



Features

- 12/ **Needed: better strategies for combating the opioid epidemic**
For decades, doctors and community advocates have worked together to combat the epidemic of substance use disorder. Lately, that battle has seemed harder than ever. *By Steve Hamm*
- 18/ **Alternatives to opioids**
How a Yale scientist is looking for painkillers that target sodium channels, not opioid receptors. *By Ashley P. Taylor*
- 22/ **The road back to good health**
Each year substance use disorder robs millions of people of health, self-respect, and even life. Patients who make their way to treatment follow an arduous but trafficable path. *By Jenny Blair, MD '04*
- 26/ **History of substance abuse**
For as long as they've had the ability, humans have sought natural sources for stimulation and relief from pain and injury.
Compiled by Adrian Bonenburger
- 34/ **How treatment for addiction came out of the dark ages**
Non-addictive pain medication has changed how experts approach therapy for substance use disorders. *By Sonya Collins*
- 38/ **A mother's love**
Spreading a Yale pediatrician's intuitive, unorthodox, effective treatment for opioid-dependent newborns. *By Christopher Hoffman*

winter 2018 departments

2 From the editor / 3 Dialogue / 4 Chronicle / 9 Round Up / 40 Capsule / 42 Faces / 46 Q&A / 48 Books / 49 End Note

Fighting addiction

For the first time since the 1960s, life expectancy declined in the U.S. two years in a row. Remarkable given the absence of a major war, this corresponds with increases in death-by-overdose among young men and women. While many hoped that the 21st century would witness significant reductions to dependent relationships with various substances and activities, the problem has endured and even proliferated.

The current crisis is relevant to every one of us. Not just because few people go unaffected by the epidemic—those lucky enough not to have lost friends or kin to addiction

almost certainly know others who have—but also owing to the way in which its intensification involved and continues to affect the medical community.

It's complicated, of course. If solving the crisis was only a matter of tactical shifts, such as different attitudes toward the treatment of physical pain, doctors could adjust their behavior and expect to see significant progress in ending the epidemic. A quick glance at the history of humankind's relationship with drugs, however, confirms the lament that there is "no new thing under the sun": crises like these have occurred before, and successfully resolving them

has required more than swift, decisive action, though that is needed too.

Some successful efforts to combat the crisis have begun here at Yale. Pioneered by students, faculty, and alumni, our community has conceived of, tested, and implemented programs and techniques that show great promise in helping to halt the epidemic. It's inspiring to be able to share stories of how the school's faculty and alumni apply their expertise to such a pressing social need. Their innovations will certainly have an impact on the struggle to gain control over the deluge of overdoses.

Shelter from the Storm is my first issue as editor of *Yale Medicine Magazine*, and I can't think of a more pressing topical theme than this to cover. Every one of us can help shape solutions by thinking more carefully about the way we talk and think about drugs and those whose lives are affected thereby. We can be more careful with the words we choose, the choices we make in describing serious health challenges. Ultimately, we're all in this together, and beating the opioid epidemic is going to take all of us, working in concert to check the rising tide of this public health crisis.

Adrian Bonenberger
Editor, *Yale Medicine Magazine*

SECOND OPINION BY SIDNEY HARRIS



Send letters and news items to

Yale Medicine Magazine, 1 Church Street, Suite 300, New Haven, CT 06510 or email ymm@yale.edu. Please limit letters to 350 words and include a telephone number. Submissions may be edited for length.

Editor

Adrian Bonenberger

Contributing Editors

John Curtis
Robert Forman
Kathy Katella-Cofrancesco
Jill Max
Kathleen Raven

Senior Writers

William Hathaway
Ziba Kashef
Karen Peart
Cathy Shufro

Contributors

Jenny Blair, M.D. '04
Sonya Collins
Steve Hamm
Christopher Hoffmann
Natasha Strydhorst
Ashley P. Taylor

Art Director

Jennifer Stockwell

Copy Editors

Elaine Alibrandi
Rebecca Frey, Ph.D.

Mailing List Inquiries

Maya Szatai
Visual Design Specialist
Cheryl R. Violante
Website Coordinator

Printing

The Lane Press

Correspondence

Editor, *Yale Medicine Magazine*
1 Church Street, Suite 300
New Haven, CT 06510-3330
Telephone: 203-785-5824
Facsimile: 203-785-4327
Email: ymm@yale.edu
Yale Medicine Magazine is distributed to alumni, faculty, students, and friends of Yale School of Medicine.

Yale School of Medicine

Robert J. Alpern, M.D.
Dean and Ensign Professor of Medicine
Mary Hu
Associate Dean for Communications and Chief Communications Officer
Charles Turner
Director of Medical Development
Deborah Jagielow
Director of Alumni Affairs

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Balancing patient pain with ethical treatment: a doctor's dilemma

THE MEDICAL PROFESSION has gone back and forth in its approach to pain treatment. Alcohol and opioids, once seen as miraculous and valid ways to assuage pain from injury or chronic disability, are now viewed—and used—differently. Dean Robert J. Alpern, M.D., discusses what has changed since he was trained as a physician—and what that bodes for the future.

Has the landscape changed in terms of how the medical community discusses individuals with substance use disorder challenges? Many years ago the treatment of pain was dominated by the traditional philosophy of “do no harm.” We as physicians undertreated pain due to the fear of causing addiction and overdoses. Then there was a period when medical professionals saw undertreatment of pain as a kind of harm, and we went through a period of increasingly aggressive pain treatment, which led to the development and expansion of pain as a specialty. Medical schools and health systems began developing and expanding pain programs, because as it turns out, it’s very difficult to treat pain effectively.

Most recently, we’ve seen that pain treatment that frequently relies on opioids has secondary and even tertiary consequences, causing an epidemic of addiction and overdoses. Now the medical profession is pulling back, trying to find the right balance.

Do you feel that part of the issue with substance use disorder surrounding pain medication involves the idea that one should not have to feel any pain? No, I don’t think so. Medically, you were always balancing the patient’s comfort with risk to the patient’s health. The ideal would be to treat pain in ways that don’t involve opiates. Steve Waxman’s research into blocking specific sodium channels that affect the sensation of pain is extremely promising. But there’s a danger, too. If you block all pain sensation, a patient could burn themselves and not know it. There’s a reason we feel pain.

What’s the School of Medicine’s role in the substance use disorder epidemic? Yale is very strong in substance use disorder research. Our faculty in psychiatry, general internal medicine, and emergency medicine are world-class experts on the subject. Substance use disorder spans many variables so, while many of them work in opioid addiction, others focus on tobacco, alcohol, food, and other things. In every case, Yale should be among the first to take the most effective practices to the bedside. I hope that in the near future, someone suffering pain will be able to receive treatment specific to their ailment that isn’t addictive.



Patient navigators address barriers to health care

PRISCILLA WANG, M.D. '17, recalled a frightening moment at her patient's house. She watched in dismay as the man, who had disabilities, clung for balance to flimsy towel bars in his bathroom.

"It made me really upset. ... He could easily fall; he could break his hip because of this unsafe arrangement," Wang said. Yet his health insurance did not make funds available to help prevent a potentially catastrophic and expensive injury.

"This experience was really eye-opening, in that it made me realize that it's in the day-to-day settings that health is determined," she said.

The home visit took place as part of a pilot patient navigators program Wang co-founded in 2016. The Yale Patient Navigator Program (PNP), pairs nine teams of senior and junior medical students with patients from Yale's primary care clinics who face serious social barriers to health. Supported by lectures from faculty, social workers, and New Haven outreach workers, and through visits with patients, the students learned to go beyond brief clinical encounters in

order to listen to and learn what patients are up against, and provide meaningful support.

"Many of the problems we address in the hospital are not necessarily biological in their root causes. There are many ways in which medical students can meaningfully address these deeper issues," said Wang, who worked on the project before her graduation last May.

Indeed, the quest for better health asks a lot of patients—literacy, transportation, disposable income. Being unable to read, travel to the doctor's office, or pay for parking can derail even the best medical advice. Many people risk being fired if they miss work for a doctor's appointment. Others contend with domestic abuse or the criminal

justice system. Cars break down, buses don't serve the neighborhood or don't arrive, and missed appointments ensue, which can lead providers to discharge patients from the clinic. People may lack information about healthful living or support for quitting tobacco, or are confused by their doctors' instructions. Some people simply mistrust the health care system. Such problems don't get much space in formal med school curricula.

So the student navigators helped their patients make sense of multiple bottles of medicine. They connected people to food assistance, discounted transportation, and low-income housing. One man lacked a phone, so his student team signed him up for a free Obama Phone (cell phones for low-income Americans).

Nisha Dalvie, then in her first year of medical school, accompanied her patient, a man in his 50s, to the courthouse for help with housing; to his physical therapy; and to the housing authority. Not only did he contend with diabetes and a condition causing muscular weakness, but he also had low literacy. He had trouble reading forms and medication instructions, but he didn't want to attend a nearby literacy program and reveal his difficulty to people he'd known since childhood. Dalvie and her teammate, fourth-year medical student Sean Maroongroge, helped him obtain tutoring in another part of town where he could study in anonymity.

“It was great to see how many things were available for him by basically just googling things and emailing people, trying to figure out what we could do,” Dalvie said. “There’s so much out there, and you really don’t learn it in medical school.”

The PNP is an outgrowth of Students for a Better Healthcare System, which M.D./Ph.D. student Lorenzo Sewanan and several other students founded in 2012 to help educate New Haven residents about the Affordable Care Act. During teach-ins they conducted in schools, churches, and at the School of Medicine, the students picked up on problems that go beyond health insurance. “Even though more and more people were having ‘access’ to health care or at least health care insurance,” Sewanan said, specifying the quotation marks, “it didn’t necessarily mean they were getting to receive the best care or getting the benefits of that care.”

The difficult world some patients inhabit was uncharted territory for students like Dalvie, who said she had a privileged upbringing.

“There’s a lot of tension in this city, I feel, between people who are impoverished and the students, who are most often not,” Dalvie said. “I hadn’t really seen it like that in any other place where I’d been, where those who didn’t have as much were so in the forefront of the city. ... We got to see how all of these issues extend beyond the clinic.”



Co-founded by Wang, Sewanan, Eamon Duffy, Julianna Berk-Krauss, and Matt Meizlish, and supported by several physician advisors, including Pinar Oray-Schrom, M.D., HS ’02, assistant professor of medicine (general medicine), the program completed its pilot year to rave reviews from students who participated. One student called it “one of the most formative experiences of my Yale career.” Another wrote, “There is nothing at Yale more patient-centered than this.”

Patient navigation has its roots in a program started by Harold P. Freeman, M.D., in Harlem in 1990 to assist primarily the poor and uninsured to access cancer care; it grew to become the Harold P. Freeman Patient Navigation Institute, which now trains navigators all

over the country. New Haven’s Gateway Community College also offers training.

Sewanan said the student program was also inspired by “hotspotting,” an approach pioneered by Jeffrey Brenner, M.D., in Camden, N.J., in which teams of providers work directly with high-risk patients who use the most health care services. The teams address social needs as well as smoothing paths through the health care system, with a resulting drop in the need for hospital services.

For Wang, learning more about her patient’s life was such a powerful experience that she switched career plans while on the residency interview trail.

First-year medical student Nisha Dalvie joined hoping to help patients navigate the health care system. Volunteering with the Patient Navigator Program offered a way to help the community while also broadening her understanding of what types of challenges patients face.



ONLINE EXCLUSIVES

Last November, Yale School of Medicine doctors, PhDs, lawyers, activists, and recovering addicts gathered to brainstorm solutions to the epidemic of opioid use.

For more on story, visit ymm.yale.edu/opioid

Wang abandoned her plans to train in categorical internal medicine, instead landing a last-minute spot in the primary care residency at Harvard's Brigham and Women's Hospital in Boston—a change of heart for someone who began medical school interested in orthopaedic surgery.

“It’s a really humbling, a really powerful experience to step into a patient’s home and see the challenges that they live with on a day-to-day basis,” she said.

This year, navigators are expanding their reach to include patients with diabetes and mental health issues. They’re also adding students from other fields, including nursing students and social work students from Southern Connecticut State University.

With the Affordable Care Act and social services under threat in the current political climate, patients and physicians face ever-stiffer headwinds. Still, Sewanan believes that patients and medical students possess the power to make an impact. “If we can’t achieve what we want at the policy level,” Sewanan said, “I think there’s still a lot that can be done at the personal, individual level.”

