Medical History (2026), 1–21
doi:10.1017/mdh.2026.10090

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ARTICLE

Beyond reasonable doubt: antidepressants and the limits of scientific critique

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Abstract

Public doubt about the usefulness of antidepressants appears to have grown, even as scientific agreement about their efficacy has become more settled. This paper examines the role that figures associated with critical psychiatry have had in promoting this doubt. It traces the long entanglement of antidepressants and their critics over the last eighty years, culminating in a 2022 review of the serotonin hypothesis, which, though it made no claims about efficacy, was widely interpreted as showing that antidepressants do not work. Drawing on Oreskes and Conway's concept of 'manufactured doubt', the paper explores how certain philosophical commitments have shaped these actors' views, at times impeding their engagement with new evidence. In doing so, it marks a distinction between productive and unproductive doubt. Whilst external scrutiny has played a significant role in shaping psychiatry, some positions are held so rigidly that the resulting critiques obscure the scientific consensus and risk undermining psychiatric care.

Keywords: Antidepressants; Critical Psychiatry; Manufactured doubt; Serotonin hypothesis; Anti-psychiatry; Meta-analysis

Introduction

Despite a growing scientific consensus that antidepressants are modestly effective, public controversy around their use has recently intensified. Selective serotonin reuptake inhibitors (SSRIs), first introduced in the 1980s, have since been extensively studied.[1] Meta-analyses, including work by the Cochrane Collaboration[2] and the researcher Andrea Cipriani's group at Oxford,[3] have shown significant benefit over placebo. Real-world, post-marketing trials also support their use.[4] On the basis of this and other evidence, national and international policy institutions – including the American Psychiatric Association (APA),[5] National Institute of Mental Health (NIMH),[6] the UK's National Institute for Health and

[1]Jay C. Fournier *et al.*, 'Antidepressant Drug Effects and Depression Severity: A Patient-Level Meta-Analysis', *JAMA*, 303, 1 (2010), 47–53; Fredrik Hieronymus *et al.*, 'Consistent Superiority of Selective Serotonin Reuptake Inhibitors Over Placebo in Reducing Depressed Mood in Patients with Major Depression', *Molecular Psychiatry*, 21, 4 (2016), 523–30.

[2]Bruce Arroll *et al.*, 'Antidepressants Versus Placebo for Depression in Primary Care', *Cochrane Database of Systematic Reviews*, 3 (2009), CD007954.

[3]Andrea Cipriani *et al.*, 'Comparative Efficacy and Acceptability of 21 Antidepressant Drugs for the Acute Treatment of Adults With Major Depressive Disorder: A Systematic Review and Network Meta-Analysis', *Lancet*, 391, 10128 (2018), 1357–66.

[4]Augustus John Rush *et al.*, 'Acute and Longer-Term Outcomes in Depressed Outpatients Requiring One or Several Treatment Steps: A STAR*D Report', *American Journal of Psychiatry*, 163, 11 (2006), 1905–17.

[5]American Psychiatric Association, *Practice Guideline for the Treatment of Patients With Major Depressive Disorder*, 3rd edn (Arlington, VA: American Psychiatric Publishing, 2010).

[6]National Institute of Mental Health, *Depression* (National Institutes of Health, 2021), accessed 18 April 2025, https://www.nimh.nih.gov/health/topics/depression.

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Care Excellence (NICE),[7] and the World Health Organization (WHO)[8] – all recommend antidepressants as a treatment for depression.

Yet in September 2022, *Newsweek* ran a cover story titled 'Hooked on Hype: Antidepressants work no better than sugar pills for most of the 43 million Americans who take them'.[9] One month later, *The Economist* published a leader claiming 'Most people on antidepressants don't need them'.[10] Both articles cited a paper by the FDA's Deputy Director of Safety for Psychiatric Drugs, Marc B. Stone, that affirmed the efficacy of antidepressants, drawing on a comprehensive analysis of all historical FDA-submitted trial data. By analysing individual-level responses rather than averaging the effect of all participants, Stone and colleagues found that approximately 1 in 6 participants experienced a large improvement and were no longer clinically depressed.[11]

How did a paper that reinforced the scientific consensus come to be used as evidence against it? Both outlets also quoted figures associated with the Critical Psychiatry Network (CPN), a UK-based group of psychiatrists and researchers advocating for a more sceptical approach to psychiatry.[12] Several months earlier, newspapers had widely reported on an article published in the journal *Molecular Psychiatry* by CPN co-founder Joanna Moncrieff and others, titled 'The Serotonin Theory of Depression: A Systematic Umbrella Review of the Evidence'[13] (henceforth, the 'umbrella review'). *The Guardian* ran an article with the headline: 'Little evidence that chemical imbalance causes depression, UCL scientists find'. Moncrieff was quoted as saying the review showed no support for the serotonin theory of depression and that antidepressants were likely overprescribed.[14]

The paper was a review of older research on serotonin's role in depression and did not address the drugs' efficacy, yet it was widely seen as evidence that they 'don't work'. The psychiatrist and media commentator Awais Aftab noted that a US radio host interviewing him seemed surprised to learn that the paper made no claims about efficacy at all.[15] This was not an interpretation imposed by journalists. In press releases and media appearances, the authors themselves argued their paper raised doubts about antidepressants' effectiveness. The 'umbrella review' would be accessed over a million times and media coverage was extensive, while methodological critiques from scientists went largely unnoticed. It would also be linked to a sharp increase in negative discussion of antidepressants on social media in the months that followed.[16]

Yet controversy around SSRIs was far from new. Since their rapid uptake in the 1980s and 1990s, these medications had been the subject of several serious challenges. In the early 2000s, research had raised

[7]National Institute for Health and Care Excellence, *Depression in Adults: Recognition and Management* (CG90) (London: NICE, 2009), https://www.nice.org.uk/guidance/cg90.

[8]World Health Organization, *mhGAP Intervention Guide for Mental, Neurological and Substance Use Disorders in Non-Specialized Health Settings: Mental Health Gap Action Programme (mhGAP)*, 2nd edn (Geneva: WHO, 2016).

[9]'Antidepressants Work Better Than Sugar Pills Only 15 Percent of the Time', *Newsweek*, 21 September 2022, accessed 18 April 2025, https://www.newsweek.com/antidepressants-work-better-sugar-pills-only-15-percent-time-1744659.

[10]'Most People on Antidepressants Don't Need Them', *The Economist*, 22 October 2022, accessed 18 April 2025, https://www.economist.com/leaders/2022/10/22/most-people-on-antidepressants-dont-need-them.

[11]Marc B. Stone *et al.*, 'Response to Acute Monotherapy for Major Depressive Disorder in Randomized, Placebo Controlled Trials Submitted to the US Food and Drug Administration: Individual Participant Data Analysis', *BMJ*, 378 (2022), e067606.

[12]Critical Psychiatry Network, *About Us* (n.d.), accessed 18 April 2025, https://www.criticalpsychiatry.co.uk/about-us/.

[13]Joanna Moncrieff *et al.*, 'The Serotonin Theory of Depression: A Systematic Umbrella Review of the Evidence', *Molecular Psychiatry*, 28 (2023), 3243–56 (published online 20 July 2022).

[14] Andrew Gregory, 'Scientists Question Widespread Use of Antidepressants After Survey on Serotonin', *The Guardian*, 20 July 2022, accessed 18 April 2025, https://www.theguardian.com/society/2022/jul/20/scientists-question-widespread-use-of-antidepressants-after-survey-on-serotonin.

[15] Awais Aftab, interview with the author conducted 16 April 2025.

[16]Julia Robinson, 'The Serotonin Theory of Depression: How the Media Got It All Wrong', *The Pharmaceutical Journal*, 309, 7964 (August 2022). E.J. Dickson, 'Who Is the Psychiatrist Behind the Antidepressant Study Taking Over Right-Wing Media?', *Rolling Stone*, 30 July 2022, accessed 24 May 2026, https://www.rollingstone.com/culture/culture-news/ssri-right-wing-attack-joanna-moncrieff-1388067/; see also Juan Pablo Chart-Pascual *et al.*, 'Understanding Social Media Discourse on Antidepressants: Unsupervised and Sentiment Analysis Using X', *European Psychiatry*, 68, 1 (2025), Article e51.

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concerns that their benefit, while statistically significant, might be too small to be 'clinically meaningful'.[17] Other studies highlighted underreporting of harms (such as suicidality in young people)[18] and over-representation of positive results in industry-funded trials, leading to publication bias.[19] These concerns prompted extensive further research and regulatory changes.[20] By the next decade, a recalibration of the scientific consensus had taken place: SSRIs came to be seen not as the 'wonder drugs' they had once been sold as, but nevertheless as useful treatments that were effective and well-tolerated for many people.[21]

Why did controversy emerge again, even as the scientific consensus had become increasingly settled? What caused this sudden intensification of doubt in the science of psychiatry?

Doubt is of course a necessary feature of science, where all conclusions retain a degree of residual uncertainty. Challenging consensus positions through scholarly debate is a key way in which scientific knowledge advances. Yet doubt can have harms as well. In their seminal work *Merchants of Doubt*, the historians Naomi Oreskes and Erik M. Conway describe how a small number of activist scientists manufactured doubt about a range of environmental issues during the twentieth century. Repeatedly cited by journalists and media figures, these contrarian voices portrayed the evidence underpinning the harms of second-hand smoke, acid rain, the ozone hole, and global warming as unsettled and contested. In doing so, they undermined the scientific consensus that had formed on each of these issues, turning doubt into a tactic to delay regulatory action and erode public trust in science more broadly.[22]

Yet Oreskes and Conway note that distinguishing reasonable from unreasonable doubt is inherently difficult. They suggest one indicator is the presence of practices that violate established scientific norms. Some hallmarks of manufactured doubt include: (i) disregarding the weight of evidence by demanding impossible standards of proof; (ii) persisting in the same objections after new evidence has addressed them; (iii) selectively misrepresenting data or the conclusions of other researchers; (iv) circumventing the peer review process by shifting debate towards public platforms; and (v) overstating one's expertise or authority in a field where it is limited.[23]

When such hallmarks are present, they prompt us to ask: what motivates these actions? In some historical cases, like tobacco science, motivations were financial and well-documented.[24] Yet in many others, Oreskes and Conway show how these figures were driven by strong ideological commitments: in particular, a right-wing libertarian suspicion of government regulation and of the scientific findings that appeared to justify it. In psychiatry, critiques may stem from philosophical, political, or ethical commitments that resist the medicalisation of mental illness.

This paper examines how a scientifically uncontroversial claim – that SSRIs are modestly effective – became the subject of renewed public doubt. It retraces how activists critical of psychiatry have promoted uncertainty about antidepressant efficacy. Most notably, the 2022 'umbrella review' was used as part of a concerted campaign to cast doubt on the use of SSRIs despite presenting no new evidence on efficacy and making no claims about it in the published paper itself. It argues that such actions went beyond the bounds of established scientific norms and could be considered an example of 'manufactured doubt' as

[17] Irving Kirsch *et al.*, 'The Emperor's New Drugs: An Analysis of Antidepressant Medication Data Submitted to the U.S. Food and Drug Administration', *Prevention & Treatment*, 5 (2002), Article 23.

[18]Tarek A Hammad, Thomas Laughren and Judith Racoosin, 'Suicidality in Pediatric Patients Treated With Antidepressant Drugs', *Archives of General Psychiatry*, 63 (2006), 332–9.

