs when resources are stretched so impossibly thin.

Oquendo's interest in how culture and psychiatry intersect has a personal element. Half Puerto Rican and half Spanish (and the only Latina president in the American Psychiatric Association's 173-year history), she grew up in a traditional household in which girls and women were in supportive roles. She says being Latina is important to her and her identity: For example, she works hard to keep her fluent Spanish from slipping away.

The flip side of this background is that Oquendo's rise through the profession has included encounters with prejudice. "Unfortunately, I can give you a lot of examples," she quips. One incident that sticks in her mind happened a few years ago at a conference at another Ivy League university. Dressed professionally for the event, she went to the registration desk but was told her name wasn't on the list. She told the staffer, "That's really strange because I'm giving a talk in about 20 minutes." It turned out the woman was checking the support staff roster instead of faculty. "She was so embarrassed, as you can imagine," Oquendo recalls. "I actually felt bad for her."

Wainberg notes that Oquendo has worked to be inclusive of diversity "of all kinds of minorities, without compromising rigor or quality." Carolyn Rodriguez, MD, PhD, an assistant professor of Psychiatry and Behavioral Sciences at Stanford who had Oquendo as her residency director, calls her a champion of diversity and inclusiveness. Rodriguez notes that Oquendo started an annual "Celebration of Diversity" dinner at her home and took actions to increase the recruitment of underrepresented minorities. She says that in one year she increased the diversity in the psychiatry residency class significantly, from 5 percent to 25 percent.

Wainberg observes that beyond having cultural competency, a psychiatrist needs to have cultural proficiency, meaning that simply providing unbiased care isn't enough. A therapist should understand and appreciate the positive role a patient's culture may play in their well-being. "With so much diversity in the United States, we see diverse patients... [We need] that sort of more nuanced understanding of how culture plays a role," Rodriquez agrees.

Oquendo's cultural background has also contributed to her value as a mentor for past trainees, including Rodriquez, who is Puerto Rican. "It's an amazing thing as an up-and-coming researcher to see people who look like you in positions of leadership and doing well scientifically," she says. Rodriguez also fondly remembers Oquendo's accessibility as a mentor. "Maria often left her door open [to visitors], which is a wonderful thing for junior faculty and residents... and hearing her jovial laugh down the hall always put everyone at ease."

As president of the APA, how did Oquendo tackle the challenge of the Goldwater Rule barring psychiatrists from discussing political figures' mental health? Find out more about this, and read more about Oquendo's efforts in global mental health, in the online version of this story at PennMedicine.org/magazine/Oquendo.

THE POWER OF PENN MEDICINE CAMPAIGN: ADVANCING KNOWLEDGE FOR GOOD

An Up-Close Look: Education

Our students are more than "the future of medicine." By caring for you, your loved ones, children and grandchildren, they will be the stewards of our family trees. Their ability to be the next great physicians depends on all of us, coming together, to ensure every generation of worthy students will be able to benefit from our superlative Penn education.

That is why our top educational priority for The Power of Penn Medicine campaign is financial aid, with an additional \$50 million being raised—because finances and tremendous personal debt should no longer to be a barrier to our world-class program.

The Power of Penn Medicine Scholarship Challenge

Establishing a named scholarship fund is now easier than ever. Donors who participate in The Power of Penn Medicine Scholarship Challenge will receive special recognition credit and have the opportunity to make a matched gift—increasing the amount of scholarship support a student will receive. For those donors who want to go even further in their support, there is an option to make a blended gift with an outright gift and estate commitment that is also matched.

Increased access to financial aid is one of the most effective tools we have to recruit and retain top students from diverse backgrounds. In fact, 28 percent of the 2018 entering class identify as members of groups underrepresented in medicine.

And in rates that far exceed national averages, Perelman School of Medicine students are enrolling in programs to receive credentials beyond their medical degrees, including dual degrees: Approximately 60 percent of the 2018 graduating class received certificates or advanced degrees.

"Our greatest minds have already shown us where biomedical research is headed. It's our turn to heed the call and provide the resources to advance medicine's next chapter."

Dean J. Larry Jameson, MD, PhD



This past spring, the world got its first look at the University of Pennsylvania's new \$4.1 billion campaign.

