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ABSTRACT Before 1980, most people experiencing common nervous problems and who sought medical help complained of anxiety and were treated for anxiety. Similar experiences increasingly led to complaints of or treatment for panic attacks in the late 1980s and early 1990s, and to complaints of or treatment for mood disorders by the mid-1990s. Today, such patients seem once again increasingly likely to complain of and be treated for anxiety. This paper reviews a series of mechanisms whereby company marketing can both transform the perceptions of physicians and shape the experiences of those seeking treatment and the self-understanding of those not in treatment. These include the standard ploys of company sales departments to increase demand for products, including celebrity endorsements, the sponsoring of educational events and a host of reminders. The portfolio of marketing manoeuvres has grown, though, by translating educational events and celebrity events into the arena of scientific research: clinical trials have increasingly become part of the marketing of disorders and their treatments; ghost-written scientific papers are authored by celebrity researchers. The portfolio of marketing manoeuvres has also grown to encompass new ways of creating fashion through medical activism, by setting up patient groups and disease awareness campaigns. The result is a transformation and growth in disorders tailor-made to fit ever more visible drugs.

Keywords antidepressants, depression, ghost-writing, globalization, marketing, neurosis

Shaping the Intimate:

Influences on the Experience of Everyday Nerves

David Healy

In the late 1960s, psychiatry and society were riven by the convulsion of anti-psychiatry (Healy, 2002a). Students stormed universities and occupied departments of psychiatry, claiming that mental illness did not exist, and that the treatments being used for mental illness were simply chemical straitjackets. By 1980, the anti-psychiatric argument that mental illness does not exist had apparently begun to lose its appeal. The advent of the third edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-III), which gave psychiatry operational criteria for diagnoses, and the rise of neuroscience, almost certainly played a part in reassuring many that the treatment of nervous problems had moved into less ideological

Social Studies of Science **34/2**(**April 2004**) **219–245**

ISSN 0306-3127 DOI: 10.1177/0306312704042620
www.sagepublications.com

and less contested waters. Positron emission tomography (PET) scans and other techniques appeared to attest to the reality of mental illness rather than just the existence of brains.

But aside from the existence or non-existence of mental illness, there had been a broader thrust to the anti-psychiatric argument, which was that the vaunted de-institutionalization of psychiatry had unrecognized consequences for all of us, not just for the relatively small group of individuals at risk of being incarcerated in asylums (Healy, 2002a). With the availability of new drugs and the prescription-only status of these drugs, the nervousness that can be found in the community at rates of 10–20% – viewed by some as being of social origin, by others as being of psychological origin and by yet others as being of biological origin – had fallen into the clutches of psychiatry. Real questions could be asked about how adequately psychiatrists had been trained to handle the many issues surrounding the experience of everyday nerves or about how psychiatry as a practice was equipped to handle the management of some of our most intimate experiences. It is this domain of influences on the experience of everyday nerves that the present paper seeks to address. It will suggest that there can be little confidence that the alienists, who had been decanted from their asylums in the 1950s and 1960s, are in control of or understand the forces shaping this domain.

Shaping Innermost Thoughts

Whatever the school of thought about the origin of the most common forms of nervous problems found in the community, there was a general consensus from the 1950s to the 1980s that these conditions were best seen as anxiety neuroses. When pharmacotherapy was turned to, the dominant management of these nervous problems was with benzodiazepines.

DSM-III, published in 1980, proposed a reorganization of the classification system within psychiatry that in combination with pharmaceutical company marketing was to change the face of psychiatry. DSM-III introduced what was described dismissively at the time as a Chinese laundry approach to psychiatry – take two symptoms from column A, two from column B and two from column C. In the case of anxiety, DSM-III broke up what had been a monolithic entity into a number of discrete disorders such as panic disorder, obsessive-compulsive disorder (OCD), social phobia, post-traumatic stress disorder (PTSD) and generalized anxiety disorder (GAD).

The impact of these new DSM categories and the marketing of new drugs on the experience of nervous problems can be seen most clearly in the case of panic disorder. Up to the mid-1980s, the average patient presenting with anxiety described periods of feeling tense and stressed, and typically indicated that these states of dysphoria would last for 30 minutes to 2 or 3 hours. By the end of the 1980s, one of the commonest complaints

of patients was that they had panic attacks – a term rarely heard of before 1980. When asked how long these attacks might last, sufferers would typically indicate duration of 30 minutes to 2 or 3 hours. This transformation occurred even though by definition panic attacks last for 1–2 minutes, and rarely much longer.[1]

Underpinning the transformation in terms that people used to express or account for their dysphoria lay the fact that in the 1980s, the Upjohn pharmaceutical company sought to market a new drug alprazolam (Xanax). As part of the development process for alprazolam, Upjohn put this new agent into clinical trials for one of the conditions newly recognized by DSM-III – panic disorder. This disorder was first described by Donald Klein in the mid-1960s. The perception was that panic disorder was a severe form of anxiety and that demonstrations that alprazolam worked for this condition would lead to it displacing other benzodiazepine drugs from the anxiety marketplace (Sheahan, 2000). In the course of their development work for alprazolam, Upjohn sponsored scientific symposia on panic disorder, often in exotic locations to which they brought some of the most distinguished figures in psychiatry. The company supported a burgeoning literature on panic attacks and a range of clinical and marketing studies on this disorder (Healy, 1990, 1998).[2] When finally launched, adverts for the new drug featured Panic even more prominently than Xanax. Sales of Xanax followed this marketing of Panic, despite the fact that, even in Upjohn-supported trials, panic disorder responded less convincingly to alprazolam than to comparators such as imipramine.

