



BRIAN CAHILL/ZUMA WIRE/ALAMY LIVE NEWS

# Against the tide in an ocean of opioids

Taking on the multibillion-dollar drugs industry to stem the US opioid epidemic has made **Andrew Kolodny** both a hero and a hate figure

**A**NDREW KOLODNY first noticed something was amiss in 2004, when his job as a medical director at New York City's health department was to reduce drug overdose deaths. An expert in addiction treatment, he opened an evening and weekend clinic with the expectation that his patients would come from New York's rougher neighbourhoods, where overdose deaths had been concentrated for decades.

But many of those who turned up came from wealthy areas like Long Island and Westchester. About a third were elderly; the rest mostly in their 20s and 30s. All were using prescription opioids, whether prescribed by their doctor or bought on the black market. "That's when I recognised we had something awful going on," he says.

By this time tomorrow, another 100 or so people in the US will have died from an

accidental overdose of opioids. The opioid epidemic has claimed more than 200,000 American lives since 1999. Many of these people defy the old stereotypes: they became addicted only after their pain prompted their doctor to prescribe painkillers derived from the opium poppy – the source of heroin.

If Kolodny had had his way, perhaps the catastrophe unfolding in slow motion across the US could have been averted. He has arguably fought harder than anyone to reduce the country's opioid prescriptions, a campaign that has made him a hero to many. Others have dubbed him "Killer Kolodny" and even "the devil". Ranged against him is a pharmaceutical industry that has spent about a billion dollars in lobbying. Kolodny is regularly attacked by the very people he is trying to save: patients who are scared of losing legal access to drugs they believe are essential to ease their pain.

Within a few years of opening his clinic, there was growing evidence of an addiction epidemic. Kolodny thought, perhaps naively, that policy-makers would curtail opioid use for long-term pain treatment. But researchers who blamed the epidemic on the rise in prescription opioids found their work "ripped apart" in the pages of academic journals and at medical conferences by well-respected pain doctors. Many critics were later revealed to have been paid handsomely by the firms making these drugs. "I realised we were going to have a harder time than I thought," says Kolodny.

Pharma firms were marketing to physicians in a big effort to destigmatise opioids. And it was working like a dream: opioid prescriptions quadrupled from 1999 to 2010. Overdose deaths involving opioids also rose sharply.

Before the late 1990s, opioids were prescribed only for severe, acute pain, and

to palliative and cancer patients. Physicians were extremely careful with the drugs, due to valid concerns about their addictiveness. But there were millions of people with poorly treated chronic pain, and opioid makers saw an opportunity. Based on scant evidence, these firms, notably Purdue Pharma, convinced doctors that addiction was very rare, thanks to the development of sophisticated, time-release formulas. It was unfair, the argument went, to withhold these new opioids from people with back injuries, arthritis and other sources of chronic pain. Wanting to help their patients, doctors agreed. In 2007, Purdue agreed to pay \$600 million in fines after pleading guilty to misleading the public about the addictive nature of opioids.

It isn't clear exactly how opioids relieve pain. They create a surge of the feel-good chemical dopamine in the brain, and one idea is that the resulting euphoria masks pain. For short-term pain, such as in post-surgical situations, opioids can be very effective. But the dopamine release also "reinforces" the drug-taking behaviour, as it does for eating or sex.

But the real driver of addiction, says Kolodny, is that "people feel really bad without the opioid". Opioids inhibit the locus coeruleus system in the brain, which regulates fight-or-flight hormones. That's why opioids are relaxing. But as the drug levels drop, the locus coeruleus begins to wake up, until it's operating on overdrive. "Your brain is responding as if there's a lion in the jungle ready to tear you to pieces," says Kolodny. The sense of impending doom, combined with other withdrawal symptoms – pain comes



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**PROFILE**

Andrew Kolodny is co-director of opioid policy research at the Heller School for Social Policy and Management at Brandeis University in Waltham, Massachusetts. He also directs Physicians for Responsible Opioid Prescribing

back with a vengeance too – makes people desperate for relief, and for that next dose. About a quarter of those given an initial 12-day opioid prescription were still using the drugs a year later, according to a study by the US Centers for Disease Control and Prevention.