— Jenny Blair, M.D. '04



YSM offers a leg up to students aspiring to medical careers

At the age of 42, Shermaine Hutchins has more life experiences under his belt than many of his classmates at the School of Public Health. He was raised in Daytona Beach, Florida, by a single mother who provided for him and his younger brother with her wages as an aide in a retirement home. He graduated from high school in 1993, unsure of his path in life, and climbed up the ladder at McDonald's from “fries to manager.” In 1998, he joined the Army, trained as a medic, and served on a humanitarian mission in Nicaragua, where he cared for his fellow troops and local villagers.

He mustered out in 2002, still not knowing where life would take him. A chance encounter in a mall led to a job as a DJ at a radio station that played rhythm and blues and hip-hop. Again, he rose up the ladder, continuing as an on-air personality while taking on behind-the-scenes roles in management and production. His career took him to Ohio, where he saw the writing on the wall for “terrestrial” radio. Spotify, MP3 players, and streaming services were changing how people listen to music and challenging radio's business model. In search of a more secure livelihood, Hutchins thought back to his time as a medic and decided to become a nurse. He began taking pre-med courses at Owens Community College in Toledo.

Then, two things happened. He decided he'd rather be in health care management than in clinical care. And he was accepted into Yale's Summer Medical

and Dental Education Program (SMDEP). Yale, along with other schools, had offered the program, funded by the Robert Wood Johnson Foundation, since 1997 to help college students from disadvantaged backgrounds learn how to navigate the med school application process and teach them basic science knowledge and communications skills.

In 2013, Hutchins was one of 80 students from around the country who came to Yale for the six-week residential program. He arrived with some trepidation. Ivy Leaguers, he was sure, would be rich stuck-up snobs. “I had all those preconceptions,” he said. Instead, he found an accepting and welcoming environment filled with “regular people who just happened to be at Yale.”

At summer's end, he returned to Toledo with not just new skills but also a new dream. He would study at an Ivy League school.

“Everybody told me I was crazy,” Hutchins said. “All I kept hearing was, ‘You can't do that.’”

He graduated from Bowling Green State University in 2016 and that fall matriculated at the School of Public Health, where he's on track to graduate with a degree in health management in May 2018. This year, he's second in the program and he's the 2017 Cornell Scott Scholar, an honor awarded each year by

the Community Foundation for Greater New Haven to a Yale public health student who demonstrates a commitment to community-based health care.

“I wouldn’t be here without SMDEP,” Hutchins said. But the program is no longer available at Yale. Because Yale has no dental school, it had to withdraw from the national program in 2016.

When word came that Yale could no longer participate in SMDEP, Linda Jackson, director of diversity, inclusion, community engagement, and equity at the medical school, and Darin Latimore, M.D., deputy dean for diversity and inclusion, decided to launch a program that would serve local community college students. Jackson reached out to officials at Gateway Community College in New Haven and Housatonic Community College in Bridgeport. Last summer, 19 students attended the inaugural Yale Summer Enrichment Medical Academy (YSEMA), a free six-week program for students interested in careers in medicine.

At an informational meeting at Gateway in November, Jackson told about 30 prospective students what to expect from this year’s course, which will accept up to 25 students.

“If you’re interested in being a physician, physician assistant, or nurse, this will help you on that road,” said Jackson, herself a graduate of Gateway. “We are getting you ready for the next step. It is a very rigorous program. You will learn a lot.”

Also at that session at Gateway was Lauren Doninger, Ph.D., a professor of psychology who coordinates YSEMA at the community college.

“We really have identified the population that the School of Medicine is seeking to develop and nurture—first-generation students, DACA students, students who are underrepresented in medicine,” she said. Too often, she added, these are students who, “when they say they want to be a doctor, hear ‘You can be an aide.’”

The program includes organic chemistry, biology, writing and communications, introduction to research, and mentoring workshops.

“Clearly, it tells them what they are in for down the road,” said Antonios Pappantoniou, Ph.D., a professor of biology at Housatonic Community College. “Students often don’t have an impression of how much work it takes to get into medical school. This gives them some training in advance.”

An integral feature of the course is meeting Yale students like Hutchins, who shares the experiences of many of the students. Last year’s inaugural YSEMA class included Felicia Williams, a 45-year-old program manager for Goodwill. She already has a bachelor’s degree from Albertus Magnus College in social science, but came to Gateway to make a career change. She’d like to become a pharmacist. She found the program challenging but encouraging. “It makes me know that I

could be whatever I want to be,” Williams said.

“It was overwhelming,” added Ama Dondorful-Amos, who took the course last summer with Williams. Dondorful-Amos arrived in the United States from Ghana two years ago, and hopes to become a pediatrician. “It opened up new perspectives. I learned how to run gels, how DNA replicates.”

For Beth Schmidt, the course sent a message that at 51, she too can aspire to medical school. Medicine has been part of her life since childhood. Both her parents were medical corpsmen in the U.S. Navy. She studied art history in college but spent a career as a marketer for medical device companies. Although she longed to study medicine, she felt she couldn’t afford medical school. After the YSEMA course ended, she secured an internship at a lab at the medical school, which became a paid position in January. She couldn’t have done it, she said, without a class called Introduction to Research, taught by Hutchins. “He was very encouraging,” she said.

Such responses are gratifying to Hutchins, who is determined to use his story as an example to others. Last summer, although he had an internship with the CFO of Partners HealthCare in Boston, he returned to New Haven twice a week to teach the research class. But he also offered pep talks in what is possible in life: such as attending an Ivy League school.

“I remember that feeling that no one is in your corner and no one believes that you can do it,” he said. “I wanted to be that voice that told them that they could do it.”

—John Curtis



The DNA repair–breast cancer connection

The gene known as *BRCA1* (for “breast cancer susceptibility gene 1”) has a storied history. It was the first gene identified as contributing to familial breast cancer risk, and its discovery in 1990 led scientists and doctors to accept the theory that breast cancer could be inherited. Now experts know that having a mutation that inactivates the breast cancer gene increases a woman’s chances of getting breast cancer about sixfold.

While scientists know much about how dysfunctional *BRCA1* protein leads to cancer, they know little about what the protein actually does in cells. In a paper published in *Nature* this fall, Patrick Sung, D.Phil., professor of molecular biophysics and biochemistry and of therapeutic radiology, reports findings that shed light on the function of the breast cancer protein in the repair of broken DNA.

Sung has been studying the homologous recombination method of DNA repair for more than 20 years. This DNA repair mechanism takes place when the cell is about to divide, after it has duplicated its chromosomes—bundles of double-stranded DNA—but before each chromosome and its duplicate have split off into separate cells. In homologous recombination, a large number of proteins function together to repair a DNA break in one chromosome by copying the broken section from

the duplicate chromosome to patch up the break. First, for a short distance on either side of the break, one strand of the DNA is shaved away to form a single-stranded end. Next, each single-stranded end inserts itself between the two strands of the duplicate chromosome in order to copy the damaged DNA section. Like an interloper at a dance, the single-stranded end gets between the other chromosome’s two strands, pushing one of them aside and forming a structure called a displacement loop or D-loop.

In 1994, working in yeast, Sung discovered that a protein called *RAD51* attaches itself to the single-stranded end of the broken DNA and leads the invasion of the duplicate chromosome. In 1997, another lab learned that this invader protein physically interacts with the breast cancer protein. “We have to study this,” Sung thought to himself when he heard the news. All of a sudden, his research became related to breast cancer.

But yeast, the model system Sung had been using, does not have the breast cancer protein. In order to study the interactions between the invader protein and the breast cancer protein, Sung had to shift his research focus from yeast to humans—or, rather, human cells and proteins.

Sung and his team developed a method to isolate a significant quantity of the *BRCA1* protein as a complex with a partner protein

called *BARD1*. The researchers performed experiments to test D-loop formation by *RAD51* with and without the breast cancer protein and its partner. Those tests revealed that the duo helps the invader protein to form D-loops, and results from experiments done in human cells confirmed these findings.

This new information suggests, Sung said, that in breast cancer patients with mutations in the breast cancer gene, defective DNA repair likely leads to cancer development. In this regard, knowledge of how the breast cancer protein works could aid in drug development.

The findings could also empower patients to make important choices about their treatment. In patients with a family history of breast cancer, for example, doctors could sequence the breast cancer gene and the gene encoding its partner to look for mutations that might impede the pair’s functioning. Further, it would be possible, Sung said, to recreate a patient’s protein duo in the laboratory and test its DNA repair abilities to better assess the patient’s cancer risk. “Being able to apply this type of system to look at patient mutations will ultimately help patients to make decisions, like whether to get a mastectomy as a preventive measure,” Sung said. “It’s a really big deal. It’s very important. Because it’s a huge decision for anyone to make.”

—Ashley Taylor



ONLINE EXCLUSIVES

2017 was a bad year for natural disasters. Hurricanes, floods, and fire hit communities across the U.S. Yale School of Medicine alumni lived and worked in many of them, and took part in leading relief efforts.

For more on story, visit ymm.yale.edu/relief

round up

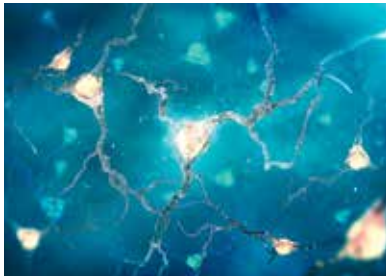
a collection of recent scientific findings



YALE RESEARCHERS HELP RESCUE EXTINCT TORTOISES

For years before his death in 2012 in the Galápagos Islands, people around the world followed the sad saga of “Lonesome George.” The hope was that George, the last saddleback tortoise of his species, would mate

before he died. While there wasn’t much anyone could do for George, an international expedition from Yale found 23 tortoises with sufficient DNA to breed a different but related saddleback species back into existence. Much will depend on the ability of the nine males and 14 females to procreate over successive generations. Announced in September through the journal *Scientific Reports*, the story may have to wait some time for a happy ending: Saddleback tortoises don’t reach sexual maturity for a quarter-century.



LESS THAN 1 PERCENT OF NEURONS ORCHESTRATE BRAIN DEVELOPMENT

It is a sign of enlightenment and sophistication for a country to adopt democratic methods of government. Not so with the brain, it seems! According to research conducted by a team including Jessica Cardin, Ph.D.,

associate professor in Yale’s Department of Neuroscience, the brain takes a more top-down approach. Just 1 percent of its neurons are responsible for its development. These “VIP” neurons don’t have to worry about gerrymandering or primaries—the other neurons obey their prompting without question or complaint!



USSR: PUBLIC HEALTH PIONEER

An exhibit at Yale’s Cushing/Whitney Medical Library in October presented viewers with an unusual spectacle—the first health campaign to create an education program using posters designed for use by the public. Developed by

graphic designers and artists working with doctors in the Soviet Union in the 1920s, the campaign sought to diminish the incidence of syphilis among an overwhelmingly rural and uneducated population. While reliable numbers are difficult to come by, one assumes that the public health campaign made some headway in reducing transmission of the disease.



TRANSLATION OF WORLD’S MOST MYSTERIOUS MANUSCRIPT IS UNMADE

In September 2017, a television writer and amateur decoder named Nicholas Gibbs claimed to have deciphered the Voynich manuscript. The Voynich is a unique codex that dates from the 15th century and resides in Yale’s Beinecke Library. It has defied codebreakers for centuries and generated a number of curious theories. Gibbs wrote in the *Times Literary Supplement* that it was “a reference book of selected remedies lifted from the standard treatises of the medieval period, an instruction manual for the health and well-being of the more well-to-do women in society.” Case closed, right? Not so fast, Lisa Fagin Davis, Ph.D. ’93, director of the Medieval Academy of America, offered a swift and authoritative rebuttal of the Gibbs theory: “Frankly, I’m a little surprised the *TLS* published it,” she said to Sarah Zhang of *The Atlantic*. And so the enigma remains unsolved.



Shelter from the storm

Improving treatment, exploring solutions
to the opioid crisis

ACCORDING TO THE CENTERS FOR DISEASE CONTROL AND PREVENTION (CDC), approximately 88,000 Americans die each year from what they describe as “excessive alcohol use.” Meanwhile, in 2016, the most recent year for which numbers are available, drug overdoses accounted for 64,000 deaths—a figure that all indications suggest will be eclipsed by 2017’s numbers, when they become available. Given that alcohol is easily available and socially acceptable, while the drugs that are killing men, women, and young people are, hypothetically, difficult to procure, is all the more disturbing that the gap between these figures is narrowing so quickly.

