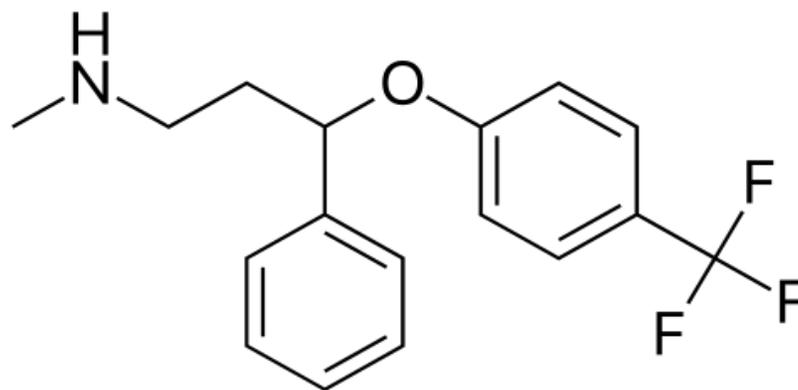


The discourse around health as a human rights issue usually focuses on access to medical treatment. However, the “right to health” begins with the right to informed consent about the merits of a treatment, which has been lacking as a US-constructed “disease” model of psychiatric care has been exported around the globe. The narrative that supported the adoption of the disease model told of how major psychiatric disorders were due to chemical imbalances in the brain, which could be treated by a second generation of psychiatric drugs that fixed those imbalances, much like “insulin for diabetes.” Randomized clinical trials had proven that antidepressants, antipsychotics, and other psychiatric drugs were safe and effective. However, missing from this narrative of medical progress were three key facts: that investigations failed to validate the chemical-imbalance theory of mental disorders; that studies of long-term outcomes regularly failed to show a benefit for the medicated patients; and that this model of care has led to poor public health outcomes in the United States and other developed countries. The principle of informed consent in medicine can be expanded to include the obligation of a medical specialty to be a reliable narrator of its own research, which provides a framework for understanding the violation of human rights that occurred with the exporting of a disease model of care to a global population.

## Without Informed Consent



The Global Export of a Failed Paradigm of Care

## Introduction

The legal right to informed consent arose out of the horrors of Nazi experiments. The Nuremberg Code stated that volunteers in research studies needed to be informed about the risks of a study before they could give consent. In the 1950s and 1960s, this principle of informed consent was extended to regular medical practice in the United States. In the 1972 case *Canterbury v. Spence*, the US Supreme Court ruled that a doctor must provide the patient with “enough information to make an intelligent choice” regarding the merits of a proposed treatment. As for the information to be disclosed, the court set this standard: “What would a reasonable patient want to know with respect to the proposed therapy and the dangers that may be inherently or potentially involved?”<sup>1</sup>

This obligation is codified in the American Medical Association’s Code of Ethics, which states that “informed consent to medical treatment is fundamental in both ethics and law.”<sup>2</sup> Similarly, the European Charter of Patients’ Rights and the World Medical Association’s Code of Medical Ethics list informed consent as a fundamental right.

While this obligation is imposed specifically on the individual doctor, it also imposes an ethical duty—by proxy—on the medical specialty to provide the public with an accurate and full summary of its research findings, because a society will organize its care around that public narrative. A medical specialty needs to be a reliable source of information about what is known about the biology of a disorder, as well as the risks and benefits of a proposed therapy. In essence, it is the medical specialty that provides society with “informed consent” for its therapies.

Moreover, the right to informed consent is a primary element of the individual’s right to health as set forth by the United Nations International Covenant on Economic, Social and Cultural Rights. The covenant states that the right to health includes “access to health-related education” and that an “important aspect is the participation of the population in all health-related decision-making at the community, national and international levels.” In other words, the individual’s right to health is dependent on the public being properly informed about scientific findings regarding the risks and benefits of any proposed treatment.

As can be shown, American psychiatry failed to meet its informed consent obligations as it promoted its disease model to the public, and this failure continued as this model was adopted in other high-income countries and exported to low- and middle-income countries.

