

The Best Drug for Quitting Smoking Can't Shake Its Suicide Stigma

WRITTEN BY KALEIGH ROGERS November 24, 2015 // 10:30 AM EST

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Image: Stephanie Monohan

One night while watching TV, Chris Kunkel decided to kill himself.

“Out of nowhere, it just came over me,” Kunkel told me over the phone.

He found a bottle of Tylenol PM in the medicine cabinet, swallowed the contents, and put himself to bed. Kunkel was home alone; his wife and two kids were out of town visiting family, but he was on call for work as an army IT specialist and had to stay behind. He had a great life, and no history of depression or mental illness of any kind. The dark thought simply bloomed in his mind, as natural as any other.

“It was like thinking, ‘I’m going to go outside for a smoke,’ or ‘I’m going to go to the bathroom,’” Kunkel said. “Except it was: ‘I’m going to kill myself.’”

Luckily, Kunkel's wife arrived home shortly after he downed the fistful of pills. She had decided to come home early to surprise him and found him unconscious next to the empty bottle. She called 911. In the hospital the next morning, Kunkel said he struggled to piece together the events of the night before.

"It took awhile for the cobwebs to clear and for me to realize what had happened, and it was tough to try to explain," Kunkel said. "Really it wasn't until we got home that we realized that the Chantix probably played a major part."

Kunkel had recently started taking Chantix, a prescription drug intended to help people quit smoking. It worked: Kunkel did quit smoking. He went from a seven-year, pack-a-day habit to cold turkey just 10 days after his first pill. Ten days after that, he tried to kill himself. His story isn't unique.

Since entering the market in 2006, hundreds of Chantix users have reported a laundry list of disturbing effects ranging from intense nightmares, to amnesia, to suicidal (and even [homicidal](#)) thoughts and behavior. There were enough reports that the Food and Drug Administration ordered Pfizer, the maker of Chantix, to include a [black-box warning label](#), the strictest possible labeling requirement.



Image: Stephanie Monohan

Yet dozens of scientific studies have failed to find any link between Chantix and adverse psychiatric effects. These are not just Pfizer's in-house trials, but independent double-blind, [placebo-controlled studies](#), focused [observational studies](#), and sweeping [meta-analyses](#).

These are studies published in illustrious journals like *The Lancet* and *the BMJ*. While some of these results come from researchers with ties to Pfizer, many do not, and all of the studies I reviewed came to the same consensus: there's no evidence Chantix is linked to adverse psychiatric events.

How can there be such a gulf between what the science is indicating and what the population is reporting? Testimonies from former Chantix users like Kunkel make it difficult to come to any conclusion other than the one he came to: that Chantix caused him to have suicidal thoughts. But a review of the scientific literature has the exact opposite effect: one can't help but conclude that something else is causing these people to feel like they're losing control.

The truth is difficult to pin down, and it's made Chantix a unique case study in how we view prescription drugs, scientific proof, and addiction. And it raises a sobering question: When it comes to risk, can we ever be truly sure that a drug is safe?

“That’s where the trouble really started.”

Ten years ago, on a Wednesday in November, Pfizer [filed an application](#) with the FDA for approval of a new drug to help people quit smoking. Included in that application was a stack of pre-market trials Pfizer had completed, testing the drug on more than 4,500 patients, many for a full year. The worst side effects that were reported were intense, vivid dreams and some nausea, but no serious psychiatric events emerged.

“In addition to being efficacious, varenicline appeared to be well tolerated by most participants,” read [a report](#) based on these clinical trials published in the *Journal of the American Medical Association* the summer after the FDA approved Chantix. “Nausea, the most common complaint, was reported as being mostly mild to moderate in severity and rarely resulted in discontinuation of study medication. [...] Varenicline may represent an advance in the treatment of tobacco dependence.”

And the drug proved very effective in helping people kick their tobacco habits: after one year, [23 percent](#) of participants were still tobacco-free, and hadn't taken a single puff since quitting, even though they were only given the drug for the first twelve weeks. Compared to other smoking cessation treatments—nicotine patches and gum, for example, have about a [6 percent](#) success rate—this was remarkable.