What is the power of Penn Medicine? It is our people and their relentless pursuit of cures, constant striving for innovation in patient care, and a commitment to educating the dynamic future leaders of medicine.

\$1.5 BILLION

to fuel THE POWER OF PENN MEDICINE

CORE PRIORITIES



\$970 MILLION for research

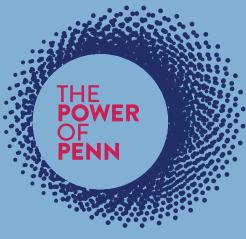


\$170 MILLION in faculty support



\$250 MILLION for patient care

\$100 MILLIONtoward medical
education, with an
additional \$50 million
for financial aid



\$2 Million Gift for Scientists in Training



Penn's 2018 Blavatnik Fellows at the Fifth Annual Blavatnik National Awards Ceremony and Gala at the American Museum of Natural History.

Financial aid isn't only about undergraduate medical education, and a visionary gift from the Blavatnik Family Foundation proves just that.

Launched with an unprecedented \$2 million gift, the Blavatnik Family Fellowship in Biomedical Research in the Penn Biomedical Graduate Studies (BGS) program will be competitively awarded to six Penn PhD students for each of the next four academic years. The fellowship ensures support for students during their work with their mentors, a pivotal relationship in their scientific journey.

"Many of our students are playing key roles in advancing major breakthroughs here at Penn thanks to BGS's expert mentors, a world-class research infrastructure, and a culture of collaboration," Dean Larry Jameson explained. "With the generous support of the Blavatnik Family Foundation, our talented Blavatnik Family Fellows will be able to transform their scientific passions into discoveries that improve human health." By 2021, the Blavatnik Family Fellowship will have impacted 24 students.

"This investment in our future will benefit cutting-edge science now and over time as these trainees grow and drive innovation in their respective fields," said Len Blavatnik, a prominent entrepreneur and philanthropist.

The inaugural class of Blavatnik Family Fellows are focusing on research projects with translational implication across many disease areas, including ocular diseases, amyotrophic lateral sclerosis, pancreatic cancer, metastasis, psychiatric disorders, and trinucleotide repeat expansion disorders, such as Huntington's disease and Fragile X Syndrome.

One Blavatnik Family Fellow, Kamen Simeonov, recently said of his research, "In the coming months, with the help of the Blavatnik Family Fellowship in Biomedical Research, we expect to have generated novel barcoded mouse models of three types of major metastatic cancers: colorectal, pancreatic, and melanoma. Using these barcoded models, we aim to create high-resolution maps of metastatic disease and ask: Why do certain cancer cells spread disease, while others do not?"

Want to learn more about supporting our students through The Power of Penn Medicine campaign and Scholarship Challenge? Visit PowerofPenn.upenn.edu, call (215) 898-5164, or drop us a line at medalum@dev.upenn.edu.

PROGRESS NOTES

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

1970s

Dennis A. Ausiello, MD'71 has joined the board of directors at Rani Therapeutics, a pioneer in oral biologics. He most recently served as chief of Medicine at



Massachusetts General Hospital (MGH) from 1996 until 2013. Currently the director of the Center for Assessment Technology and Continuous Health, he founded this program as a joint effort between MGH and Massachusetts Institute of Technology physicians, scientists, and engineers to provide real-time measurement and analysis of the human phenotype in wellness and disease.

Robert J. Spiegel, MD'75 has joined the Scientific Advisory Board in Oncology at CERENIS Therapeutics, an international biopharmaceutical company dedicated to the discovery and development of HDL-based innovative therapies for treating cardiovascular and metabolic diseases, as well as new HDL-based vectors for targeted drug delivery in the field of oncology. He has over 30 years of extensive R&D and operational experience

in biopharmaceuticals including Big Pharma, biotech, and academic startups, as well as interactions advising venture capital and private equity.

1980s

Francisco A. Arabia, MD'83 has been appointed physician executive of advanced heart failure and mechanical circulatory support at Banner Health. He is an internationally recognized surgeon and executive leader in thoracic, cardiothoracic vascular, and transplant surgery. He most recently worked at Cedars-Sinai Medical Center in Los Angeles, where he served in several leadership roles focused on advanced heart disease, mechanical circulatory support, cardiothoracic surgery, and comprehensive heart transplant programs. He will also serve as professor of Surgery at the University of Arizona College of Medicine – Phoenix, with a joint appointment at the University of Arizona College of Medicine - Tuscon.