## **The American Psychiatric Association adopts a disease model of care**

Prior to the publication of DSM-3 (the Diagnostic and Statistical Manual of Mental Disorders, third edition), American psychiatry had conceptualized psychiatric disorders as arising from multiple factors: family and social tensions, social inequalities (poverty, racism, and so forth), and, on occasion, biological illnesses. However, this was a diagnostic medley that lent credence to the criticism that psychiatrists were not “real doctors,” and in the 1970s, the American Psychiatric Association (APA) faced criticisms from so many quarters that its leaders spoke of their field as being under siege. Expatients formed psychiatric survivor groups; popular movies suggested that psychiatrists were crazier than their patients; psychiatrists’ diagnostics were seen as unreliable; and outcome studies failed to show that psychoanalysis was more effective than less-expensive therapies provided by psychologists and other mental health counselors.

With psychiatry’s public image in freefall, the APA created a task force to produce a new DSM. As this effort took hold, APA leaders spoke about how adopting a disease model could serve to remake psychiatry’s public image. The shrink tending to a patient on a couch would be replaced by a doctor in a white coat, treating “diseases” of the brain. With this new model, APA leaders stated, the focus would be on “the symptoms and signs of illness ... the medical model is clearly related to the concept of disease.”<sup>3</sup>

In 1984, Nancy Andreasen, who would later become editor-in-chief of the *American Journal of Psychiatry*, presented the field’s new thinking in a best-selling book, *The Broken Brain: The Biological Revolution in Psychiatry*. “Major psychiatric illnesses are diseases,” she wrote. The thought was that each “different illness has a different specific cause ... there are many hints that mental illness is due to chemical imbalances in the brain and that treatment involves correcting these chemical imbalances.”<sup>4</sup>

This was the soundbite that was used to sell the disease model to the American public. In 1988, Eli Lilly brought Prozac (fluoxetine) to market, and it was touted as a breakthrough medication that fixed a serotonin imbalance in the brain. Other pharmaceutical companies brought selective serotonin reuptake inhibitor (SSRI) antidepressants to market, and throughout the 1990s the American public was informed, both through pronouncements from leaders in American psychiatry and pharmaceutical advertisements, that these drugs fixed a chemical imbalance in the brain.

As APA President Richard Harding wrote in a 2001 *Family Circle* article, “We now know that mental illnesses—such as depression or schizophrenia—are not ‘moral weaknesses’ or ‘imagined’ but real diseases caused by abnormalities in brain structure and imbalances of chemicals in the brain.”<sup>5</sup> In that same issue of *Family Circle*, Nada Stotland, who subsequently became president of the APA, informed the public that antidepressants “restore brain chemistry to normal.”<sup>6</sup>

During the mid-1990s, pharmaceutical companies also introduced a second generation of “atypical” antipsychotics, which were said to fix the dopamine imbalance that caused schizophrenia, while also fixing irregularities in the serotonergic system. As psychiatrist Peter Weiden wrote in a book titled *Breakthroughs in Antipsychotic Medications*, the newer antipsychotics “do a better job of balancing all of the brain chemicals, including dopamine and serotonin.”<sup>7</sup>

This narrative told of an astonishing medical advance. Researchers had discovered the very molecules that caused depression, psychosis, and other major disorders, and the field now had drugs that corrected those chemical imbalances. Patients diagnosed with such disorders now understood that they suffered from a known pathology and that psychiatric drugs provided an antidote.

Indeed, in 2005, an APA survey proved that this understanding had taken hold in the public mind. The APA announced that “75% of consumers believe that mental illnesses are usually caused by chemical imbalances in the brain.” A psychiatrist, the APA added in its press release, is “a specialist specifically trained to diagnose and treat chemical imbalances.”<sup>8</sup>

The APA continued to tell this story in the years that followed, with visitors to its website in 2014 able to read, in a section titled “Let’s Talk Facts” about depression, that “antidepressants may be prescribed to correct imbalances in the levels of chemicals in the brain.”<sup>9</sup> Other mental health organizations, such as the National Alliance for the Mentally Ill, the Depression and Bipolar Support Alliance, and the Child and Adolescent Bipolar Foundation, told this to the public as well.<sup>10</sup> These organizations had scientific advisory councils composed of prominent American psychiatrists, and so the public had reason to conclude that the chemical-imbalance story was a well-established fact.