Overdose deaths have become the number one public health crisis in our country. This issue of *Yale Medicine Magazine* explores how courageous faculty, students, and alumni from Yale School of Medicine are working to gain control over the storm that is raging through our country. From research into new types of pain treatment and patient care (“How treatment for addiction came out of the Dark Ages,” “Alternatives to opioids”) to policy based on clinical experience (“Needed: better strategies for combating the opioid epidemic”), YSM clinicians and researchers actively seek to reduce and destigmatize preventable death from this disease. It’s a daunting task.

The war over how to describe and treat substance use disorder has tremendously high stakes. Yale School of Medicine has produced and continues to produce leaders capable of posing ethical, empathetic, system-wide solutions to a deeply subversive affliction that, more than ever, holds American citizens in its grip.

Needed: better strategies for combating the opioid epidemic	12
Alternatives to opioids	18
The road back to good health	22
History of substance abuse	26
How treatment for addiction came out of the Dark Ages	34
A mother’s love	38



Needed: better strategies for combating the opioid epidemic

For decades, doctors and community advocates have worked together to combat the epidemic of substance use disorder. Lately, that battle has seemed harder than ever.

BY STEVE HAMM | GREG HALL ILLUSTRATION

In 2000, a doctor from tiny St. Paul, Virginia, asked the School of Medicine for help with a terrible problem. Art Van Zee, M.D., a physician in a community clinic, reported that opioid abuse was sweeping Appalachian coal country like a tsunami. People he had cared for since infancy were overdosing on the prescription painkiller OxyContin®. How could this disaster be stopped?

“Art was the canary in the coal mine,” recalls David A. Fiellin, M.D., HS ’95, professor of medicine (general medicine), emergency medicine, and of public health. Fiellin traveled to Virginia with Richard S. Schottenfeld, M.D. ’76, HS ’82, FW ’84, then a professor of psychiatry. They learned about the emerging rural opioid abuse problem and gave treatment advice to about 150 community members, health professionals, and counselors gathered in a community center building near the Kentucky border.

Appalachia was ground zero of an epidemic that has since ravaged the nation, with the drug of choice shifting from OxyContin to the semi-synthetic opioids heroin and fentanyl. “Unfortunately,” says Fiellin, “a lot of what Art was concerned about has come true—al over the country.”

More than 60,000 people died of drug overdose, mostly from opioids, in the United States in 2016. Opioids presently account for more deaths than gun homicides and car crashes combined.

“Even though the country has been focused on this issue for several years, the problem is getting exponentially worse, not better,” says U.S. Senator Christopher Murphy, a Democrat from Connecticut. “The scope of the epidemic is absolutely staggering. It’s not young or old, black or white, rich or poor. It’s everybody.” Murphy is pressing in Congress for increased funding for crisis intervention, long-term treatment, and medication therapy, and a crackdown on the drug companies and physicians who push painkillers that aren’t necessary.

THE STATE TURNS TO YALE

Addiction experts at Yale have been at the forefront of treatment innovations since the 1970s, so it was no surprise when in 2016 Connecticut Governor Dannel P. Malloy asked Fiellin and colleagues at Yale to take the lead in designing a strategy to reduce opioid overdose deaths. (The death toll in Connecticut reached 723 in 2015, 917 in 2016, and was projected to exceed 1,000 in 2017.) The result was the Connecticut Opioid REsponse (CORE) initiative. In October 2016 the initiative issued, in Yale’s Medical Historical Library, a report based on input from Yale faculty, state agencies, hospitals, physicians, nonprofit groups, and citizens.

“The solution to the opioid crisis has to be a multi-pronged approach,” says Fiellin. “We need to decrease the availability of all types of opioids, and we need to increase the availability of the most effective forms of treatment.”

The CORE group recommended six strategies—all of which are being acted on by state government leaders. The first five were sharply focused—increased access to treatment with methadone and buprenorphine; accelerated entry into treatment for individuals at high risk of overdose; reduction of over-prescription of opioids; increased access to naloxone to reverse the effects of overdose; and increased sharing of data among state agencies, medical clinics, and treatment centers. The goal was a more rapid response to overdose outbreaks.

The sixth strategy was more sweeping: to increase understanding of the nature of opioid use disorder and

the most effective ways to deal with it. This strategy is critical, according to the Yale team, because much of the conventional wisdom about how to deal with opioid use disorder is wrong.

“In essence,” says Gail D’Onofrio, M.S., M.D., professor and chair of emergency medicine and a member of the CORE team, “the goals are to reduce the stigma associated with addiction and understand that it is a chronic, relapsing disease. It has nothing to do with a moral failing, and all to do with a remodeling of the brain’s reward system that is not easily corrected by short-term approaches such as detoxification and enforced abstinence.”

AN ALTERNATIVE TO REHAB

The conventional wisdom, endorsed by some government leaders and health care professionals, is that the solution is to send people to residential rehabilitation centers where, after detoxification, patients are told to abstain completely. Not so, says D’Onofrio. She describes this treatment of addiction through abstinence as “potentially contributing to the worst possible scenario. ... When they are released, the craving associated with certain cues is still there, but now they have less tolerance. The risk of overdose and death is very high.”

Research has shown that more than 90 percent of those who go through detoxification and attempt abstinence will relapse within six months. Opioids rewire the brain, causing intense cravings often impossible to resist. Rather than detox and abstinence, which do little to blunt the craving or undo the remodeling in the brain, Yale experts advocate medication-based therapy. The long-term use of such opioid agonists as methadone and buprenorphine, they say, should not provide a “high” but address the underlying cravings and allow people to lead productive lives. Treatment with these medications has been shown to keep people in treatment while decreasing cravings, withdrawal, criminal activity, and death. Individuals can work, maintain interpersonal relationships, and lead productive lives. Methadone has, over five decades, proven effective in combating heroin addiction. Buprenorphine was approved by the U.S. Food and Drug Administration in 2003 after years of advocacy by Yale faculty. Unlike methadone, it can be prescribed by physicians outside of licensed opioid treatment programs.

A study published by Fiellin and colleagues in *JAMA: The Journal of the American Medical Association* makes a strong case for long-term use of buprenorphine. In a clinical study of people with prescription opioid dependence, those in the detoxification group who tested positive for illicit opioid use 33 percent more often than those in the buprenorphine maintenance group. Of the 57 patients in the detoxification group, only six stayed in treatment, compared to 37 of 56 people in the group that received ongoing buprenorphine.

“Treating people with buprenorphine has been one of the most meaningful things I’ve done in 40 years as a physician,” says Van Zee, the Virginia physician. “It can transform people’s lives.”

One of Fiellin’s patients, Jay C., who did not want his full name used, can attest to that. He was working as a graphic designer 16 years ago when a dentist prescribed an opioid painkiller after a tooth extraction. Jay loved the euphoria, and soon he couldn’t live without the drug—partly because he couldn’t face the agony of withdrawal. He holed up in his house after he lost his job, and ultimately sold half of his possessions to buy drugs.

Buprenorphine “saved my life,” he says. Now, at age 49, he’s the co-owner of an office cleaning company, has tapered his daily dose, and plans to get off buprenorphine entirely. Still, he’s shaken by his experience. “Opioids sink their claws in your soul, and they never let go,” he says.

The Yale substance use disorder experts advocate much more widespread use of buprenorphine and naloxone, the overdose antidote.

SCREENING FOR CARE

For years, Yale clinicians have been using naloxone in the emergency department for overdose victims. Increasingly, police, first responders, and emergency medical professionals use naloxone, but advocates want to make the drug as prevalent as automatic defibrillators are in offices, stores, and restaurants. Currently, patients who overdose in the Yale New Haven Hospital ED are given a take-home dose of naloxone and instructions for use. As early as 1999, Yale physicians began screening ED patients for opioid and other substance use disorders as part of a pioneering program,

Project ASSERT (Alcohol & Substance Abuse Services, Education, and Referral to Treatment). Using a brief negotiation interview (formerly known as an intervention) to motivate patients to change their substance use, patients are directly linked by Health Promotion Advocates employed by Yale New Haven Hospital to community partners offering specialized care. The program has been very successful over the past 17 years; almost two-thirds of all patients with a direct linkage to community providers and programs enroll in treatment. In 2015 D’Onofrio, Fiellin, and Yale colleagues published the results of their study testing negotiation interviews for patients with opioid use disorder in *JAMA*. Patients offered a brief negotiation interview and ED-initiated treatment with buprenorphine, followed by 10 weeks of medical management in primary care led by Fiellin, were compared with referral only and brief negotiation interview with a facilitated referral. ED-initiated buprenorphine was found to be twice as effective as the other negotiation interviews in engaging patients in formal addiction treatment at 30 days, at lower costs.

Buprenorphine and methadone have been found effective for up to 80 percent of people with opioid use disorder. Because buprenorphine is not as powerful as methadone, it carries less risk of an overdose—doctors can prescribe the medication after taking an eight-hour course.

Prescribing buprenorphine in an office-based practice—as opposed to methadone in the clinic—allows patients to preserve their anonymity if they choose. It also helps them avoid running into former opioid-using associates—chance encounters that might promote relapse.

The U.S. Substance Abuse and Mental Health Service Administration reports that 968 clinicians in Connecticut are certified to prescribe buprenorphine as of the end of September 2017, up from 594 at the end of 2014. Yet, while the numbers are up significantly here and nationally, public health experts say some communities remain underserved. “We have to increase the number of prescribers,” says Robert Heimer, M.Sc. ’80, Ph.D. ’88, professor of epidemiology (microbial diseases) and of pharmacology at the School of Public Health, and a member of the CORE team.

Needed, he says, are far-reaching education

programs aimed at physicians. Caregivers in suburban and rural areas, where opioids were not a major problem in the past, must be trained to spot and treat substance use disorders and reduce their misprescribing of opioids, Heimer says.

Another critical need: increasing the capacity of long-term treatment programs and expanding them in underserved parts of Connecticut. Too often, people who are referred for treatment must wait weeks or even months to begin, or travel long distances to clinics. As a result, there’s a high potential for continued opioid use with its attendant risks of overdose, arrest, and such bloodborne infections as HIV, hepatitis C, endocarditis, and soft tissue infections. New Haven’s APT Foundation, founded by Yale faculty in 1970 and one of the country’s first methadone clinics, has scaled up services to help everybody who walks in the door. Its open-access model means a person with a drug problem can walk in without proof of insurance, be evaluated by a clinician, and obtain medication before the end of the day. “We have reduced waiting time to zero,” says Lynn M. Madden, APT’s chief executive officer. The organization serves more than 8,000 patients a year in Connecticut.

“We need APT Foundations all over the country,” says Schottenfeld, now chair of psychiatry at Howard University in Washington, D.C. APT’s open-access model, he said, should be applied around the country in areas where treatment slots become available only when a patient dies or relapses. “That has been the traditional model, and it doesn’t work.”

A PARTNERSHIP WITH THE STATE

Expanding services means more resources will be needed. Despite Connecticut’s budget crisis (the state is facing a deficit of more than \$5 billion over the next two years), the governor and legislators have committed to finding money to combat opioid addiction.

A host of state agencies, including the Department of Mental Health & Addiction Services (DMHAS), has partnered with Yale faculty on the CORE Initiative. The DMHAS is now modifying or amplifying its efforts in response to the group’s recommendations.

Miriam Delphin-Rittmon, Ph.D., FW ’02, the commissioner of DMHAS, applauds the CORE team for

using data to show what works—and what doesn't. "We don't just implement these things and hope they work. We implement them and measure their impacts," says Delphin-Rittmon, who is on leave from the faculty of the School of Medicine.

One of the most innovative programs funded by DMHAS in partnership with the Connecticut Community for Addiction Recovery dispatches "recovery coaches" who help ED patients who seek longer-term treatment. When necessary, the coaches even drive patients to treatment facilities. The program recently expanded from four to seven hospitals around the state. Still, Connecticut has 27 acute care hospitals, so it is available to only a fraction of state residents.

A new program encouraging people to turn in unused prescription opioid pills is off to a fast start. More than 33,000 pounds of pills were collected last year. Also, responding to new state regulations and professional guidance, physicians are cutting back on opioid prescriptions.

But doctors warn that responses to the opioid epidemic must be thought through—lest they adversely affect patients. Jane L. Andrews, M.D., assistant professor of medicine, says limiting prescriptions puts physicians in a bind. "What do I tell my 70-year-old patient with arthritis who is getting 30 milligrams of OxyContin a day, but still hurts? We need to find new alternatives to opioids for long-term pain relief."