[19]Erick H. Turner *et al.*, 'Selective Publication of Antidepressant Trials and Its Influence on Apparent Efficacy', *The New England Journal of Medicine*, 358, 3 (2008), 252–60.

[20]Stone *et al.*, *op. cit.* (note 11); U.S. Food and Drug Administration, 'Public Health Advisory: Suicidality in Children and Adolescents Being Treated With Antidepressant Medications', October 2004, accessed 19 April 2025, https://www.fda.gov/ohrms/dockets/ac/04/briefing/2004-4065bl.htm.

[21]David Herzberg, *Happy Pills in America: From Miltown to Prozac* (Baltimore, MD: The Johns Hopkins University Press, 2009).

[22]Naomi Oreskes and Erik M. Conway, *Merchants of Doubt: How a Handful of Scientists Obscured the Truth on Issues From Tobacco Smoke to Global Warming* (New York, NY: Bloomsbury Press, 2010).

[23]*Ibid.*, 7–8, 244–5, 268–71.

[24]Robert N. Proctor, *Golden Holocaust: Origins of the Cigarette Catastrophe and the Case for Abolition* (Berkeley, CA: University of California Press, 2011).

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articulated by Oreskes and Conway. Furthermore, it suggests that the motivations behind these actions stemmed from underlying philosophical commitments that impeded disinterested scientific inquiry.

In doing so, the paper advances an argument about the role of doubt in science. It posits that whilst critique can and has helped to bring about change in psychiatry, there may be a point at which it becomes unproductive and harmful. This includes criticism originating from careful scholarship. Oreskes and Conway – and others writing under the rubric of agnotology[25] – offer a normative vision of science as self-correcting, cumulative, and open to challenge, but also vulnerable to bad-faith distortion. This sits in conflict with a broader critical stance towards science sometimes observable in the history of medicine, and psychiatry in particular. However, where questions of mind, body, and social meaning are entangled, distinguishing reasonable and unreasonable doubt becomes especially difficult. This paper argues that examining antidepressant controversy through this lens can clarify the epistemic, ethical, and political consequences of doubt in psychiatry today.

Psychiatry and its discontents

Critics of psychiatry emerged long before the rise of antidepressants. The dire state of psychiatric institutions had already drawn public ire in the 1940s,[26] although their most famous critique was not published until 1961 by the sociologist Erving Goffman.[27] By this time, large state-run hospitals had already begun to close, spurred on by patients' rights activism,[28] financial pressures, and the introduction of the first antipsychotic, Thorazine (chlorpromazine), in 1952.[29]

While the term 'anti-psychiatry' has been broadly applied to figures challenging institutional psychiatry in the 1950s and 1960s, few identified with the label.[30] More precisely, it describes a group of British psychiatrists, such as R.D. Laing and David Cooper (who first coined the term in 1967).[31] They gained fame and a degree of notoriety as figures in Britain's counter-cultural movements, although their early reputations rested on establishing alternative therapeutic communities.

As Michael Staub has argued, Laing and the other British anti-psychiatrists echoed an already widely held position at the time, that the causes of mental illness were to be found not in the biology of the brain, but in the social and relational fabric of everyday life.[32] Their success stemmed in part from their ability to blend this idea with an increasingly wide array of countercultural sources – from the Beat Generation to eastern mysticism – in a way that resonated with the left-wing liberation politics of the 1960s. Madness, in this view, was an unreasoned yet reasonable response to a schizophrenogenic world: one to be celebrated and even emulated.[33]

US psychiatry was at the time dominated by psychoanalytic thought, where much mental illness was believed to be the consequence of repressed unconscious conflict – a position the anti-psychiatrists implicitly shared.[34] Yet the loose diagnostic formulations that Freudian thought produced soon invited

[25]Robert N. Proctor and Londa Schiebinger (eds), *Agnotology: The Making and Unmaking of Ignorance* (Stanford, CA: Stanford University Press, 2008).

[26]Anne Harrington, *Mind Fixers: Psychiatry's Troubled Search for the Biology of Mental Illness* (Berkeley, CA: University of California Press, 2018). Harrington cites Albert Q. Maisel's article 'Bedlam 1946', published in *Life* on 6 May 1946, as an early critique.

[27]Erving Goffman, *Asylums: Essays on the Social Situation of Mental Patients and Other Inmates* (Garden City, NY: Anchor Books, 1961).

[28]Jonathan Toms, 'MIND, Anti-Psychiatry, and the Case of the Mental Hygiene Movement's "Discursive Transformation"', *Social History of Medicine*, 33, 2 (2020), 622–40.

[29]David Healy, *The Creation of Psychopharmacology* (Cambridge, MA: Harvard University Press, 2002).

[30]Tom Burns, 'A History of Antipsychiatry in Four Books', *The Lancet*, 387, 10025 (2016), 845–6.

[31]See also Oisín Wall, *The British Anti-Psychiatrists: From Institutional Psychiatry to the Counter-Culture, 1960–1971* (London: Routledge, 2018).

[32]Michael E. Staub, *Madness Is Civilization: When the Diagnosis Was Social, 1948–1980* (Chicago, IL: University of Chicago Press, 2011).

[33]*Ibid.*, 20.

[34]*Ibid.*; Kenneth S. Kendler, Rodrigo A. Muñoz and George Murphy, 'The Development of the Feighner Criteria: A Historical Perspective', *American Journal of Psychiatry*, 167 (2010), 134–42.

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another kind of critique. While often grouped with the anti-psychiatrists, Thomas Szasz rejected the label outright.[35] A Hungarian émigré who had fled Nazi Europe, Szasz trained and practised as a psychiatrist in the USA, but his most enduring legacy came from questioning the very basis of psychiatric diagnosis. In *The Myth of Mental Illness* (1961), Szasz argued that medicine concerns itself with diseases with observable biological correlates, such as lesions or physiological dysfunction. Since psychiatric diagnoses lacked such correlates and were instead defined by behaviour, he claimed they could not be diseases at all but should be understood as 'problems in living'.[36] If a biological cause were found, the condition would cease to be psychiatric and be reclassified as neurological. Psychiatric illness, in this view, was a category error.

Szasz's critique was motivated in part by his libertarian political beliefs; he shared a loathing of totalitarian regimes common among intellectuals who had fled Europe. He saw mental illness as a way for individuals to shirk their responsibilities and psychiatry as a fundamentally coercive institution at odds with individual liberty. This left little space to account for psychological distress or 'pain', and Szasz saw claims of 'illness' as a form of unconscious malingering.[37]

His critique of psychiatry, however, was a philosophical one. On the one hand, he reified all 'real' disease as based in an identifiable biological lesion, an essentialist criterion that many physical diseases could not fulfil, and on the other, claimed human 'behaviour' and experience more broadly to be outside of this realm. Some have argued that Szasz relies on a form of mind-body dualism, and as medicine applies only to one side of that division, psychiatry becomes a logical impossibility. This position – along with strong dualistic claims more generally – has been widely critiqued on philosophical grounds.[38] Nevertheless, the simplicity of its logic, and its ethical appeal to autonomy, proved compelling to many American libertarians. His work was frequently cited by jurists in civil liberties cases involving involuntary psychiatric commitment during the 1970s, helping to shape case law that significantly curtailed psychiatry's coercive powers.[39]

Unlike his British counterparts, who retained some standing within mainstream psychiatry, Szasz's radicalism alienated him from many colleagues. After a confrontation at the APA's 1964 conference where he was publicly challenged, he sought allies outside the psychiatric establishment.[40] He eventually aligned with the Church of Scientology, which had itself become a vocal critic of psychiatry, and co-founded its activist organisation, the Citizens Commission on Human Rights, which promoted the abolition of psychiatry. Although he claimed it was a tactical alliance, he remained associated with them until his death in 2012, something many felt damaged his credibility.[41]

Nevertheless, the alliance illustrates the wide ideological spectrum – from radical left to libertarian right – united in opposition to psychiatry by the 1970s. While the intentions of their critiques varied, both Szasz and the British anti-psychiatrists shared a common belief that psychiatry threatened individual autonomy. These critiques had real-world consequences. They influenced reforms to the legal frameworks governing coercive psychiatric care and forced the profession to confront the philosophical accusation of social constructionism. Psychiatry's response was not one these critics were likely to endorse, however, as it increasingly discarded psychoanalysis and reoriented itself towards a new 'biological' conception of disease, searching for the physical underpinnings that it was criticised as lacking.[42]

[35]Burns, *op. cit.* (note 30).

[36]Thomas Szasz, *The Myth of Mental Illness: Foundations of a Theory of Personal Conduct* (New York, NY: Hoeber-Harper, 1961).

[37]Staub, *op. cit.* (note 32), 104; 'in the hysterical transaction, disability is used as a coercive manoeuvre to force others to provide for one's needs', Szasz, *op. cit.* (note 36).

[38]SeePeter Sedgwick, *PsychoPolitics* (London: Pluto Press, 1982).

[39]Arthur R. Williams and Arthur L. Caplan, 'Thomas Szasz: Rebel With a Questionable Cause', *The Lancet*, 380, 9851 (2012), 1378–9.

[40]Harrington, *op. cit.* (note 26).

[41]Donald A. Westbrook, 'The Enemy of My Enemy Is My Friend: Thomas Szasz, the Citizens Commission on Human Rights, and Scientology's Anti-Psychiatric Theology', *Nova Religio*, 20, 4 (2017), 37–61.

[42]Staub, *op. cit.* (note 32), ch. 7; Hannah S. Decker, *The Making of DSM-III®: A Diagnostic Manual's Conquest of American Psychiatry* (Oxford: Oxford University Press, 2013).

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The rise of antidepressants

Even within an era of Freudian dominance, psychiatrists had long used medications to treat their patients. Thorazine was quickly regarded as a 'wonder drug', both in terms of its clinical effects and its economic success.[43] It was not the first psychiatric drug to be discovered, but it spurred on an eager search for others.[44] Whilst looking for analogues to Thorazine, researchers discovered that the drug imipramine caused some depressed patients to become elevated and energetic. After promising trial results, it was released in 1958, closely followed by amitriptyline in 1961, the first two tricyclic antidepressants (TCAs). Around the same time, iproniazid, a drug originally developed to treat tuberculosis, was also found to have mood-lifting effects.[45]

The idea that a chemical substance could alter one's mental experience pushed the new field of neurophysiology to sudden prominence. The discovery of neurotransmitters (the chemical messengers between nerve cells) in the brain prompted researchers to investigate their effects on behaviour,[46] especially after LSD was found to be structurally similar to serotonin.[47] One group showed that using a drug that lowered concentrations of serotonin caused a depression-like state in rats, which was then reversed when serotonin was restored.[48] However, the Swedish pharmacologist Arvid Carlsson demonstrated that another class of neurotransmitters – catecholamines – also affected behaviour.[49] Further studies showed that TCAs worked by preventing the reuptake of serotonin and catecholamines from the synapse,[50] while iproniazid prevented their breakdown. Both drugs seemed to work by increasing synaptic concentrations of neurotransmitters.

Other evidence began to push researchers towards the idea of the brain as a chemical organ and led some to hypothesise that mental illnesses may arise from neurochemical imbalances.[51] Schizophrenia was linked to elevated catecholamine levels,[52] which could be blocked by Thorazine, and Carlsson later demonstrated that movement disorders could be treated with the catecholamine precursor, L-DOPA, paving the way for its use as the first effective medication for Parkinson's disease.[53] In 1965, low catecholamine levels were proposed as a cause of depression,[54] while others suggested low serotonin.[55] Both camps recognised that chemical imbalance theories were likely to be 'simplifications', as did prominent figures like Carlsson.[56] Yet as the best fit for the limited evidence at the time, they were meant to help organise further research and push future discovery.[57]

[43]Advertisements for minor tranquilisers couched their efficacy in Freudian language: Herzberg, *op. cit.* (note 21), ch. 1.