*I spent 13 years at NIMH really pushing on the neuroscience and genetics of mental disorders, and when I look back on that I realize that while I think I succeeded at getting lots of really cool papers published by cool scientists at fairly large costs—I think \$20 billion—I don’t think we moved the needle in reducing suicide, reducing hospitalizations, improving recovery for the tens of millions of people who have mental illness .*<sup>63</sup>

Indeed, in 2025, the World Health Organization called for a “paradigm shift” in mental health care, one that moved away from historic “over-reliance on the biomedical approach and psychotropic drugs,” and toward “approaches that are more person-centred, recovery-oriented, and grounded in human rights.”<sup>64</sup> That is an approach that would honor the principle of informed consent, which should be the centerpiece of global mental health.

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care professionals; and greater spending on mental health as a percentage of total spending on health in the country.<sup>61</sup>

Finally, in 2013, Rajkumar and researchers in Denmark assessed the level of psychiatric services in 191 countries, with a combined population of more than six billion people. This was a comprehensive global study, and, like Shah, they found that “countries with better psychiatric services experience higher suicide rates.” Both the “number of mental health beds and the number of psychiatrists per 100,000 population were significantly associated with higher national suicide rates (after adjusting for economic factors),” they wrote.<sup>62</sup>

## Discussion

The principle of informed consent in medicine tells of a basic human right: patients have a right to be told what is known about the pathology associated with a medical diagnosis and to be informed of the risks and benefits of any proposed treatment. The honoring of this obligation requires that the medical specialty overseeing a domain of medicine provide a reliable accounting of research findings to the public and to the larger medical community. However, American psychiatry never fulfilled this obligation, and that failure remained present as the disease model took hold globally.

The informed consent failure was twofold. Although research in the 1980s and 1990s regularly failed to validate the chemical-imbalance theory of mental disorders, with the APA’s own textbook in 1999 telling of this failure, the APA publicly doubled down on that story, and like a medical meme, it spread around the globe.

The other failure was that American psychiatry never publicized the studies that told of poor longterm outcomes and poor public health outcomes associated with this paradigm of care. This was information that belied the narrative of progress that American psychiatry was telling the public, and as the disease model of care was exported to the rest of the world, the public narrative remained much the same. This was a story of medical progress, and the exporting of this model of care was touted as an effort to bring this new standard of mental health treatment to a global public.

However, the disease model of care is now 45 years old, and that false narrative of medical progress is now falling apart. American psychiatry has stopped promoting the chemical-imbalance story, and there is increasing recognition, within the United States and abroad, that the disease model has failed. In a 2017 interview, former NIMH director Thomas Insel drew this very conclusion:

## Economies of influence

Any study of institutional corruption requires identifying the “economies of influence” that can lead an institution to betray its public duties. In this instance of institutional corruption, there were two such influences that led American psychiatry astray.

The first was that American psychiatry had an evident guild interest in promoting the chemical-imbalance story, as it told of an extraordinary medical advance that elevated the prestige of psychiatry and its influence on American society. It also provided psychiatry with superiority in what might be dubbed the therapeutic marketplace. Psychiatrists had prescribing powers, while other mental health providers—psychologists, counselors, and so forth—did not.

The second was that pharmaceutical companies were eager to help the APA sell the disease-model story to the public. Drug companies provided funding for the APA through grants, advertisements in APA journals, and fees for display booths, and they sponsored talks at the APA’s annual conferences. With pharma money flowing into its coffers, the APA’s annual revenues increased from US\$10.5 million in 1980 to US\$65.3 million in 2008, with 30% of this 2008 revenue coming from pharmaceutical companies.<sup>11</sup>

Pharmaceutical companies also began paying academic psychiatrists to serve as their advisors, consultants, and key opinion leaders, with this financial influence so complete that in 2000, when the *New England Journal of Medicine* sought to commission a review on the efficacy of antidepressants, it found it difficult to find an expert in mood disorders who was not receiving money from industry.<sup>12</sup> A subsequent investigation by Senator Charles Grassley revealed that prominent thought leaders had received six-figure payments from industry, with several reaching the million-dollar club.<sup>13</sup>

With pharmaceutical companies providing the funding and academic thought leaders the scientific legitimacy for the disease-model narrative, spending on psychiatric drugs in the United States dramatically increased—from US\$2.4 billion in 1986 to US\$58 billion in 2012.<sup>14</sup> In 2020, one in six adults in the United States was treated with a psychiatric medication.<sup>15</sup>

## Without consent: The science that belies the disease model

The chemical-imbalance story lies at the heart of the disease-model narrative that was told to the American public and subsequently the world. However, decades of research failed to find such chemical imbalances, and it is the disparity between those findings and what was told to the public that reveals

psychiatry's failure to provide informed consent to the public.

