

Books & arts

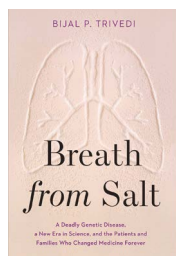
the O'Donnells, have extensive political and financial resources. Even so, it took staggering effort, dedication and perseverance to marshal these resources in the search for treatments.

The grief-worn families in *Breath from Salt* put their efforts and money into the Cystic Fibrosis Foundation, a charity based in Bethesda, Maryland, that has become a trailblazer in venture philanthropy. Business- and science-savvy, it actively directs research and drug development, and makes payouts to academics or companies when the research reaches milestones such as getting a candidate drug ready for animal testing, or succeeding in a clinical trial.

Genetic link

The foundation helped to fund research that discovered the genetic cause of the disease: mutations in the gene encoding the protein CFTR, which is key to transporting ions from salt across cell membranes, explaining the skin taste. The charity pushed pharmaceutical companies to take on a daunting task: designing drugs to fix a broken protein and mend an ailing body. Despite widespread scepticism, Vertex Pharmaceuticals, now in Boston, Massachusetts, ultimately prevailed – largely because the Cystic Fibrosis Foundation could foot much of the bill.

Plenty has been written about cystic fibrosis



Breath from Salt: A Deadly Genetic Disease, a New Era in Science, and the Patients and Families Who Changed Medicine Forever
Bijal P. Trivedi
BenBella (2020)

over the years. But it is in the details of that struggle – from the relentless fundraising to the slow and uncertain medicinal chemistry to perfect an experimental drug – that *Breath from Salt* enlightens.

Trivedi chronicles the evolution of drug discovery and biomedical research as it moves towards individualized therapies, offering a realistic portrait of the meticulous processes involved. One crucial step, separating a sweat gland from skin, is “like extracting a transparent hair from a bowl of clear Jell-O”, she writes.

She also delves into the motivations of scientists, fundraisers and trial participants, and the emotional toll on all of them. “Can you guys hurry up?” a bereaved mother begs a Vertex executive at the funeral for one of her three children with cystic fibrosis. The same executive cries when he learns that his company’s first drug against cystic fibrosis has dramatically succeeded in clinical trials. That drug,

ivacaftor, was approved in 2012.

There are controversies, including the eye-popping US\$294,000 annual price tag that Vertex slapped on ivacaftor. The Cystic Fibrosis Foundation received royalties, and found itself accused of benefiting at the expense of families who had sacrificed to support it. By 2019, after decades of hard work, the foundation had developed targeted treatments for the vast majority of people with cystic fibrosis; none was a cure. It sold the rights to its royalties for \$3.3 billion in 2014, making it the world’s richest charity focused on a specific disease. The foundation pledged to plough those funds back into research, supporting bold efforts to cure cystic fibrosis once and for all.

The tools for that might at last be available. In the decades since Joey O’Donnell died, it has become more common for companies to develop treatments for rare diseases. Many charities have adopted the Cystic Fibrosis Foundation model. Still, it is sobering to think of other genetic disorders that don’t receive the same attention – including sickle-cell disease, which affects mainly people of African descent, who are less likely to have access to financiers and politicians. Those children, too, deserve a formidable research rescue.

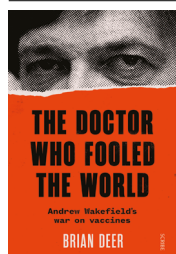
Heidi Ledford is a senior reporter for *Nature* in London.

The discredited doctor hailed by the anti-vaccine movement

Riveting biography is a cautionary lesson in the legacy of hubris. **By Saad B. Omer**

Since Edward Jenner’s first scientific description of vaccination in 1798 – using cowpox pus to protect against smallpox – there has been pushback. Throughout the nineteenth century, in the United States and the United Kingdom, there were cycles of increased smallpox vaccination, rising opposition, drops in immunization coverage, outbreaks, better appreciation of vaccination, more of it, and more protests. This stand-off eased around the start of the twentieth century when, with sanitation and medical care improving, public health placed less emphasis on compulsory vaccination. Probably the last time the world waited with bated breath for a vaccine – against polio in the 1950s – it was welcomed with open arms. The modern wave of vaccine scepticism has

its origins in the 1970s. That was when concerns (later determined to be unfounded) about the safety of a whole-cell vaccine against pertussis, or whooping cough, came to the fore in many high-income countries. In the 1980s and 1990s, a few organized groups opposed to vaccines emerged in many countries, including the United Kingdom.



The Doctor Who Fooled the World: Andrew Wakefield's War on Vaccines
Brian Deer
Scribe UK (2020)

It was in this context that, in 1998, Andrew Wakefield and his colleagues published a now-infamous and retracted paper in *The Lancet*, following which, in 2010, Wakefield was struck off the UK medical register for misconduct by the country’s General Medical Council. The fraudulent work on 12 children promoted a non-existent connection between autism and the MMR vaccine, used against measles, mumps and rubella. It propelled Wakefield to notoriety and turbocharged the anti-vaccine movement. He remains a headliner on the international vaccine-sceptic circuit as diseases once vanquished return because of falling rates of immunization. Many large epidemiological studies have found no difference in risk of developmental delays between children who receive the MMR vaccine and those who don’t¹.



