

STEPPING OFF "THE

PITT PEOPLE LOOK TO NEW WAYS TO END THE OPIOID EPIDEMIC | BY JENNY BLAIR WITH ERICA LLOYD AND KATY RANK LEV

PATH TO HELL"



In August 2015, a 26-year-old mother in a Walgreens southwest of Pittsburgh collapsed from an opioid overdose, her toddler locked in the bathroom stall with her. It was part of a rash of opioid poisonings in Washington County, Pa., which led to 25 overdoses and three deaths in two days. David Hickton, U.S. attorney for the Western District of Pennsylvania, called the outbreak "apocalyptic."

A bad situation had gotten worse. Since its origins around 2000, the opioid abuse epidemic has devastated the United States. What began with a well-intended rise in pain reliever prescriptions has led to widespread, entrenched pill and heroin addictions. Heroin is now increasingly laced with fentanyl, as was probably the case in that Washington County outbreak, often without the user knowing (though some now seek out its high); and fentanyl is many times more potent and deadly. Accidental drug overdose is now the leading cause of death by injury in this country, with 78 people dying of an opioid-related poisoning every day.

ILLUSTRATIONS | STACY INNERST

Amid the wreckage, Pitt Health Sciences faculty are studying the problem and developing new ways to approach it. They're also tackling the issue in Western Pennsylvania, an especially hard-hit area. Pitt faculty were a part of the U.S. Attorney's Working Group on Drug Overdose and Addiction, which issued its first action plan in 2014. Mark Nordenberg, Pitt chancellor emeritus, has made the issue a priority at the University's Institute of Politics, of which he is chair. The institute catalyzes public-private sector conversations about regional policy. In 2014, an institute advisory group led by Hickton issued a set of recommendations relating to pill abuse; it released another in October about the opioid epidemic as a whole. Nordenberg also connected Hickton (JD '81), who is his former law student, to Donald Burke, dean of the Graduate School of Public Health, sparking new conversations about Pitt's role in addressing the epidemic.

"Nobody's saying we should never use opioids," says Susan Meyer, the School of Pharmacy's associate dean for education, who codirects the Pitt Center for Interprofessional Practice and Education. "We just have to understand better about avoiding indiscriminate use of them."

On March 29, the Association of American Medical Colleges released a letter signed by 69 medical schools, including Pitt, that pledged a renewed commitment to training students to meet the epidemic. (The Schools of Nursing and Pharmacy have signed similar pledges.)

For Pitt Health Sciences students about to graduate, Arthur S. Levine, senior vice chancellor for the Health Sciences who is the John and Gertrude Petersen Dean of the School of Medicine, charged his staff with rapidly organizing an April 14 panel on the topic. The event included harrowing talks by Hickton; Burke, who holds the UPMC Jonas Salk Chair in Global Health; and Gwendolyn Sowa, who is now chair of the Department of Physical Medicine and Rehabilitation.

Levine attributed the epidemic to inappropriate pain medication prescribing, noting that the medical profession, the pharmaceutical industry, and failed federal regulatory mechanisms sowed the seeds of its creation.

We now know that between 5 and 15 percent of people who are prescribed opioids for pain will develop an abuse problem. They might receive opioids for chronic or acute pain in an internist's office, in the ED, in a pain management clinic, or for surgery.

Hickton called this "the worst epidemic in our history." He noted, "A person who gets addicted to prescription pills is basically on the path to hell at the rate of a dollar a milligram."

As part of the panel discussion, Hickton shared details of the outbreak in Washington County. Burke showed a time-lapsed map of accidental poisoning deaths in the United States, with counties colored according to their death rates. In the 1980s, sporadic counties showed elevated death rates; by the mid-2000s, the map displayed explosive color all around the nation (with a red hot spot indicating poisonings in Western Pennsylvania). Sowa explained how little evidence there is to recommend opioids for low back pain, yet how commonly physicians prescribe them anyway, contradicting guidelines.

"It's very challenging to change provider behavior," Sowa noted. It's easier, of course, to persuade students; and Pitt and UPMC will be training both emerging and established providers.

In the pages that follow, we show how Pitt people are working to help end the devastation. The first steps involve changing how people think about the problem.

—Jenny Blair with Erica Lloyd

DOCTORS COME CLEAN

When it comes to treating pain, health professionals across the country are embarking on a massive shift of mind-set—their second in recent history.

Opioids include morphine and its relatives, all of which can relieve pain and cause euphoria and dependence. Less than two decades ago, doctors tended to be cautious about prescribing these drugs for fear of addicting patients.