The chemical-imbalance hypothesis arose in the 1960s based on an understanding of the mechanism of action of antipsychotics and antidepressants. Antipsychotics were found to block dopamine receptors in the brain, thereby decreasing dopamine transmission, and this led researchers to hypothesize that schizophrenia was due to too much dopamine. Both classes of the new antidepressants—monoamine oxidase inhibitors and tricyclic antidepressants—increased monoamine activity, prompting researchers to hypothesize that depression was due to a monoamine deficiency (serotonin is a monoamine).<sup>16</sup>

With these hypotheses in mind, researchers then sought to determine whether patients diagnosed with schizophrenia or depression actually suffered from such chemical imbalances prior to being medicated. In neither instance did they find compelling evidence that this was so, and that was particularly true regarding the low-serotonin theory of depression (also known as the monoamine theory of depression).

Even by the early 1970s, researchers were reporting that they were not finding evidence that low serotonin was a cause of depression.<sup>17</sup> In a 1984 report, National Institute of Mental Health (NIMH) researchers came to the same conclusion, writing that “elevations or decrements in the functioning of serotonergic systems per se are not likely to be associated with depression.”<sup>18</sup>

Still, the hunt for a chemical imbalance continued, and over the next 15 years, researchers utilized a number of methods for assessing serotonergic activity in depressed patients, but none bore fruit. The 1999 edition of the APA's *Textbook of Psychiatry* traced this research history and pointed out the faulty logic that had led to the hypothesis in the first place:

*Inferring neurotransmitter pathophysiology from an observed action of a class of medication availability is similar to concluding that because aspirin causes gastrointestinal bleeding, headaches are caused by too much blood and the therapeutic action of aspirin in headaches involves blood loss. Additional experience has not confirmed the monoamine depletion hypothesis.*<sup>19</sup>

The following year, Stephen Stahl, in his textbook *Essential Psychopharmacology*, put this conclusion even more bluntly: “There is no real clear and convincing evidence that monoamine deficiency accounts for depression; that is, there is no ‘real’ monoamine deficit.”<sup>20</sup>

treatment in its “intervention guide.”<sup>56</sup>

The title of Ethan Watters's 2010 book *Crazy Like Us: The Globalization of the American Psyche*, neatly summarized the results of this medical crusade, telling how it supplanted Indigenous methods for treating psychiatric difficulties with DSM diagnoses and treatments.<sup>57</sup> From 2008 to 2019, the prescribing of psychiatric drugs rose at an annual rate of 8% in upper-middle-income countries and 3% in lower-middle-income countries—evidence, once again, of the disease model taking hold.<sup>58</sup>

### Global mental health outcomes

The expectation was that the adoption of a Western model of care, together with greater access to psychiatric drugs, would lead to a drop in suicide rates and improved mental health outcomes in countries around the world. However, that has not proven to be the case in high-income countries, and outcomes have been similarly dispiriting in low- and middle-income countries.

In 2004, Australian researchers, in a study of 100 countries, found that “contrary to the hypothesized relation,” the “introduction of a mental health policy and mental health legislation was associated with an increase in male and total suicide rates.”<sup>59</sup> They quantified the negative impact of specific initiatives:

- The adoption of mental health legislation was associated with a 10.6% increase in suicides.
- The adoption of a therapeutic drugs policy designed to improve access to psychiatric medications was associated with a 7% increase in suicides.

“It is a concern,” the researchers concluded, “that national mental health initiatives are associated with an increase in suicide rates.”