In 2010, outraged by what he saw as the failure of the US Food and Drug Administration (FDA) to tighten restrictions on opioids, Kolodny co-founded an advocacy group, Physicians for Responsible Opioid Prescribing (PROP). It created guidelines

pointing out that the benefits of long-term opioids for chronic pain were not established and that physical dependence and tolerance can develop within days. In other words, patients need ever greater doses to achieve the same painkilling effect.

Pain doctors painted Kolodny and his peers as the "lunatic anti-opioid fringe", and PROP's guidelines were largely ignored. But if anything, this made Kolodny more resolute. The way he describes it, it was as if he and the other nine initial PROP members were witnessing a disaster that no one in authority seemed to see. Convincing others of the reality he saw in his clinic and in national overdose statistics became an obsession.

He spent his spare time filing Freedom of Information Act requests for details of the pharmaceutical industry's influence on FDA committees and major medical foundations. He shared his findings with journalists and created a series of educational videos. In one, he interviews Russell Portenoy, a pain-management specialist who benefited from substantial payments from opioid manufacturers. In a surprisingly candid moment, Portenoy admits to Kolodny: "Because the primary goal was to destigmatise [opioids], we often left evidence behind."

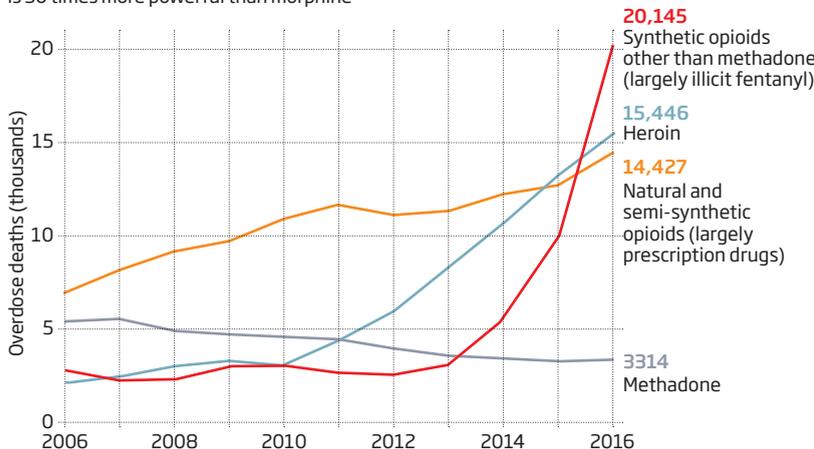
In 2013, Kolodny finally got what he wanted: a key opportunity to make his case to the FDA. He was given 20 minutes to argue that a certain class of opioid drugs be put in a more restrictive category. The heavily lobbied FDA had resisted the move for years, but in 2013, law-makers pushed it to consult experts on the issue. The drugs in question, including Vicodin, combine the opioid hydrocodone with acetaminophen (paracetamol). The "vast majority" of addicted people got there through these combination drugs, says Kolodny, because all other opioids were in stricter categories and harder to obtain.

When the day came, Kolodny was so nervous he forgot to shave. "I got there looking like a total mess, but I knew this was it," he tells me. He told the FDA: "All of us should be pretty lucky that we were born at a time when our environment wasn't flooded with pain pills, because if we weren't, some of us might not be here today. We have a responsibility to protect this generation, and we're failing. We're losing a generation."

It was a powerful speech. Judy Rummmler remembers it well. "He was just so eloquent and so knowledgeable," she recalls. Rummmler was there because her son, Steve, became addicted to opioids after taking them medically for five years. In 2011, days after he successfully completed rehab, Steve walked into a

**Too hard to handle**

With more than 50,000 US deaths from overdoses involving opioids in 2016, the sharpest increase was a result of synthetic ones such as fentanyl, which is 50 times more powerful than morphine



SOURCE: CDC WONDER

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