Quite aside from an increase of sales to and through psychiatrists, television, radio, and newspaper editors and journalists, from the BBC to NBC, and from *The Times* and *Guardian* to *The New York Times* and *The Washington Post*, became aware of interest in this new disorder. This led to programmes and articles featuring panic attacks. Even though many of these programmes and articles recommended behaviour therapy as the appropriate treatment rather than drug treatment, the net result of media exposure was that the way patients understood and expressed their experiences changed and the way physicians viewed those experiences also changed. This was true even in the UK, where Xanax never became widely available. Pharmaceutical funding strategically placed in academia had leveraged a much wider change in consciousness in society generally.

There is more than a simple change of labels for personal experiences involved here. The term panic in the late 1980s connoted a biological disturbance, whereas anxiety neurosis had indicated a psychosocial problem best managed by non-drug means. (A further implication of these changing labels in the marketing of depression will be outlined later.) Quite aside from the true nature of the problems and their most appropriate treatment, this example of pharmaceutical company marketing gives evidence of a new force at work with capacities to transform some of our most intimate experiences, and there is nothing in the training of psychiatrists that would lead anyone to think they were likely to be aware of what

was happening. A few more examples will help indicate the scope of this issue.

In the early 1990s, Roche had hoped to market moclobemide for the treatment of another of this new cluster of disorders – social phobia. In preparation for the launch of moclobemide, Roche commissioned an educational booklet produced apparently disinterestedly by a working party of the World Psychiatric Association, aimed at helping clinicians to recognize the features of social phobia. One hundred thousand copies of this were prepared for distribution to clinicians. Moclobemide was eventually only licensed in a small number of markets for social phobia, but the methods of marketing it, which involved selling social phobia, have been documented in some detail (Moynihan, 2002) and have subsequently been pursued on a much wider scale by SmithKline, the marketers of paroxetine (Paxil), when it was licensed for social phobia. Since then a literature has burgeoned, and even though much of it recommends non-drug treatments for 'shyness', sales for Paxil increase in line with awareness of both shyness and social phobia among physicians and consumers.

What can be seen here is a pattern of marketing diseases that can also be seen in the rest of medicine in the marketing of problems such as osteoporosis, leading to hormone replacement therapy or calcium-enhancing drugs (Berman, 1999); elevated lipid levels, leading to the use of lipid-lowering drugs; erectile dysfunction leading to the use of sildenafil; or bipolar disorder by a range of different companies, leading to the use of so-called 'mood-stabilizers'.

Within the domain of everyday nerves, these unfolding events were shaped by an earlier set of developments. In the mid-1980s, the benzodiazepine group of tranquillizer drugs, of which Valium, Librium, and Ativan were among the best known, were linked with the production of physical dependence. Concerns about benzodiazepines dependence rapidly escalated into a crisis that helped establish health as both an item of news and an object of study within the social sciences (Bury, 1996; Bury & Gabe, 1990; Gabe & Bury, 1991).

In the late 1980s, the first of the new drugs acting on the serotonin system, buspirone, was marketed as a non-dependence-producing tranquillizer. This failed in the marketplace, even though its mechanisms of action and treatment effect sizes for both anxiety and depression are similar to the mechanisms of action and treatment effect sizes of selective serotonin reuptake inhibitors (SSRI) and other serotonergic drugs for either anxiety or depression. This development made it clear that the new generation of serotonergic drugs coming on-stream would have to be developed as antidepressants rather than tranquillizers. The idea of a non-dependence-producing tranquillizer had no credibility in the market place, whereas antidepressants were not thought to be dependence-producing. The SSRIs became antidepressants, and it was predictable even then that companies would seek to branch out from the beachhead of depression into the hinterlands of anxiety (Healy, 1991).

Although it is now well-recognized that nervous disorders are shaped by history (for example, see Hacking, 1995) there have been few commentators within either the social sciences or mental health fields who have been prepared to contemplate the possibility that the Era of Depression we have recently been living through in the West has stemmed primarily from the need of pharmaceutical companies to market compounds such as Prozac, Zoloft and Paxil.