However, in the 1990s, patient- and physician-activists began to call attention to the serious problem of undertreated pain. The American Academy of Pain Medicine and other professional societies adopted pain as the "fifth vital sign." Physicians accepted the supposition that addiction was unlikely if opioids were given for significant chronic pain, an optimistic claim later found to be based on thin evidence.

Around the same time, drug companies manufactured and began marketing powerful new opioid formulations, like the extended-release form of oxycodone, OxyContin.

"One of the only tools that primary care physicians had was providing opioids," recalls Ajay Wasan, an MD professor of anesthesiology and vice chair for pain medicine. Pain clinics offering multidisciplinary treatment—considered cutting-edge prior to the opioid epidemic—have been in short supply for decades.

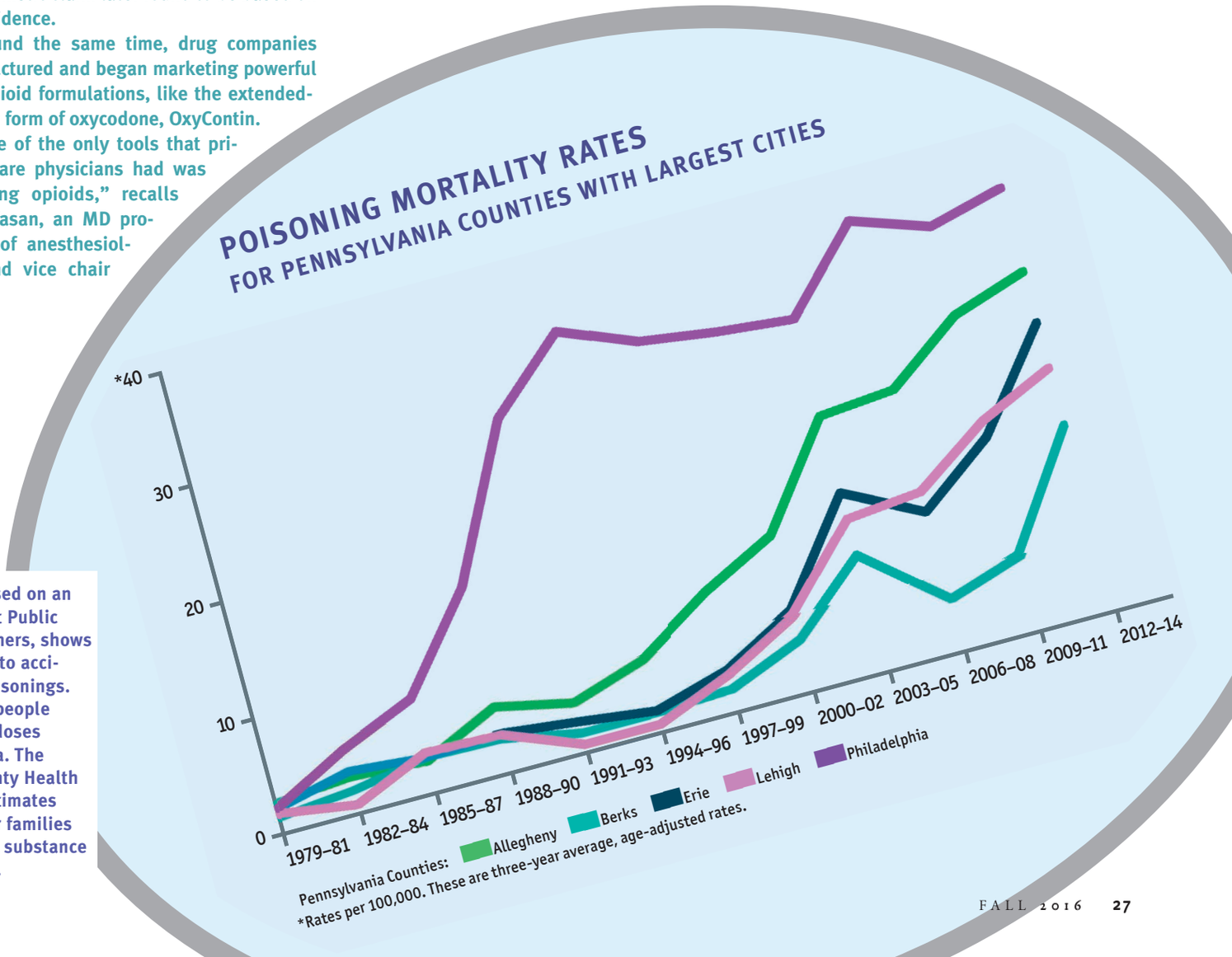
Several years into this movement, signs of a crisis emerged. Opioid painkillers did addict a substantial portion of patients, as well as their families and friends. In the meantime, dealers hawking cheap heroin began to fan out in U.S. cities, tempting people whose pill habit had gotten expensive. Deaths began to rise.