Varenicline, the drug Pfizer would market as Chantix, is a combination of nicotinic partial agonist and antagonist. Agonist means it stimulates receptors in the brain, and antagonist means it blocks those receptors from being stimulated by other chemicals. Chantix does both.

When a smoker takes a puff of a cigarette, the nicotine in the smoke is absorbed through the lungs into the bloodstream, hitching a ride to the brain. The nicotine binds to nicotinic receptors in the brain, which causes a release of dopamine, [giving the brain](#) a feeling of reward. It's a short-lived little high that helps contribute to the addictive qualities of tobacco.

Varenicline works by binding to those receptors before the nicotine can get there, which does two things to help someone quit smoking. First, it causes the brain to release a little bit of dopamine (about 40 percent of what nicotine would, that's the “partial” part of a partial agonist), which helps curb the craving for a cigarette—your brain already got its dopamine reward, so it's not seeking it from another source. Second, it blocks nicotine from being able

to bind to those receptors (that's the antagonist function), so even if you do smoke, the nicotine doesn't have the same effect.

In May, 2006, the FDA gave the green light to start marketing Chantix.

“Initially, there was tremendous uptake. There was just a huge, pent-up demand of these drugs,” said Dr. Frank T. Leone, the director of comprehensive smoking treatment programs at the University of Pennsylvania’s Abramson Cancer Center. (Leone has no affiliation to Pfizer and his research, which focuses on smoking cessation tactics and nicotine addiction, has never been funded by Pfizer.)

Varenicline is not the only smoking cessation drug on the market (Zyban, or bupropion, is another popular choice that’s been around since 1997) but with a [slightly higher](#) success rate than its predecessor, it quickly became one of the most frequently prescribed drugs in the world. Since it came on the market in 2006, Chantix has been prescribed to more than 11 million unique patients in the US and more than 22 million unique patients globally, according to Pfizer. Leone said Chantix followed a similar arc to Zyban, with an initial burst of popularity that later fizzled out.

“The sales would go through the roof, and then shortly after, sales would taper off when comments about weird side effects emerged,” Leone said.

For Chantix, the honeymoon ended a little more than a year after the drug hit the market. It started with a smattering of online posts from users claiming they were having suicidal thoughts after taking the drug. It hit a climax with the death of Carter Albrecht.

Albrecht was a musician best known for his work as a keyboardist and guitarist for the New Bohemians. In August 2007, Albrecht started taking Chantix. A week later, after a night of drinking, he started behaving erratically, [yelling at and attacking](#) his long-time girlfriend. When she locked him out of the house, he went to the neighbor’s and began yelling at the house from the yard. The neighbor [fired a “warning shot”](#) through the door, which struck Albrecht in the head and killed him.

Albrecht’s girlfriend and family publicly blamed Chantix for his sudden change in behavior and subsequent death. His parents even [tried to sue Pfizer](#). After Albrecht’s death, the FDA began receiving hundreds of reports through its adverse events reporting system, a kind of hotline where anyone can report side effects for any drug. By November, 2007, the reports had totaled enough that the FDA [alerted the public](#), launched an investigation, and ordered Pfizer to update its label.

In 2009, as the reports from the public continued to mount—[hundreds](#) of adverse effects have been reported each year since Albrecht’s death—the FDA ordered Pfizer to add a black box warning. A black box warning is the most severe labeling requirement the FDA has, and is “designed to call attention to serious or life-threatening risks,” [according](#) to the agency. The warning Pfizer is required to use on all of its Chantix literature, including a large disclaimer on [its website](#), includes pretty ominous language warning patients that “some people have had changes in behavior, hostility, agitation, depressed mood, suicidal thoughts or actions while using Chantix to help them quit smoking.”

Chantix's alleged dark side was a topical enough to warrant a Saturday Night Live skit.

At the same time as it issued the black box warning, the FDA ordered Pfizer to do trials specifically looking for evidence of neuropsychiatric adverse events, and how the drug affects people with existing mental health issues.