[44]Healy, *op. cit.* (note 29).

[45]David Healy, *The Antidepressant Era* (Cambridge, MA: Harvard University Press, 1997), 45.

[46]It had previously been thought that brain cells communicated via electricity, a legacy of nineteenth-century vitalism. *Ibid.*, 71; Healy, *op. cit.* (note 29).

[47]Healy, *op. cit.* (note 29), ch. 5.

[48]Bernard B. Brodie, Alfred Pletscher and Paul A. Shore, 'Evidence That Serotonin Has a Role in Brain Function', *Science*, 122, 3177 (1955), 968.

[49]Arvid Carlsson, Margit Lindqvist and Tor Magnusson, '3,4-Dihydroxyphenylalanine and 5-Hydroxytryptophan as Reserpine Antagonists', *Nature*, 180, 4596 (1957), 1200.

[50]Julius Axelrod, Lionel Gordon Whitby and Georg Hertting, 'Effect of Psychotropic Drugs on the Uptake of H^3-Norepinephrine by Tissues', *Science*, 133, 3450 (1961), 383–384.

[51]The idea that depression is caused by a chemical imbalance has an older precedent in Thomas Willis's *De Anima Brutorum* (1672). Stanley W. Jackson, *Melancholia and Depression: From Hippocratic Times to Modern Times* (New Haven, CT: Yale University Press, 1986), ch. 6.

[52]Jacobus M. van Rossum, 'The Significance of Dopamine-Receptor Blockade for the Mechanism of Action of Neuroleptic Drugs', *Archives Internationales de Pharmacodynamie et de Thérapie*, 160, 2 (1966), 492–4.

[53]Arvid Carlsson *et al.*, 'On the Presence of 3-Hydroxytyramine in Brain', *Science*, 127, 3296 (1958), 471.

[54]Joseph J. Schildkraut, 'The Catecholamine Hypothesis of Affective Disorders: A Review of Supporting Evidence', *American Journal of Psychiatry*, 122, 5 (1965), 509–22.

[55]Alec Coppen, 'The Biochemistry of Affective Disorders', *British Journal of Psychiatry*, 113, 504 (1967), 1237–64.

[56]Interview with Arvid Carlsson in David Healy, *The Psychopharmacologists* (London: Arnold, 2001).

[57]See Haixin Dang and Liam Kofi Bright, 'Scientific Conclusions Need Not Be Accurate, Justified, or Believed by Their Authors', *Synthese*, 199 (2021), 8187–203.

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Nevertheless, these theories motivated a growing chorus of biological psychiatrists who pushed against the Freudian establishment.[58] Although depression had long been recognised as a psychiatric condition, it was generally considered to be severe and fairly rare, involving symptoms like suicidality or psychosis.[59] Milder cases tended to be seen in psychoanalytic terms as anxious reactions. But the medications' direct effects on mood prompted some researchers in the 1960s to argue that more common everyday symptoms were the manifestations of 'true' depression instead.[60] This view was encouraged by early epidemiological findings that suggested depression was indeed both common and under-recognised.[61] But it also rode a wave of optimism in the science of neurophysiology, evidenced by the retrospective christening of drugs like iproniazid and TCAs as 'antidepressants', giving an after-the-fact precision to fit the emerging chemical narrative.[62]

The biological turn in psychiatry came to a head in the 1980s, as the profession battled both itself and its critics over how to define the conditions it treated. US regulatory changes in the 1960s meant drug companies had to prove the effectiveness of new drugs in clinical trials,[63] and the pharmaceutical industry began to push for more standardised diagnostic criteria for use in these trials. This became an opportunity for some actors to finally displace the Freudian hegemony. When, in 1980, the APA published the third edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-III), it was a revolution – stripping away the vague psychoanalytic descriptors that had long occupied it. Diagnoses became sharply defined categories made up of specified lists of symptoms.[64] Although it was supposedly atheoretical – and agnostic about the causes of mental illness – in reality, the redrafting committee had leaned heavily towards a biological approach.[65] A new catch-all category, Major Depressive Disorder, subsumed previous classifications like reactive or endogenous depression, and arguably opened the way for simplistic chemical imbalance theories to become its dominant explanatory framework.[66]

Yet even by this point, evidence against monoamine theories had begun to mount. The catecholamine hypothesis was at first the more popular, but a 1984 study by the NIMH found no correlation between catecholamine metabolite levels and depression, challenging a straightforward deficit model.[67] In Europe, researchers had focused on serotonin as the mood-altering chemical – especially after low levels of its precursor, tryptophan, were associated with depression.[68] At Carlsson's urging, pharmaceutical companies began to develop drugs that selectively inhibited the reuptake of serotonin.

When SSRIs came to market in the 1980s (Prozac was released in the US in 1988), they were the first class of psychiatric drugs to appear only after they had undergone evaluation in clinical trials. Studies had shown that they were more effective than a placebo pill,[69] although no more effective than earlier drugs

[58]Supporters of a biological approach publicly encouraged a shift from 'blaming mother' to 'blaming brain': Herzberg, *op. cit.* (note 21), 170.

[59]There is divergence among historians between 'continuity' framings of depression (like Jackson, *op. cit.* [note 51]) and those who argue that depression was fundamentally remade (Healy, *op. cit.* [note 45]). For a thoughtful resolution, see Jonathan Sadowsky, *The Empire of Depression: A New History* (Cambridge: Polity Press, 2021).

[60]Herzberg, *op. cit.* (note 21).

[61]Such as the UK Goldberg–Blackwell Study (1970) and later the US Epidemiologic Catchment Area Study (1980). Christopher M. Callahan and German E. Berrios, *Reinventing Depression: A History of the Treatment of Depression in Primary Care 1940–2004* (Oxford: Oxford University Press, 2005).

[62]They were originally described as 'psychic energizers': Healy, *op. cit.* (note 45), 56.

[63]Following the 1962 Kefauver–Harris Amendments: Harry M. Marks, *The Progress of Experiment: Science and Therapeutic Reform in the United States, 1900–1990* (Cambridge: Cambridge University Press, 1997); Healy, *op. cit.* (note 29).

[64]Kendler *et al.*, *op. cit.* (note 34).

[65]Decker, *op. cit.* (note 42).

[66]Harrington, *op. cit.* (note 26); Healy, *op. cit.* (note 45), 174.

[67]James W. Maas *et al.*, 'Pretreatment Neurotransmitter Metabolite Levels and Response to Tricyclic Antidepressant Drugs', *American Journal of Psychiatry*, 141, 10 (1984), 1159–71.

[68]Alec J. Coppen and D.P. Doogan, 'Serotonin and Its Place in the Pathogenesis of Depression', *The Journal of Clinical Psychiatry*, 49, suppl. 8 (1988), 4–11.

[69]John P. Feighner, 'A Comparative Trial of Fluoxetine and Amitriptyline in Patients with Major Depressive Disorder', *The Journal of Clinical Psychiatry*, 46, 9 (1985), 369–72.

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(and potentially less).[70] Nevertheless, they were sold as the climax of years of scientific progress, a clean drug specifically designed to target a single neurotransmitter, meaning fewer side effects.

What remained unknown, however, was how they actually worked – what scientists refer to as their 'mechanism of action'. By the time they were released, further research had challenged any simple relationship between low serotonin and depression. Scientists could induce a serotonin-depleted state by starving individuals of the amino acid and serotonin precursor, tryptophan. However, healthy participants did not become depressed when starved, although those with a prior history of depression experienced a relapse in their symptoms, and some with a family history also experienced a mood drop.[71]

As SSRIs' mechanism became more uncertain, another challenge emerged from neuroscience itself. By the 1980s, researchers began to conceptualise the brain as a complex network and recast neurotransmitters as modulators of these systems.[72] Serotonin was found to play a role in how animals learnt about threat and punishment.[73] As the dominant metaphor for the brain began to shift from chemical organ to dynamic network, it no longer yielded a simple disease model for psychiatry to map clinical conditions onto. Increasingly challenged by new evidence, the serotonin hypothesis became the orphan of an abandoned theory of the brain.

Nevertheless, SSRIs proved extraordinarily popular. In 1992, Prozac became the most prescribed drug in the United States,[74] driven in part by SSRIs' favourable safety profile, which made them easier to prescribe for the primary care physicians who treated most cases of depression.[75] However, their success also owed much to the growing cultural acceptance of new biological models of depression, pushed by aggressive marketing campaigns. In the United States, direct-to-consumer drug advertising was legalised in 1985, and some advertisements portrayed SSRIs as correcting 'low levels' of serotonin.[76]

The ethics of this approach have since been widely debated.[77] Although many scientists initially supported the serotonin hypothesis as a plausible explanation, by the time these drugs were marketed, evidence had clearly begun to complicate this. In presenting an increasingly disputed theory as established fact, this advertising strategy created a misperception that would last for decades. As subsequent scandals soon began to mount, the use of an obsolete theory to promote SSRIs left the pharmaceutical industry open to accusations of bad faith.

Psychiatry's biological reorientation, which began in part as a response to its critics, had been made possible by the success of these medications. As they became a source of controversy, it would hand those same critics new grounds to remake their case.

After the decade of the brain

In July 1990, President George H. W. Bush issued a Presidential Proclamation declaring the new decade the 'Decade of the Brain'. It would turn out to be the high-water mark for public acceptance of biological

[70]Edward Shorter, *Before Prozac: The Troubled History of Mood Disorders in Psychiatry* (Oxford: Oxford University Press, 2009).

[71]Pedro L. Delgado *et al.*, 'Serotonin Function and the Mechanism of Antidepressant Action', *Archives of General Psychiatry*, 47, 5 (1990), 411–8; H.G. Ruhé, N.S. Mason, and A.H. Schene, 'Mood Is Indirectly Related to Serotonin, Norepinephrine and Dopamine Levels in Humans: A Meta-Analysis of Monoamine Depletion Studies', *Molecular Psychiatry*, 12 (2007), 331–59.

[72]Eric R. Kandel, 'The Molecular Biology of Memory Storage: A Dialogue Between Genes and Synapses', *Science*, 294, 5544 (2001), 1030–38; Ronald S. Duman, George R. Heninger and Eric J. Nestler, 'A Molecular and Cellular Theory of Depression', *Archives of General Psychiatry*, 54, 7 (1997), 597–606; Eric J. Nestler *et al.*, 'Neurobiology of Depression', *Neuron*, 34, 1 (2002), 13–25.

[73]Philippe Soubrie, 'Reconciling the Role of Central Serotonin Neurons in Human and Animal Behavior', *Behavioral and Brain Sciences*, 9, 2 (1986), 319–64; N.C. Tye, Barry J. Everitt and Susan D. Iversen, '5-Hydroxytryptamine and Punishment', *Nature*, 268, 5622 (1977), 741–43.

[74]Harrington, *op. cit.* (note 26).

[75]Callahan and Berrios, *op. cit.* (note 61).

[76]See Herzberg, *op. cit.* (note 21), for an extensive discussion of pharmaceutical advertisement tactics, many of them borrowed from (or adapted to avoid the critiques of) earlier approaches with minor tranquilisers.

