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# Bad science misled millions with chronic fatigue syndrome. Here's how we fought back

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EROS DERVISHI FOR STAT

If your doctor diagnoses you with [chronic fatigue syndrome](#), you'll probably get two pieces of advice: Go to a psychotherapist and get some exercise. Your doctor might tell you that either of those treatments will give you a 60 percent chance of getting better and a 20 percent chance of recovering outright. After all, that's what researchers concluded in a 2011 study published in the prestigious medical journal the Lancet, along with later analyses.

Problem is, the study was bad science.

And we're now finding out exactly how bad.

Under court order, the study's authors for the first time released their raw data earlier this month. Patients and independent scientists collaborated to analyze it and posted [their findings](#) Wednesday on Virology Blog, a site hosted by Columbia microbiology professor Vincent Racaniello.

The analysis shows that if you're already getting standard medical care, your chances of being helped by the treatments are, at best, 10 percent. And your chances of recovery? Nearly nil.

The new findings are the result of a five-year battle that chronic fatigue syndrome patients — me among them — have waged to review the actual data underlying that \$8 million study. It was a battle that, until a year ago, seemed nearly hopeless.

When the Lancet study, nicknamed the PACE trial, first came out, its inflated claims made headlines around the world. “Got ME? Just get out and exercise, say scientists,” wrote the Independent, using the acronym for the international name of the disease, myalgic encephalomyelitis. (Federal agencies now call it ME/CFS.) The findings went on to influence treatment recommendations from the [CDC](#), the [Mayo Clinic](#), [Kaiser](#), the [British National Institute for Health and Care Excellence](#), and more.

But patients like me were immediately skeptical, because the results contradicted the fundamental experience of our illness: The hallmark of ME/CFS is that even mild exertion can increase all the other [symptoms of the disease](#), including not just profound fatigue but also cognitive deficits, difficulties with blood pressure regulation, unrestorative sleep, and neurological and immune dysfunction, among others.

Soon after I was diagnosed in 2006, I figured out that I had to rest the moment I thought, “I’m a little tired.” Otherwise, I would likely be [semi-paralyzed](#) and barely able to walk the next day.

The researchers argued that patients like me, who felt sicker after exercise, simply hadn’t built their activity up carefully enough. Start low, build slowly but steadily, and get professional guidance, they advised. But I’d seen how swimming for five minutes could sometimes leave me bedbound, even if I’d swum for 10 minutes without difficulty the day before. Instead of trying to continually increase my exercise, I’d learned to focus on staying within my ever-changing limits — an approach the researchers said was all wrong.

## **A disease ‘all in my head’?**

The psychotherapy claim also made me skeptical. Talking with my therapist had helped keep me from losing my mind, but it hadn’t kept me from losing my health. Furthermore, the researchers weren’t recommending ordinary psychotherapy — they were recommending a form of cognitive behavior therapy that challenges patients’ beliefs that they have a physiological illness limiting their ability to exercise. Instead, the therapist advises, patients need only to become more active and ignore their symptoms to fully recover.

In other words, while the illness might have been triggered by a virus or other physiological stressor, the problem was pretty much all in our heads.

By contrast, in the American research community, no serious researchers were expressing doubts about the organic basis for the illness. Immunologists found clear patterns in the [immune system](#), and exercise physiologists were [seeing](#) highly unusual physiological changes in ME/CFS patients after exercise.

I knew that the right forms of psychotherapy and careful exercise could help patients cope, and I would have been thrilled if they could have cured me. The problem was that, so far as I could tell, it just wasn't true.

## **A deeply flawed study**

Still, I'm a science writer. I respect and value science. So the PACE trial left me befuddled: It seemed like a great study — big, controlled, peer-reviewed — but I couldn't reconcile the results with my own experience.

So I and many other patients dug into the science. And almost immediately we saw enormous problems.

Before the trial of 641 patients began, the researchers had announced their standards for success — that is, what “improvement” and “recovery” meant in statistically measurable terms. To be considered recovered, participants had to meet established thresholds on self-assessments of fatigue and physical function, and they had to say they felt much better overall.

But after the unblinded trial started, the researchers weakened all these standards, by a lot. Their revised definition of “recovery” was so loose that patients could get worse over the course of the trial on both fatigue and physical function and still be considered “recovered.” The threshold for physical function was so low that an average 80-year-old would exceed it.

In addition, the only evidence the researchers had that patients felt better was that patients said so. They found no significant improvement on any of their objective measures, such as how many patients got back to work, how many got off welfare, or their level of fitness.

But the subjective reports from patients seemed suspect to me. I imagined myself as a participant: I come in and I'm asked to rate my symptoms. Then, I'm repeatedly told over a year of treatment that I need to pay less attention to my symptoms. Then I'm asked to rate my symptoms again. Mightn't I say they're a bit better — even if I still feel terrible — in order to do what I'm told, please my therapist, and convince myself I haven't wasted a year's effort?

Many patients worked to bring these flaws to light: They wrote blogs; they contacted the press; they successfully submitted carefully argued [letters](#) and [commentaries](#) to leading medical journals. They even [published papers](#) in peer-reviewed scientific journals.

They also filed Freedom of Information Act requests to gain [access to the trial data](#) from Queen Mary University of London, the university where the lead researcher worked. The university denied most of these, some on the grounds that they were “[vexatious](#).”

## Critics painted as unhinged

The study’s defenders painted critics as unhinged crusaders who were impeding progress for the estimated 30 million ME/CFS patients around the world. For example, Richard Horton, the editor of the Lancet, [described](#) the trial’s critics as “a fairly small, but highly organised, very vocal and very damaging group of individuals who have, I would say, actually hijacked this agenda and distorted the debate so that it actually harms the overwhelming majority of patients.”