“I never thought that it would give me the results that it did, that it would throw my life into complete disarray,” said Derek De Koff, a journalist who penned [a feature](#) for *New York* magazine in early 2008 on his experience using Chantix. De Koff wrote that he had bizarre, vivid nightmares, that he felt tired, paranoid, and depressed. He wrote that he contemplated suicide without even really grasping that that’s what he was doing.

“Maybe I should just go downstairs and leap in front of a tour bus,” De Koff wrote, recalling his experience. “Or launch my head through the computer screen. All this seemed logical, but also weirdly funny, even at the time: I could see how crazy these impulses were, I could recognize them as suicidal clichés. But I couldn’t make them go away.”

De Koff still believes Chantix was responsible for his dark thoughts and feelings—he hasn’t experienced any since going off of the drug seven years ago. In his story, he questioned the quality of the premarket trials of varenicline, which were limited by only including people who had no history of certain illnesses including depression and alcohol and drug abuse. De Koff told me he still thinks the initial results were flawed because of this limitation.

“Somebody who smokes a lot, there’s a very good chance they drink as well and there were no studies as to how this drug would impact somebody who was drinking,” De Koff said. “A lot of the stories come from people who were on Chantix and drinking. It’s a dangerous mix, or it was a dangerous mix for me. That’s where the trouble really started.”

When the concern about Chantix’s possible dark side first started to build, the only data we had to rely on about varenicline were these consumer reports and Pfizer’s few premarket trials. There wasn’t enough information to say with any certainty whether Chantix was causing these sometimes terrifying symptoms. But we’ve come a long way since then.

“It’s not the Chantix.”

The FDA’s adverse effects reporting system is a useful tool for the agency. It’s a quick and easy way for patients, doctors, and families to report any potential side effects. If reports start to show a pattern, it’s usually a clue that more scientific research needs to be conducted.

The reports on Chantix show a definite pattern. From January 1 of this year to October 16, the Food and Drug Administration received 1,811 reports of adverse effects attributed to varenicline, according to documents obtained by Motherboard through a Freedom of Information Act request. Of those, 98 included suicidal thoughts, 18 reported a completed suicide, and two reported a homicide.

It’s disturbing to read through hundreds of cold, clinical reports dotted with terms like “nightmare,” “hallucination, auditory,” and “completed suicide.” But it’s important to view these reports in context: these are anecdotal, unproven associations. They can’t be taken as proof of a causal relationship. Just as an anti-vaxxer could report autism as a side-effect of the MMR vaccine, anyone can report any symptom and attribute it to Chantix.



FDA Adverse Event Reporting System (FAERS)
Freedom of Information Act (FOIA)

Detailed Report

FDA Received Date	Case #	Case Type	Health Professional	Outcomes	Manufacturer Control #	Age	Sex	Country	
13-Feb-2015	10792901	NON-EXPEDITED			US-PFIZER INC-2015058001	57 YR	Female	USA	
Preferred Term		Product		Role Route		Dosage Text		Duration	Manufacturer
Fatigue		Chantix		S		UNK			PFIZER
Somnolence		LISINOPRIL		C		25 mg, 1x/day			
Feeling abnormal		OMEPRAZOLE		C		UNK			
FDA Received Date	Case #	Case Type	Health Professional	Outcomes	Manufacturer Control #	Age	Sex	Country	
13-Feb-2015	10793322	NON-EXPEDITED		DE	US-PFIZER INC-2015056952	56 YR	Male	USA	
Preferred Term		Product		Role Route		Dosage Text		Duration	Manufacturer
Completed suicide		Chantix		S		UNK			PFIZER
FDA Received Date	Case #	Case Type	Health Professional	Outcomes	Manufacturer Control #	Age	Sex	Country	
13-Feb-2015	10793348	NON-EXPEDITED			US-PFIZER INC-2015056924		Unknown	USA	
Preferred Term		Product		Role Route		Dosage Text		Duration	Manufacturer
Cardiac disorder		Chantix		S		UNK			PFIZER

Some of the reports filed through the FDA's adverse event reporting system.

“It’s completely uncontrolled and anyone can call in and say ‘I had this effect while taking Chantix,’” said Suzanne Colby, a tobacco researcher and the associate director of the center for alcohol and addiction studies at Brown University. Colby has no affiliation with Pfizer and none of her research has ever been funded by Pfizer (nor any other drug company, she noted).