[77]Jeffrey R. Lacasse and Jonathan Leo, 'Serotonin and Depression: A Disconnect Between the Advertisements and the Scientific Literature', *PLoS Medicine*, 2, 12 (2005), e392.

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explanations for mental illness.[78] SSRIs became potent cultural symbols. Psychiatrist Peter Kramer captured the prevailing enthusiasm in his best-selling book *Listening to Prozac*, in which he famously suggested that SSRIs could make people 'better than well', coining the provocative term 'cosmetic pharmacology' to describe this phenomenon.[79] First-person memoirs such as *Prozac Nation* by journalist Elizabeth Wurtzel and *Prozac Diary* by psychologist and writer Lauren Slater portrayed these drugs in a positive, although somewhat ambivalent, light.[80]

However, this wave of optimism quickly gave way to a growing body of criticism. Figures like R.D. Laing and Thomas Szasz had seen their influence wane in the 1980s, marginalised by the biological turn, but their critiques began to find new audiences in the wake of SSRIs. In 1994, the American psychiatrist Peter Breggin – a student and acolyte of Szasz who also questioned the biomedical model – published *Talking Back to Prozac.* Though seen as highly alarmist, Breggin's book raised concerns that would persist in critiques of SSRIs: that their efficacy was overstated due to industry bias, that their risks were under-recognised, and that they could induce serious side effects, including suicidality and aggression.[81] Breggin went further, however, comparing SSRIs to recreational drugs and attracting controversy by attributing the violent behaviour of one of the perpetrators of the 1999 Columbine High School massacre to their use.[82]

Concerns about SSRIs and suicidality had, however, already begun to surface. As early as 1990, case reports suggested that fluoxetine might be associated with increased suicidal ideation.[83] Initially met with scepticism – suicidal thoughts being closely linked with depression itself – the claims eventually prompted the APA to launch a task force. Eli Lilly, the manufacturer of fluoxetine, vigorously defended the drug, even as it quietly settled several legal cases out of court.[84] Subsequent studies and meta-analyses did reveal a small but measurable increase in self-reported suicidal thoughts among individuals under eighteen, although no conclusive link with aggression was established.[85] In 2004, the FDA issued a black-box warning regarding this risk, and in the UK, NICE restricted SSRI use in those under eighteen to fluoxetine alone.[86]

Similar concerns were echoed by David Healy, an Irish psychopharmacologist and medical historian, in his 2004 book *Let Them Eat Prozac.*[87] Healy accused the pharmaceutical industry of manipulating clinical trial data to downplay safety concerns. Blurring the roles of historian and historical actor, Healy became a whistle-blower and described how his public criticisms had led to the withdrawal of a job offer, which he interpreted as industry retaliation.

Although some questioned Healy's motives – he, like Breggin, began serving as an expert witness in SSRI-related legal cases[88] – further evidence emerged to support his claims. Perhaps the most infamous

[78]National Institutes of Health, *Decade of the Brain: Research Plan*, NIH Publication No. 91-2782 (Bethesda, MD: U.S. Department of Health and Human Services, 1991).

[79]Peter Kramer, *Listening to Prozac: A Psychiatrist Explores Antidepressant Drugs and the Remaking of the Self* (New York, NY: Viking, 1993).

[80]Elizabeth Wurtzel, *Prozac Nation: Young and Depressed in America* (Boston, MA: Houghton Mifflin, 1994); Lauren Slater, *Prozac Diary* (New York, NY: Random House, 1998).

[81]Peter R. Breggin and Ginger R. Breggin, *Talking Back to Prozac: What Doctors Won't Tell You About Today's Most Controversial Drug* (New York, NY: St. Martin's Press, 1994).

[82]In comparing them to addictive drugs, he borrowed arguments made about hypnotics a decade earlier. Herzberg, *op. cit.* (note 21).

[83]Martin H. Teicher, Carol Glod and Jonathan O. Cole, 'Emergence of Intense Suicidal Preoccupation During Fluoxetine Treatment', *The American Journal of Psychiatry*, 147, 2 (1990), 207–10.

[84]Natalie Angier, 'Suicidal Behavior Tied Again to Drug', *New York Times*, 7 February 1991.

[85]Hammad *et al.*, *op. cit.* (note 18).

[86]Unintended harms of the black-box warning have since been highlighted: Richard A. Friedman, 'Antidepressants' Black-Box Warning – 10 Years Later', *New England Journal of Medicine*, 371, 18 (2014), 1666–8; NICE, *op. cit.* (note 7).

[87] David Healy, interview with the author conducted 24 April 2025; David Healy, *Let Them Eat Prozac: The Unhealthy Relationship Between the Pharmaceutical Industry and Depression* (New York, NY: New York University Press, 2004).

[88]James Coyne, 'Lessons in Conflict of Interest: The Construction of the Martyrdom of David Healy and the Dilemma of Bioethics', *The American Journal of Bioethics*, 5, 1 (2005), W3–W14.

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example was Study 329, sponsored by SmithKline Beecham. Published in 2001, the study concluded that paroxetine was safe and effective in treating adolescent depression.[89] Yet a subsequent re-analysis of the original data contradicted this conclusion.[90] Moreover, the original article was revealed to have been ghostwritten by pharmaceutical copywriters, raising serious concerns about scientific integrity and misleading authorship.[91]

Concerns extended beyond individual studies to encompass the wider issue of selective publication. A 2008 analysis of both published and unpublished trials held by the FDA found that, of 74 studies on 12 antidepressants, only 51 were published – 94% of which reported positive results, despite only 51% being deemed positive by the FDA. This clear publication bias substantially overstated the efficacy of antidepressants.[92]

In a series of papers, Irving Kirsch analysed unpublished FDA trial data and suggested that SSRIs were only marginally more effective than placebo – not enough, he argued, to be considered 'clinically meaningful'.[93] A researcher at Harvard's Placebo Studies unit, he argued that their benefits were better explained by an 'amplified placebo effect'.[94] However, Kirsch was later criticised for misrepresenting the difference between drug and placebo effects: Placebos work quickly and then tend to wane; antidepressants only begin to take effect weeks after starting, and their benefits are sustained.[95]

As doubt regarding the effects of SSRIs mounted, it spilled into other debates. Many began to reconsider the very concept of depression that these drugs' success was built on. There was a flourishing of scholarly critique from historians and philosophers, challenging the checklist diagnoses that the DSM-III made possible. Some argued that this had allowed the category to expand and include much of what was once thought of as 'normal sorrow'.[96] Historians of medicine began to reconstruct this transformation, emphasising how the meaning of depression had changed under the influence of psychiatry's biological turn.[97]

Some argued that psychiatry had been fundamentally altered by this new conception of mental illness, leading to an over-reliance on prescribing at the expense of psychotherapy, a trend often attributed to cost-containment by health insurers.[98] In the UK, concerns about antidepressant overuse led NICE to recommend psychotherapy as a first-line treatment for depression, and in 2008 the government launched the Improving Access to Psychological Therapies (IAPT) programme, a self-referral scheme designed to expand access to NHS-funded talking therapies.[99]

The sense of scandal precipitated other changes. Concerns around bias in industry-funded trials were not unique to psychiatry and extended to the whole of academic medicine.[100] Still, antidepressants loomed

[89]Martin B. Keller *et al.*, 'Efficacy of Paroxetine in the Treatment of Adolescent Major Depression: A Randomized, Controlled Trial', *Journal of the American Academy of Child & Adolescent Psychiatry*, 40, 7 (2001), 762–72.

[90]Joanna Le Noury *et al.*, 'Restoring Study 329: Efficacy and Harms of Paroxetine and Imipramine in Treatment of Major Depression in Adolescence', *BMJ*, 351 (2015), h4320.

[91]Leemon B. McHenry and Jon N. Jureidini, 'Industry-Sponsored Ghostwriting in Clinical Trial Reporting: A Case Study', *Accountability in Research*, 15, 3 (2008), 152–67.

[92]Turner *et al.*, *op. cit.* (note 19).

[93] Irving Kirsch, interview with the author conducted 22 July 2025; Kirsch *et al.*, *op. cit.* (note 17).

[94]Irving Kirsch, *The Emperor's New Drugs: Exploding the Antidepressant Myth* (New York, NY: Basic Books, 2010).

[95]Peter Kramer, *Ordinarily Well: The Case for Antidepressants* (New York, NY: Farrar, Straus and Giroux, 2016).

[96]Jerome Wakefield's philosophical conception of Harmful Dysfunction was itself a response to the lack of contextual characterisation in the DSM-III, and he expanded it in a later book critiquing the DSM-III's conception of depression: Allan V. Horwitz and Jerome C. Wakefield, *The Loss of Sadness: How Psychiatry Transformed Normal Sorrow Into Depressive Disorder* (Oxford: Oxford University Press, 2007).

[97]Healy, *op. cit.* (note 87); Shorter, *op. cit.* (note 70); Callahan and Berrios, *op. cit.* (note 61); Gary Greenberg, *Manufacturing Depression: The Secret History of a Modern Disease* (New York, NY: Simon & Schuster, 2010).

[98]Greenberg, *op. cit.* (note 97).

[99]David M. Clark, 'Implementing NICE Guidelines for the Psychological Treatment of Depression and Anxiety Disorders: The IAPT Experience', *International Review of Psychiatry*, 23, 4 (2011), 318–27; National Institute for Clinical Excellence, *Depression: Management of Depression in Primary and Secondary Care* (Clinical Guideline 23) (London: NICE, 2004).

[100]Marcia Angell, former editor of the NEJM, published a scathing exposé: Marcia Angell, *The Truth About the Drug Companies: How They Deceive Us and What to Do About It* (New York: Random House, 2004). See also: Ben Goldacre, *Bad Pharma: How Drug Companies Mislead Doctors and Harm Patients* (London: Fourth Estate, 2012).

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large in this broader debate, and they were frequently cited in congressional hearings leading to the 2007 FDA Amendments Act.[101] This marked a shift in government oversight in how trials were run, requiring drug companies to preregister trials and publish all results – not just positive ones. This legislation coincided with other grassroots science-activism movements that helped to establish a new ethical standard in scientific publishing, including authorship declarations and conflict-of-interest disclosures.[102]

As scientists began to restore faith in their methods, doubt about the effectiveness of antidepressants seemed to settle as well. Following Kirsch, other researchers reanalysed the same datasets and found that antidepressant efficacy remained significant – albeit with less hyperbole than in earlier decades. Jay Fournier and colleagues, for instance, found that antidepressants produced significant benefit, but primarily in cases of severe depression.[103] Later meta-analyses confirmed modest but meaningful efficacy in milder cases as well.[104] Between 2001 and 2006, the NIMH conducted the STAR*D trial, involving over 4,000 patients, many of whom had not responded to previous treatments or presented with complex comorbidities (unlike the simpler patients typically included in industry trials). The trial – then the largest and most expensive of its kind – found that remission could be achieved in 67% of cases when non-responders were switched to alternative antidepressants, although these findings were later scrutinised.[105]

The STAR*D trial used other, newer antidepressants that had emerged since SSRIs, like bupropion (Wellbutrin) and venlafaxine (Effexor). In the wake of the monoamine hypothesis, researchers had looked at other neurotransmitters like dopamine and noradrenaline and found that drugs targeting these (with or without serotonin) could relieve depression in some people as well.[106] What remained unclear, however, was which drug to use in which person. The trial helped to establish the principle that depression was a heterogeneous condition: If one class of antidepressants didn't help, a different one might.[107]

By the late 2000s, however, the hope of ever more treatment options was fading quickly. Faced with growing regulatory and financial burdens, and a lack of new neurotransmitter targets, the pharmaceutical industry largely retreated from psychiatric drug development.[108] Aside from a few notable exceptions, psychopharmacology's half-century of promise had stalled.[109]

Two decades after the so-called 'Decade of the Brain', a more sober scientific consensus had emerged about antidepressants. Peter Kramer summarised the two decades of scientific controversy following *Listening to Prozac* by concluding that they worked 'ordinarily well' – that is, they were moderately effective in a substantial proportion of cases, with effect sizes comparable to those of other common medications such as beta-blockers or NSAIDs.[110] As David Healy argued in 1997, surveying the history of twentieth-century psychopharmacology before SSRIs, 'many drugs follow a pattern of being hailed as a

[101]Patricia Guthrie, 'US Senate passes FDA Revitalization Act', *CMAJ*, 177, 1 (2007), 23.

