



HEALTH

# We Have No Drugs to Treat the Deadliest Eating Disorder

There are pills for bulimia and binge-eating disorder. Why not anorexia?

By Rachel Gutman-Wei

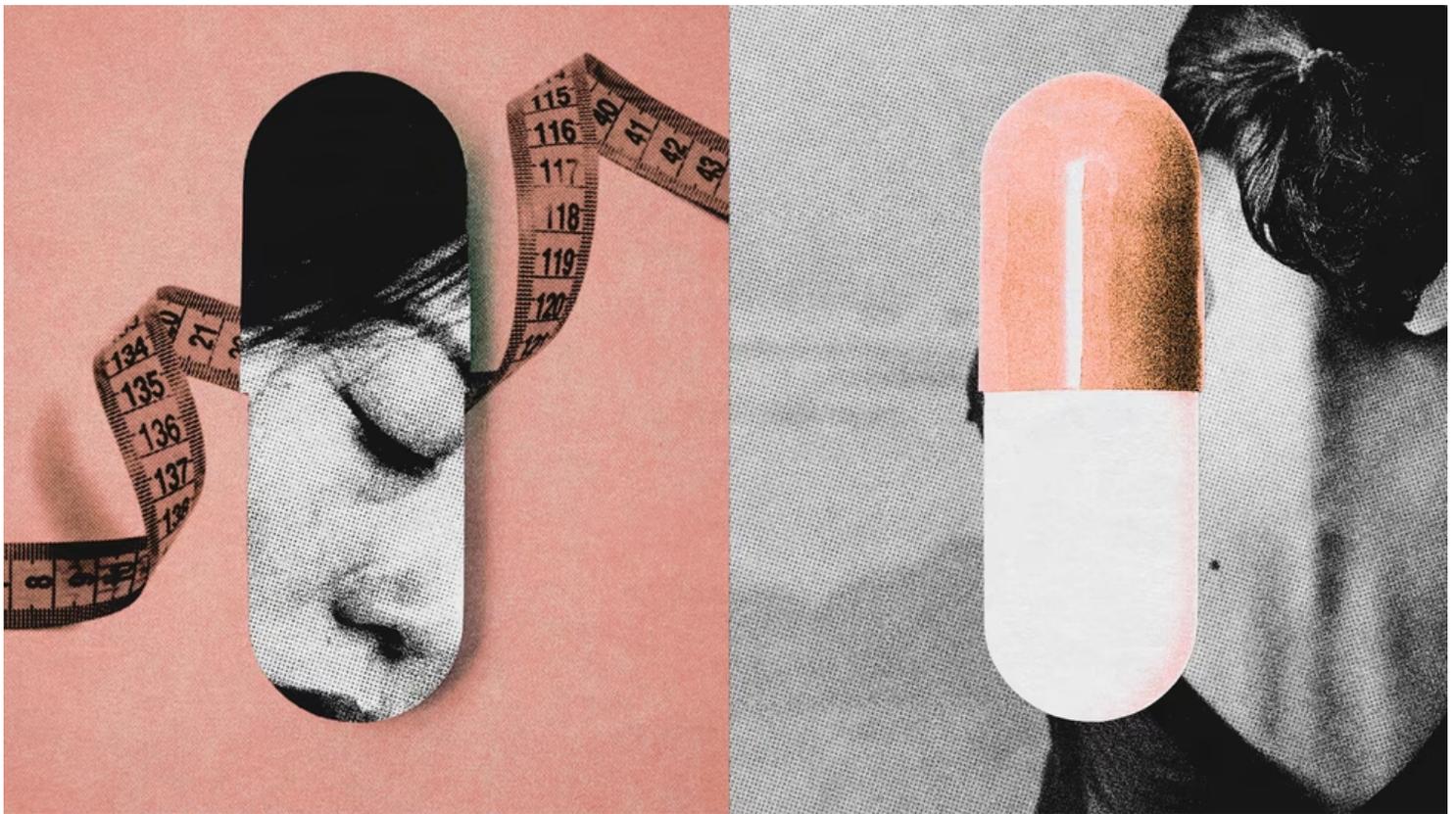


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In the 1970s, they tried lithium. Then it was zinc and THC. Anti-anxiety drugs had their turn. So did Prozac and SSRIs and atypical antidepressants. Nothing worked. Patients with anorexia were still unable to bring themselves to eat, still stuck in rigid thought patterns, still chillingly underweight.

A few years ago, a group led by Evelyn Attia, the director of the Center for Eating Disorders at New York Presbyterian Hospital and the New York State Psychiatric Institute, tried giving patients an antipsychotic drug called olanzapine, normally used to treat schizophrenia and bipolar disorder, and known to cause weight gain as a side effect. Those patients in her study who were on olanzapine increased their BMI a bit more than others who were taking a placebo, but the two groups showed no difference in their cognitive and psychological symptoms. This was the only medication trial for treating anorexia that has shown any positive effect at all, Attia told me, and even then, the effects were “very modest.”