Andrew Wakefield (centre) in 2010, shortly before being struck off the UK medical register.

Wakefield is the subject of *The Doctor Who Fooled the World*, a riveting new book by investigative journalist Brian Deer. It was Deer's reporting in *The Sunday Times* and *The BMJ* that helped to debunk the 1998 study as fraught with ethical, financial and methodological impropriety. It was eventually found to have involved undisclosed conflicts of interest, and to have subjected minors to unwarranted procedures and mischaracterized their samples. Wakefield continues to defend his actions and conclusions.

Over nearly two decades, Deer has covered Wakefield's demise and second act in detail. Yet there's plenty of new material here, even for those (like me) who have been following the saga as detailed in a shelf-ful of books since, including Paul Offitt's *Autism's False Prophets* (2008) and Seth Mnookin's *The Panic Virus* (2012). For example, we gain insights from interviews with Wakefield's family and colleagues. The result is a compelling portrait of hubris and the terrible shadow it can cast. For example, MMR-vaccine coverage in the United Kingdom fell to around 80% in the mid-2000s (from the necessary 95%), leading to outbreaks.

So how and why did an English physician from a long line of medics become one of the most prominent faces of the global anti-vaccine movement? As his mother (also a doctor) tells it: "Even as a little boy he used to sew patches on his trousers, and they were always beautifully sewn on. And he always wanted to be a surgeon." Wakefield switched to full-time research to focus on ideas such as the aetiology of Crohn's disease.

Deer paints a picture of a privileged man with charisma and big ideas, who was a little too confident of his hypotheses – and a little too certain of his imperfect understanding of the topics he was investigating. We are reminded that the disastrous 1998 *Lancet* paper was preceded by several other Wakefield studies, not always methodologically strong. For example, Wakefield authored a paper in 1995, also in *The Lancet*, claiming that measles

"It shows how self-importance can be self-destructive and harmful to others."

vaccination was associated with inflammatory bowel disease². That paper compared disease occurrence in two unrelated cohorts – a child-health study from before measles vaccines were introduced, and a study of another group after its introduction. The cohorts were selected using dissimilar recruitment and follow-up methods, and from different populations. This apples-with-brussels-sprouts comparison was criticized at the time by scientists at the US Food and Drug Administration and at the Department of Health in England, and by others with expertise in statistics, epidemiology, virology and related disciplines^{3,4}.

This unauthorized biography is also a story of Wakefield's enablers. Some had understandable incentives, including parents of sick children desperate for answers. Others' motives

seem indefensible, among them anti-vaccine politicians, and (in Deer's telling) institutional power players who should have known better.

How did Deer come to uncover one of the most significant scientific frauds of our time? He describes a lunch meeting in London in 2003 with a newly promoted editor at *The Sunday Times* that became the starting point of his investigation. We learn how a discrepancy between an interview with the mother of one of the children included in the 1998 study and the descriptions in the paper itself gave Deer one of the first clues that something sinister was afoot.

What follows is a roller-coaster ride. Wakefield's findings were questioned in an interdisciplinary meeting at England's Royal College of Surgeons in 1998, although it took a further 12 years for him to be stripped of his licence to practise. Deer has reported indefatigably throughout, including on Wakefield's move to the United States, where he convinced an ever-expanding list of benefactors to support his various ventures. Among them was two-time Oscar winner Robert De Niro – who has spoken up for the 2016 film *Vaxxed* made by Wakefield and producer Del Bigtree.

The book is not without imperfections. For example, Deer notes too many times that Wakefield was a "doctor without patients" because, despite having a medical degree and surgical training, he, like many in biomedicine, became a full-time researcher – as if that in itself makes him worthy of our scepticism.

As with all good biographies, *The Doctor Who Fooled the World* is about more than the life it covers. Written pre-pandemic, it is a timely warning for the rest of us. It shows how self-importance can be self-destructive and harmful to others. The Herculean efforts of so many researchers during COVID-19 have been marred by a few individuals going well beyond their areas of expertise and endorsing outlandish hypotheses. As Deer writes: "Courage in science isn't proving yourself right. It's in your efforts to prove yourself wrong." More than anything, we are reminded that investigative reporting is worth paying for, whether it is by subscribing to a local newspaper or through buying a book written by a journalist who asked the right questions.

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1. Di Pietrantonj, C. et al. *Cochrane Database Syst. Rev.* **4**, CD004407 (2020).
2. Thompson, N. P., Pounder, R. E., Wakefield, A. J. & Montgomery, S. M. *Lancet* **345**, 1071–1074 (1995).
3. Patriarca, P. A. & Beeler, J. A. *Lancet* **345**, 1062–1063 (1995).
4. Farrington, P. et al. *Lancet* **345**, 1362–1364 (1995).