[102]Peter Doshi *et al.*, 'Restoring Invisible and Abandoned Trials: A Call for People to Publish the Findings', *BMJ* 346 (2013), f2865, doi:10.1136/bmj.f2865.

[103]Fournier *et al.*, *op. cit.* (note 1).

[104]Cipriani *et al.*, *op. cit.* (note 3); Stone *et al.*, *op. cit.* (note 11).

[105]Rush *et al.*, *op. cit.* (note 4); see Kramer, *op. cit.* (note 95), for a discussion of the trial including Kirsch. For examples of reanalyses, see Hitoshi Sakurai *et al.*, 'Cumulative Remission Rate After Sequential Treatments in Depression: Reappraisal of the STAR*D Trial Data', *World Psychiatry*, 23 (2024), 156–7; H. Edmund Pigott *et al.*, 'What Are the Treatment Remission, Response and Extent of Improvement Rates After up to Four Trials of Antidepressant Therapies in Real-World Depressed Patients? A Reanalysis of the STAR*D Study's Patient-Level Data With Fidelity to the Original Research Protocol', *BMJ Open*, 13 (2023), e063095.

[106]Sadowsky, *op. cit.* (note 59).

[107]Maurizio Fava *et al.*, 'Background and Rationale for the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) Study', *Psychiatric Clinics of North America*, 26, 2 (2003), 457–94.

[108]See former NIMH director Steve Hyman's autopsy: Steven E. Hyman, 'Revolution Stalled', *Science Translational Medicine*, 4, 155 (2012), 155cm11.

[109]Ketamine and psychedelics were just emerging as potential novel antidepressants. Sadowsky, *op. cit.* (note 59); Carlos A. Zarate Jr. *et al.*, 'A Randomized Trial of an N-Methyl-D-Aspartate Antagonist in Treatment-Resistant Major Depression', *Archives of General Psychiatry*, 63, 8 (2006), 856–64; Robin L. Carhart-Harris *et al.*, 'Psilocybin With Psychological Support for Treatment-Resistant Depression: An Open-Label Feasibility Study', *The Lancet Psychiatry*, 3, 7 (2016), 619–27.

[110]Kramer, *op. cit.* (note 95).

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panacea at first, only to be later dismissed as poisons before achieving pedestrian status years or decades later'.[111] SSRIs too had become pedestrian.

Doubt had once again transformed psychiatry: It had driven the evolution of new methods in data analysis and a recalibration of its research ethics. It had also helped to force a reckoning with the reductionist overconfidence of biological psychiatry. These criticisms would continue to shape the discipline in the coming years. Yet alongside it, another, less productive form of doubt began to gain prominence. Buoyed by this reckoning, some critics turned to older philosophical critiques which no scientific answer seemed to satisfy.

The new critics

By 2010, psychiatrists were calling for 'a paradigm shift'.[112] Many researchers had recognised the flaws in the DSM checklist criteria and began to argue for new diagnostic frameworks that recognised both the porous boundaries of mental illnesses and the need to characterise their heterogeneous underpinnings.[113] There were renewed calls for pluralism both in research methods and underlying philosophy.[114] This latter, more reflexive stance came to be called 'critical psychiatry' – consciously absorbing insights proffered by historians and social theorists, and their critiques of biological reductionism.[115]

Yet critical psychiatry was a diverse movement. The term originated in the late 1990s from a group of British psychiatrists and professionals called the Critical Psychiatry Network (CPN): a UK-based 'lobbying, campaigning and mutually supportive body' that aimed to challenge the 'hegemony of the now dominant biological view' in psychiatry.[116] The CPN started as a psychiatric trainee reading group established by Joanna Moncrieff and others in 1997 at the UK's Institute of Psychiatry. They invited speakers critical of mainstream psychiatry, including Thomas Szasz, the historian Andrew Scull, and the sociologist Nikolas Rose.[117] Szasz's influence in particular weighed heavily on the group. In 1999, they formalised as an activist group in reaction to new mental health legislation that allowed compulsory community-based treatment with medication.[118]

An NHS psychiatrist and professor at UCL, Moncrieff published theoretical work that drew on a range of philosophical influences. Citing Nikolas Rose and others, she developed an explicitly Marxist critique of psychiatry, arguing that it reinforces neoliberal political economy by framing economic non-productivity and broader human distress as individual pathology to be medicated.[119] Yet, once again illustrating the unlikely alliances within this debate, she also drew heavily on libertarian figures like Szasz

[111]Healy, *op. cit.* (note 45), 4.

[112]Thomas R. Insel *et al.*, 'Innovative Solutions to Novel Drug Development in Mental Health', *Neuroscience and Biobehavioral Reviews*, 37 (2013), 2438–44.

[113]Robert Spitzer, the original architect of DSM-III, accepted Wakefield's critique: Robert Spitzer, 'Preface', Horwitz and Wakefield, *op. cit.* (note 96); Hyman, *op. cit.* (note 108); Kendler *et al.*, *op. cit.* (note 34). Novel diagnostic framings included RDoC and HiTOP: Thomas Insel *et al.*, 'Research Domain Criteria (RDoC): Toward a New Classification Framework for Research on Mental Disorders', *American Journal of Psychiatry*, 167, 7 (2010), 748–51; Roman Kotov *et al.*, 'The Hierarchical Taxonomy of Psychopathology (HiTOP): A Dimensional Alternative to Traditional Nosologies', *Journal of Abnormal Psychology*, 126, 4 (2017), 454–77.

[114]Awais Aftab, 'Psychiatry and the Critical Landscape', in *Conversations in Critical Psychiatry* (Oxford: Oxford University Press, 2024).

[115]*Ibid.*; Robert Chapman, 'A Critique of Critical Psychiatry', *Philosophy, Psychiatry, & Psychology*, 30, 2 (2023), 103–19.

[116]Critical Psychiatry Network, *op. cit.* (note 12).

[117] Awais Aftab, 'Joanna Moncrieff', *op. cit.* (note 114).

[118]The Ritchie Inquiry recommended compulsory treatment orders after a psychiatric patient murdered a stranger on the London Underground in 1992. Nicholas Timmins, 'Christopher Clunis Report: Schizophrenic Made Series of Violent Attacks', *The Independent*, 24 February 1994.

[119]Nikolas Rose, *Governing the Soul: The Shaping of the Private Self*, 2nd edn (London: Free Association Books, 1999); Joanna Moncrieff, 'Psychiatric Drug Promotion and the Politics of Neoliberalism', *The British Journal of Psychiatry*, 188, 4 (2006), 301–302; Joanna Moncrieff, 'Psychiatric Diagnosis as a Political Device', *Social Theory & Health*, 8, 4 (2010), 370–82; Joanna Moncrieff, 'The Political Economy of the Mental Health System: A Marxist Analysis', *Frontiers in Sociology*, 6 (2022), Article 771875.

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and Breggin. She frequently recapitulated Szasz's view of psychiatry as biologically untenable,[120] and adopted Breggin's claims about antidepressants functioning as mood-blunting or numbing agents.

In the CPN's foundational paper, Moncrieff argued that, unlike the earlier anti-psychiatry movement, which 'called for the abolition of psychiatry on what have been perceived as ideological grounds', critical psychiatry's goal was to offer 'constructive criticism of clinical psychiatry'.[121] Although, as we have seen, self-identified anti-psychiatrists like Laing never called for psychiatry's abolition but rather for its liberatory reform, it was Szasz (and Scientology) who declared it philosophically impossible and demanded its abolition.

Alongside her philosophical interventions, Moncrieff's early work focused on challenging the evidence for antidepressant efficacy. Whilst at the Institute of Psychiatry, she was involved in a research unit that used new methods from evidence-based medicine. During this time, she published a meta-analysis suggesting that the efficacy of antidepressants was lower in trials with active placebos. She proposed that efficacy in other trials could be explained by 'unblinding', where participants realise they are taking a medication due to its side effects. Co-authored with the unit director Simon Wessely, the paper's conclusions were highly cautious and inconclusive, reflecting the significant limitations of the data.[122] Later, however, Moncrieff adopted a more definitive stance, asserting that unblinding largely accounted for antidepressant effects in trials in her 2008 book, *The Myth of the Chemical Cure*.[123] Studies subsequently challenged this view: trial data showed participants remained mostly unaware of whether they were taking the drug or not.[124]

In the same book, she also advanced a conceptual distinction between the 'drug-centred' and 'disease-centred' models of psychiatric medication. In the disease-centred model, drugs target an underlying pathology to relieve symptoms; in the drug-centred model, medications produce altered mental states – akin to recreational drugs or alcohol – that may mask or suppress symptoms. This was a reformulation of Szasz's claim that psychiatry involved a categorical error: because mental disorders were not biologically based, drugs could not treat them in the conventional medical sense. Moncrieff's argument was circular: If psychiatry lacked biologically defined disease entities, then psychiatric drugs could not treat disease, and could only produce drug effects. It also reified medications used elsewhere in medicine as always targeting pathology, even though many do not.

Her insistence on separating 'mental states' from biology also implied that any attempt to correlate conscious experience with brain functioning was untenable. In a later interview, she said: 'we cannot pin down the biological mechanisms of complex human thoughts, feelings and behaviours … we cannot do this now and we have no indication that we will be able to in the future'.[125] Once again, the Szaszian categorical dualism rendered psychiatry – and now cognitive neuroscience – essentially futile.

While her philosophical commitments were distinctive, Moncrieff's scepticism about antidepressants was at that time reflective of the prevailing view. Rejecting the possibility of a biological basis for depression made her more inclined to doubt medication efficacy, but she was not alone in doing so. She continued to publish critiques of SSRIs and found common ground with Irving Kirsch. Together they

[120]Joanna Moncrieff, '"It Was the Brain Tumor That Done It!": Szasz and Wittgenstein on the Importance of Distinguishing Disease From Behavior and Implications for the Nature of Mental Disorder', *Philosophy, Psychiatry, & Psychology*, 27 (2020), 169–81.

[121]Hugh Middleton and Joanna Moncrieff, 'Critical Psychiatry: A Brief Overview', *BJPsych Advances*, 25, 1 (2019), 47–54.

[122]Joanna Moncrieff, Simon Wessely and Rebecca Hardy, 'Active Placebos Versus Antidepressants for Depression', *Cochrane Database of Systematic Reviews*, (2004), CD003012. https://doi.org/10.1002/14651858.CD003012.pub2.