Harry L. Leider, MD'83 has been appointed chief medical officer and executive vice president of Gelesis, a biotechnology company developing first-in class mechanotherapeutics to treat obesity and other chronic diseases related to the gastrointestinal pathway. He most recently served as chief medical officer and group vice president at Walgreens.

Richard S. Levy, MD'83, GME'86 has joined the board of directors at Kodiak Sciences Inc., a clinical stage biopharmaceutical company specializing in novel therapeutics to treat high prevalence ophthalmic diseases. He served as executive vice president and chief drug development officer of Incyte Corporation for many years.

Kathleen A. Cooney, MD'84 has been appointed chair of the Department of Medicine at Duke University School of Medicine. She is a medical oncologist and internationally known physician scientist. She most recently worked at the University of Utah



School of Medicine, where she was the H.A. and Edna Benning Presidential Endowed Professor, chair of the Department of Internal Medicine, and member of the Huntsman Cancer Institute.

David A. Mankoff, MD'85 has joined the scientific advisory board at ImaginAb Inc., an immune-oncology imaging company. He is Gerd Muehllehner Professor of Radiology, vice chair for research in Radiology, and director of the PET Center at the Perelman School of Medicine.

Ronald Alan Paulus, BS'84, MD'88, MBA'88 has joined the board of directors of Vocera Communications, Inc., a leader in clinical communication and workflow solutions. He has been the president and CEO of Mission Health, a \$1.9 billion regional integrated delivery system serving western North Carolina. He has published numerous peer-reviewed articles and speaks regularly on the topics of healthcare quality and efficiency, humancentered innovation, physician leadership, and new models of care.

1990s

Gary M. Phillips, BA'87, MBA'91, MD'92, GME'97 has been appointed president and chief executive officer of OrphoMed, Inc., a clinical-stage biopharmaceutical company developing first-in-class dimer therapeutics. He has over two decades of experience in the pharmaceutical and health care industries, leading commercial operations, clinical medicine, business strategy and development functions. He maintains an active medical license and practiced as



a general medicine clinician/officer in the U.S. Navy, from which he was honorably discharged as Lieutenant Commander.

Jin-Moo Lee, MD, GME'97 has been named Norman J. Stupp Professor of Neurology at Washington University School of Medicine in St. Louis. He studies how the brain "rewires" itself after injury to find ways to enhance recovery. He has also been instrumental in improving care for stroke patients as co-chief of the Stroke and Cerebrovascular Disease Center at Barnes-Jewish Hospital. He has worked to integrate patient care across the Barnes-Jewish network to allow smooth transitions from inpatient to rehab.

Nahush A. Mokadam, BA'94, MD'98 has been appointed division director for Cardiac Sugery at The Ohio State University Wexner Medical Center. He is an



international leader in heart failure who specializes in heart transplants and ventricular assist devices. He most recently worked at the University of Washington Medical Center as the LeRoss Endowed Professor in Cardiovascular Surgery, surgical director of heart transplant and mechanical circulatory support, and program director for the cardiothoracic residency.

Christina M. Coughlin, MD'99, PhD'99 has been appointed chief medical officer and executive vice president at Tmunity Therapeutics, Inc., a private clinical-stage biotherapeutics company focused on saving and improving lives by delivering the full potential of T cell immunotherapy. She is responsible for clinical development, program leadership, and regulatory affairs.

of the Center for Aortic Disease, co-director of the Heart Valve Repair Center, and medical director of International Medicine at Mount Sinai Health System in New York.

D. Chimene Richa, MD'05 has been appointed medical director at Knowledge to Practice (K2P), a leading provider of personalized, competency-based lifelong learning for practicing physicians, hospitals, and health care systems. Prior to this position, he was a clinical assistant professor of Ophthalmology at University of Maryland School of Medicine and also served as associate program director and director of medical student education for the department. As the medical director for K2P, he will continue limited clinical practice at the University.

2000s

Nishan M. de Silva, MD'00, MBA'00 has been appointed chief executive officer at Dermtreat, a clinical-stage biopharmaceutical company focused on mucosal diseases. He has nearly 20 years of experience in biotechnology, venture capital and health care management consulting. He most recently served as president of Poseida Therapeutics, where he helped build a clinical-stage oncology pipeline and raise more than \$70 million in funding.