In 2008, Ajit Shah and Ravi Bhat found higher rates of suicide among elderly patients “in countries with greater provision of mental health services, including the number of psychiatric beds, psychiatrists and psychiatric nurses, and the availability of training mental health [programs] for primary care professionals.”<sup>60</sup>

In 2009, Shah and colleagues reported on suicide rates for people of all ages in 76 countries and once again found that suicide rates were higher in countries with mental health legislation. They also reported that there was a correlation between higher suicide rates and a higher number of psychiatric beds, psychiatrists, and psychiatric nurses; more training in mental health for primary

attend conferences, where pharmaceutical freebies flowed.

Paulo Amarante, a well-known psychiatrist in Brazil, described the scene at one such conference in his country, where psychiatrists lined up at a pharmaceutical exhibit to get industry handouts:

*There, they received vouchers for free dinners at restaurants with their families, and even other benefits for non-family members, according to the proud account of a department head who boasted of being “sponsored” by a [pharmaceutical] laboratory, along with his “lover.” The laboratory had paid for the airfare, the luxury hotel, and other perks. All with great honor and pride! They also received various gifts, such as CDs, ice cream cones named after psychotropic drugs. There were raffles for flights to Europe and the US, laptops, and many other things. There were so many gifts! So many that the [department head] had a suitcase with wheels and a long handle, one that can be carried on the plane. This was so he could collect more gifts, as the bags distributed by the laboratories were considered too small for him.*<sup>53</sup>

As for the symposia, Amarante wrote, “many of the speakers were funded by pharmaceutical companies, and their speeches were blatant advertisements for the drugs.”

Beyond such commercial influences, the globalization of mental health proceeded under the banner of science. After Prozac was brought to market, US and European researchers began reporting that mental disorders were quite common in low- and middle-income countries and that in the absence of access to “evidence-based” treatments, many patients resorted to “traditional or spiritual healers and healing,” which were said to be useless or even harmful. “The impact of mental illness in these settings can be devastating, in terms of symptoms, stigma and functional impairment,” researchers wrote.<sup>54</sup>

With this argument in place, in 2007 *The Lancet* issued an “urgent call for action to scale up services for people living with mental health problems and to close a substantial treatment gap, especially in low-income and middle-income countries, where the proportions of people receiving treatment are lowest.”<sup>55</sup>

This was a clarion call by Western psychiatry to export the medical model to all corners of the world. The World Health Organization, for its part, urged countries around the world to pass legislation that would increase access to mental health treatment, with psychiatric drugs presented as a first-line

The history of research into the dopamine hypothesis of schizophrenia is a bit more complicated, but it too began to fall apart in the 1970s and 1980s. In 1994, John Kane, who was a leader in schizophrenia research, concluded that there is “no good evidence for the perturbation of the dopamine system in schizophrenia.”<sup>21</sup> Seven years later, Eric Nestler, former NIMH director Steven Hyman, and Robert Malenka, in their book *Molecular Neuropharmacology*, echoed this conclusion, writing that “there is no compelling evidence that a lesion in the dopamine system is a primary cause of schizophrenia.”<sup>22</sup>

With both pillars of the chemical-imbalance theory of mental disorders having been investigated and found wanting, other prominent figures in the research community pronounced the chemical-imbalance theory dead. In 2005, Kenneth Kendler, coeditor-in-chief of *Psychological Medicine*, summed it up this way: “We have hunted for big simple neurochemical explanations for psychiatric disorders and not found them.”<sup>23</sup>

Such were the conclusions that could be found in psychiatric texts. However, the public heard little of this, and many were shocked in 2022 when UK psychiatrist Joanna Moncrieff and colleagues published an exhaustive review of research on the serotonin theory of depression and concluded that there was “no convincing evidence that depression is associated with, or caused by, lower serotonin concentrations or activity.”<sup>24</sup>

Moncrieff said in an interview:

*People were staggered, really surprised. I went on one television program and the presenter said it blows your mind that this is not true. It revealed that the general public has been persuaded by the pharmaceutical industry and medical propaganda that depression had been established to be caused by a deficiency of serotonin. That’s what people thought, and so people were blown away to find out that it wasn’t true.*<sup>25</sup>

Yet as Tufts Medical School psychiatrist Nassir Ghaemi wrote after Moncrieff and colleagues published their 2022 paper, “nothing is new here. And the fuss surrounding the paper reveals much ignorance about psychiatry. The serotonin hypothesis of depression, which became popular from the 1990s until now, is false, and has been known to be false for a long time, and never was proven to begin with.”<sup>26</sup>

Ghaemi was accurately summarizing the history of research into the chemical-imbalance theory of mental disorders. The APA had been telling the public one

story, and scientific research had been telling another, and that disparity tells of a medical discipline that failed to fulfill its public duty to be a reliable narrator of its own research.