[123]Joanna Moncrieff, *The Myth of the Chemical Cure: A Critique of Psychiatric Drug Treatment* (London: Palgrave Macmillan, 2008).

[124]Stone *et al.*, *op. cit.* (note 11); Yi-Hsuan Lin *et al.*, 'Assessment of Blinding in Randomized Controlled Trials of Antidepressants for Depressive Disorders 2000–2020: A Systematic Review and Meta-Analysis', *eClinicalMedicine*, 50 (2022), 101505, https://doi.org/10.1016/j.eclinm.2022.101505.

[125]Aftab, *op. cit.* (note 114), 218, 228.

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co-authored several papers, combining her focus on unblinding with his on the clinical insignificance of antidepressant effect sizes.[126]

Other scholars had already begun to scrutinise how the mechanism of SSRIs had been communicated to the public. Research showed that many laypeople still believed that the 'serotonin hypothesis' was established science, due in part to aggressive marketing. By contrast, they found scientists and clinicians largely dismissed it as a simplification. Some commentators worried that this disconnect could cause harm, for instance, by fostering a reductive understanding of one's condition.[127] Moncrieff included these arguments in *The Myth of the Chemical Cure*, as well as an evaluation of the early research into the hypothesis. She argued that there was no evidence to support it and that its uncritical acceptance reflected a collusion between psychiatry and industry to distort public understanding.[128]

Meanwhile, other figures associated with the CPN began to gain public visibility. One was British psychotherapist James Davies, who had also been influenced by Peter Breggin. In *The Importance of Suffering* (2011), Davies argued that psychological distress should be seen as a 'healthy call to change' and not suppressed by medication.[129] Like Moncrieff, he later adopted Marxian critiques of neoliberalism and psychiatry.[130] In 2014, Davies and British aristocrat Luke Montagu co-founded the Council for Evidence-Based Psychiatry (CEP), with Moncrieff on its board. At the organisation's launch in the House of Lords on 30 April 2014, they warned of rising antidepressant prescription rates, claiming that benefits were overstated, harms minimised, and scientific evidence lacking.[131] UK media coverage was extensive, with headlines such as 'Antidepressants do more harm than good, research says'.[132] Figures from the CEP began making regular media appearances. Montagu shared his experience of withdrawal symptoms in *The Times*, whose editor he knew personally.[133] In April 2014, Davies appeared on *Sky News*, asserting that antidepressants 'work no better than placebo pills' for most people, and that 'most people taking antidepressants are not suffering a mental illness but rather understandable, albeit painful, human responses to difficult life factors that these pills may be exacerbating'.[134]

As the CEP's media profile grew, there was concern that these figures were no longer offering critique but presenting themselves as experts to cast doubt on the effectiveness of antidepressants. Instead of focusing on legitimate uncertainty, they asserted with increasing certainty that antidepressants were ineffective and unsafe. As work by Cipriani's Oxford group continued to reaffirm evidence of efficacy, this position diverged from most scientists' understanding.[135] Some observers argued that these activists

[126]Joanna Moncrieff and Irving Kirsch, 'Efficacy of Antidepressants in Adults', *BMJ*, 331, 7509 (2005), 155–9; Irving Kirsch and Joanna Moncrieff, 'Clinical Trials and the Response Rate Illusion', *Contemporary Clinical Trials*, 28, 3 (2007), 348–51.

[127]Lacasse and Leo, *op. cit.* (note 77); Christopher M. France, Paul H. Lysaker and Ryan P. Robinson, 'The "Chemical Imbalance" Explanation for Depression: Origins, Lay Endorsement, and Clinical Implications', *Professional Psychology: Research and Practice*, 38, 4 (2007), 411–20.

[128]Moncrieff, *op. cit.* (note 123), 222–4.

[129]James Davies, *The Importance of Suffering: The Value and Meaning of Emotional Discontent* (London: Routledge, 2011). He also appeared on Breggin's podcast: Peter Breggin, 'The Dr. Peter Breggin Hour – 04/19/17', *The Dr. Peter Breggin Hour* Podcast audio, 59:43 (19 April 2017), accessed 19 April 2025, https://drpeterbregginshow.podbean.com/e/the-dr-peter-breggin-hour-%E2%80%93-041917/.

[130]James Davies, *Sedated: How Modern Capitalism Created Our Mental Health Crisis* (London: Atlantic Books, 2021).

[131]Council for Evidence-based Psychiatry, 'Council for Evidence-Based Psychiatry Launches Today With Data Showing Dramatic Rise in Mental Health Disability', *Council for Evidence-Based Psychiatry*, 30 April 2014, accessed 19 April 2025, https://cepuk.org/2014/04/30/council-evidence-based-psychiatry-launches-today-data-showing-dramatic-rise-mental-health-disability/.

[132] Julia Llewellyn Smith, 'Lives "Left in Ruin" by Rising Tide of Depression Drugs', *The Telegraph*, 27 April 2014, accessed 19 April 2025; Chris Smyth, 'Antidepressants Do More Harm Than Good, Research Says', *The Times*, 30 April 2014, accessed 19 April 2025.

[133] Julia Llewellyn Smith, 'How Antidepressants Ruined My Life', *The Times*, 18 July 2015, accessed 19 April 2025, https://www.thetimes.co.uk/article/how-antidepressants-ruined-my-life-rjknv5zj5nh.

[134] James Davies, 'Interview on Sky News', *Sky News*, 26 April 2014, accessed 26 April 2025, https://cepuk.org/2014/04/28/video-dr-james-davies-interview-sky-news-26-april-2014/.

[135]Andrea Cipriani *et al.*, 'Comparative Efficacy and Acceptability of 12 New-Generation Antidepressants: A Multiple-Treatments Meta-Analysis', *Lancet*, 373, 9665 (2009), 746–58.

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were deliberately shifting the debate outside of scientific forums and into the public sphere.[136] Despite this, the CEP received relatively little pushback from mainstream psychiatrists.[137]

Some figures associated with the CPN did continue to challenge evidence for efficacy in academic venues. Michael Hengartner, later a co-author on the 2022 'umbrella review', published several studies and meta-analyses questioning antidepressant efficacy and safety.[138] But by this point, the disagreement had become increasingly technical, with each side critiquing the other's methodology, and decoupled from an intensifying public debate driven by media commentary and social media activism.

Then, in 2018, a new meta-analysis gained widespread public attention. Cipriani's group, responding to criticisms of their earlier 2009 study, conducted their most methodologically rigorous analysis yet. Including 522 RCTs and over 116,000 participants, with extensive inclusion of unpublished trial data, they published their findings in *The Lancet*. Once again, they concluded that most antidepressants were modestly effective and well tolerated.[139] It was the largest meta-analysis ever published in psychiatry. Despite some lingering criticisms, the scale and rigour of this article gave it particular weight among clinicians and researchers. It was regarded as a landmark contribution that further consolidated the consensus.[140]

In an interview, Moncrieff described the paper and its public reception as a 'setback' in a debate she felt 'we were starting to win'.[141] Along with Davies, Montagu and other CPN associates, she published a response claiming there was 'nothing new or clinically useful' in the findings.[142] Their critique repeated earlier arguments – unblinding, publication bias – but neglected to comment on how Cipriani et al. had accounted for these concerns. Paradoxically, they argued that the paper showed antidepressants should be used 'far less or perhaps not at all'. The certainty of this stance suggested they were unlikely ever to have been persuaded by its findings. The idea that antidepressants could be moderately effective was incommensurate with their belief that depression is not a meaningful disease category rooted in some element of biology.

The umbrella review

Shortly after the publication of Cipriani's 2018 meta-analysis, Moncrieff assembled a team of like-minded researchers whom she said she 'could trust' to undertake a new meta-review on the serotonin hypothesis.[143] They preregistered the protocol in 2020,[144] although Moncrieff had already critiqued the early science underpinning it at length in her 2008 book, casting doubt on the idea that this was a disinterested scientific inquiry, as she would later claim in media appearances.

Why take up the issue again? As the position that antidepressants were effective became settled within the scientific community, Moncrieff sought to shift the debate towards the unresolved question of their mechanism of action. For most scientists, these were distinct issues. Many drugs are used clinically despite an unclear or evolving understanding of how they work. But for Moncrieff and her collaborators, the lack of an established mechanism was itself discrediting. There remained widespread public belief in the 'low

[136]Aftab, *op. cit.* (note 15).

[137]One of the few professional responses: David Nutt *et al.*, 'In Defence of Antidepressants', *The Times*, 2 May 2014, accessed 19 April 2025. https://www.thetimes.com/travel/destinations/uk-travel/scotland-travel/in-defence-of-antidepressants-wdt5ms0vmwr?eafs_enabled=false.

[138]Michael P. Hengartner *et al.*, 'Efficacy of New-Generation Antidepressants Assessed With the Montgomery-Asberg Depression Rating Scale, the Gold Standard Clinician Rating Scale: A Meta-Analysis of Randomised Placebo-Controlled Trials', *PLoS One*, 15, 2 (2020), e0229381.

[139]Cipriani *et al.*, *op. cit.* (note 3).

[140]Sagar V. Parikh and Sidney H. Kennedy, 'More Data, More Answers: Picking the Optimal Antidepressant', *Lancet*, 391, 10128 (2018), 1333–4. Methodological criticisms continued, e.g., from the sceptical Nordic Cochrane Centre (whose lead Peter Gøtzsche was expelled from Cochrane's board in 2018): Klaus Munkholm, Asger Sand Paludan-Müller and Kim Boesen, 'Considering the Methodological Limitations in the Evidence Base of Antidepressants for Depression: A Reanalysis of a Network Meta-Analysis', *BMJ Open*, 9, 6 (2019), e024886.

[141] Joanna Moncrieff, interview with the author, conducted 31 July 2025.

[142]Sami Timimi *et al.*, 'Network Meta-Analysis of Antidepressants', *correspondence,* Lancet, 392, 10152 (2018), 1011–2.

[143]Moncrieff, *op. cit.* (note 141).

[144] Joanna Moncrieff *et al.*, 'The Serotonin Theory of Depression: An Umbrella Review of the Evidence' (PROSPERO, 2020), accessed 19 April 2025, https://www.crd.york.ac.uk/PROSPERO/view/CRD42020207203.

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serotonin' theory, and the review was intended to provoke debate about the paucity of its evidence. This created an opportunity to reiterate the group's longstanding claims: that there is no meaningful biological basis for depression; that antidepressants are better understood as recreational drug-like substances rather than disease-targeting treatments; and that any perceived efficacy could be attributed to unblinding or bias.

Yet for most researchers and clinicians, the inconsistent evidence around serotonin's role did not invalidate the possibility of a biological underpinning. Although no simple correlation between serotonin levels and depression had been found, broader evidence implicating neurotransmitter systems continued to motivate investigation. The consistent clinical efficacy of SSRIs was itself indirect evidence of serotonin involvement. Drawing on decades of research, scientists now framed depression as a disorder of brain networks, where negative self-beliefs and aversive behaviours became increasingly reinforced, producing distress and disability.[145] By increasing levels of neurotransmitters, antidepressants were thought to work by promoting plasticity and the updating of these fixed beliefs.[146] These ideas echoed neuroscience's broader paradigm shift – from 'chemical brain' to 'networked brain' – and reflected a form of 'normal science': the positing of provisional models revised in response to new evidence. Moncrieff and her co-authors did not engage with these new theories.