Beau M. Ances, BA'93, MSc, PhD'00, MD'01 has been named the inaugural Daniel J. Brennan, MD, Professor of Neurology at Washington University School of Medicine in St. Louis. He develops diagnostic tools and treatments for Alzheimer's disease.

Allan S. Stewart, MD, GME'02 has been appointed chief of Cardiac Surgery at Miami Cardiac & Vascular Institute, part of Baptist Health South Florida. He has over 13 years of experience in transcatheter aortic valve replacement procedures, being the second to ever perform this procedure in the United States, and has completed 1,200 since. He most recently served as director



Ali Behbahani, MD'07, MBA'07 has been promoted to general partner at New Enterprise Associates, Inc. He is a health care investor focused on the biopharmaceutical and medical devices sectors. He joined NEA in 2007 and was promoted partner in 2013.

2010s

Janet Haas, MD, GME'10 has been appointed honorary chairwoman of the Pennsylvania Early Learning Investment Commission. She is also the chairwoman and a past president of the William Penn Foundation. She practices palliative medicine at the Abramson Cancer Center of Pennsylvania Hospital. She is board-certified in Rehabilitation Medicine and has cared for brain-injured patients at Temple University and Moss Rehabilitation Hospital.

OBITUARIES

1950s

Luther W. Brady, MD, GME'56, a radiation oncologist; July 20. He was a renowned radiation oncologist and authority on tumors of the eyes, and practiced medicine for more than a half century at Hahnemann University Hospital. In 2006, he founded Philadelphia CyberKnife, a Havertown center featuring the first linear accelerator with a robotic arm for performing precise radiation treatment. In the 1940s, he earned a bachelor's degree in zoology and a medical degree from George Washington University. He received post-graduate training at the U.S. Naval Hospital in Bethesda, Md.; Jefferson Medical College; and the Hospital of the University of Pennsylvania.

David Faegenburg, BA'52, MD'56, a radiologist; May 10. For nearly 50 years, he was a committed and esteemed radiologist. He excelled in school and attended the University of Pennsylvania on full scholarship, first as an undergraduate and then at its medical school.

John M. Akin Jr., MD'53, GME'60, a surgeon; March 1, 2013. He attended Birmingham-Southern College where he was president of the student body, an SAE, ODK, Magna Cum Laude, and voted by faculty as Senior Contributing Most To The School. In 1949, he entered the University of Pennsylvania and was elected to AOA honorary society. He interned and completed his surgical residency at the Hospital of University of Pennsylvania. He became chief surgical resident and diplomate of the American Board of Surgery. In addition, he was a captain in the United States Air Force Medical Corps at Eglin Air Force Base in Florida from 1955

until 1957. He entered the private practice of general surgery at Montclaire Baptist Hospital in Birmingham, Ala., and was director of the surgical residency program, which he helped establish, for many years. He taught thirdyear medical students at the University of Alabama School of Medicine. He was president of the Jefferson County Medical Society in 1976, vice president of the Medical Association of the State of Alabama in 1978, president of the Birmingham Academy of Medicine in 1974, on the board of directors for the American Cancer Society, a member of American College of Surgeons, and a member of Norton Board of Birmingham-Southern College.

1960s

Joseph H. Wearn, MD'64, a former pediatrician; Dec. 16. He was a pediatrician for three generations of children in the region of Tacoma, Wa. He was an early advocate and leader in establishing Mary Bridge as a regional medical center for children and the newborn intensive care unit at Tacoma General. He served in the U.S. Army and was an Eagle Scout. He received the Wright Brothers Master Pilot Award for 50 years of safe aviation flying, and he was an advisor and mentor for Aviation Explorers, Post 1735, at Tacoma Narrows Airport.