Researchers in Yale's Department of Psychiatry are exploring nonpharmacological methods of dealing with pain—everything from cognitive behavior therapy and biofeedback to tai chi and massage. They see chronic pain as something to be managed rather than "cured," and they want to place greater responsibility for managing pain on the individual. They're investigating the effectiveness of smartphone apps that help people care for themselves. "We're trying to promote a cultural shift away from dependency on doctors and drugs to solve problems," says Robert D. Kerns, Ph.D., a research psychologist at VA Connecticut Healthcare System, West Haven Campus, and professor of psychiatry, neurology, and psychology.

Other Yale researchers are exploring non-addictive drug therapies that may eventually replace opioids for some uses. Stephen Waxman, M.D., Ph.D., the Bridget

M. Flaherty Professor of Neurology, and director of the Center for Neuroscience and Regeneration Research, is working with pharmaceutical companies to develop drugs that block sodium channels, which transmit pain impulses through the nervous system (see story on page 18).

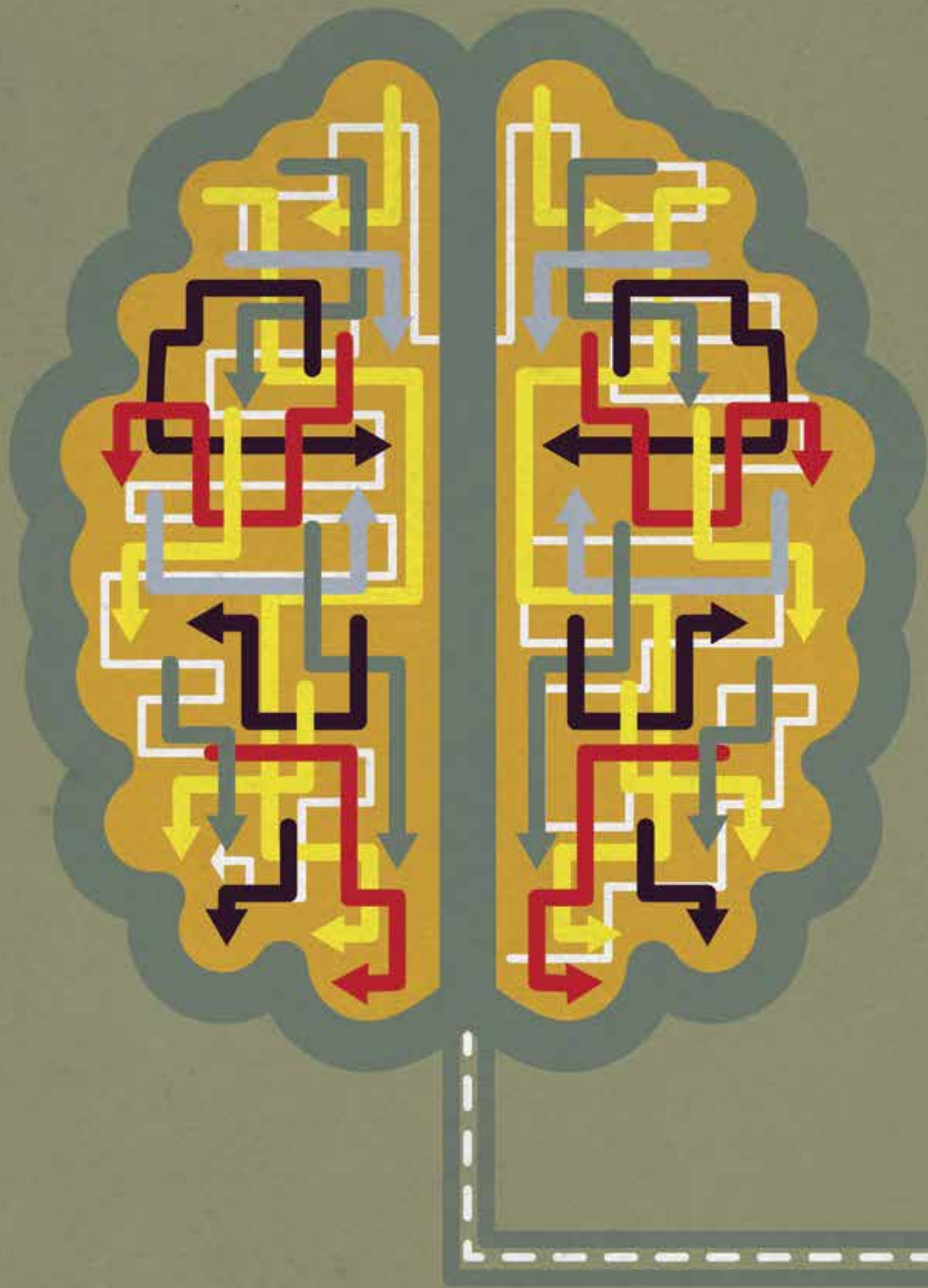
CHANGING ATTITUDES

In the meantime, Yale's addiction experts believe it will be difficult to address today's opioid epidemic without changes in attitudes. To many people, addiction signals a personal failing. Too often, those with drug problems are shunned or treated like criminals, or they try to hide their problems rather than seek help.

To meet Rachel Moore (not her real name), you would never suspect that she's recovering from heroin addiction. The 29-year-old lab tech in New Haven is bright and cheerful, and loves her job. She started shooting heroin at age 16 "to fill a hole" in her life. Now, after 11 years of methadone treatment and counseling, no relapses, and two college degrees, she'd like to help break the stereotypes about drug addiction. Yet none of her work colleagues know her secret. "Maybe if I was more open and told people my story, I could help change attitudes," she says. "But I'm worried it would change the way people viewed me. I think people forget there is a unique individual behind the addiction."

Heimer of the School of Public Health says it's time for our society to replace shame with empathy and understanding of addiction as a chronic relapsing disease. "We have to reduce the stigma associated with addiction," he says. "We have to stop calling people names. They're not 'junkies' or 'addicts.' They're people with a disease, and we have to get them into treatment." */yale medicine magazine*

Steve Hamm is a contributor to Yale Medicine Magazine.



Alternatives to opioids

How a Yale scientist is looking for painkillers that target sodium channels, not opioid receptors

BY ASHLEY P. TAYLOR | GREG HALL ILLUSTRATION



Since ancient times, humans have used opium and its derivatives to block pain. Yet in all that time, no one has found a solution to two main side effects of opioids—addiction and overdose.

Opioids block pain signals by stimulating opioid receptors in the spinal cord and brain. But they don't work for all types of chronic pain, says Stephen Waxman, M.D., Ph.D., the Bridget M. Flaherty Professor of Neurology at Yale School of Medicine and director of the Center for Neuroscience and Regeneration Research at the VA Connecticut Healthcare System in West Haven. Many patients with neuropathic pain—the result of nervous system injury or dysfunction—get little or no relief.

Neuropathic pain, says Waxman, is “a very important unmet medical need.” It can occur after nerve injury or shingles; in association with diabetes; or as a response to chemotherapy.

“For all of these diseases, a common thread is that we need better therapies,” Waxman says. He's working to develop such therapies, and he's found a new target—not opioid receptors but sodium channels, which neurons need to fire.

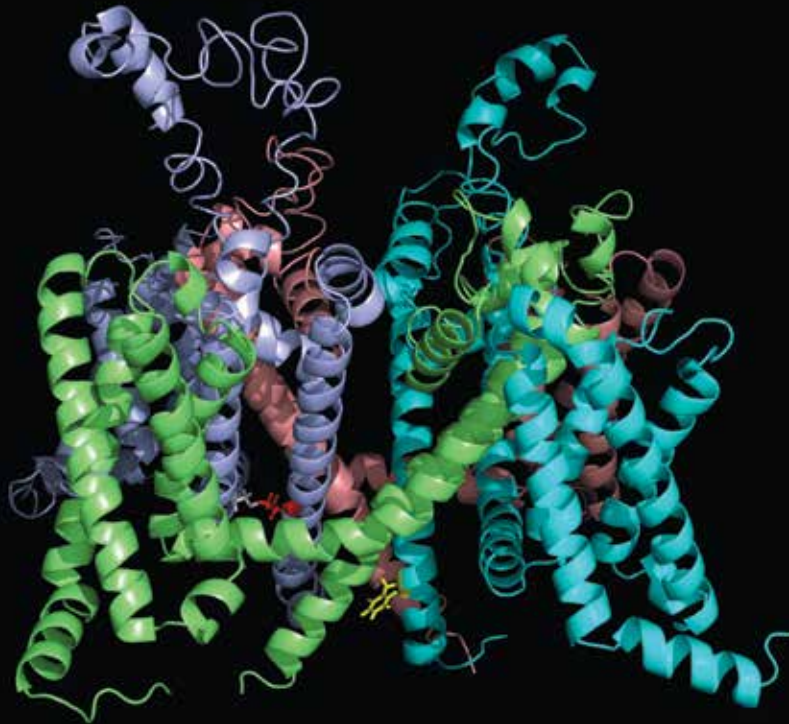
For several years he's been testing painkillers that block sodium channels in patients with a rare genetic disorder that sends their pain neurons into overdrive. Waxman hopes to find treatments that will not only ease common types of chronic pain but also reduce opioid use.

His search for non-opioid painkillers began at the dentist's office. Lidocaine, Novocaine, and all of the “-caine” drugs in dentists' needles are local anesthetics

that stop neurons from transmitting pain signals by blocking their sodium channels. But in pill form, those drugs would have such unacceptable side effects as double vision, seizures, sleepiness, and confusion, all a consequence of blocking sodium channels in the brain. A “holy grail of pain research,” Waxman says, is to find a sodium channel that is essential to the function of peripheral nerves that lie outside the brain and spinal cord, but that does not play a major role in the brain. Exploiting such a channel, he says, could block pain without leading to side effects or addiction.

In the 1990s, scientists found such a channel, Nav1.7, and Waxman's lab began to study it. But drug companies wouldn't pursue drugs targeting that channel without proof that it had an important role in human health. In 2003 Waxman began scouring the world for people with inherited neuropathic pain, in hopes of linking pain disorders to their particular mutations, genes, and proteins.

He was still searching when a lab in China reported in March 2004 that mutations in a gene, *SCN9A*, which encodes Nav1.7, were the likely cause of the rare genetic disorder inherited erythromelalgia (IEM). “Mild warmth triggers intense burning pain, and many patients keep their hands and feet on ice, to the point of getting tissue damage, sometimes even gangrene,” Waxman says of the disorder, also known as man-on-fire syndrome. At



Atomic-level model of the Nav1.7 sodium channel, which is a master switch for pain. This model is permitting scientists at Yale to advance toward “precision,” genomically guided medications for pain, which will not have such side effects as sleepiness or confusion, and will not have the potential for addiction.

first Waxman thought that the Chinese lab had beaten him to the punch. But although the Chinese scientists had linked the sodium channel to the disorder, they had not shown how the channel works or how damage to the sodium channel causes IEM. The Waxman lab began investigating and later that year published their results. The mutations in *SCN9A*, says Waxman, “make the Nav1.7 channel overactive. And that makes pain-signaling nerve cells shriek when they should be whispering.” Soon, Waxman’s lab received a grant from The Erythromelalgia Association and what Waxman calls “a much bigger gift”—access to a community of families with erythromelalgia who have shared their DNA and medical histories and participated in clinical trials.

In 2009 Waxman and colleagues reported that patients with a particular *SCN9A* mutation responded well to carbamazepine, which blocks all sodium channels. Later, they used computer modeling of the sodium channel to predict that people with IEM who had a different *SCN9A* mutation might also respond to the drug. A 2016 study at Yale confirmed their hypothesis. Waxman hopes to use genetics and computer modeling in a “precision medicine” approach to predict drug responses in patients with other variations in their genes.

In 2016, Waxman collaborated with Pfizer to test another drug that, unlike carbamazepine, targets only

the sodium channel Nav1.7. Three of the five study participants responded to the drug in at least one of two trials, and two participants responded to the drug on both trials. In general, patients reported a three-point reduction in pain on the 10-point scale. Waxman cautions that the number of patients studied was small. Nevertheless, “That’s a fairly large improvement,” Waxman says.

The scope of this research extends beyond IEM. Waxman hopes that work on sodium-channel blockers will lead to the development of non-opioid medications to treat many kinds of chronic pain. Already the British company Convergence Pharmaceuticals, recently acquired by Biogen, has tested one Nav1.7 blocker as a treatment for trigeminal neuralgia, which causes attacks of facial pain. Waxman is collaborating on that study, and early results are promising, he says. Eventually, Waxman believes, these opioid alternatives will be tested as treatments for back pain, diabetic neuropathy, and more. “We need to do a lot more work, and the numbers will tell the story, but I am hopeful.” */yale medicine magazine*

Ashley P. Taylor is a frequent contributor to Yale Medicine Magazine.