This helps explain the disconnect between the scientific community's puzzled reaction to the paper and its authors' own assessment of its significance. When the 'umbrella review' was published in *Molecular Psychiatry*, a prominent *Nature* Portfolio journal, on 20 July 2022, it drew intense media attention. The article summarised 17 studies on serotonin levels and activity in the brain – including blood serotonin, tryptophan depletion studies, and genetic data – and concluded that these provided no support for the serotonin hypothesis.

But many scientists challenged the paper's 'adamantine certainty'.[147] A group of 36 experts published a formal rebuttal, highlighting what they saw as serious methodological flaws.[148] Responding to Moncrieff's claim that the paper was an 'objective' systematic review, they argued that it was selective and incomplete, since it cited only 17 of over 360 potentially relevant studies. For example, it ignored several tryptophan depletion studies showing that previously depressed patients could relapse when serotonin levels were lowered. Critics also challenged Moncrieff's public characterisation of the findings as 'new', when in fact the review relied largely on historical literature. And, as another response pointed out, the serotonin hypothesis comprised multiple related propositions, not a single falsifiable claim.[149]

As these methodological critiques were being voiced in academic forums, a very different – and disconnected – debate had begun to emerge in the media and online. Whilst the paper itself was careful to avoid making claims about efficacy, a press release written by Moncrieff and co-author Mark Horowitz explicitly linked the umbrella review to a lack of efficacy in antidepressants. Press releases, unlike academic articles, do not go through peer review. Even so, staff in the UCL media office were uneasy about including comments on efficacy as this diverged from the article's content. They worked with the authors on a revised version. However, the authors pre-emptively circulated their own version that included comments on efficacy.[150]

[145]E. Castrén and H. Antila, 'Neuronal Plasticity and Neurotrophic Factors in Drug Responses', *Molecular Psychiatry*, 22, 8 (2017), 1085–95; Quentin J.M. Huys, Nathaniel D. Daw and Peter Dayan, 'Depression: A Decision-Theoretic Analysis', *Annual Review of Neuroscience*, 38, 1 (2015), 1–23.

[146]Catherine J. Harmer, Ronald S. Duman and Philip J. Cowen, 'How Do Antidepressants Work? New Perspectives for Refining Future Treatment Approaches', *The Lancet Psychiatry*, 4, 5 (2017), 409–18.

[147]Science Media Centre, 'Expert Reaction to a Review Paper on the "Serotonin Theory of Depression"', *Science Media Centre*, 20 July 2022, quoting Prof Phil Cowen, accessed 29 January 2026, https://www.sciencemediacentre.org/expert-reaction-to-a-review-paper-on-the-serotonin-theory-of-depression/.

[148]Sameer Jauhar *et al.*, 'A Leaky Umbrella Has Little Value: Evidence Clearly Indicates the Serotonin System Is Implicated in Depression', *Molecular Psychiatry*, 28 (2023), 3149–52.

[149]H. Möller and P. Falkai, 'Is the Serotonin Hypothesis/Theory of Depression Still Relevant? Methodological Reflections Motivated by a Recently Published Umbrella Review', *European Archives of Psychiatry and Clinical Neuroscience*, 273, 1 (2023), 1–3.

[150]Glyn Lewis, correspondence with the author, 29 July 2026. Confirmed by a staff member from the UCL Media Relations team, correspondence with the author, 30 July 2026. UCL media office press release: 'No Evidence That Depression Is Caused by Low Serotonin Levels, Finds Comprehensive Review', UCL News, 20 July 2022, accessed 29 July 2026, https://www.ucl.ac.uk/

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The article was quickly picked up by media outlets across the globe, far outstripping earlier CEP efforts. Within days it had gone viral: it was read over 413,000 times in the first few weeks and became the 217th most-shared scientific paper ever recorded by Altmetric.[151,152] In media appearances, Moncrieff frequently suggested that the paper discredited the efficacy of antidepressants. She appeared on ITV's This Morning and the right-wing news platform GB News, claiming the umbrella review showed there was 'no biological cause for depression' and that this meant that antidepressants had little or no benefit.[153]

When some scientists attempted to clarify the distinction between mechanism and efficacy, Moncrieff responded by claiming that researchers were backtracking, that they had long promoted the serotonin theory and were now dishonestly claiming it had been abandoned years earlier.[154] She thus recast clarification as evidence of deception.

As the media coverage continued, the paper was widely reported as showing that antidepressants do not work – a view encouraged by its authors. It fuelled a vast amount of negative discussion about antidepressants and their efficacy in US right-wing media outlets, podcasts, online blogs and social media (it was referenced nearly 9,000 times on Twitter by 2023).[155] Even as the paper itself faded from view, it left a widespread public perception that scientists disagreed among themselves about the efficacy of these medications. Tarred by this obfuscating sense of controversy, psychiatrists struggled to offer convincing correctives. And the profession was soon challenged by Secretary of Health and Human Services Robert F. Kennedy Jr., who took up antidepressant use as a cause célèbre in his Make America Healthy Again campaign in 2026, referencing the review's authors.[156] By promoting this disconnect between the paper's findings and its portrayal in the media – and between the scientific consensus and public understanding – the 'umbrella review' thus became a powerful tool for the manufacture of doubt.

Reasonable and unreasonable doubt

'Doubt is crucial to science', Oreskes and Conway argue: 'healthy scepticism drives science forward'.[157] Disagreement among scientists is extremely common, even when reviewing the same evidence. Do the debates around the efficacy and use of antidepressants represent healthy, reasonable doubt?

news/2022/jul/no-evidence-depression-caused-low-serotonin-levels-finds-comprehensive-review. Moncrieff and Horowitz distributed a separate press release a week earlier, unseen by the press team and without their knowledge: Joanna Moncrieff and Mark A. Horowitz, 'Comprehensive Review Finds No Evidence That Depression Is Caused by Low Serotonin Levels', Press Release, 20 July 2022. Copy in the author's possession. This made similar claims to an article they published the same day in The Conversation: Joanna Moncrieff and Mark A. Horowitz, 'Depression Is Probably Not Caused by a Chemical Imbalance in the Brain - New Study', The Conversation, 20 July 2022, archived capture, accessed 29 July 2026, https://web.archive.org/web/20220720053811/https:/theconversation.com/depression-is-probably-not-caused-by-a-chemical-imbalance-in-the-brain-new-study-186672.

[151]See note 16; Julia Llewellyn Smith, 'Do Antidepressants Work? This British Professor Says They Don't', The Sunday Times, 12 January 2025, accessed 26 April 2025, https://www.thetimes.co.uk/article/do-antidepressants-work-this-british-professor-says-they-dont-2025. Altmetric, *op. cit.* (note 152).

[152]Altmetric (n.d.), accessed 26 April 2025, https://www.altmetric.com/details/132834624?src=bookmarklet#score.

[153] Joanna Moncrieff, *This Morning*, hosted by Phillip Schofield and Holly Willoughby (ITV, 21 July 2022); J. Moncrieff, 'Antidepressants May Not Be the Best Treatment for Depression: Professor Joanna Moncrieff', interview by GB News, YouTube video, 24 April 2024, accessed 26 April 2025, https://www.youtube.com/watch?v=6eF6f3tQ6aw.

[154]Joanna Moncrieff *et al.*, 'The Serotonin Hypothesis of Depression: Both Long Discarded and Still Supported?', *Molecular Psychiatry*, 28, 6 (2023), 3160–63

[155]Dickson, *op. cit.* (note 16).

[156]Moncrieff was quoted in an HHS press release: U.S. Department of Health and Human Services, 'WTAS: HHS Launches MAHA Action Plan to Curb Psychiatric Overprescribing', 6 May 2026, accessed 31 May 2026, https://www.hhs.gov/press-room/wtas-hhs-launches-maha-action-plan-curb-psychiatric-overprescribing.html. Some months earlier, she appeared on an FDA panel on antidepressant use during pregnancy where she claimed, 'there is very little evidence that antidepressants have actual benefits in depression'. Joanna Moncrieff, remarks at 'FDA Expert Panel on Selective Serotonin Reuptake Inhibitors (SSRIs) and Pregnancy', US Food and Drug Administration, 21 July 2025, accessed 2 August 2026, https://www.youtube.com/watch?v=2Nha1Zh63SA.

[157]Oreskes and Conway, *op. cit.* (note 22), 39.

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There was a great deal of scepticism about the usefulness of SSRIs both within and outside psychiatry after their early years of hype. This doubt provoked intensive scientific inquiry: it led to further trials, including the largest post-marketing clinical trial ever conducted in psychiatry (STAR*D). It generated many meta-analyses of these clinical trials that contributed to innovation in the methodologies of meta-analysis more broadly. It helped to establish new ethical standards about the pre-registering of trials that are now the benchmark across the whole of academic medicine. Despite their many controversies, SSRIs survived intensive scientific scrutiny and re-analysis. Today, every major expert body and evidence-based guideline endorses them as an effective and appropriate treatment for depression.[158]

Yet, recently, there has emerged a widespread public misperception that they do not work, that they are 'no better than placebo' for most of those who take them. Claims like this are regularly repeated by journalists and media commentators, and circulate widely on social media. This paper has argued that figures associated with the Critical Psychiatry Network have helped to manufacture this doubt. They rejected the growing scientific consensus and, rather than contesting the evidence for efficacy directly, shifted focus to mechanism of action, hoping that uncertainty in this domain would undermine confidence in the drugs' broader use. The 'umbrella review' did not engage with the ongoing internal scientific debate about the aetiology of depression or recent theories of antidepressant action. Most of its authors have no prior expertise in these areas. Instead, they aimed their challenge at an outdated mechanistic theory and misrepresented the paper's findings in the media by suggesting that this challenged the evidence of efficacy. By arguing their paper supported claims that it did not, they bypassed scholarly debate altogether. In doing so, they adopted the stance of scientific sceptics, but not the practices of scientific inquiry.

When should doubt raise suspicion? When it persists in the face of further scientific inquiry, when it ignores the consensus that this inquiry generates, when it is promoted primarily outside the normal sites of scientific debate, and when it obscures or denies the broader balance of evidence. The authors of the 'umbrella review' demonstrate many of the hallmarks of the manufacture of doubt, as articulated by Oreskes and Conway. Where these hallmarks are found, they prompt us to consider the underlying commitments that may motivate them.

In her writings, Moncrieff articulates a consistent ethical and political critique of psychiatry: that it is coercive, that it medicalises social suffering, and that it reinforces neoliberal logics of personal responsibility. Yet as we have seen, these concerns are not inherently anti-scientific. Many psychiatrists, researchers, and historians share them, and such critiques have played a valuable role in shaping both policy and clinical practice. Indeed, they are deeply intuitive if you hold the kind of liberal values common in Western cultures. What distinguishes Moncrieff is her philosophical stance, inherited from Szasz, that there is a fundamental and irreducible distinction between the realm of human experience – which encompasses all mental phenomena including mental illnesses – and the biology of the brain. My aim here is not to refute this position but rather to draw attention to its implications. Holding it seems to significantly impair one's ability to engage with scientific inquiry into psychiatric conditions, especially the careful and open-minded testing and updating of hypotheses that Oreskes and Conway argue characterises normal science. Strongly endorsing this stance has meant that, throughout her career, Moncrieff has repeatedly rejected scientific findings that support any such biological underpinning. It has also meant she has rejected the idea that psychiatric medications can meaningfully treat mental diseases.