"The supposition was wrong," says associate professor of anesthesiology Michael Mangione, an MD. "[Patients'] pain isn't controlled indefinitely. They don't go back to work. They do have side effects. Tolerance is a big issue. They get opioid-induced hyperalgesia, where being on the opioids chronically actually makes their pain worse. And, obviously, it has led to an enormous addiction and abuse problem."

Indeed, many opioid abusers overdose and die—some 28,000 of them in 2014, the highest rate of opioid-related deaths on record. Eighty percent of all new heroin users got their start using prescription pain pills. And physicians widely acknowledge their role in starting it all.

"In retrospect, sometimes we rely on experience and a consensus of experts when we don't have good objective data. We truly believed 10, 12, 14 years ago that what we were doing was correct," Mangione says. "But we were wrong.

"Over the first 10 years of my career physicians were part of the culture that created this problem," Mangione adds. "I'm spending the latter part of my career trying to clean it up." *—JB*



This graph, based on an analysis by Pitt Public Health researchers, shows deaths related to accidental drug poisonings. In 2015, 3,500 people died from overdoses in Pennsylvania. The Allegheny County Health Department estimates that one in four families struggle with a substance abuse problem.

GRAPH BY PICTOGRAM STUDIO BASED ON "PATTERNS AND TRENDS IN ACCIDENTAL POISONING DEATHS: PENNSYLVANIA'S EXPERIENCE 1979-2014," FIGURE 4, BALMERT L, BUCHANICH J, PRINGLE J, WILLIAMS K, BURKE DS, MARSH G, PLOS ONE, MARCH 10, 2016.



OLD WAY

A CASE THAT ENDS BADLY (c. 2000)



A man gets hurt at work lifting something. His low back pain becomes chronic. Eventually, he goes to his doctor. The physician hands him an opioid prescription, saying, "There's no serious injury, but this will help with the pain."



Patient fills it, takes it. He finds himself sitting more, thinking, *I'm afraid that if I move I'll really hurt myself*. This inclination is called "fear avoidance."



Turns out the man is in the unfortunate subset of patients who develop tolerance and dependency to the drug.



Pills get expensive; he switches to heroin.

"Where we've really missed the boat as a medical community is getting these patients reactivated. They start taking pain medications, they start having a little lower energy and motivation, they become less and less active, their pain becomes worse, they start taking more pain medications, and it becomes this vicious cycle. Maybe a decade or so ago, we would have told them to rest for a few days. Now we're doing quite the opposite. We're telling them that they need to keep moving."

—Gwendolyn Sowa, Chair, Department of Physical Medicine and Rehabilitation

"Between 5 and 15 percent of patients who are prescribed opioids for pain will develop either an abuse or addiction problem."

—Ajay Wasan, Vice Chair, Pain Medicine, Department of Anesthesiology

About one in four people who try heroin become addicted. In 2014, 586,000 people in the United States had a heroin abuse problem.

Fear avoidance can make low-back pain related disability worse and can block recovery.

An illicit prescription opioid habit can cost hundreds of dollars a day.



NEW WAY A CONSERVATIVE APPROACH



A man gets hurt at work lifting something. Eventually, he goes to his doctor. The physician tries a conservative approach, newly recommended by the Centers for Disease Control and Prevention.



In 2016, the CDC released these best practices for chronic pain unrelated to cancer or palliative care. Conservative practices are being folded into Pitt's Health Sciences curricula, as well.

- Use nonopioid therapies, such as acetaminophen, nonsteroidal anti-inflammatory drugs, anticonvulsants, antidepressants, physical therapy, assessment for anxiety and depression, cognitive behavioral therapy, and nerve blocks.
- Start low and go slow: if using opioids, begin with a low dose.
- Follow up: monitor patients for efficacy and possible harm.