### **The efficacy of psychiatric drugs**

There are three principal types of evidence present in the scientific literature regarding the efficacy of antidepressants and antipsychotics. First, in randomized clinical trials, both of the two classes of drugs reduced symptoms of the disorder better than placebo, with the difference statistically significant. Second, in randomized controlled trials (RCTs) conducted in patients who had responded well to the drug, those who were withdrawn from the drug relapsed at higher rates than those who were maintained on it, which was seen as evidence that the drugs help prevent relapse.

Together, these two types of RCTs became the pillars for assertions that the use of psychiatric drugs was evidence based, which enabled the globalization of the disease-model of care. The relapse studies, in particular, fit neatly into the chemical-imbalance narrative that antidepressants and antipsychotics needed to be taken on a continual basis, because they provided evidence for this practice.

However, the deficiency of the relapse studies, as a source of evidence supporting maintenance use of the drugs, is of a fundamental sort. As Ghaemi noted, the design of these studies “is biased from the start by excluding acute symptomatic non-responders” and thus is not a “scientifically valid design.”<sup>27</sup> Moreover, the studies do not tell how patients are faring over the long term, particularly in regard to functional and quality-of-life outcomes, and in comparison to unmedicated patients.

There is a third line of research that exists in the literature that can provide insight into that last question. The research is of several types—a few randomized studies, research comparing the change in the course of the “disorder” following the introduction of psychiatric drugs, and naturalistic studies—which together have raised arguments, made within the research literature, that both of these classes of drugs, in the aggregate, have worsened long-term outcomes. Much of this research consists of landmark NIMH investigations into the long-term impact of these two classes of drugs.

### **Depression**

In the 1970s, mood experts in the United States told of how depression was an episodic disorder. Various studies in the pre-antidepressant era found that at the end of one year, around 85% of hospitalized patients had recovered.<sup>28</sup> However, after antidepressants were introduced, studies began to find that depression was

### **Public health outcomes in high-income economies**

At a societal level, the public—if the principle of informed consent in medicine is applied—should have been told that the chemical-imbalance hypothesis never panned out and that the biology of mental disorders remained unknown. It also should have been informed of public health outcomes associated with the disease model of care. Here is a brief summary of public health outcomes:

- In 2013, Finnish investigators reported that long-term recovery rates for schizophrenia patients had declined since the introduction of the atypical antipsychotics in the mid-1990s, with only 6% “recovering” from the illness.<sup>48</sup> That is worse than any recovery rate reported since the schizophrenia diagnosis first appeared in asylum medicine 100 years earlier.
- Recovery rates for depressed patients worsened after the adoption of this disease model. The same is true for bipolar disorder.<sup>49</sup>
- The number of people receiving disability payments due to mood disorders soared in the United States following the introduction of SSRIs, increasing threefold from 1987 to 2007. A sampling of disability rates in other high-income countries shows a similar increase in disability payments, an increase that correlated with a rise in antidepressant prescriptions.<sup>50</sup>
- Standard mortality rates for patients with schizophrenia and bipolar disorder have worsened in high-income countries.<sup>51</sup>

In a 2025 article, Dost Öngür, editor of *JAMA Psychiatry*, validated this description of outcomes, writing that “life expectancy and long-term functional outcomes have worsened in recent decades for those with severe mental illnesses, including schizophrenia, severe mood disorders, and obsessive-compulsive disorder, despite greater availability of treatments.”<sup>52</sup>

Öngür did not blame the worsening outcomes on the medications. However, the general public, having organized its use of psychiatric drugs for the past 40 years around a narrative of great medical progress, would surely be stunned to learn of this worsening of outcomes in modern times.

### **Exporting the disease model to low- and middle-income countries**

As pharmaceutical companies marketed their drugs to middle-income countries, they once again relied on the same formula that had been successful in the United States and high-income countries. They paid academic psychiatrists to serve as their speakers and key opinion leaders, and paid for psychiatrists to

income countries with large populations) to attend the conference, where they would enjoy free lunches and dinners that featured presentations by academic “thought leaders” telling of advances in treating psychiatric diseases.