“When you don’t see these effects in the context of controlled trials but you do see it reported in this type of database, it makes me think it’s not the Chantix,” Colby said. “As a scientist, that’s my conclusion.”

Though the scientific literature has shown Chantix can cause abnormal dreams (the kind of intense nightmares often reported by users), this has been a long-known side effect, one that was evident in Pfizer’s original drug application. When it comes to the reported paranoia, dark thoughts, and suicide attempts linked to Chantix, there are dozens of studies that fail to show a connection.

A [massive study](#) published in last month’s issue of *The Lancet: Respiratory Medicine* pulled data from the National Health Service in the UK to look for evidence of a link between Chantix and neuropsychiatric risks as well as cardiovascular risks. Looking at more than 160,000 patients, the researchers found no increased risk of neuropsychiatric events when compared to bupropion (the other popular stop smoking drug) or nicotine replacement therapy (things like the patch and gum). (Two out of the six study authors have received grants from Pfizer, though those grants were not used on this study.)

Earlier this year, [a review](#) of the current scientific literature on varenicline was published in *Nicotine & Tobacco Research*. The review was written by Dr. John Hughes, who has previously received funding from Pfizer, but is also considered one of the foremost experts on nicotine. Hughes looked at 46 studies, 41 of which were not funded by Pfizer, specifically looking at suicidal outcomes. He found the studies consistently showed no increased risk of suicide with varenicline, and in the handful where there was an increased risk, it was very low.

And if the Pfizer affiliations are making you suspicious, there are plenty of examples of completely independent studies finding the same results. A [study](#) published in the February issue of *BMJ* reviewed 39 trials involving 5,817 patients who were taking Chantix and 4,944 patients taking placebos. The researchers found “no increased risk of suicide or attempted suicide, suicidal ideation, depression, or death in individuals treated with varenicline.” None of the study authors have any affiliation with Pfizer or have received any funding from Pfizer. A [study](#) from 2013, also with no ties to Pfizer, looked at 120,000 patients undergoing some form of smoking cessation treatment and found no evidence of association between varenicline and an increased risk of suicide or depression.

There are also studies that focus on specific groups, like people with [schizophrenia](#) or [bipolar disorder](#). Even with pre-existing neuropsychiatric issues, researchers found no risk of adverse effects linked to Chantix.

“You can’t discount the observational data. There’s something going on and we don’t know what it is.”

Colby suspects there are a number of factors that could be leading to the reports of negative side effects, ranging from fodder for courtroom defenses to the very real side effects of nicotine withdrawal. The fact is that Chantix is a pretty effective stop-smoking aid, so many people who report scary side effects have recently kicked two or three-pack-a-day habits, and that takes a toll on the brain, Colby said.

“The most common things are cravings, irritability, frustration, sleep disturbance, difficulty concentrating, negative affect generally, depression,” Colby said. “For people who have various forms of mental illness, maybe those are exacerbated. These things that happen very idiosyncratically, how do we know that it’s the Chantix versus something that would have happened anyway? The only way to answer that question is with clinical trials.”

It’s worth noting that Pfizer’s fingerprints are littered throughout the scientific literature—it’s a bit of a hazard with this field of study, in general. Many studies have one or more authors with some kinds of ties to the company, ranging from accepting research grants from Pfizer to testifying as expert witnesses for Pfizer in court. This doesn’t mean the studies are invalid, but it does show Pfizer clearly is investing a lot of money into studying, and possibly exonerating, Chantix.

And the company's motivations are worth considering. Just weeks after Albrecht’s death, lawyers began advertising for lawsuits. These rounds of early suits have cost Pfizer millions of dollars in settlements. By February of 2013, the company had settled most of its claims at a total cost of \$273 million, according to [SEC filings](#). It estimated it would need to spend another \$15 million on the outstanding cases, and a [class action suit](#) in Canada is still pending, according to this year’s filing.