Despite nearly half a century of attempts, no pill or shot has been identified to effectively treat anorexia nervosa. Anorexia is well known to be the deadliest eating disorder; the only psychiatric diagnosis with a higher death rate is opioid-use disorder. A 2020 review found people who have been hospitalized for the disease are more than five times likelier to die than their peers without it. The National Institutes of Health has devoted more than \$100 million over the past decade to studying anorexia, yet researchers have not found a single compound that reliably helps people with the disorder.

Other eating disorders aren't nearly so resistant to treatment. The FDA has approved fluoxetine (a.k.a. Prozac) to treat bulimia nervosa and binge-eating disorder (BED); doctors prescribe additional SSRIs off-label to treat both conditions, with a fair rate of success. An ADHD drug, Vyvanse, was approved for BED within two years of the disorder's official recognition. But when it comes to anorexia, “we've tried, I don't know, eight or 10 fundamentally different kinds of approaches without much in the way of success,” says Scott Crow, an adjunct psychology professor at the University of Minnesota and the vice president of psychiatry for Accanto Health.

The discrepancy is puzzling to anorexia specialists and researchers. “We don’t fully understand why medications work so differently in this group, and boy, do they ever work differently,” Attia told me. Still, experts have some ideas. Over the past few decades, they have been learning about the changes in brain activity that accompany anorexia. For example, Walter Kaye, the founder and executive director of the Eating Disorders Program at UC San Diego, told me that the neurotransmitters serotonin and dopamine, both of which are involved in the brain’s reward system, seem to act differently in anorexia patients.

Perhaps some underlying differences in brain chemistry and function play a role in anorexia patients’ extreme aversion to eating. Or perhaps, the experts I spoke with suggested, these brain changes are at least in part a result of patients’ malnourishment. People with anorexia suffer from many effects of malnutrition: Their bones are more brittle; their brain is smaller; their heart beats slower; their breath comes shorter; their wounds fail to heal. Maybe their neurons respond differently to psychoactive drugs too.

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Psychiatrists have found that many patients with anorexia don't improve with treatment even when medicines are prescribed for conditions other than their eating disorder. If an anorexia patient also has anxiety, for example, taking an anti-anxiety drug would likely fail to relieve either set of symptoms, Attia told me. "Time and again, investigators have found very little or no difference between active medication and placebo in randomized controlled trials," she said. The fact that fluoxetine seems to help anorexia patients avoid relapse—but only when it's given *after* they've regained a healthy weight—also supports the notion that malnourished brains don't respond so well to psychoactive medication. (In that case, the effect might be especially acute for people with anorexia nervosa, because they tend to have lower BMIs than people with other eating disorders.)

Why exactly this would be true remains a mystery. Attia noted that proteins and certain fats have been shown to be crucial for brain function; get too little of either, and the brain might not metabolize drugs in expected ways. Both she and Kaye suggested a possible role for tryptophan, an amino acid that humans get only from food. Tryptophan is converted into serotonin (among other things) when we release insulin after a meal, Kaye said, but in anorexia patients, whose insulin levels tend to be low, that process could end up off-kilter. "We suspect that that might be the reason why [SSRIs] don't work very well," he said, though he emphasized that the theory is very speculative.

In the absence of meaningful pharmacologic intervention, doctors who treat anorexia rely on methods such as nutrition counseling and psychotherapy. But even non-pharmaceutical interventions, such as cognitive behavioral therapy, are more effective at treating bulimia and binge-eating disorder than anorexia. Studies from around the world have shown that as many as half of people with anorexia relapse.

Colleen Clarkin Schreyer, a clinical psychologist at Johns Hopkins University, sees both patients with anorexia nervosa and those with bulimia nervosa, and told me that the former can be more difficult to treat—"but not just because of the fact that we don't have any medication to help us along. I often find that patients with anorexia nervosa are more ambivalent about making behavior change." Bulimia patients, she said, tend to feel shame about their condition, because binge eating is stigmatized and, well, no one likes vomit. But anorexia patients might be praised for skipping meals or rapidly losing weight, despite the fact that their behaviors can be just as dangerous over the long term as bingeing and vomiting.

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Researchers are still trying to find substances that can help anorexia patients. Crow told me that case studies testing a synthetic version of leptin, a naturally occurring human hormone, have produced interesting data. Meanwhile, some early research into using psychedelics, including ketamine, psilocybin, and ayahuasca, suggests that they may relieve some symptoms in some cases. But until randomized, controlled trials are conducted, we won't know whether or how well any psychedelic really works. Kaye is currently recruiting participants for such a study of psilocybin, which is planned to have multiple sites in the U.S. and Europe.

Pharmaceutical companies just don't seem that enthusiastic about testing treatments for anorexia, Crow said. "I think that drug makers have taken to heart the message that the mortality is high" among anorexia patients, he told me, and thus avoid the risk of having deaths occur during their clinical trials. And drug development isn't the only area where the study of anorexia has fallen short. Research on eating disorders tends to be underfunded on the whole, Crow said. That stems, in part, from "a widely prevailing belief that this is something that people could or should just stop ... I wish that were how it works, frankly. But it's not."

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