Herbert M. Loyd, MD, GME'66, a retired radiologist; Aug. 20, 2017. He graduated magna cum laude from the University of Texas in 1955 with a BA in Zoology and was elected to Phi Beta Kappa. He was voted the outstanding pre-medical student by the faculty. He received his medical degree from Louisiana State University in New Orleans in 1959, was elected to AOA honorary society, and served a rotating internship as senior assistant surgeon at the Public Health Service Hospital in Baltimore. Following the internship, he fulfilled his military obligation at the National Institutes of Health in Bethesda, Md. and later began a four-year residency program in radiology at the Hospital of the

University of Pennsylvania, and served a fifth year as a staff radiologist to complete his specialty training. He joined Houston Methodist Hospital in the Texas Medical Center in 1967 as a diagnostic radiologist, became chief of the Scurlock Outpatient Department in 1980, and retired in 1997. During that time, he also served as clinical associate professor at Baylor College of Medicine, Houston, where he was recognized as a gifted teacher. He was a Diplomate of the American Board of Radiology, a member of the Radiological Society of North America, Texas Radiological Society, and Houston Radiological Society. In retirement, he enjoyed volunteering and teaching weekly seminars to transitional radiology residents and technicians at Methodist Hospital.

Irving S. Wiesner, BA'62, MD'66, a psychiatrist; April 9. He received a fellowship in Child and Adolescent Psychiatry at the Pennsylvania Child Guidance Center, and completed his residency at the University of Pennsylvania Health System and the Albert Einstein Montefiore Medical Center. He was a practicing psychiatrist at Swarthmore Medical Center with prior training in internal medicine and gastroenterology. He was the past chairman of the Committee on Religion, Spirituality, and Psychiatry of the American Psychiatric Association; the past president of the Psychiatry Section of the Christian Medical and Dental Association; and the author of three books dealing with psychiatry and the Christian faith.

1970s

Herbert I. Goldberg, MD, GME'71, an emeritus professor in Radiology; March 26, 2017. He graduated from the University of Vermont College of Medicine in 1956 and completed an internship at Bellevue Hospital. He completed his residency at Penn Presbyterian Medical Center and received a fellowship at New York Presbyterian Hospital-Columbia Presbyterian Center. In 1967, he became a professor of Radiology; in 1978, he became a

professor of Radiation Oncology; and in 1984, he became a professor of Neurosurgery. In 1992, he joined the 25-Year Club at Penn, and became emeritus professor of Radiology in 1998.

Norma O. Goldstein, PhD'71, a retired biologist; April 12. She received her bachelor's degree from New York University in 1942, her master's degree from Columbia University in 1949, and her PhD from the University of Pennsylvania in 1971. She was a cell biologist whose work spanned peri-

ods at Woods Hole Marine Biological Laboratory (now Woods Hole Oceanographic Institution), the University of California at Berkeley Department of Zoology, Memorial Sloan Kettering Cancer Center and multiple research laboratories at the University of Pennsylvania. She worked at the University of Pennsylvania for the last several decades of her career, where she studied animal and human gene sequencing to illuminate their relationship to aging and pathology of human heart, lung and skin diseases.

Morris Tobin, BS'67, MD'71, a nephrologist; June 18. He graduated from the University of Pennsylvania with a Bachelor of Science in Chemistry in 1967 and a Doctor of Medicine in 1971. He went on to receive his specialty training in Internal Medicine and a fellowship in Nephrology at the University of Buffalo. After completing his training, he relocated to Paris, Tex., to start his private practice in 1979. He served the Northeast Texas and Southeast Oklahoma community for almost 40 years

In Memoriam: Jerry Rabinowitz, BA'73, MD'77



Jerry Rabinowitz, MD, was a family physician known for his warmth and compassion, his smile, and his signature bow tie. He was a president of his congregation, Dor Hadash, which met at the Tree of Life synagogue in Pittsburgh. On Oct. 27, 2018, Rabinowitz was among 11 congregants killed there in a mass shooting in which the perpetrator reportedly expressed anti-Semitic hate.

"He was one of the finest people I've ever met in my life. He had a moral compass stronger than anyone I have ever known," his practice partner Ken Ciesielka, BA'74, MD'80, told the *Pittsburgh Post-Gazette* in the aftermath of the shooting.

Rabinowitz was born and raised in New Jersey and attended the University of Pennsylvania for his undergraduate and medical degrees. He completed a residency at what is now UPMC Shadyside Hospital. After his graduation from Penn, he was a member of the Thistle Society and Ivy Stone Society, signifying multiple consecutive years of philanthropic support to the University and Penn Medicine.