"A lot of times we've been, as providers, a little too quick to pull out the prescription pad and try to quickly fix the problem, as opposed to spending the time and resources needed to tease out all these other complicating factors." *—Gwendolyn Sowa*

Fear Itself

Pitt's School of Health and Rehabilitation Sciences is leading a $12 million national trial to see if patients with fear avoidance who are given extra cognitive behavioral therapy heal faster than patients given conventional treatment.

"We're trying to identify patients who tend to think in this way [i.e., are afraid to move] and intervene with them early on when they're still acute, to characterize their pain in the right way and encourage activation and encourage confrontation of the pain process. [We will] see if that reduces the incidence of an acute situation becoming chronic.

"All the while, we're monitoring opioid use in both of the groups."
—Anthony Delitto, Dean, School of Health and Rehabilitation Sciences



With a new kind of prescription plan built into UPMC's electronic medical record system, a man with back pain is likely to hear this from his doctor: "I want to help you address the root cause of your back injury and pain. I'm writing you a prescription to help you with your activity level and fitness. Call this health coach. In six weeks, let me know how you're doing."



Lessen Suffering

Pain has two components. The sensory component, called nociception: *Ouch. I feel that.* And the suffering component: *This is horrible—make it stop!* The latter is the emotional, behavioral, and cognitive interpretation of the pain stimulus—the story we tell ourselves about it, so to speak.

It's prolonging suffering—perhaps from dread, anxiety, anger, or sadness—that mires us in misery. Pitt physical therapy students are being taught to observe this distinction and explore ways to mitigate suffering for patients. Opioids treat the sensory part of pain—not suffering.

PREVENTION PLAN

A doctor's prescription carries an aura of authority that helps motivate the patient to fill it. Mike Parkinson, an MD and UPMC Health's senior medical director of Health and Productivity, wants to employ what he calls the "power of the white coat" toward addressing the root causes of disease.

The National Institutes of Health has recognized the School of Medicine as a Center of Excellence in Pain Education. Pitt has been developing online case-based teaching modules on how to handle opioids in patients with problems like low back pain, dental pain, and fibromyalgia.

UPMC Health Plan's Prescription for Wellness lets doctors click a box in the electronic medical record (EMR) to print a paper prescription for health coaching. The coaches help patients take on unhealthy behaviors and habits (like smoking or not exercising). The prescription comes with the coach's phone number; Parkinson says many patients call from the parking lot right after a visit. The EMR then periodically reminds office staff to call patients and check if they've "filled" the prescription.

Parkinson says, "These types of innovations give [staff] the opportunity to engage patients and their families in the prevention, treatment, and even reversal of some of these conditions with lifestyle." Physicians say, *It makes me feel like a doctor again*, he notes.

Begun as a pilot in the General Internal Medicine Clinic, Prescription for Wellness doubled tobacco-cessation and weight-loss rates compared to standard coaching. It's rolling out across UPMC this fall. "We're the only system in the country that does [EMR-based lifestyle-change prescriptions]," says Parkinson. "We're getting calls from leading systems in the country asking, *How did you guys do this?*" *—JB*

POST-OP DEPENDENCE DROP

Surgery is a big reason why patients get opioids. But cutting back on narcotics, doing without them, and using other pain-control approaches can help post-op patients heal faster. An approach called enhanced recovery after surgery (ERAS) is getting patients home as much as three days sooner.

For colorectal surgery, at least, standard surgical practice means patients get opioids while asleep during the operation. After the operation, they're put on a patient-controlled intravenous narcotics pump (called patient-controlled analgesia, or PCA). The drugs naturally slow bowel activity, which is already a problem after surgery, so patients might sit in the hospital for almost a week before being able to eat, switch to oral opioids, and go home.

"The more opioids patients take before surgery and the more they're given during their surgery, the more they require after their surgery," says Pitt assistant professor of anesthesiology Stephen Esper, an MD and MBA.

By contrast, ERAS patients get other pain medications—like acetaminophen, ibuprofen, and ketamine—before, during, and after a procedure (as well as some opioids). That means the bowel "wakes up" sooner, so many patients are eating solid food just hours after their operations. They might get oral opioids, but only 17 percent wind up needing a PCA pump. By the time they go home, the pain tends to be modest. And these patients aren't more likely to be readmitted to the hospital than patients treated the old way.

"We don't want [patients] to be tethered to an IV or other catheters. We want them to walk. We want them to get out of bed," says Esper. "Many patients and providers feel that physicians, nurses, PAs, or CRNPs are responsible for patient recovery. Truly, it is the patient who is the team leader. We are the patients' support staff and encourage and empower them to take responsibility for those healthier steps toward a recovery, which includes walking after surgery, on the same day."