The road back to good health

Each year substance use disorder robs millions of people of health, self-respect, and even life. Patients who make their way to treatment follow an arduous path.

BY JENNY BLAIR, MD '04 | GREG HALL ILLUSTRATION

Before Kevin M.'s drinking problem began, before he became what he calls a "frequent flyer" in the Yale New Haven Hospital emergency department (ED), he was a policeman in Hollywood, Florida. There, he became involved in several shooting incidents. Though a civilian review board determined he had been justified, he says, he was asked to "leave the department quietly."

Next, Kevin became a successful salesman of automatic doors. Even as his business thrived and he found himself in demand as an expert witness in automatic-door liability cases, he began to drink alone in hotels.

Then a \$50 million lawsuit hit. It ruined his finances as well as his marriage.

"That's when my alcoholism really started to flourish," says Kevin, now a 64-year-old retiree living in New Haven. "I came back up north, broke, enraged, and just kept drinking and drinking. My whole family didn't want me around." Often homeless, hospitalized, or in jail, Kevin spent over seven years in and out of the Yale ED. And it was in the ED that Kevin connected with Project ASSERT—and turned his life around.

The project's deceptively simple mission: to screen patients for substance use disorders, conduct a brief negotiation interview, and refer patients to treatment (a trio of actions abbreviated to SBIRT). It staffs the EDs of both Yale New Haven Hospital (YNHH) and the Saint Raphael campus with Health Promotion Advocates (HPAs) trained to conduct the short interviews, which help patients explore the pros and cons of substance use, and begin to think about the possibility of change. For those who feel ready, project staff can arrange for transfers to detox or rehab directly from the ED. Since the program's founding, it has arranged treatment for some 48,000 people. "We are their voice in the ED," says HPA Shevonne Mack.

In 2016, of all the patients the HPAs met with in the ED, 22 percent went straight into treatment, while another 43 percent received treatment referrals. Getting people the substance abuse treatment they need is not

only good patient care and good public health, resulting in fewer ED visits due to injury, it may also be good economics. One 2005 study found that an ED-based program saved \$3.81 for every \$1.00 it spent on an SBIRT program.

Gregory Johnson is a founding member of Project ASSERT and one of several HPAs who worked with Kevin. Johnson attributes the project's successes to its home base in the ED. Accosting people with substance use disorders on the street may or may not lead anywhere—it's all too easy to toss an informational flyer, for instance. But an ED visit can bring long waits and time for reflection—the perfect opportunity for a caring outsider to offer help.

"If the patient recognizes that he has arrived at the chest pain center because of cocaine and alcohol use and I tell them 'I can get you directly into treatment from the ED, from point A to point B', they're more likely to say, 'Let's go for it,'" Johnson says.

The project began in 1999 as a one-year, grant-funded initiative to help people with substance problems self-reflect via the brief negotiation interview. Within a few months, its mission grew, according to Johnson. Not only were HPAs finding at-risk drinking and drug use, they were uncovering severe substance use disorders.

The normal procedure in such cases was to alert social workers, who would refer patients for treatment. But social workers often did not show up in the ED when called, Johnson says. So he took matters into his own hands. Having previously worked at New Haven's South Central Rehabilitation Center, he knew how to get people into treatment, and he started doing so. After the grant ran out, the hospital hired the team as permanent employees.

“We became the substance treatment people,” Johnson says.

In addition to short detox programs for the physically addicted, HPAs also arrange longer stays in rehab. Project ASSERT also emphasizes harm reduction, offering naloxone antidote kits, suboxone, and methadone clinic appointments for some patients.

The idea of bringing public health initiatives like this to the ED is partly that of Gail D’Onofrio, M.D., M.S., the chief of Emergency Services. D’Onofrio is a renowned federally funded SBIRT expert who sees to it that all primary-care resident physicians at Yale learn the technique.

The HPAs credit much of their success to personal connections—among the community as well as to the patients they serve. Being on a first-name basis with rehab and detox workers all over the state can often open doors, for instance, especially for patients whose insurance doesn’t

For Kevin, an HPA’s words at a crucial moment made all the difference. One morning, he went to Yale New Haven Hospital to collect belongings he’d left during a discharge the previous day. He planned to hit the liquor store next. But as he waited in the hospital atrium, one of the HPAs spotted him and came to say hello. She asked him if he’d been drinking that morning. He had.

“She sat and talked to me,” he recalls. “Something went on in my head that said, ‘Are you ready to stop?’”

Kevin walked to the ED, where his blood pressure and heart rate were found to be sky-high. That morning’s drink turned out to be his last. After his discharge, he became deeply involved with Alcoholics Anonymous. No longer homeless, he spends up to four days a week at Yale New Haven Hospital and the Saint Raphael campus, talking with others who struggle with alcoholism.

“I try to give them what was given to me, which is that little light in your head that’s in that very dark place that

Gregory Johnson

“If I say I can provide immediate help for them, and I actually come through on my word, that leaves an imprint on them.”

cover treatment or who lack it altogether. And, recognizing patients’ difficult life circumstances, which can make relapse hard to avoid, the team also works to connect them to other area resources wherever possible.

That personal connection with patients can be especially important after relapse. Those who decide to try again often ask for help from an HPA they’ve come to trust.

“I’ve had patients who call their mother and their mother hangs up on them because they burned so many bridges,” Johnson says. “If I say I can provide immediate help for them, and I actually come through on my word, that leaves an imprint on them.”

says, ‘You don’t have to live this way anymore,’” Kevin says. “That’s what the folks over at the ER with the project over there do. ... They never gave up on me.”

“You can’t be judgmental, and you’ve got to be compassionate, and you’ve got to understand it’s a disease,” says HPA Damaris Navarro. “They come back, they’re going to come back, but that’s a part of getting better.” *yale medicine magazine*

Jenny Blair, M.D. '04, a freelance writer based in Montpelier, Vermont, has written frequently for Yale Medicine Magazine.

History of substance abuse

For as long as they've had the ability, humans have sought natural sources for stimulation and relief from pain and injury.

COMPILED BY ADRIAN BONENBERGER

12th century BCE Early references to “drink madness” from ancient Egypt and Greece.



7,000–5,000 BCE Grapes cultivated for wine in what is now modern-day Georgia. And they’re still making wine outside Tblisi today!

5,000 BCE Likely oral origins of the Ayurveda, Hinduism’s traditional medical system, in which alcohol is prescribed as a cure for certain ailments, but not in excessive quantities—too much use of alcohol is seen as damaging.



3,400 BCE The opium poppy is cultivated in lower Mesopotamia. Sumerians refer to it as Hul Gil, the “joy plant.” The Sumerians would soon pass along the plant and its euphoric effects to the Assyrians. The art of poppy-culling would continue from the Assyrians to the Babylonians, who in turn would pass their knowledge on to the Egyptians.



9th century BCE In Homer’s *Odyssey*, Helen is described as giving soldiers and veterans of the Trojan War drugged wine according to a recipe discovered in Egypt—a magical potion called *Nepenthes pharmakon*, or the anti-sorrow drug.



5th Century BCE Herodotus makes references to drunkenness as a sickness of body and soul.

4th Century BCE Aristotle (384–322), in comparing licentiousness to drunkenness, noted that the former was a functional disorder while the latter resulted from an organic disorder. He viewed licentiousness as permanent, but drunkenness as curable. When Alexander the Great (Aristotle’s most famous pupil) died in 323 BCE, his death was ascribed partly to years of immoderate drinking.



1st Century BCE *The Yellow Emperor’s Classic of Internal Medicine*, an organized and systematic explanation of acupuncture recognizable to practitioners today, is published in China. “These days, people have changed their way of life,” says the Yellow Emperor Huang Di in the opening chapter. “They drink wine as though it were water, indulge excessively in destructive activities, drain their *jing* (the body’s essence that is stored in the kidneys) and deplete their *qi* [life force].” The text treats alcoholism (and other diseases or ailments) as a behavioral problem, and recommends adjusting one’s behavior to compensate.



98 AD Tacitus writes in *Germania*, that German tribes “do not show the same self-control in slaking their thirst. If you indulge their intemperance by plying them with as much drink as they desire, they will be as easily conquered by this besetting weakness as by force of arms.”



1st Century AD The Roman philosopher Seneca (4 BCE–65 AD) defines drunkenness as a type of insanity. “The word *drunken* is used in two ways—in the one case of a man who is loaded with wine and has no control over himself; in the other, of a man who is accustomed to get drunk, and is a slave to the habit ... there is a great difference between a man who is drunk and a drunkard.”

4th Century AD St. John Chrysostom compares inebriation to other known diseases. He is, however, in favor of using wine because of its sacramental role in the Eucharist and its centrality in one of Jesus’ best-known miracles.



5th century AD St. Benedict writes the *Rule of Saint Benedict*, in which alcohol is not prohibited. He notes that monks who abstain from alcohol tend to be more virtuous.

6th century AD Germanic tribesmen prone to abusing alcohol or drugs are encouraged to binge before battle. Wearing wolf or bear skins, given plenty of space by their allies, these men were deployed as berserkers (from the Norse word for bear shirt) and feared by their enemies. Three of these tribes, the Angles, Saxons, and Jutes claim Britain between 450 and 550 AD.



7th century AD Islam founded. Islam’s attitude toward alcohol differs from that of Christianity. Lacking the New Testament descriptions of Christ’s use and blessing of wine, Islam is free to prohibit alcohol completely, a prohibition that stands to this day. Although the prohibition broadly concerns “intoxicants,” thus providing a religious rationale for banning narcotics as well, early Islam seems to have been less strict in its attitude toward the consumption of nonalcoholic substances, including coffee.

The Middle Ages (5th–13th century AD) attitudes toward drunkenness varied. Some religious sects prohibited the use of substances (the Ismaili Naziri or “Assassins”), while others permitted or encouraged it (Benedictine and Franciscan monks); use varied by culture and religious context. Overall, addiction was regarded as vice, and treatment was either nonexistent or focused on spiritual redemption.



11th–12th century AD Medical students from Salerno, Italy, build the first stills, enabling the distillation of spirits. This greatly increased the potency of beverage alcohol and spurred a worldwide surge in alcoholism.

12th–13th century Zhang Sanfeng, whose exercises allowed him to (allegedly) live 152 years, establishes the basis for Tai Chi, which does not recognize a division between the physical body and the spirit. In addition to exercises, Sanfeng’s teaching recommends abstaining from alcohol, meat, beans, and grains.



14th century Italian scholar Petrarch's rediscovery of humanist, pagan texts from classical thinkers lays the groundwork for the Renaissance and the Enlightenment. Humanist scholarship also plays a major role in the Protestant Reformation. While some Protestant churches (Lutheran, Anglican) continue to permit the use of alcohol, others adopt strict prohibitions against its use, including some of the smaller groups that help establish the English colonies of North America.



1517 Sigismund de Dietrichstein organizes the Order of Temperance in Germany. The order calls for an end to the custom of “pledging healths” (toasts)—a practice thought to promote intemperance.



1560s–90s An early description of narcotic withdrawal, cravings, and compulsions: European explorers and scientists, in describing the opium traffic among the Turks, Chinese, Moors, and Persians, note of opium consumers: “If they leave off somewhat taking it, then they feel physically ill.”

1600 Dietrichstein's Order of Temperance allowed members no more than seven alcoholic drinks per meal, and only two meals per day. Well, as the saying goes: “you have to start somewhere.”



1606 Shakespeare's *Macbeth* offers a guarded evaluation of the ills of drink—Lady Macbeth drinks for courage to assassinate (“That which hath made them drunk hath made me bold; what hath quenched them hath given me fire”) while King Duncan and his guards have become vulnerable through drink. The play may reflect evolving Elizabethan attitudes toward drunkenness. Alcohol was not viewed as the problem, but rather human dependence on it for comfort. Drunkenness was therefore a sign of moral weakness rather than disease.



1620 Separatists, members of a Puritan sect, settle New England, and bring judgmental attitudes toward the use of substances with them.

1747 The French philosopher Condillac refers to inebriety as a disease and calls for state-sponsored treatment.



1772 Physician and social reformer Benjamin Rush calls for the abandonment of distilled spirits and the substitution of cider, beer, wine, and non-alcoholic drinks in his sermons to *Gentlemen Upon Temperance and Exercise*. Later, he calls for the creation of special hospitals for “inebriates,” following the notion that drink (and not the drinker) was to blame for alcoholism.