"PSOM joins Dr. Rabinowitz's family, his patients, and his community in mourning his untimely and tragic loss," Dean J. Larry Jameson, MD, PhD, and Senior Vice Dean for Medical Education Suzi Rose, MD, MSEd, wrote to the Perelman School of Medicine

community and alumni. "We share our outrage as well as sadness over these horrific events," they added, referencing a series of hate-filled acts within a 96-hour period that included, in addition to the synagogue shooting, multiple attempted bombings of public figures and a racially targeted shooting in a grocery store.

Rabinowitz's life exemplified the highest ideals of compassion and care in medicine. In his primary care practice with his long-time friend Ciesielka, Rabinowitz cared for multiple generations. He was known for visiting patients at home, sometimes just to check in and talk, and for spending time helping patients understand their conditions.

In the early days of the AIDS crisis, when the disease remained poorly understood, Rabinowitz made a mark as a beloved physician for his caring focus on his vulnerable patients, including those in the LGBT community. "Before there was effective treatment for fighting HIV itself, he was known in the community for keeping us alive the longest," an HIV-positive former patient from that time, Michael Kerr, wrote on Facebook. "He often held our hands (without rubber gloves) and always, always hugged us as we left his office."

"He was my doctor and doctor to my entire family—three generations of us," one patient wrote in a comment in the *Pittsburgh Tribune.* "More than that, he was God's hands in the material world: healing, upholding, caring. He healed so much brokenness in this city."

as a devoted physician and helped establish the first dialysis unit in NE Texas along with the Sisters of Charity of the Incarnate Word from San Antonio. Throughout his career he served as chief of Medicine at St. Joseph's Hospital in Paris, Tex., and served on various committees at St. Joseph's and McCuistion hospitals, including ICU, Pharmacy, and Infection Control. He worked as a consulting physician for the Choctaw Nation in Oklahoma since starting his practice. Most recently he was on staff at Trinity Mother Francis in Sulphur Springs, Tex. He was a large advocate and supporter of Doctors Without Borders.

Janet De Hoff Sparks, MT'72, PhD'80, a professor; Dec. 3. She earned a degree in medical technology from the University of Pennsylvania School of Allied Medical Professions, followed by a PhD at Penn and a post-doctoral fellowship at the Wistar Institute. For 35 years, she was a professor of Pathology and Laboratory Medicine at the University of Rochester. Throughout her entire life, she worked in cardiovascular diabetes research and was a member of many organizations and a fellow of the American Heart Association. She authored numerous scientific publications and was involved in peer review activities serving as a member or chairman of multiple review panels. She served as director of a graduate cluster as well as a member of departmental and university committees.

Donald B. Thornton, MD'72, a physician of pulmonary disease; Dec. 10. He graduated from the University of Michigan with a BSE in Bioengineering and worked for North American Rockwell Corp as a Human Factors Engineer where he worked on life support systems and workspace analysis for the Apollo 7 mission. He received a fellowship from the University of Pennsylvania School of Medicine and studied further at the University of Washington School of Medicine where he had a Post-Doctoral Fellowship in Pulmonary Disease Research. Following internship and residencies, he

joined the U.S. Navy Reserve as a medical officer. Beyond his private practice in San Diego, he provided medical services to poverty-stricken communities in Africa and serviced incarcerated populations in Michigan.

Harvey E. Bernstein, MD'73, a pediatrician; April 6. He received his medical degree from the University of Pennsylvania and completed his residency at Albert Einstein College of Medicine at Jacobi Medical Center. He worked at Smithtown Pediatric Group as a pediatrician.

Dong Myung Kwak, MD, GME'75, a physician; May 5. He received his bachelor's and medical degree from Pusan National University in South Korea and completed his residency at the University of Pennsylvania in Philadelphia. He was a physician at Overlook Medical Center in Summit for over two decades and, most recently, at various surgical centers in New Jersey.

1980s

Lawrence Scott Linder, MD'88, a former director of emergency medicine at the University of Maryland Baltimore-Washington Medical Center; May 1. He received his bachelor's degree at Franklin & Marshall College and his medical degree at the University of Pennsylvania. During medical school, he sang in the university choir and once performed at Carnegie Hall. He conducted his internship and residency at Christiana Hospital in Newark, Del. In 1991, he moved to Maryland and joined the staff of then-North Arundel General Hospital where he served as chief of Medicine. His final post was chief executive officer of the University of Maryland Community Medical Group where he retired.