"I can't say [the rate of opioid] abuse is high after colorectal surgery, but I think abuse altogether is high, so we have to be careful as to how we're sending patients home [and how we're] controlling their pain," says UPMC colorectal surgeon and Pitt assistant professor of surgery Jennifer Holder-Murray.

She and Esper, a cardiothoracic anesthesiologist, learned about ERAS during their fellowships at Mayo Clinic and Duke, respectively. The ERAS approach was developed in the late 1990s in Denmark but has been slow to make inroads in the United States.

At three UPMC hospitals, however, it's now standard practice in colorectal and pancreatic operations. The physicians plan to expand to other surgical specialties and more UPMC hospitals. (And there's much more to ERAS than easing up on narcotics for pain. Watch for more *Pitt Med* coverage in future issues.)

Shorter hospital stays, no extra re-admissions, better patient satisfaction. Is there a downside? "No," says Holder-Murray. "There's really none." *—JB*

No Tolerance?

A hallmark of opioids is that people can develop tolerance, or the need to take ever-higher doses to maintain the same pain-relieving (or euphoria-inducing) effects. In the lab, Pitt's Howard Gutstein and his team have discovered a mechanism that causes tolerance—they've also found a way to completely eliminate it. They're about to start clinical trials of tolerance-blocking compounds to see if they can prevent or reverse tolerance. Such an approach could help people suffering from addiction and/or pain cut down on opioid doses.

"These are revolutionary breakthroughs. If it works in humans the way it does in rodents and monkeys, Pitt may be able to provide the first effective treatment to help eradicate the opioid epidemic."

—Howard Gutstein, Chair, Department of Anesthesiology

FORECASTING AN EPIDEMIC

Donald Burke, dean of Pitt's Graduate School of Public Health, notes opioid overdose deaths have surpassed motor vehicle accidents and are now the leading cause of years of life lost for persons under age 65 in Pennsylvania. Yet in terms of the scope of the epidemic, he points out that those deaths are just the tip of the iceberg.

Pitt Public Health researchers made headlines in recent years with a modeling platform (called FRED), which they developed for predicting infectious disease outbreaks. The platform helped one California legislator, Richard Pan (MD '91), persuade colleagues of the need to vaccinate against measles. Burke believes his team can use the same kinds of tools to pinpoint outbreaks and activity around the noninfectious epidemic of opioid use disorder. Such a model would predict actions of "virtual people" without infringing on privacy rights. Burke and his team are now working on a model of all 4 million people in Western Pennsylvania that simulates and forecasts prescription drug use, addiction, overdoses, and deaths into the future. They then will use the model to evaluate the effectiveness of public health interventions, such as reducing the number of opioid prescriptions.

In an October report on opioid use disorder released by Pitt's Institute of Politics, U.S. Attorney for the Western District of Pennsylvania David Hickton notes that we can't prosecute or incarcerate our way out of this epidemic. What's needed, he says, is a true partnership between law enforcement and health care to get people help when they need it. Burke says his model would offer decision support for leaders to "contain and reverse the opioid epidemic." *—EL*

ACCIDENTAL POISONING DEATHS IN PENNSYLVANIA*

		1979		2014	
		Deaths	*Rate*	*Deaths*	*Rate*
Overall		**134**	**2.04**	**2458**	**29.16**
Sex	Male	96	3.02	1633	38.89
	Female	38	1.12	825	19.50
Age Group	15-24	43	2.38	277	16.25
	25-34	30	2.04	654	39.87
	35-44	18	1.70	555	36.69
	45-54	24	2.17	616	34.10
	55-64	19	1.70	356	20.10
Race	White	118	1.98	2160	30.73
	Black	16	2.85	283	27.00
	Other	0	0.00	15	4.24

** Poisonings linked to drugs. Rates are per 100,000 accidental poisoning deaths among persons age 15 to 64, by selected characteristics.*

GRAPH BY PICTOGRAM STUDIO BASED "PATTERNS AND TRENDS IN ACCIDENTAL POISONING DEATHS: PENNSYLVANIA'S EXPERIENCE 1979-2014, TABLE 1, BALMERT L, BUCHANICH J, PRINGLE J, WILLIAMS K, BURKE DS, MARSH G, PLOS ONE, MARCH 10, 2016.

