New strategies to combat opioid addiction

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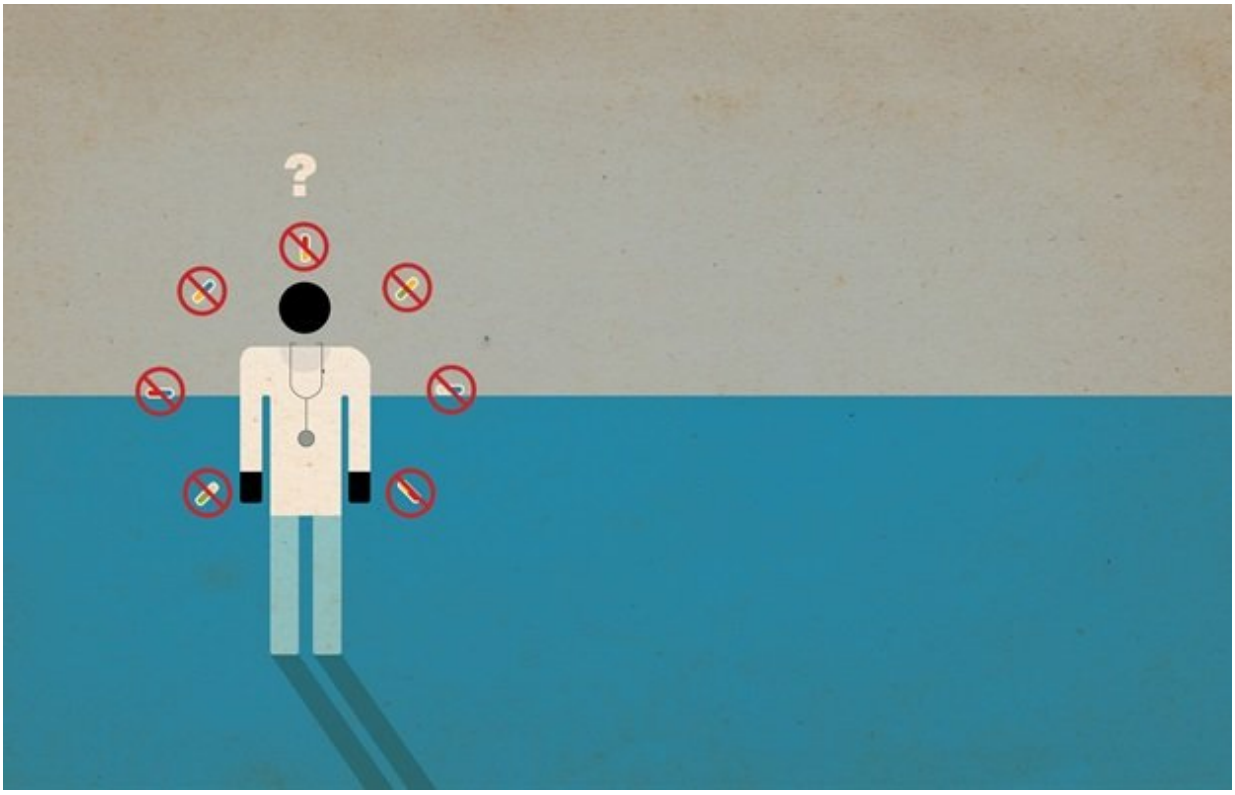

Credit: Yale University

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—all 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 multipronged 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 Alternatives to opioids).

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."

Provided by Yale University