FACULTY

Herbert I. Goldberg, MD. See Class of 1971.

Norma O. Goldstein, PhD. See Class of 1971.

LEGACY GIVING

The Heart of the Matter

An IRA Gift Honors HUP's Life-Giving Transplant Team

Over the course of six years, pharmacist Bill Jaeger, of Reading, Pa., would suffer a staggering seven cardiac arrests. Even after receiving a pacemaker/defibrillator and, later, undergoing a heart ablation, his heart just couldn't recover.



"We learned a few months after the ablation that Bill would need a transplant," Doris, his wife of more than 40 years, said. "The ten-and-a-half-month wait for a new heart was long and worrisome. His transplant doctor at Penn Medicine, Mariell Jessup, and the heart failure team—always just a phone call away—made us feel that everything would be fine, and we couldn't have been more grateful for their confidence and comfort."

The Penn Heart Transplant Center is the largest such center in the Mid-Atlantic region, and one of the top three heart transplant programs in the U.S.—with more than 1,000 procedures performed since the program's 1988 inception.

It was September 2014 when Bill received his new heart at Penn Medicine. "There are no words to describe the power of 'the [transplant] call,'" Doris said.

"Penn Medicine gave me a second chance at life, and I plan to use it to make a difference," Bill said. "It is very important to future generations that Penn Medicine be here to provide the quality care and experience that we have available to us now."

The Jaegers chose to show their enduring gratitude by supporting Penn Medicine through annual gifts and by initially including a bequest in their will. But then they learned that naming the Division of Cardiovascular Surgery as a beneficiary of their IRA might produce additional tax advantages for their children. Their new planned gift of retirement assets will make a future impact at Penn in a way that makes sense for the entire family.

"Using an IRA beneficiary designation allows us to make our gift tax-free to Penn," Bill and Doris said. "The IRA would be taxable if inherited by our children, so we decided it made a better gift for Penn Medicine."

"And with Doris in good health, we were able to purchase an additional life insurance policy with her as the insured. This allowed us to replace the funds we are gifting because the death benefit of the insurance policy can go to our children without being subject to taxes," they explain. "The required minimum distributions we must take from our IRA each year more than cover the premiums of the life insurance policy. It is a win-win for us, our children and Penn Medicine."

Naming Penn Medicine as a beneficiary of your IRA is a wonderful and easy way to supplement the generous support you provide during your lifetime. Figuring out how a beneficiary designation can work best for you, your family, and your philanthropic goals is what we do best. Speak with us to learn more about giving options. Contact Christine S. Ewan, JD, Senior Executive Director of Planned Giving, at 215-898-9486 or cewan@upenn.edu.

For more information, please visit our website at: www.plannedgiving.med.upenn.edu.

Penn Medicine Innovators Aim to Redefine the Electronic Health Record



ew innovations in modern medicine are simultaneously as celebrated and maligned as electronic health records (EHRs). Progressing far beyond the premise of a paper chart—simply documenting a patient's symptoms, diagnoses, and clinical care plans—they have grown into a vital tool in delivering care. They are a platform for ordering tests and prescriptions, for processing billing to insurers, for coordinating care across inpatient and ambulatory settings, and even for preventing errors.

But at the same time, when it comes to using this vital tool, it's clear that EHRs have some problems. For physicians and other clinicians to keep an electronic health record populated with all the essential information, and for physicians to find the most important information to make decisions about a patient's care, one side effect is what some describe as "death by a thousand clicks."

Some providers worry about a general decline of humanism in medicine: schedules are busier, workdays are longer and they may spend less time looking patients in the eye and more with eyes on the screen. "There is an increasing sense

that current day EHRs play a significant role in contributing to provider burnout," said C. William Hanson III, MD'83, GME'89, chief medical information officer at Penn Medicine. "It's time to turn our attention from deployment to refinement, to help doctors provide better care to our patients."

In that context of balancing promise, practicality, and pain, Penn Medicine has launched an ambitious new plan to transform EHRs—turning them into more streamlined, interactive, smarter tools that ease the work of clinicians, expedite care, and drive the best possible patient outcomes.

