Many People Taking Antidepressants Discover They Cannot Quit

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By Benedict Carey and Robert Gebeloff April 7, 2018

Victoria Toline would hunch over the kitchen table, steady her hands and draw a bead of liquid from a vial with a small dropper. It was a delicate operation that had become a daily routine — extracting ever tinier doses of the antidepressant she had taken for three years, on and off, and was desperately trying to quit.

“Basically that’s all I have been doing — dealing with the dizziness, the confusion, the fatigue, all the symptoms of withdrawal,” said Ms. Toline, 27, of Tacoma, Wash. It took nine months to wean herself from the drug, Zoloft, by taking increasingly smaller doses.

“I couldn’t finish my college degree,” she said. “Only now am I feeling well enough to try to re-enter society and go back to work.”

Long-term use of antidepressants is surging in the United States, according to a new analysis of federal data by The New York Times. Some 15.5 million Americans have been taking the medications for at least five years. The rate has almost doubled since 2010, and more than tripled since 2000.

Nearly 25 million adults, like Ms. Toline, have been on antidepressants for at least two years, a 60 percent increase since 2010.

The drugs have helped millions of people ease depression and anxiety, and are widely regarded as milestones in psychiatric treatment. Many, perhaps most, people stop the medications without significant trouble. But the rise in longtime use is also the result of an unanticipated and growing problem: Many who try to quit say they cannot because of withdrawal symptoms they were never warned about.

Some scientists long ago anticipated that a few patients might experience withdrawal symptoms if they tried to stop — they called it “discontinuation syndrome.” Yet withdrawal has never been a focus of drug makers or government regulators, who felt antidepressants could not be addictive and did far more good than harm.

The drugs initially were approved for short-term use, following studies typically lasting about two months. Even today, there is little data about their effects on people taking them for years, although there are now millions of such users.

Expanding use of antidepressants is not just an issue in the United States. Across much of the developed world, long-term prescriptions are on the rise. Prescription rates have doubled over the past decade in Britain, where health officials in January began a nationwide review of prescription drug dependence and withdrawal.

In New Zealand, where prescriptions are also at historic highs, a surveyof long-term users found that withdrawal was the most common complaint, cited by three-quarters of long-term users.

Yet the medical profession has no good answer for people struggling to stop taking the drugs — no scientifically backed guidelines, no means to determine who’s at highest risk, no way to tailor appropriate strategies to individuals.

“Some people are essentially being parked on these drugs for convenience’s sake because it’s difficult to tackle the issue of taking them off,” said Dr. Anthony Kendrick, a professor of primary care at the University of Southampton in Britain.

With government funding, he is developing online and telephone support to help practitioners and patients. “Should we really be putting so many people on antidepressants long-term when we don’t know if it’s good for them, or whether they’ll be able to come off?” he said.

Antidepressants were originally considered a short-term treatment for episodic mood problems, to be taken for six to nine months: enough to get through a crisis, and no more.

Later studies suggested that “maintenance therapy” — longer-term and often open-ended use — could prevent a return of depression in some patients, but those trials very rarely lasted more than two years.

Once a drug is approved, physicians in the United States have wide latitude to prescribe it as they see fit. The lack of long-term data did not prevent doctors from placing tens of millions of Americans on antidepressants indefinitely.

“Most people are put on these drugs in primary care, after a very brief visit and without clear symptoms of clinical depression,” said Dr. Allen Frances, a professor emeritus of psychiatry at Duke University. “Usually there’s improvement, and often it’s based on the passage of time or placebo effect.

Image

Robin Hempel began taking an antidepressant on the advice of her gynecologist. “A year and a half after stopping, I’m still having problems,” she said. “I’m not me right now.”CreditCheryl Senter for The New York Times

“But the patient and doctor don’t know this and give the antidepressant credit it doesn’t deserve. Both are reluctant to stop what appears to be a winner, and the useless prescription may be continued for years — or a lifetime.”

The Times analyzed data gathered since 1999 as part of the National Health and Nutrition Examination Survey. Over all, more than 34.4 million adults took antidepressants in 2013-4, up from 13.4 million in the 1999-2000 survey.

Adults over 45, women and whites are more likely to take antidepressants than younger adults, men and minorities. But usage is increasing in older adults across the demographic spectrum.

White women over 45 account for about one-fifth of the adult population but account for 41 percent of antidepressant users, up from about 30 percent in 2000, the analysis found. Older white women account for 58 percent of those on antidepressants long term.

“What you see is the number of long-term users just piling up year after year,” said Dr. Dr. Mark Olfson, a professor of psychiatry at Columbia University. Dr. Olfson and Dr. Ramin Mojtabai, a professor of psychiatry at Johns Hopkins University, assisted The Times with the analysis.