Press reports also [alleged](#) that ME/CFS researchers had received death threats, and they lumped the PACE critics in with the purported crazies.

While grieving for my fellow patients, I seethed at both the scientists and the journalists who refused to examine the trial closely. I could only hope that, eventually, PACE would drown under [a slowly rising tide of good science](#), even if the scientific community never recognized its enormous problems.

But with the National Institutes of Health only funding \$5 million a year of research into chronic fatigue syndrome, it seemed like that could take a very long time.

Then last October, David Tuller, a lecturer in public health and journalism at the University of California, Berkeley, wrote in Virology Blog a devastating [expose of the](#) scientific flaws of the trial. Tuller described all the problems I had seen, along with several more. The project was a remarkable act of public service: He isn’t a patient, yet he spent a year investigating the trial without institutional support, legal backing, or remuneration.

And, at last, the criticisms gained traction.

Racaniello and 41 other scientists and clinicians published an [open letter](#) to the Lancet calling for an independent investigation into the trial and saying “such flaws have no place in published research.” Rebecca Goldin, the director of Stats.org, an organization that works to improve the use of statistics in journalism, [eviscerated](#) the trial’s design in a 7,000-word critique.

In the meantime, a Freedom of Information Act request from Australian patient Alem Matthees was making its way through the legal system.

Matthees had asked for the anonymized data necessary to analyze the study using its original standards for success, but Queen Mary University of London had refused the

request, arguing that malicious patients would break the anonymization and publish the participants' names to discredit the trial. It again cited the death threats.

The court rejected these claims a month ago, [calling](#) them “wild speculations” and pointing out that the researchers themselves acknowledged in court that neither they nor PACE participants had received death threats.

## Startling results from a re-analysis

Just before releasing the data, Queen Mary University of London did its own [re-analysis](#) on the question of how many patients got better, at least a little bit. Their data showed that using the study's original standards, only 20 percent of patients improved with cognitive behavior therapy or exercise in addition to medical care, not 60 percent as claimed in the Lancet.

And even the 20 percent figure might be misleading, because the re-analysis also found that 10 percent of participants improved after receiving only standard medical care. That suggests that 10 percent in each of the treatment groups would likely have improved even without the exercise or therapy, leaving only 10 percent who were significantly helped by those interventions.

As for the claim that 22 percent of patients who received either treatment made an actual recovery? That went up in smoke when Matthees analyzed the raw data with the help of his colleagues and statisticians Philip Stark of the University of California, Berkeley, and Bruce Levin of Columbia University.

Their analysis showed that had the researchers stuck to their original standards, only 4.4 percent of the exercise patients and 6.8 percent of the cognitive behavior therapy patients would have qualified as having recovered, along with 3.1 percent of patients in a trial arm that received neither therapy.

Importantly, there was no statistically significant difference between these recovery rates.

The PACE researchers, the editor of the Lancet, and the editors of Psychological Medicine (which published the follow-up study on recovery) all declined to comment for this article.

Simon Wessely, president of the UK Royal College of Psychiatrists, defended the trial in an email exchange with me. He argued that some patients did improve with the help of cognitive behavior therapy or exercise, and noted that the improvement data, unlike the recovery data, was statistically significant. “The message remains unchanged,” he wrote, calling both treatments “modestly effective.”

Wessely declined to comment on the lack of recovery. He summarized his overall reaction to the new analysis this way: “OK folks, nothing to see here, move along please.”

## ‘A classic bad study’

But it doesn’t appear that outside researchers are ready to “move along.”

After reviewing the new analysis, Jonathan Edwards, a professor emeritus of medicine at University College London said he was unconvinced that these small subjective improvements indicated the patients genuinely felt better. “They’ve set this trial up to give the strongest possible chance of there being a placebo effect that you can imagine,” he said.

“This is a classic bad study,” said Ron Davis, director of the [Stanford Genome Technology Center](#) and director of the Science Advisory Board of the [End ME/CFS Project](#). He emphasized an additional problem: The study used such a broad definition of the disease that it likely included many patients who didn’t truly have ME/CFS at all.

“The study needs to be retracted,” Davis said. “I would like to use it as a teaching tool, to have medical students read it and ask them, ‘How many things can you find wrong with this study?’”

[Retractions are rare](#), however, and erasing the impact of this flawed research will take much work for years to come.

After a [sustained effort](#) by ME/CFS advocates, the federal Agency for Healthcare Research and Quality, just [changed](#) its recommendation to read that there is insufficient evidence to justify cognitive behavior therapy or graded exercise. But many more public health agencies continue to point patients toward them.

And efforts to propagate this approach continue: A [trial](#) of graded exercise in children with ME/CFS has recently begun, and patients are [protesting](#) it.

Watching the PACE trial saga has left me both more wary of science and more in love with it. Its misuse has inflicted damage on millions of ME/CFS patients around the world, by promoting ineffectual and possibly harmful treatments and by feeding the idea that the illness is largely psychological. At the same time, science has been the essential tool to repair the problem.

But we shouldn’t take solace in the comforting notion that science is self-correcting. Many people, including many very sick people, had to invest immense effort and withstand vitriol to use science to correct these mistakes. And even that might not have

been enough without Tuller's rather heroic investigation. We do not currently have a sustainable, reliable method of overturning flawed research.

And rectifying PACE will take more than exposing its flaws. The lingering doubt it has cast on the illness will only be fully dispersed when we've finally figured out what's really going on with the disease.

For that, we need to invest in some serious, good science. The kind I continue to love.

*[Julie Rehmeyer](#) is a math and science writer. Her memoir "Through the Shadowlands," describing the science and politics of chronic fatigue syndrome and other poorly understood illnesses, will be published by Rodale in May.*