The foreign attendees could then be expected to return to their home countries and promote the disease model to their colleagues. And just as they had done in the United States, pharmaceutical companies paid academic psychiatrists in Europe, Canada, and Australia to serve as their advisors and consultants and to speak at conferences throughout the developed world.

In a 2002 article titled “The Going Rate on Shrinks,” psychiatrist E. Fuller Torrey told of how the 7th World Congress of Biological Psychiatry in Berlin included 23 symposia sponsored by pharmaceutical companies:

*Each [symposium] brought in two to four psychiatric experts, whom the sponsoring pharmaceutical company usually gave business-class air tickets, four-star hotel accommodations, and an honorarium, typically \$2,000 to \$3,000 ... Honoraria and future invitations are directly dependent on how experts present their data. Emphasizing adverse effects of a drug, for example, may well cost the expert a trip to future congresses. Some of the psychiatric experts sponsored by a pharmaceutical company are also on the company’s speakers bureau; many own stock and thus have a direct financial interest in the success of the company’s products.*<sup>45</sup>

With pharmaceutical money putting its thumb on the scale, psychiatric associations in high-income countries embraced the disease model that had originated in the United States, which produced the same commercial result. Websites in developed countries around the world now told of psychiatric drugs that fixed chemical imbalance in the brain, and psychiatric guilds promoted the RCT results from short-term studies and the relapse studies as evidence of the efficacy of psychiatric drugs.<sup>46</sup> The third line of research that told of drugs worsening long-term outcomes was not introduced into that story of medical progress, but rather conveniently forgotten or dismissed as not having come from RCTs.

In Europe, the prescribing of antidepressants rose 250% from 2000 to 2020, a commercial marker of the disease model taking hold.<sup>47</sup>

now running a more chronic course, with only about 15% of patients remitting and staying well.<sup>29</sup> In 1994, Italian psychiatrist Giovanni Fava raised the question of whether antidepressants were the cause of this increased chronicity:

*Within the field of psychopharmacology, practitioners have been more cautious, if not fearful, of opening a debate on whether the treatment is more damaging [than helpful] ... I wonder whether the time has come for debating and initiating research into the likelihood that psychotropic drugs actually worsen, at least in some cases, the progression of the illness which they are supposed to treat.*<sup>30</sup>

A number of NIMH studies conducted between the late 1980s and early 2000s provided reason to bring this “debate” to the public. For instance, in a one-year NIMH study of 108 real-world outpatients, only 6% remitted and stayed well until the end of the study, whereas in a NIMH study of 85 unmedicated depressed patients, 85% were well at the end of one year.<sup>31</sup>

With such questions about antidepressants swirling in the research literature, in the early 2000s the NIMH launched the STAR\*D study, which it touted as the largest and longest trial of antidepressants ever conducted. The results from this study in “real-world” patients would guide future clinical care in the United States. “Given the dearth of controlled data [in real-world patient groups] results should have substantial public health and scientific significance, since they are obtained in representative participant groups/settings, using clinical management tools that can easily be applied in daily practice,” the STAR\*D investigators wrote.<sup>32</sup>

The STAR\*D study had two phases. In the first, or “acute,” phase, patients were given up to four tries to remit. If they did not remit on a first antidepressant, they could try a second one, and so on. In the second, or follow-up, phase, those who remitted would be treated with the best possible clinical care for one year. This would provide a final count of patients who remitted and then stayed well and in the trial to its end.