"Increasingly, health information technology plays a foundational role in each domain of our work: patient care, educating the next generation of physicians and scientists, and biomedical research," said J. Larry Jameson, MD, PhD, executive vice president of the University for the Health System and dean of the Perelman School of Medicine. "Electronic health records innovations are key to advancing our impact in each of those missions."

Penn Medicine experts have already begun to map new approaches to EHR design. In a recent Perspective piece

published in the *New England Journal of Medicine*, David A. Asch, MD, MBA'89, GME'87, executive director of the Penn Medicine Center for Health Care Innovation, and his colleagues suggested that a restructuring of the EHRs should allow doctors to "subscribe" to their patients' clinical information to receive real-time updates when an action is required, similar to social media feeds and notifications.

The Penn Medicine Nudge Unit within the innovation center has developed approaches to ensure that patients are referred for lifesaving cardiac rehabilitation following heart attacks, that statins are prescribed to those who need their cholesterol managed, and advanced CT scan imaging is provided to all patients who need it, but not to those who don't. Each of these care improvements was facilitated through a redesign of Penn's electronic record system to serve physicians' needs as they care for patients. And Penn Medicine data scientists and clinicians working in teams across the health system are developing other innovations that also may be built into the EHR in the future after being piloted in clinical settings; an example is "Palliative Connect," which empowers palliative care specialists to proactively reach out to front-line physicians caring for seriously ill patients who would be likely to benefit from a palliative care consultation, as identified by a predictive algorithm.

"Ultimately, we need to move past the idea that the EHR is just an administrative tool, and see it as a clinical tool—like a scalpel, or a medication, or an X-ray machine," Asch said. "We judge these tools by the degree to which they facilitate good patient care, and we should be judging the EHR against the very same standard."

Penn Medicine is asking everyone involved with EHRs to step forward and develop their innovative ideas. This fall, a new innovation tournament launched to identify the earliest targets for EHR transformation. Teams from across the health system including IT experts, data scientists, and clinical educators will work alongside clinicians and staff to help develop, test, and refine improvements. The health system will also be introducing "sprints" in which clinical groups can work together with the different teams to streamline and improve EHR interactions and engagement with email and other digital media.

"Every day, we're supporting, learning and running tests to investigate new ideas in the clinic, lab, and the classroom. Our best ideas come from within our walls," said Ralph W. Muller, CEO of the University of Pennsylvania Health System. "With this initiative, the future of electronic medical records will be written by those working each day at Penn Medicine." □

More from Penn Medicine Online

Has Penn Medicine's recent growth left you wondering about new and unfamiliar buildings in the illustrations for this issue's cover story? Find a key to these illustrations and more explanations of this issue's art in the online version of the magazine. The online version also includes behind-the-scenes insights into how photos in this issue's pages were created. Find all the extras at PennMedicine.org/magazine.

In the Spring Issue: Leadership in a New Era of Health Care

"Health care in the United States suffers from a persistent and worsening disconnect between the capacity of the physician-leadership workforce and the needs of our expanding and increasingly complex health systems," write Dean J. Larry Jameson, MD, PhD, and Caryn Lerman, PhD, vice dean for strategic initiatives in the Perelman School of Medicine. "Closing this gap will require leadership skills that are not acquired during traditional medical training." In the next issue of *Penn Medicine*, we look at how these words, published in the *New England Journal of Medicine* this spring, are prompting Penn's medical and business leaders into action.



Penn Medicine and Wharton Executive Education are joining forces to launch an executive health care leadership program that will offer participants from across the country a strategic toolkit to cement their ability to lead at a time when science, technology, and economics are reshaping the practice of medicine and altering the field's economic landscape.

There is still time to be part of the program! "Leadership in a New Era of Health Care" begins with a four-day course in March 2019. For more information, visit WhartonPennMedLeadership.com.

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A quarter century ago, the University of Pennsylvania Health System (UPHS) formed as one of the first integrated academic health systems in the U.S. "If you look at the top hospitals in the country today, most are part of integrated systems," said UPHS CEO Ralph W. Muller. "But integration alone is not what makes us great." There are five key ingredients, Muller and other Penn Medicine leaders say, that have made the organization a success.

Find out more on p. 14.