1787–1813 Delirium tremens (acute alcohol withdrawal syndrome) recognized and medically described by Lettsom, Armstrong and Pearson, and then named by Thomas Sutton.



1789 First American temperance society organized in Litchfield, Connecticut.



1799 China's emperor, Kia King, bans opium, making trade and poppy cultivation illegal.



Early 1800s In Boston, temperance advocates found a brewery to provide beer to those who pledged to forsake “ardent spirits”—what we call hard liquor.

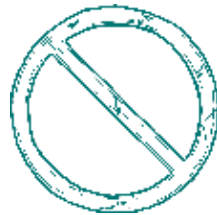


1811 A temperance society in Fairfield, Connecticut calls for total abstinence, acknowledging that this is a harsh remedy, “but the nature of the disease absolutely requires it.”



1819 Christopher Wilhelm Hufeland coins the term *dipso-mania* to describe the uncontrollable craving for spirits that triggers “drink storms.”

1826 American Temperance Society formed—first national temperance organization.



1825–1850 Temperance movement abandons temperance (moderation) and embraces total abstinence as a goal and legal prohibition of alcohol as a means of collectively achieving that goal.

1830 The Connecticut State Medical Society calls for creation of inebriate asylums.



1833 Dr. Samuel Woodward, superintendent of the Worcester Insane Hospital and Women's Lunatic Asylum in Massachusetts, writes a series of essays that are published in 1836 and again in 1838. “A large proportion of the intemperate in a well-conducted institution would be radically cured, and would again go into society with health reestablished, diseased appetites removed, with principles of temperance well grounded and thoroughly understood, so that they would be afterwards safe and sober men.”



1839 Lin Tse-Hsu, imperial Chinese commissioner in charge of suppressing opium traffic, orders all foreign traders to surrender their opium. To protect its opium trade, the British send expeditionary warships to the coast of China, beginning the first Opium War. By 1841, the Chinese have lost the war, and cede Hong Kong to the United Kingdom.



1840–1890 More than 200 American water cure institutions include alcoholics and addicts among their devoted clientele and solicit their patronage through such media as *The Water Cure Journal*.



1849 The Swedish physician Magnus Huss introduces the term “alcoholism” in his text, *Chronic Alcoholism*; it does not appear in the United States until after the Civil War.



1853 The hypodermic syringe is developed as a refinement of the use of cannulae to introduce drugs beneath the skin. Morphine is one of the first drugs for which the syringe is commonly used to treat such conditions as facial neuralgia.



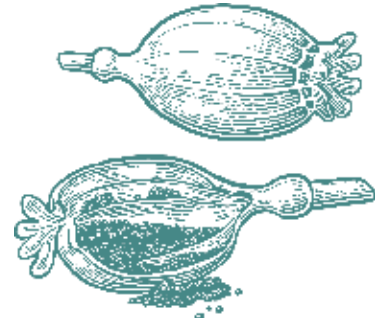
1856 The British and French renew hostilities against China during the Second Opium War. The import of opium is legalized in China again.



1860 Alexander Peddie, a Scottish physician practicing in Edinburgh, calls for legal commitment of dipsomaniacs to inebriate asylums. He distinguished between common drunkards whose excessive drinking was a vice and the “insane drinker” whose vice had been transformed into a disease no longer under his volitional control. Peddie believed this disease could be inherited or acquired.



1861–65 Widespread use of morphine during America’s Civil War, along with the introduction of the hypodermic syringe, lead to an epidemic of opioid addiction among veterans of the conflict; so much so that opioid addiction temporarily becomes known as “soldier’s disease.”



1878 Britain passes the Opium Act with hopes of reducing opium consumption. The selling of opium is restricted to registered Chinese opium smokers and Indian opium eaters, while the Burmese are strictly prohibited from smoking opium.



1890 The U.S. Congress, in its earliest law-enforcement legislation on narcotics, imposes a tax on opium and morphine. Tabloids owned by William Randolph Hearst publish stories of white women being seduced by Chinese men and their opium to invoke fear of the yellow peril disguised as an anti-drug campaign.



1895 Heinrich Dreser, working for The Bayer Company of Elberfeld, Germany, finds that diluting morphine with acetyls produces a drug without the common side effects of morphine. Bayer begins production of diacetylmorphine and coins the trade name “Heroin.” Within a few years, the philanthropic Saint James Society in the United States has mounted a campaign to supply free samples of heroin through the mail to morphine addicts trying to break their habit. By 1902, physicians have begun to note in various medical journals the side effects of using heroin as a morphine step-down cure. Several physicians argued that their patients suffered from heroin withdrawal symptoms equal to morphine addiction.



1905 U.S. Congress bans opium.



1906 Several physicians experiment with treatments for heroin addiction. Alexander Lambert and Charles B. Towns tout their popular cure as the most “advanced, effective, and compassionate cure” for heroin addiction. The Towns-Lambert Cure consists of a seven-day regimen, which includes a five-day purge of heroin from the addict’s system with doses of belladonna (nightshade) that often produces delirium. The patient also receives other drugs thought to be beneficial.



1914 The Harrison Narcotics Act passes. It requires doctors, pharmacists, and others who prescribe narcotics to register and pay a tax.



1923 The U.S. Treasury Department’s Narcotics Division (the first federal drug agency) bans narcotics sales. As a result, substance users are forced to buy from illegal street dealers.



1939 The first edition of the basic text of Alcoholics Anonymous (AA), notes: “Then we have a certain type of hard drinker. He may have the habit badly enough to gradually impair him physically and mentally. It may cause him to die a few years before his time. If a sufficiently strong reason—ill health, falling in love, change of environment, or the warning of a doctor—becomes operative, this man can also stop or moderate, although he may find it difficult and troublesome and may even need medical attention.”

1944 Two “Yale Plan” clinics open in Connecticut, one in New Haven and one in Hartford. The Clinics hope to develop a plan for cost-effective assessment and treatment of people suffering from alcoholism.



1960s Expansion of drug use into white middle class youth transforms attitudes and approaches toward treatment. Shifting patterns of substance use addiction during the Vietnam War and Civil Rights era lead to a massive cultural divide in the U.S., leading to a fundamental split between conservative and progressive lawmakers in their approach to treating drug and alcohol dependence.



1965-75 Involvement in Vietnam is blamed for the surge in illegal heroin being smuggled into the United States.



1970 The Controlled Substances Act of 1970 classifies marijuana along with heroin and LSD as a Schedule I drug—high abuse potential, with no accepted medical use.



1973 President Richard Nixon creates the DEA (Drug Enforcement Administration) under the Justice Department to consolidate federal powers of drug enforcement in a single agency.



1985-93 New research extols the positive effects of moderate drinking; the first “how-to” books on controlled drinking are published, contributing to “Moderation Management,” a moderation-based support group alternative to AA.



1994 The Clinton Administration orders a shift in policy away from the anti-drug campaigns of previous administrations. Instead focus includes “institution building”—included harsh sentences for repeat offenders (also known as the “Three Strikes” law).



2000 The Drug Addiction Treatment Act facilitates the treatment of chronic opioid users by qualified doctors in a clinical setting using approved Schedule III, IV, and V narcotics.

2002 Buprenorphine is approved as a Schedule III drug, and becomes the first approved as safe to use as treatment in a doctor’s office.

With gratitude to William White, MD, whose papers and timelines on the subject supplied much of the background and information for this timeline.



How treatment for addiction came out of the Dark Ages

Non-addictive pain medication has changed how experts approach therapy for substance use disorders.

BY SONYA COLLINS | GREG HALL ILLUSTRATION



“It’s not often that a psychiatrist gets to hear ‘Doctor, you saved my life,’ ” said Ellen Edens, M.D., FW ’09, assistant professor of psychiatry and associate fellowship director in addiction psychiatry. But she gets that a lot from patients receiving outpatient treatment for opioid use disorder. “They tell me, ‘I have my children back, I’m working, I feel good.’ ”

Treatment for opioid use disorder hasn’t always brought such clear rewards. Throughout the 1960s, abstinence-based detox was the only widely available treatment despite high relapse rates. Then, in 1965, methadone clinics emerged as a game-changer.

Rockefeller University clinicians Vincent Dole, M.D., and Marie Nyswander, M.D., reported in *JAMA: Journal of the American Medical Association* that year that they had used once-daily oral methadone—an opioid painkiller—to stabilize 22 young men who were addicted to heroin. Methadone relieved both withdrawal and cravings, and allowed patients to resume their lives. On September 15, 1969, Robert DuPont, M.D., who would become the first director of the National Institute on Drug Abuse, started the first methadone maintenance treatment program, which served 25 parolees in Washington, D.C.

“That is when treatment for opioid use disorder emerged from the Dark Ages,” said Patrick G. O’Connor, M.D., M.P.H. ’88, FW ’88, the Dan Adams and Amanda Adams Professor of General Medicine, and chief of general internal medicine.

As methadone clinics opened in cities around the country, studies showed that the treatment decreased drug use and opioid overdoses, lowered hepatitis B and C rates, improved pregnancy and birth outcomes, increased overall survival, and—crucially—lowered risk for HIV infection.

But the groundbreaking treatment wasn’t perfect. Patients who landed a coveted spot in one of a handful of licensed clinics had to show up every day for their dose until they were deemed trustworthy enough to take a supply home. That process could take months. As heroin users

tried to escape the soaring risk of HIV infection in the late 1980s, the model could barely support the demand.

“Here in New Haven, we had waiting lists of six to 12 months for a slot in a methadone clinic,” said O’Connor. “People were literally dying while they were waiting for this highly effective treatment.”

O’Connor and colleagues at Yale knew there had to be a better way. “What if we developed an approach to treating opioid dependence that didn’t rely on one or two methadone programs in New Haven, but rather was available in primary care clinics and physicians’ offices all over the city?” O’Connor asked.

CHRONIC CARE FOR ADDICTION

In a 1992 article in the *Journal of General Internal Medicine*, O’Connor and colleagues showed that they could manage withdrawal from heroin with clonidine, a drug introduced in 1966 to treat high blood pressure and that was found to manage opioid withdrawal. Once opioid-free, patients received naltrexone, an opioid blocker which renders them less able to feel “high” or to overdose when they use heroin. Theoretically, the medication would eliminate the stimulus to use opioids. But cravings persisted and patients often gave up naltrexone and returned to using opioids.

Still, says O’Connor, “We showed that patients would come to primary care for treatment and that we had an effective protocol that could get them to a drug-free state in an outpatient setting.” Integrating addiction treatment into primary care has additional benefits. This model would allow patients to receive both addiction treatment and general medical care

“under one roof,” without the stigma of an addiction treatment program.

Because patients often abandoned naltrexone, O’Connor explored a new approach—using opioid maintenance therapy in primary care. Since methadone could be used only in specialized programs, he performed the first randomized trial of primary care-based buprenorphine—an experimental medication that had been found as effective as methadone in specialized treatment programs.

“Our study found that patients who received buprenorphine in primary care did just as well as those who received it in specialized addiction treatment settings,” said O’Connor.

Soon, the Drug Addiction Treatment Act of 2000 permitted physicians who met certain criteria to treat opioid addiction in outpatient offices using FDA-approved Schedule III, IV, and V narcotics, although none were available at that time. Two years later, the FDA approved two drugs that fit the bill.

Subutex (buprenorphine hydrochloride), the partial opioid agonist that O’Connor studied, could alleviate withdrawal and cravings with less risk of overdose or abuse than methadone. Suboxone (buprenorphine hydrochloride and naloxone hydrochloride) added naloxone to decrease the risk of misuse. Both formulations could be administered in a doctor’s office.

Medication-assisted therapy—Subutex or Suboxone in addition to such psychosocial treatment as counseling—became the standard of care. “It was revolutionary,” said Edens. “One patient could be waiting to get their blood pressure checked next to another who is waiting to get Suboxone for opioid use disorder, and nobody knows the difference.”

Researchers, including David A. Fiellin, M.D., HS ’94, FW ’96, professor of medicine, challenged a long-standing belief when they began to show that treatment with buprenorphine combined with primary care physician management was as effective as buprenorphine combined with cognitive behavioral therapy.

ALIGNING EVIDENCE WITH POLICY

While treatment has advanced over the last 50 years, policy and medical education lag. Medical school curricula spend little time on addiction. In part because

of this neglect, physicians who want to treat patients with buprenorphine must first attend an all-day course. Federal law limits them to treating up to 275 patients at a time in a “qualified setting” that complies with information technology requirements and makes counseling services available. For practical reasons clinicians rarely if ever treat the full 275 patients allotted to them.