However, we cannot expect scientists (or indeed anyone) to be free of prior moral or political commitments. This issue has been widely discussed in the philosophy of science: The philosopher Heather Douglas has argued that it is neither possible nor desirable for scientists to exclude ethical or social values from their work. Scientific hypotheses often carry consequences that extend beyond the lab, and so decisions about which theories to pursue, accept, or reject will inevitably involve normative judgement.[159] Psychiatry is an exemplary case of this principle: The consequences of its conclusions are

[158]See notes 5–8. For a recent expert evidence review: Raymond W. Lam *et al.*, 'Canadian Network for Mood and Anxiety Treatments (CANMAT) 2023 Update on Clinical Guidelines for Management of Major Depressive Disorder in Adults', *The Canadian Journal of Psychiatry*, 69 (2024), 641–87.

[159]Heather Douglas, 'Inductive Risk and Values in Science', *Philosophy of Science*, 67, 4 (2000), 559–79.

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far-reaching, and it benefits from scrupulous and value-driven practitioners to guide its research. Many scientists working in psychiatry have ethical critiques to make of it. Yet only for some do their values lead them to persistently discount new evidence in this way.

Others have elaborated this point with reference to Bayesian probability: that all empirical assessments we make necessarily take into account both current evidence and prior experience. Yet this position sets up a tension as Bayesian priors are also correlated with a degree of certainty: If one's prior beliefs are held with a very high degree of certainty, then one is much less likely to allow novel data to challenge them. So whilst recognising the inevitability and normative benefit of our non-epistemic values and their involvement in our work, I would also suggest that the degree of certainty with which those priors are held is key in their evaluation. If one holds a philosophical position that means excluding the possibility of a certain kind of evidence – that depression might be a disease with a biological cause – then you will be highly predisposed to dismiss supporting evidence as weak, inconclusive or flawed. Holding such a prior strongly thus appears to impede one's ability to engage with balanced scientific inquiry.

Where do we draw the line? In this paper, I have tried to mark a distinction between two kinds of doubt in science. Many of the critiques made of psychiatry have been both effective and productive: earlier criticisms contributed to the de-institutionalisation movement and shaped the laws that regulate the use of coercive practices in psychiatry. In the last few years, legal debate around human rights law led to the WHO recently calling for an end to coercive practices as an infringement on human rights. Critiques of biological reductionism have led to changes in diagnostic frameworks and promoted calls for more philosophically grounded approaches.[160] This productive kind of doubt allowed for a degree of eventual convergence between science and its critics: scientists had to respond – to change their methods, beliefs and attitudes.

Another kind of doubt appears, however, singularly unproductive: attempts to address concerns, through further research into efficacy, provoked only louder and more vehement critique. Their doubt appears unresolvable: to demand an unreasonably high burden of proof. This incorrigible form of doubt seems to be driven in this instance – and perhaps others too – by strongly held philosophical beliefs that are irreconcilable with the premise of scientific inquiry. It drove these critics to repeatedly question emerging evidence and, eventually, disengage from scholarly debate altogether and redirect their efforts towards the public sphere. In their ever-greater efforts to discount new evidence, they turned to the tactics of manufactured doubt.

What are the consequences of this position? Oreskes and Conway argue that unreasonable doubt can be harmful to science, as evidenced by the climate change denialism that was propagated by contrarian scientists in the twentieth century. Can we find examples of such harms here? After all, antidepressant prescription rates have continued to rise.

However, as the philosopher and disability-rights campaigner Robert Chapman has argued, insisting on the invalidity of psychiatric diagnoses and treatments risks epistemic harm to marginalised groups, including disabled and neurodivergent individuals who would otherwise find value in them as a means to overcome stigmatisation and source agency.[161] Drawing an equivalence between antidepressants and recreational drugs stigmatises those who use them. This unreasonable doubt has been remarkably effective at generating controversy, evidenced by the widely held belief that the science remains unsettled. In promoting a disconnect between scientific and public understanding, it has impaired public trust in psychiatry more broadly, and risks alienating individuals from the mental health services that support them.[162] Finally, unreasonable doubt may also impoverish psychiatry of the benefits of productive external critique which, given the legal powers psychiatrists can employ and the vulnerability of the patients they manage, may be of particular importance to it.

[160]Aftab, *op. cit.* (note 114).

[161]Chapman, *op. cit.* (note 115).

[162]More recently, Breggin has published conspiracy-theory-laden books about the origins of COVID-19 vaccines: Peter Breggin and Ginger Breggin, *COVID-19 and the Global Predators: We Are the Prey* (Ithaca, NY: Lake Edge Press, 2021). Moncrieff, too, has expressed discontent with vaccine mandates on personal-freedom grounds: Joanna Moncrieff, Peter C. Gøtzsche and Robert May, 'Evidence Does Not Justify Mandatory Vaccines – Everyone Should Have the Right to Informed Choice', *rapid response to* BMJ, 375 (2021), n2957.

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Figures from the CPN have responded to critiques by pointing out the harms that antidepressant medication can have, such as withdrawal effects, which they argue are under-recognised in psychiatry. They make an important point that continues to generate further inquiry. It is an example of how figures associated with the CPN have used such activism to spur on meaningful scientific inquiry, including the publishing of new guidelines on antidepressant withdrawal.[163] However, whilst research to determine how common these experiences are is ongoing, there are also risks of over-emphasising the potential harms of antidepressants. Arguing that SSRIs can cause aggressive states that motivate school shootings, as Peter Breggin did, seems to be one such example. It is irresponsible not to represent the balance of risks and benefits that these medications offer.

And again, there is a question of motivation. Many figures in this debate, like Luke Montagu, are motivated by personal experiences of distressing side-effects, experiences they felt were under-recognised and mismanaged by the doctors who prescribed these medications. Yet, at the same time, others are motivated by the political position that psychiatric drugs are a coercive tool that suppresses individual selfhood and reinforces neoliberal hegemony. If one's priors are that antidepressants can have no meaningful benefit as a result of these beliefs, then they will likely bias judgement towards over-emphasising the harms of antidepressants. So, whilst acknowledging the very real possibility of unrecognised and poorly managed withdrawal effects, I want to draw attention to the potential harms for these same patients in using the issue to further delegitimise antidepressant use when one is motivated primarily by a strong belief that they do not work.

This debate speaks to a broader tension between prior beliefs and scholarly inquiry. Many of the activist figures in this story are also published historians of psychiatry, including Moncrieff and David Healy. This reflects the broader critical stance that historians of psychiatry have taken towards their subject matter.[164] As historian Jonathan Sadowsky has observed, the historiography has often framed psychiatry as a 'special case', repeatedly emphasising its ignorance or failures whilst obscuring its therapeutic benefits, with few engaging with the question of efficacy at all.[165] We should note that the philosophical and political positions that drive the critics of psychiatry have influenced some historians at times, arguably leading them to recapitulate in their histories their own strongly held priors.

More broadly, historians of science and scholars of science studies are notable for the critical stance they take towards their subject matter, driven in part by a sense of unease at the normative authority that science has held for a long time. Yet as science has been seen to come under threat, prominent scholars in this field, such as Latour and Oreskes, have drawn attention to the risks of such critiques.[166] Critique can go too far, and unreasonable critique should be called out, as science has a degree of fragility and can be undermined. There is then an essential tension between the position taken by scholars like Oreskes, who give a normative account of science as a privileged domain of inquiry by nature of its method and organisation, and others who argue that there is no such distinction to be made.[167]

Psychiatry and its critics are interesting examples to introduce into this debate. On the one hand, it points to some of the limitations of the analytic that Oreskes and others offer: it is far easier to critique unreasonable doubt where those promoting it are more obviously fringe, due to right-wing libertarian politics, for example, or through their association with financial interests. It is harder to critique it when

[163]Mark Horowitz has contributed to new deprescribing guidelines. Mark Horowitz and David M. Taylor, *The Maudsley Deprescribing Guidelines: Antidepressants, Benzodiazepines, Gabapentinoids and Z-drugs* (Chichester: Wiley-Blackwell, 2024).

[164]Two recent examples: Owen Whooley, *On the Heels of Ignorance: Psychiatry and the Politics of Not Knowing* (Chicago: University of Chicago Press, 2019); Andrew Scull, *Desperate Remedies: Psychiatry's Turbulent Quest to Cure Mental Illness* (Cambridge, MA: Belknap Press of Harvard University Press, 2022).

[165]Jonathan Sadowsky, 'Before and After Prozac: Psychiatry as Medicine, and the Historiography of Depression', *Culture, Medicine, and Psychiatry*, 45 (2021), 479–502.

[166]Bruno Latour, 'Why Has Critique Run out of Steam? From Matters of Fact to Matters of Concern', *Critical Inquiry*, 30, 2 (Winter 2004), 225–48; Erik Baker and Naomi Oreskes, 'It's No Game: Post-Truth and the Obligations of Science Studies', *Social Epistemology Review and Reply Collective*, 6, 8 (2017), 1–10.

[167]For a particularly sensitive articulation of this, see Lorraine Daston, 'The History of Science and the History of Knowledge', *Know: A Journal on the Formation of Knowledge*, 1, 1 (Spring 2017), 131–54.

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the motivating ideologies are widely held – as they are among psychiatry's critics who, as we have seen, are drawn from across the political spectrum by an underlying liberal suspicion of an institution that seems to threaten individual liberty (however that liberty is coloured politically).

As I have tried to show, liberalism continues to sit uncomfortably with any medically coercive practice, yet the critiques it motivates have both benefits and harms. One such harm has been to either obscure or romanticise suffering from mental illness, in particular severe mental illnesses which are profoundly debilitating and deeply stigmatised. Support for people with these conditions remains disproportionately under-resourced. We need critiques that will help this, not exacerbate it.

Conclusion

This paper has examined how recent critiques of antidepressants from activist figures contributed to the intensification of public doubt about their efficacy, in opposition to a growing scientific consensus. Although the 'umbrella review' offered no new evidence and made no claims about their effectiveness, its authors used the public controversy it generated to undermine their broader use. In doing so, they employed many of the hallmarks of what Oreskes and Conway have termed the 'manufacture of doubt'.

These critics were motivated by philosophical and ethical concerns about psychiatry's coercive potential, the over-medicalisation of distress, and neoliberal logics in healthcare. Yet, many of these concerns are shared broadly and have helped to drive debate and institutional reforms in other contexts. This demonstrates the role of non-epistemic values in scholarly inquiry. However, the epistemic rigidity of certain philosophical commitments these authors hold has limited the extent to which they can meaningfully engage with scientific evidence as it has evolved. Their doubt could not be answered; attempts to redress it provoked ever greater doubt. Eventually, it prompted them to disengage from the scientific debate and turn their focus to the public sphere, employing an obfuscatory approach that has fuelled broader distrust in psychiatry.

This example prompts us to consider how underlying ethical and political commitments can be both generative and problematic in science and science studies. This may depend both on the underlying compatibility of a critique with scientific inquiry and the strength with which those commitments are held: whether prior beliefs remain sensitive to evidence; whether, as new inquiry accumulates, this doubt can ever be resolved.

Acknowledgements. The author would like to thank Naomi Oreskes, Anne Harrington, and David Jones for reviewing earlier drafts of the manuscript and their helpful feedback.

Funding statement. Part of the research for this article was funded by the Frank Knox Memorial Fellowship granted by Harvard University's Committee on General Scholarships.

Competing interests. The author declares none.

Cite this article: Goulder J (2026). Beyond reasonable doubt: antidepressants and the limits of scientific critique. *Medical History* 1–21, https://doi.org/10.1017/mdh.2026.10090

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