Still, it is not at all clear that everyone on an open-ended prescription should come off it. Most doctors agree that a subset of users benefit from a lifetime prescription, but disagree over how large the group is.

Dr. Peter Kramer, a psychiatrist and author of several books about antidepressants, said that while he generally works to wean patients with mild-to-moderate depression off medication, some report that they do better on it.

“There is a cultural question here, which is how much depression should people have to live with when we have these treatments that give so many a better quality of life,” Dr. Kramer said. “I don’t think that’s a question that should be decided in advance.”

Antidepressants are not harmless; they commonly cause emotional numbing, sexual problems like a lack of desire or erectile dysfunction and weight gain. Long-term users report in interviews a creeping unease that is hard to measure: Daily pill-popping leaves them doubting their own resilience, they say.

“We’ve come to a place, at least in the West, where it seems every other person is depressed and on medication,” said Edward Shorter, a historian of psychiatry at the University of Toronto. “You do have to wonder what that says about our culture.”

Patients who try to stop taking the drugs often say they cannot.In a recent survey of 250 long-term users of psychiatric drugs — most commonly antidepressants — about half who wound down their prescriptions rated the withdrawal as severe. Nearly half who tried to quit could not do so because of these symptoms.

In another study of 180 longtime antidepressant users, withdrawal symptoms were reported by more than 130. Almost half said they felt addicted to antidepressants.

“Many were critical of the lack of information given by prescribers with regard to withdrawal,” the authors concluded. “And many also expressed disappointment or frustration with the lack of support available in managing withdrawal.”

Drug manufacturers do not deny that some patients suffer harsh symptoms when trying to wean themselves from antidepressants.

“The likelihood of developing discontinuation syndrome varies by individuals, the treatment and dosage prescribed,” said Thomas Biegi, a spokesman for Pfizer, maker of antidepressants like Zoloft and Effexor. He urged that patients work with their doctors to “taper off” — to wean themselves by taking shrinking doses — and said the company could not provide specific withdrawal rates because it did not have them.

Drugmaker Eli Lilly, referring to two popular antidepressants, said in a statement the company “remains committed to Prozac and Cymbalta and their safety and benefits, which have been repeatedly affirmed by the U.S. Food and Drug Administration.” The company declined to say how common withdrawal symptoms are.

Nausea and ‘Brain Zaps’

As far back as the mid-1990s, leading psychiatrists recognized withdrawal as a potential problem for patients taking modern antidepressants.

At a 1997 conference in Phoenix sponsored by drug maker Eli Lilly, a panel of academic psychiatrists produced a lengthy report detailing the symptoms, like balance problems, insomnia and anxiety, that went away when the pills were restarted.

But soon the topic faded from the scientific literature. And government regulators did not focus on these symptoms, seeing rampant depression as the larger problem.

“What we were concentrating on was recurrent depression,” said Dr. Robert Temple, deputy director for clinical science in the F.D.A.’s Center for Drug Evaluation and Research. “If people’s heads went through the roof from withdrawal, I think we would have seen it.”

Drug makers had little incentive to mount costly studies of how best to quit their products, and federal funding has not filled the research gap.

As a result, the drugs’ labels, on which doctors and many patients rely, provide very little guidance for ending a prescription safely.

“The following adverse events were reported at an incidence of 1 percent or greater,” reads the label for Cymbalta, a leading antidepressant. It lists headaches, fatigue and insomnia, among other reactions in patients trying to stop.

The few studies of antidepressant withdrawal that have been published suggest that it is harder to get off some medications than others. This is due to differences in the drugs’ half-life — the time it takes the body to clear the medication once the pills are stopped.

Brands with a relatively short half-life, like Effexor and Paxil, appear to cause more withdrawal symptoms more quickly than those that stay in the system longer, like Prozac.

In one of the earliest published withdrawal studies, researchers at Eli Lilly had people taking Zoloft, Paxil or Prozac stop the pills abruptly, for about a week. Half of those on Paxil experienced serious dizziness; 42 percent suffered confusion; and 39 percent, insomnia.

Among patients who stopped taking Zoloft, 38 percent had severe irritability; 29 percent experienced dizziness; and 23 percent, fatigue. The symptoms appeared soon after people were taken off the drugs and resolved once they resumed taking the pills.

Those on Prozac, by contrast, experienced no initial spike in symptoms when they stopped, but this result was not surprising. It takes Prozac several weeks to wash out of the body entirely, so one week's interruption is not a test of withdrawal.