“It sends a message to physicians,” said Edens, “that this is a dangerous or abusable system, but buprenorphine is so easy to use, and when it’s misused, it’s usually for the exact reason we would use it: to treat withdrawal.”

But treatment for opioid use disorder won’t stop, now that it’s treated as a chronic condition in an outpatient setting in a manner similar to such other chronic diseases as diabetes. “As with any other chronic disease,” said O’Connor, “we’ll continue to search for new and more effective medication and psychosocial treatment approaches to improve health and save lives.” *yale medicine magazine*

Sonya Collins is a freelance writer in Atlanta, Georgia.



A mother's love

Spreading a Yale pediatrician's intuitive, unorthodox, effective treatment for opioid-dependent newborns.

BY CHRISTOPHER HOFFMAN | GREG HALL ILLUSTRATION

More than six months after his paper on his new treatment for babies born to mothers addicted to opiates appeared in the journal *Pediatrics*, Matthew Grossman, M.D., HS '06, assistant professor of pediatrics, is seeing his methods slowly but steadily take hold. [See “More mom, fewer drugs,” *Yale Medicine Magazine*, Autumn 2016].

Boston Medical Center and Christus Regional Medical Center in Santa Fe, New Mexico, have adopted his approach, which reduces babies' withdrawal time by replacing drug therapy with increased contact with their mothers. Hospitals in Camden, New Jersey, and Canada, and state health collaboratives in New Hampshire, Vermont, Maine, and Maryland are all talking to him about introducing the protocol. Articles highlighting his methods have appeared in *The New York Times* and other publications. Inquiries from medical institutions have grown over the past 18 months from infrequent to one or two a week in 2017, and Grossman has traveled extensively to give talks and help with implementation. “I don't say no,” he says.

While he is gratified by the growing recognition and use of his treatment, Grossman wishes it would be adopted more quickly. Additional data collected at Yale New Haven Hospital and other institutions have only confirmed how well it works, he says.

Grossman's key insight came in 2009 when he realized that babies who spent more time with their mothers left the hospital after an average of 22 instead of 29 days. That flew in the face of the all-but-universal and long-standing practice of taking babies born addicted to opiates from their mothers, putting them in intensive care, and following a rigid protocol to assist their withdrawal from morphine and other drugs. Grossman and his team

at Yale New Haven Hospital started experimenting to see whether even more time with mom would further speed withdrawal. The results were dramatic: the average hospital stay plummeted by more than two-thirds to just 5.9 days, with most of the infants needing far less, (if any), medication. “More mom, fewer drugs,” is how Grossman sums it up.

Grossman is now working on a second paper that expands on and reinforces his findings. He and his team compared their actions under the new method with the traditional method, the Finnegan Neonatal Abstinence Scoring System. That method tracks 29 symptoms to determine whether a baby should receive morphine or another drug. They found improvement, for example, in 70 percent of babies who would have received medication under the old system. Amazingly, the Finnegan scoring method has never been extensively studied, he said.

Other works in progress include following the babies to see how they do long term—Grossman has met with the Yale Child Study Center about setting up a monitoring program—and ensuring that the infants receive any necessary services.

In retrospect, Grossman finds it amazing that hospitals have for so long used and continue to use the Finnegan method. “The idea that we were separating these babies from their source of love and their family just seems terrible,” Grossman says, sitting in his narrow, unadorned office at Yale New Haven Children's Hospital. “We have something that's really good for babies and really good for moms, really good for everyone. We think it's a much better way.” [/yale medicine magazine](#)

Christopher Hoffman is a freelance writer in North Haven, Connecticut.



Real Life Comics, Advocates for Medicine and Public Health

In their Golden Age in the 1940s, comic books saluted medicine and public health ... and paved the way for improvements in human welfare.

By John Curtis

About two years ago the Medical Historical Library began adding a new category to its collection of scholarly tomes and ancient treatises—comic books. Along with the works of Osler and Vesalius, library shelves now house issues of *Real Life Comics* that tell stories like “Edward Jenner, Plague Fighter,” “The Conquest of Yellow

Fever,” and “The Story of Medicine.”

The comics are now source material for an undergraduate course on medicine and the media, and are available to researchers exploring

a question for which there is little historical documentation.

“How do we know what ordinary people and patients thought about medicine, how they envisioned it, and what their attitudes toward it were?” said Bert Hansen, Ph.D., professor emeritus of the history of medicine and science at Baruch College

in New York, and the donor of the comic books. “Published imagery in popular journals and magazines would be an important source of evidence.”

Hansen began collecting comic books in the 1980s after shifting his research from 14th-century medicine. Advances in medicine—stories of medical progress and breakthroughs like Walter Reed’s vanquishing of yellow fever in Cuba and Edward Jenner’s discovery of vaccination to prevent smallpox—found their way into the popular imagination. By the 1920s, medical stories had become fodder for novels like Sinclair Lewis’s *Arrowsmith*. In the 1930s and 1940s Hollywood joined in with movies like *Dr. Ehrlich’s Magic Bullet*, which dramatized a cure for syphilis. And in their Golden Age in the 1940s, comic books rhapsodized about the likes of Louis Pasteur, Alexander Fleming, Howard Florey, and Clara Barton.

“The narrative of my book, *Picturing Medical Progress from Pasteur to Polio*,” said Hansen, “is the story of how we get the idea of medical progress and medical breakthroughs.”

To be sure, the comic books took some license in focusing on the eureka

moments rather than long, fruitless days in the lab. And, added John Warner, Ph.D., chair and Avalon Professor of the History of Medicine, the stories often portrayed an “under-dog,” a scientist with an unconventional idea bucking the establishment, and “this notion of a breakthrough moment.”

Even as medical and scientific accuracy took a back seat to a good yarn, Warner said, this popularization helped make medical progress possible by lionizing heroes of medicine, research, and public health. Their stories helped lay the groundwork for clinical trials of the Salk polio vaccine in the 1950s. “[The trials] very much depended on public health education and the expectation of medical progress and medical citizenship,” Warner said.

About seven years ago, Warner and Gretchen Berland, M.D., associate professor of medicine, launched a course in which Yale College students would explore how the public has viewed medicine over the years—Media and Medicine in Modern America. Along with lectures and sessions with teaching assistants in history, law, medicine, and public health, the course includes

a visit to the historical library. There, Melissa Grafe, Ph.D., the John R. Bumstead Librarian for Medical History, and Susan Wheeler, curator of prints and drawings and historical medical posters, lead the students through displays of popular health

imagery that include comics, magazines, and posters. Among the questions posed are how media portrayals shape perceptions of the medical profession as well as perceptions of health and illness within the medical community.

The course is one of the reasons that Hansen donated his collection to the School of Medicine. He knew Warner from professional conferences, but he

also knew that the School of Medicine has a vigorous program in the history of medicine and faculty who are interested in media.

“I felt that the comics would be preserved and actually used,” Hansen said. “That made Yale a special place.”



During their Golden Age in the 1940s, comic books went beyond Superman and Batman to tell the stories of unsung heroes in such fields as medicine and public health. These heroes solved medical puzzles and surmounted obstacles to improve medicine and save lives. Their stories popularized medicine and public health and, scholars say, inculcated the notion of “medical citizenship.”

TOP *Real Life Comics* issue of April 1946 told the story of Stephen Smith, a reform-minded doctor in New York City during the 19th century, who campaigned for cleaner cities, public housing, and public health. His advocacy led to the founding of the Metropolitan Health Board in New York.

BOTTOM Ronald Ross, a British physician in India, and Giovanni Battista Grassi, an Italian physician, separately demonstrated the role of mosquitoes in the transmission of malaria. *Marvels of Science* told their story in November 1943.

OPPOSITE PAGE, LEFT In May 1946, *Science Comics* told the story of Horace Wells, a dentist who realized that nitrous oxide, also known as laughing gas, could lead to painless dentistry and surgery.

OPPOSITE PAGE, RIGHT The summer 1946 issue of *Picture Stories from Science* described how Walter Reed conducted experiments with human volunteers to defeat the scourge of yellow fever.



Riding for all the right reasons

SIX FLATS, THREE CHAINS, TWO TIRES. Five thousand one hundred miles, two legs, one patriotic and philanthropic Yale physician. Those numbers sketch the cross-country odyssey of Andrés Martin, M.D., M.P.H. '02, the Riva Ariella Ritvo Professor in the Child Study Center and professor of psychiatry, who climbed onto a bicycle on August 17 in Seattle, Washington, and arrived over two months later in Washington, D.C., no worse for wear.

“I loved every minute of it,” Martin said.

The goal of that ambitious ride, called Break the Cycle: to raise awareness of and funding for pediatric mental illness. Along the road, Martin was joined by a rotating cast of 49 fellow riders, including physicians and family members of children

with mental illness. They did media interviews, held one-off fundraising events—including a spin class—and ultimately raised over \$200,000 for the American

Academy of Child and Adolescent Psychiatry (AACAP). The organization represents what he calls one of medicine’s most underserved specialties.

“The need is huge—even if we quintupled the number of child psychiatrists, it wouldn’t be close to enough,” said Martin. The money raised by the ride will support research and help to train new child psychiatrists, as well as assisting children with mental illness to access the care they need.

A typical day on the road saw Martin up by 5 a.m., climbing onto his carbon-fiber Trek bike by 7, and pedaling until midafternoon—about 100 miles a day. Every evening, the experienced triathlete climbed into an ice bath to protect his legs from inflammation, a routine so effective that he never needed Tylenol. Martin got lucky with the weather, too: in 500 hours on the road, he endured only about four hours’ rain.

It was also Martin’s first journey through the country as a naturalized United States citizen. The son of Slovakian Jewish Holocaust survivors who emigrated to Mexico, he earned his medical degree in Mexico City. He continued his medical training at the University of Miami and at Massachusetts General Hospital before joining Yale’s faculty in 1996.

The trip was a “wonderful, very granular way of getting to



know the country,” Martin said. “I’ve been grateful for all the opportunities that America has opened for me and for my family. I’m incredibly patriotic Crossing the country coast to coast, to feel the textures and the smells and the sights, it’s really, really deep and meaningful.” Some favorite memories: Badlands National Monument in South Dakota; a short ride

in Portland, Oregon, whose pace was set by children; a man with schizophrenia who thanked the cyclists for their work on his behalf.

Martin himself has faced mental illness, and the ride

began as a personal journey. Seven years ago, he took up cycling as a way to cope with a bout of serious depression, the fourth such episode of his life. Along with professional help and a “dash of apt chemicals,” Martin wrote in an AACAP editorial called “Cyclotherapy,” cycling helped him overcome depression. After adding a cross-country trip to his bucket list, he realized he

Andrés Martin, M.D., M.P.H. '02, in Boston, Massachusetts, nearing the end of his epic months-long cross country bicycle fundraiser. Over \$200,000 was donated to Martin's ride on behalf of the American Academy of Child and Adolescent Psychiatry (AACAP), and he raised awareness about the crucial issue of child mental illness, as well as how to service those children who need attention.



ONLINE EXCLUSIVE

Digitized medical student theses have been downloaded tens of thousands of times by researchers around the world. Part of an ongoing project to bring as much human knowledge as possible online and advance scientific inquiry, it is run through the Medical Library with assistance from the office of Alumni Affairs.

For more on digitized theses, visit ymm.yale.edu/theses

could use the ride to give back to his profession.

Given that stigma surrounding mental illness adds to the difficulty many children face in accessing psychiatric care, Martin says it's important to speak openly about his own issues.

"If I as a psychiatrist don't talk about it, who will?" he asked. "If all this is about stigma, stigma, stigma, and we dare not say the dirty name of depression or other mental illnesses, who will?"

At the end of 2017, Martin stepped down after a 10-year term as editor of the AACAP's journal. He is also AACAP's secretary-elect and a visiting professor at Tel Aviv University. In addition to mentorship, research, and patient care, Martin is a prolific writer with many essays and reviews of popular and scholarly books in publication. He lives in New Haven with his wife, Rebecca, and their four children.

Break the Cycle was such a success that Martin plans to make it a franchise of sorts in the child psychiatry community. For next year, he's planning a two-day journey from Vancouver, British Columbia, to Seattle. A trip through Sweden is also in the works for 2019.

In the process, Martin hopes more of his colleagues will begin to think of themselves as clinician-philanthropists, helping the organizations that helped them at earlier stages of their careers.

"The mentorship, training, education, and early exposure of folks going into this field—that's something that I'm really excited about," he said. "No matter what branch of medicine you are in, what you're passionate about, there's a way of giving back."