ADDICTION TREATMENT

With its relapses and remissions, life-threatening complications, and periods of stable control, opioid addiction (to painkillers and heroin) is a chronic disease, also called substance use disorder. It's not curable, but it's "very treatable," says Antoine Douaihy, a Pitt professor of psychiatry and medicine and an addiction specialist. Unfortunately, up to 80 percent of patients aren't in treatment, not even a 12-step program. The most effective approach is multidisciplinary and long-term—much more than expecting a patient to "stop using," says Douaihy. Some medications help. Naltrexone is an opioid antagonist that prevents opioids from activating receptors, thereby helping to control cravings and prevent relapse. A long-acting form of naltrexone, originally approved for alcohol addiction, is FDA approved to treat opioid addiction. Other medications like buprenorphine and methadone can help patients control their opioid use, prevent cravings and relapse, and also achieve social stability and better functioning. This year the FDA approved a long-acting implant of buprenorphine that releases a constant low dose for six months. Douaihy is conducting clinical trials of medications that target heroin and prescription opioid painkillers.

Douaihy says, "Research has demonstrated that the combination of behavioral therapies, motivational interviewing, psychoeducation, family interventions, mutual support groups such as [Narcotics Anonymous], and medication-assisted treatments produces long-lasting positive outcomes and helps patients to establish and follow a recovery program." Starting this fall, Pitt med students are learning about treating clinical addiction with these approaches. *—JB*

HAVEN FOR MOMS

"Are you thirsty?" The question rocked Jenifer Lake (not her real name) as she sat in the intake room at Magee-Womens Hospital of UPMC's Pregnancy Recovery Center (PRC). Not once before in her pregnancy had anyone asked how she was feeling. She began to cry as staff members congratulated her for both her pregnancy and her decision to battle her substance use disorder.

"We understand that addiction is a chronic illness, and that the women coming to us are taking steps to control that disease, doing the best thing for themselves and their children," says PRC medical director and Pitt clinical assistant professor Michael England, an ob/gyn, whose patients tend to hug him both in the halls of Magee and on the streets of Pittsburgh. (He choked up when he mentioned a patient's recent relapse to this writer.)

A couple of years ago, Lake and her mother had driven from Pittsburgh to Texas, stopping at each state along the way in search of a rehabilitation program that would accept a woman pregnant with twins. Despairing, they returned home only to learn of a new program beginning here, at Magee, in July 2014.

Encouraged by research suggesting babies have better health outcomes when their mothers take buprenorphine (a stabilizing drug that prevents mothers from going through withdrawal) compared to methadone, Magee researchers partnered with Medicaid insurance providers to develop a comprehensive outpatient program for pregnant women with substance use disorder: the PRC.

Lake joined nearly 200 other women in the PRC receiving behavioral health and social services as well as prenatal care, while taking buprenorphine. Lake was able to remain living at home and even continue working throughout her pregnancy.

England feels the true benefit of the PRC lies in the behavioral health services branch of the program because, although medication manages the symptoms of the disease, it doesn't help anyone "understand why [patients] are using substances, what led to the behavior initially, and how we can help them control this disease." Each woman gets help navigating housing, transportation, and legal issues. The program also helps with job training in addition to providing individual counseling, group sessions, and classes ranging from yoga to art therapy.

"Our philosophy is to focus on the pregnancy and wrap recovery around this major life event," says England.

Pregnancy was certainly a turning point for Lake, who had attempted sobriety several times, only to relapse. Her inability to find help terrified her, because she knew withdrawal could trigger miscarriage, but she desperately wanted to stop taking illicit drugs.

The PRC became a haven for her. Lake feared cesarean delivery for her twins because of the pain medication she'd likely have to take post-surgery, so the PRC supported her through vaginal delivery of healthy, full-term babies.

England says the PRC results have been promising. More than half of the babies born at Magee to women on methadone had neonatal abstinence syndrome, which can occur when babies are exposed to opioids in the womb. Those newborns can go through withdrawal after birth and may need pharmacological treatment to help with symptoms. However, the PRC's neonatal abstinence syndrome rate is 34 percent, which means the majority of the babies born in the program require no medication or NICU stay.

England says of the PRC mothers, "They should feel proud—we are proud of them."

Lake stays home full-time with her twin daughters, now 2 years old. Both are thriving, as is their mother. After delivery, Lake transferred her care to an outpatient rehabilitation facility near her home. She visits support groups once a week but feels her daughters are the real ticket to her continued recovery.

"I don't have time for cravings when I'm constantly keeping toddlers from climbing the bookshelves," she says.

—Katy Rank Lev