“Pfizer believes there is no reliable scientific evidence establishing a causal relationship between Chantix and serious neuropsychiatric events,” said Steven Danehy, a spokesperson for Pfizer, in an email. “Smoking is one of the leading preventable causes of death in the world. Stopping smoking is one of the most important steps a person can take to improve their health, and the benefits of quitting are immediate and substantial. However, many people who want to quit struggle to do so without help. The risks of Chantix should be weighed against the benefits of its use.”

Pfizer is also just months away from publishing the results of a [massive clinical trial](#) looking at the effects of varenicline specifically on patients who have a history of psychiatric disorders, an undertaking requested by the FDA as the agency [considers](#) rewording or lifting the black-box warning requirement.



Image: Stephanie Monohan

“You have a tricky conundrum: you want to be cautious and provide every possible piece of info to the public to help them make a decision, but on the other hand you don’t want to put people off using what is probably the most effective stop smoking method we’ve got,” said Robert West, a professor of health psychology and the director of tobacco studies at University College London. West was a co-author on the *Lancet* study and has received grants from Pfizer.

“You can’t discount the observational data [from consumer reports,]” West continued. “There’s something going on and we don’t know what it is, but when you have a drug taken by millions of people, the laws of chance for this kind of thing are always against you.”

“How do you prove a negative?”

Cigarette smoking causes close to half a million deaths in the US annually, [according](#) to the Centers for Disease Control and Prevention. Life expectancy for smokers is ten years shorter than nonsmokers, and if you can quit smoking before you turn 40, your chance of dying from a smoking-related disease drops by 90 percent. With a higher effectiveness than any other smoking cessation treatment, Chantix can quite literally extend people’s lives.

But the reams of testimonies from patients who have suffered scary, even life-threatening, side effects from the drug online and in the media, combined with the alarming warnings issued by the FDA, could make anyone hesitant to try, and stick with, the drug.

And there's another factor at play. Despite the clear health benefits of quitting smoking, people don't view Chantix or drugs like it as "life-saving." We accept the truly [awful side effects](#) of treatments like chemotherapy (which include vomiting, mouth sores, diarrhea, and burning sensations) because we know the trade off is the chance for a longer life. But when the benefits of a drug are delayed by years or even decades, like with a smoking cessation aid, we're less willing to endure any possible negative side effects in the short term.

"If we had done this study with anything other than Chantix, I think people would have said 'yeah, absolutely, fine. No evidence of an effect, we'll move on. That's good news,'" West told me via Skype. "But with Chantix, that idea is there."

There are also pervasive cultural ideas that might make someone weigh the risks of Chantix more strongly than the risks of continuing to smoke. The public generally [perceives addiction](#) as a shortcoming, something you should just be able to overcome on your own. Why would you risk feeling suicidal to fix a problem you really ought to be able to just solve on your own?

"It's a common perspective in smokers and particularly in smokers with substance use disorders," Colby told me. "And adolescents and young adults in particular are very unlikely to take a pharmacotherapy to quit smoking, because they don't really perceive smoking as something that should require treatment to quit."

And there's the issue with proof. Can we ever truly say a drug is 100 percent safe? West said once an idea that a drug is dangerous has made its way into the public consciousness, the burden of proof becomes much higher. Instead of looking for evidence of a relationship between Chantix and negative effects, the researcher is tasked with seeking out evidence that there *isn't* a relationship.

"It's probably not related [to neuropsychiatric effects], but the key is in the 'probably,' because you can't say definitely," West said. "How do you prove a negative? You can't."

The FDA assesses drug risks all the time. If it thinks there is enough evidence that a drug causes more harm than good, it pulls it from the market (and that's if a drug company hasn't already pulled it). The FDA's label requirements on Chantix aren't proof that the drug causes people to come undone, it's just relaying the information we have: there have been reports of serious neuropsychiatric adverse effects. [Thousands of reports](#). And at the end of the day, there's no way to know for sure that a drug is 100 percent safe for every person.

As for Kunkel? He stopped taking Chantix and started smoking again as soon as he got home from the hospital, but recently quit by switching to vaping. He told me he hasn't had any issues with depression or suicidal thoughts since he stopped taking Chantix.

"I truly believe it just depends on the person," Kunkel said. "Everyone's built differently."

Lit Up is a series about drugs and drug-like substances and practices. Follow along [here](#)