—Jenny Blair, M.D. '04



Straddling science and spirituality

Anna Yusim, M.D. '06, a psychiatrist in New York City, has spent much of the last decade meditating on the often-invisible intersection of science and spirituality—that ethereal sense of connection to something greater than oneself. Yusim herself took to science seamlessly, but to spirituality slowly. Now, she's demonstrating—in her practice and her writing—how the two are far from mutually exclusive.

"Science is the study of the objective, measureable, quantifiable, testable, repeatable," Yusim said, "and spirituality, by definition, is the opposite: It's transcendent, personal, immanent, subjective, difficult to measure quantifiably." But opposites need not be in conflict, Yusim maintains. Indeed, their reconciliation is where she found her own fulfillment—and now invites readers to find theirs in her debut book, *Fulfilled: How the Science of Spirituality Can Help You Live a Happier, More Meaningful Life*.

Until her residency at New York University in 2006, "living spiritually wasn't a part of who I was," Yusim said. It was, however, a significant part of how her mother saw the world during Yusim's childhood in Moscow.

Despite the difficulty of finding religious and spiritual texts in the Soviet Union, Yusim's mother avidly pursued books on Judaism, Hare Krishna, and Buddhism, among others. Yusim's grandfather, Yefim, asked his deceased wife to intercede when Yusim's family was awaiting visas to immigrate to the United States in 1981. The visas came two weeks later. At the age of 5, Yusim arrived in Chicago with her family. She took more after her physics professor father, however, who saw his Judaism as a cultural rather than a spiritual identity. The same scientific mindset carried Yusim into her time at the Yale School of Medicine.

"Science was the currency of knowledge and of exchange," Yusim said. "What led me to pursue medicine was that I had always been so interested in the mind and how the mind works." But then came residency. On paper, Yusim's life looked mapped out, tidy, *fulfilled*: trudging valiantly through the most rigorous step of her medical education, in a relationship with a kind man, with a future in a field she loved.

"Here I was, training to be a psychiatrist and to help people lift depression and anxiety from their lives," Yusim said. "So why

was I feeling kind of depressed and anxious myself? ... I was ready for my spiritual education to begin.”

While maintaining her natural skepticism and a physician’s analytic mindset, Yusim took her first tentative steps into where and how the “world of spirit interacts with the world of science.” She describes her decade-long quest to unite the two sides of human experience as a key component of her life’s purpose (alongside helping her patients and nurturing her marriage)—and the impetus for writing *Fulfilled*. Having found and defined that life purpose, Yusim set out, through her psychiatric practice and the stories of herself and her patients, to help others—patients and readers—do the same.

“There’s no cookie-cutter approach,” Yusim said. Psychiatric and spiritual guidance is a relationship, she said. “It’s really working with individuals to help them connect to the soul in the most essential and real way to them.” Integrating medicine and spiritual practices like meditation has helped Yusim identify goals for finding a fulfilled life. “All of us face critical decision points where we can choose to be authentic or not ... to align with our true selves or with who we think we have to be,” Yusim writes. “I know that I am not alone in having lived much of my life out of alignment with who I really am.” Her realization of this misalignment



Anna Yusim, M.D. '06, spent her childhood in secular Soviet Moscow. Her father, a physics professor, viewed his Judaism in cultural terms, and Yusim entered Yale School of Medicine similarly predisposed toward agnosticism. Since that time, although studying and practicing in a scientific field, she has come to appreciate the importance of spirituality in her own life, as well as its capacity to help others.

came early in her psychiatry residency. Yusim acknowledged the veneer of perfection she’d built around the emptiness she felt inside, and set her sights on abandoning that perfectionism to address that root emptiness.

In Yusim’s experience, the point of connection between science and spirituality is everywhere. Literally. Spirituality sees the world as more complicated and connected than people perceive with their senses—quantum physics says the same. “According to quantum physics, at a level of reality that is invisible to the human eye, everything and everybody

is interconnected with one another and to all living organisms,” Yusim writes.

“My hope is that people will get a sense of how to integrate more traditional medical training with the slightly less conventional spiritual approach,” Yusim said. “They’re actually not incompatible—you can tap in and utilize many spiritual principles and ideas in the service of healing.”

—Natasha Strydhorst

Putting children first

AFTER THE GREAT RECESSION, researchers in pediatric health worried that their field might suffer a permanent loss of funding. That concern faded as U.S. research dollars increased in recent years, but Cliff Bogue, M.D., FW '93, chair of Yale School of Medicine's pediatric department, believes even more money should be invested today in child health research. Before and since taking the department's helm in August 2017, Bogue has traveled to Washington, D.C., to advocate for more pediatric research funding and resources from lawmakers and the National Institutes of Health (NIH). For him, the calculus couldn't be simpler. "Think of the results a treatment could have on a 5-year-old who lives to 95, versus an 80-year-old who lives 15 more years," Bogue says.

Recent advances in genetics research suggest that many adult diseases have origins that can be traced to childhood. If more data could be gathered from studies that include children, those relationships could be examined with greater certainty, Bogue said. "One of the next broad themes in pediatric research will be what we call research across the life span," added Bogue, who has served as chief medical officer of Yale New Haven Children's Hospital since 2014.

Starting this year, the Yale Center for Clinical Investigation (YCCI) will roll out a pilot funding program on life span research. Researchers from across departments at Yale will be encouraged

to gather preliminary data on collaborative projects and use the results to apply for larger NIH grants. Bogue imagines projects that push the edges of medicine. "You could have a geriatrician working with a geneticist to identify biomarkers in Alzheimer's disease that can be found in childhood," he says.

Just like his childhood hero, Sherlock Holmes, Bogue thrives on asking the right questions about patient care or a new scientific study. He recalls making his career decision after shadowing a pediatrician as a high schooler in his hometown of Tampa, Florida. Bogue earned his medical degree at the University of Virginia in 1985 and completed his pediatrics residency at Vanderbilt University. He then devoted time to his passion for developmental biology

research. After finishing a critical care fellowship at Yale, Bogue joined its faculty in 1993.

Since then, pediatric research has moved at warp speed, Bogue says, especially as genetic sequencing costs have settled to affordable levels. He expects it to continue apace. "Up to 30 percent of patients we see in the pediatric intensive care unit are there because something in their body didn't form correctly from birth. Most of the time it's a genetic mutation," Bogue said.

He sat down with *Yale Medicine Magazine* to talk more about research across the life span, the single most important activity for young children, and the perils of too much screen time.



watch an interview
with Cliff Bogue at
ymm.yale.edu/bogue

{ To nominate a subject for Q&A, contact
Yale Medicine Magazine, 1 Church Street, Suite 300, New Haven, CT 06510 or email ymm@yale.edu

What does research across the life span mean?

We are finding that a surprising number of diseases have their origins very early in the life span and they may not manifest until years later. If we understand these and can identify them, then we can intervene much earlier. For our YCCI pilot program, the idea is to get groups of people together and started on a project. We want to investigate the biological, environmental, social, and psychological aspects of disease—many of which have their origins in childhood and even prenatally.

What is the single most important thing a parent can do for his or her child?

I think we should worry about the increasing amount of time children spend watching a screen, whether it be TV or video games or iPads, and less time spent interacting with others. This constant screen time can actually change the neural networks in the brain. One way to counteract this is through reading and actively playing. If there was a single greatest predictor of how someone will do in life, it is based on how much vocabulary

they were exposed to early in life. So much evidence suggests the importance of reading to children at an early age.

What is the most memorable moment of your career?

There are quite a few memorable moments. All of them include patient recovery. A year ago, I had visit from a former patient, a young man now in his 20s, who had had a severe head injury. We didn't think he would do much except be in bed the rest of his life. But he pulled through and went through rehabilitation therapy. He came back to see me because he had just won a gold medal at the Paralympics in Brazil.

What will be your priority as chair?

Much of my focus will be what all chairs must focus on, which is being an international leader in research, education, clinical care, innovation, and collaboration. Another thing that is important to me is that our department maintains an environment in which people feel valued and excited to be here. There's been a lot of discussion in our medical

school and at a lot of schools about physician burnout, about the culture, and if clinicians feel valued. I've always felt like this department has a personal touch, and that people are its greatest resource. I think that's important to continue. It's nice to remember what we are all about: our privilege to care for children and their families. To make lives better. It's something that most people don't get to do.



The Schmuck in My Office: How to Deal Effectively with Difficult People at Work

By Cathy Shufro

Move over, *Birds of North America* and *World's Top Restaurants*. Make room for a new field guide—to obnoxious co-workers.

The Schmuck in My Office: How to Deal Effectively with Difficult People at Work helps readers reduce friction with unruly colleagues by understanding the psychological and biological causes of their behavior. The authors, both psychiatrists, identify disruptive personality types and offer strategies for working with them.

Jody J. Foster, M.D., M.B.A. and Michelle Joy, M.D. '12, use stories to illustrate the traits of 10 personality types that include the Narcissist, the Bean Counter, the Venus Fly Trap, the Distracted, and the Robotic. The Narcissist, for example, is someone (usually male) who expects others to cater to him, seeks attention, fishes for compliments, sulks, frames insults as jokes, and spreads rumors. Colleagues may find themselves treating a narcissist like a glass ornament for fear of offending him. The book explores what

underlies these behaviors, explaining that the arrogance and bluster are compensatory: “In his most private moments, the Narcissist fears that he isn’t all that great.”

So how to endure the narcissist who wreaks havoc in the workplace? It helps if co-workers respond promptly to requests or invitations, because narcissists are quick to feel snubbed. Managers can prevent them from hogging credit by rewarding teamwork more than solo efforts. And colleagues can help narcissists digest criticism by delivering it inside a “compliment sandwich” that begins and ends with praise.

Readers will benefit from such strategizing, Joy noted in a recent interview. “If you’re having a hard time at work because of a difficult person, it can make a huge proportion of your life uncomfortable. But it’s not just about how happy we are at work. It’s also about the

safety of our patients.” The Joint Commission issued a Sentinel Event Alert in 2008 warning that workplace strife can lead to errors. Disruptive and intimidating behaviors may also hasten employee turnover and increase costs.

Joy met Foster, the principal author, in 2013 when Foster was her attending on the acute psychosis unit at Pennsylvania Hospital in Philadelphia. Foster chairs the hospital psychiatry department and serves as a clinical professor at the University of Pennsylvania’s Perelman School of Medicine. Joy now works at the Philadelphia VA Medical Center.

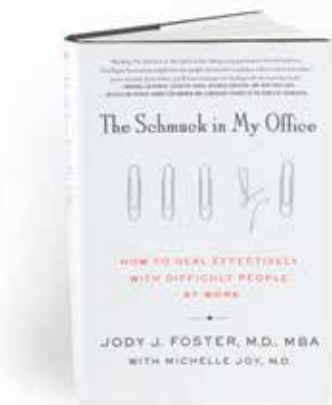
During the five years required to pitch, write, and edit the book, Joy said the partnership worked well because Foster has experience at the intersection of psychiatry and institutional culture, and a master’s from the Wharton School, while Joy has a long-time interest in writing.

Joy found time to write while at Yale School of Medicine. Physician-author Randi Hutter Epstein, M.D. '90,

M.P.H., M.S., served as a mentor when Joy edited the *Yale Journal of Humanities in Medicine*. Joy also worked with the late gastroenterologist and writer Howard M. Spiro, M.D., and participated in a writing group led by psychiatrist John Strauss, M.D. '59, now professor emeritus of psychiatry.

Joy and Foster don’t intend the book to be a diagnostic tool, but rather a rough guide to what makes co-workers irritating. “No person is going to exactly fit into one category and not the other,” Joy said. “You can get a sense of what ballpark to go to: ‘OK, the Robotic fits, but maybe the Bean Counter kind of fits, too.’ Because often there’s an overlap.”

Foster and Joy counsel empathy (and sometimes therapy) for the irritating co-worker. “They’re not setting out to be a difficult person,” said Joy. “They’re struggling with their own anxieties, their own insecurities.”



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Auction raises \$13,000 for hunger and homelessness

OVER 25 YEARS, through an annual auction, students in the health professions have supported New Haven nonprofits that address issues of hunger and homelessness. “They are taking a more holistic approach to the issue of not having access to food,” said second-year medical student David Dupee, one of the auction organizers, as he addressed the crowd at the auction in Café Med on Dec. 7. “They are providing access to health care providers, social workers, and other resources that really address the context in which social inequality occurs. All of these programs depend on us.”

This year, the 25th Annual Hunger and Homelessness Auction raised \$13,000 that will be distributed to Y2Y New Haven, Jewish Family Services, and Integrated Refugee and Immigrant Services.

—John Curtis