In a study of Cymbalta, another Eli Lilly drug, people in withdrawal experienced two to three symptoms on average. The most common were dizziness, nausea, headache and paresthesia — electric-shock sensations in the brain that many people call brain zaps. Most of these symptoms lasted longer than two weeks.

"The truth is that the state of the science is absolutely inadequate," said Dr. Derelie Mangin, a professor in the department of family medicine at McMaster University in Hamilton, Ontario.

"We don't have enough information about what antidepressant withdrawal entails, so we can't design proper tapering approaches."

In interviews, dozens of people who had experienced antidepressant withdrawal recounted similar stories: The drugs often relieved mood problems, at first. After a year or so, it wasn't clear whether the medication was having any effect.

Yet quitting was far harder, and stranger, than expected.

"It took me a year to come completely off — a year," said Dr. Tom Stockmann, 34, a psychiatrist in East London, who experienced lightheadedness, confusion, vertigo and brain zaps, when he stopped taking Cymbalta after 18 months.

To wind the prescription down safely, he began opening the capsules, removing a few beads of the drug each day in order to taper off — the only way out, he decided.

"I knew some people experienced withdrawal reactions," Dr. Stockmann said, "but I had no idea how hard it would be."

Robin Hempel, 54, a mother of four who lives near Concord, N.H., began taking the antidepressant Paxil 21 years ago for severe premenstrual syndrome on the recommendation of her gynecologist.

Image
Dr. Anthony Kendrick, professor of primary care at the University of Southampton, has received funding from the British government to develop an antidepressant withdrawal strategy.CreditAlex Atack for The New York Times

"He said, 'Oh, this little pill is going to change your life,' " Ms. Hempel said. "Well, did it ever."

The drug blunted her PMS symptoms, she said, but also caused her to gain 40 pounds in nine months. Quitting was nearly impossible — at first, her doctor tapered her too quickly, she said.

She succeeded in her last attempt, in 2015, by tapering over months to 10 milligrams, then five, down from 20 milligrams and “finally all the way down to particles of dust,” after which she was bedridden for three weeks with severe dizziness, nausea and crying spells, she said.

“Had I been told the risks of trying to come off this drug, I never would have started it,” Ms. Hempel said. “A year and a half after stopping, I’m still having problems. I’m not me right now; I don’t have the creativity, the energy. She — Robin — is gone.”

At least some of the most pressing questions about antidepressant withdrawal will soon have an answer.

Dr. Mangin, of McMaster University, led a research team in New Zealand that recently completed the first rigorous, long-term trial of withdrawal.

The team recruited more than 250 people in three cities who had been taking Prozac long-term and were interested in tapering off. Two-thirds of the group had been on the drug for more than two years, and a third for more than five years.

The team randomly assigned the participants to one of two regimens. Half tapered slowly, receiving a capsule each day that, over a period of a month or longer, contained progressively lower amounts of the active drug.

The other half believed they were tapering but got capsules that in fact maintained their regular dosage. The researchers followed both groups for a year and a half. They are still working through the data, and their findings will be published in the coming months.

But one thing is already clear from this effort and other clinical experience, Dr. Mangin said: Some people’s symptoms were so severe that they could not bear to stop taking the drug.

“Even with a slow taper from a drug with a relatively long half-life, these people had significant withdrawal symptoms such that they had to restart the drug,” she said.

For now, people who haven’t been able to quit just by following a doctor’s advice are turning to a method called microtapering: making tiny reductions over a long period of time, nine months, a year, two years — whatever it takes.

“The tapering rates given by doctors are often way, way too fast,” said Laura Delano, who had severe symptoms while trying to get off several psychiatric drugs. She has created a website, The Withdrawal Project, that provides resources on psychiatric drug withdrawal, including a guide to tapering off.

She is hardly the only one bewildered by the scarcity of good medical advice about unwinding prescriptions that have become so common.

“It has taken a long, long time to get anyone to pay attention to this issue and take it seriously,” said Luke Montagu, a media entrepreneur and co-founder of the London-based Council for Evidence-Based Psychiatry, which pushed for Britain’s review of prescription drug addiction and dependence.

“You’ve got this huge parallel community that’s emerged, largely online, in which people are supporting each other though withdrawal and developing best practices largely without the help of doctors,” he said.

Dr. Stockmann, the psychiatrist in East London, wasn’t entirely convinced withdrawal was a serious issue before he went through it himself. His microtapering strategy finally worked.

“There was a really significant moment,” he recalled. “I was walking down near my house, past a forest, and I suddenly realized I could feel the full range of emotions again. The birds were louder, the colors more vivid — I was happy.”

“I have seen lots of people — patients — not being believed, not taken seriously when they complained about this,” he added. “That has to stop.”