In 2006, the STAR\*D investigators announced the study results.<sup>33</sup> They reported that nearly 70% of the patients had remitted after the four rounds of acute treatment, and this became the result that was promoted to the media, cited within the profession and by *The New York Times* and other media as evidence of the real-world effectiveness of antidepressants.<sup>34</sup>

However, a team of independent investigators, led by psychologist Ed Pigott,

relied on Freedom of Information requests to review these findings, and in a series of articles, they reported that the STAR\*D investigators had violated the protocol in various ways to inflate the announced remission rate. If the protocol had been followed, Pigott and colleagues concluded, the remission rate at the end of the acute treatment would have been 35%.<sup>35</sup> Moreover, they reported on the one-year results from the second stage of the study, which the STAR\*D investigators had failed to do. Of the 4,041 patients who entered the trial, only 108 remitted and then stayed well and in the trial to its one-year end. The remaining 3,933 patients either never remitted, remitted and then relapsed, or dropped out.<sup>36</sup>

There have been a number of government-funded studies from other countries, including the Netherlands, France, Switzerland, and Canada, that have similarly told of better long-term outcomes and lower disability rates for depressed patients off medication compared to those who took antidepressants.<sup>37</sup> Such results have led Fava and several others to publish articles exploring the possibility that antidepressants might worsen long-term outcomes and positing a biological explanation for why this might be so. Antidepressants increase serotonergic activity, and in response, the brain dials down its own serotonergic machinery as it tries to maintain a homeostatic equilibrium. “Continued drug treatment may induce processes that are the opposite of what the medication originally produced,” wrote Rif El-Mallakh and his two co-authors. This may “cause a worsening of the illness, [may] continue for a period of time after discontinuation of the medication, and may not be reversible.”<sup>38</sup>

Although it takes a little sleuthing to find this history in the scientific literature, it is easy to see that if the STAR\*D results had been honestly reported, and if the public had been advised of the evidence that antidepressants were turning an episodic disorder into a chronic one, then the public’s understanding of the risks and benefits of antidepressants would have been profoundly altered.

## Schizophrenia

While this may seem surprising, a similar counter-narrative can be dug out from the research literature regarding the long-term impact of antipsychotics.

In the 1970s, the NIMH funded three studies that assessed the impact of antipsychotics over longer periods of times, and the results led NIMH researchers to worry that antipsychotics induced brain changes that made schizophrenia patients more biologically vulnerable to psychosis over the long term.<sup>39</sup> Canadian researchers then posited an explanation for why this could be so, telling of how antipsychotics could induce a “dopamine supersensitivity” that could lead to more severe and persistent psychotic symptoms.<sup>40</sup> Next, in the

1990s and early 2000s, MRI studies showed that antipsychotics shrink brain volumes and that this shrinkage is associated with a worsening of negative symptoms and functional impairment.<sup>41</sup>

In 2007, Martin Harrow announced the 15-year results from a NIMH-funded longitudinal study of schizophrenia. Most of the patients enrolled in the study were young, suffering from a first or second episode of psychosis, and all were treated in the hospital with antipsychotics and discharged. Harrow then periodically assessed their status over the next 15 years. Those who stopped taking antipsychotics were eight times more likely to be in recovery at the end of 15 years (40% versus 5%) and, as a group, had better cognitive function, were less anxious, and much more likely to work.<sup>42</sup>

Harrow and colleagues pointed to drug-induced dopamine supersensitivity as a possible explanation for the poor outcomes for patients who remained medication compliant: “How unique among medical treatments is it that the apparent efficacy of antipsychotics could diminish over time or become ineffective or harmful? There are many examples for other medications of similar longterm effects, with this often occurring as the body readjusts, biologically, to the medications.”<sup>43</sup>

Other studies of various types—in the Netherlands, Australia, Germany, Denmark, and Finland—have reported higher long-term recovery rates for those off antipsychotic medication.<sup>44</sup> Yet little of this information, while available in the research literature, is told to the public. The standard of care is to maintain schizophrenia patients on antipsychotics indefinitely, and if patients resist taking the drug, they are said to do so because they lack “insight” into their illness. This is the narrative that governs psychiatric care in most of the developed world, which becomes a justification for forced treatment.

## The spread of the disease model to high-income countries

Although the World Health Organization has its own classification system for medical disorders—the International Classification of Diseases—the NIMH is by far the largest public funder of psychiatric research, and at least in the 1980s and 1990s, the majority of trials of psychiatric drugs were conducted in the United States. This outsized influence led psychiatric journals throughout the developed world to require researchers to use DSM categories to report their results, which in turn led to a reification of the APA’s disease model.

At the same time, the APA turned its annual conference into an international gathering of psychiatrists. Pharmaceutical companies provided grants to psychiatrists from high-income countries (and to psychiatrists from middle-