In the West, cases that would have been treated by Valium and Ativan were being converted into cases to be treated by Prozac, Zoloft and Paxil. This situation is reflected in data on pharmaceutical sales, which show clearly that sales of antidepressants soared in the UK and the USA through the 1990s, while sales of tranquillizers flattened and dropped, so that by the middle of the 1990s the sales of the antidepressants had overtaken those of the tranquillizers (Rose, 2003). The overall volume of sales of drug treatments for nervousness remains, however, approximately constant, which indicates that what is involved at least in part is not a detection of new cases of depression, but a transformation of cases of anxiety into cases of depression.

This switch did not happen in Japan, where benzodiazepine dependence had never become a crisis. The Japanese pharmaceutical market is a high volume market with many features in common with Western pharmaceutical markets. In both Japan and the West, the antidepressant market had been a much smaller one than the tranquillizer market through the 1980s. For every person put on an antidepressant, three or four were put on tranquillizers. In Japan, this distribution of sales continued: the market for tranquillizers remained robust through the 1990s, while sales of antidepressants remained what they had been during the 1980s. There were no SSRI antidepressants on the Japanese market until 1999, when fluvoxamine was licensed for the combination of OCD and depression. In 2000, Paxil was licensed for the combination of social phobia and depression. As of 2003, Prozac is still not on the Japanese market. Far from being anomalous, the Japanese were closer to the global norm. It was the UK and US that proved the exception. Figures from South America and elsewhere during this period show trends comparable with those found in Japan (Rose, 2003).

The move from anxiety to depression can be seen in a different form in advertisements for antidepressants and tranquillizers during the period. The images of nervous problems from the 1960s through to the late 1980s showed young to middle-aged women in good health after treatment with tranquillizers. In contrast, the image of depression during this period was of older women, and occasionally of older men. Depression was a relatively rare disorder of middle-aged or older people. In the 1990s, the women featured in advertisements for SSRI antidepressants, such as those for Lilly's Prozac, Solvay's Luvox and GlaxoSmithKline's Paxil become progressively younger; by the late 1990s these women appear to be in their mid-20s.

By the mid-1990s, patients presenting with nervous problems typically talked about problems with their mood. When asked how long these problems might last, it was common to have patients say the problem might last for 30 minutes to several hours. This by definition is not a classical mood disorder, which involves a pervasive and persistent abnormality of mood, a dysthymia, lasting typically for several months, but at the very least for several weeks.[3]

Whether these conditions are appropriately called mood or anxiety disorders is immaterial. The problem that patients experienced as anxiety in the mid-1970s or early 1980s was transmuted first of all into panic attacks, and is now more likely to be called a mood disorder. Where aspects of the experience tied into physiological changes may remain constant, and may differ between anxiety and depression, it seems likely that a diagnosis of depression will demoralize, where a diagnosis of anxiety will lead to anxiety about being anxious. In so far as this happens, these changes of label seem capable of affecting significant parts of the overall experience that is anxiety or depression

There are further aspects to this. Even though drugs were used in its treatment, anxiety up through to the 1980s had been seen primarily as a psychological problem, and a slew of psychodynamic terms linked to its psychological management had penetrated into popular language. Terms such as defence mechanisms, libido and ego were bandied around, commonly divorced from their theoretical frames of reference. This psychobabble had consequences for notions of legal and moral responsibility, as well as for child-rearing and educational practices. By 1997, however, the front page of the G2 section of *The Guardian*, one of the UK's leading liberal broadsheets, featured the image of a depressive thinker agonizing over the fact that the UK had become so depressed. On the inside the author wonders whether the British have become a low-serotonin people (James, 1997). The psychobabble is rapidly being replaced by a biobabble that equally has pervasive consequences for the ways we view and experience ourselves and not just for the labels we give to our discontents.

By 1996, the World Health Organization had reported that depression was the second greatest source of disability on the planet (Murray & Lopez, 1996). The response from psychiatry to this news appeared to be satisfaction that the discipline was now the second most important in medicine after cardiology. Nobody seemed to question how a society could have become so depressed so fast. Depression was being touted as a serious illness; but the emergence of a comparable epidemic of any other serious illness on this scale would have led to serious questioning as to what had happened. There appeared to be no such questioning in the case of depression.

Despite the element of scepticism here, it should be noted that many regard this switch from diagnosing anxiety to diagnosing depression as evidence of scientific progress rather than one more instance of disease marketing. The recent rebranding of SSRIs as anxiolytics, which is outlined later, has however considerably strengthened the sceptical position.

Marketing Disorders

A more sceptical position also depends on being able to explain how pharmaceutical companies achieve such transformations. With colleagues, I recently tracked reviews of antidepressants used to treat depression in people with *physical* illnesses. This aspect of the literature on depression essentially only appears during the mid-1980s, even though the antidepressants had been available since the late 1950s. Similarly, when tracking articles on depression from periodicals such as *Vogue*, one can again see a literature appearing on depression and antidepressants in the mid-1980s (Shorter, 2001).

The most parsimonious explanation of the emergence of this literature on depression and antidepressants in the mid to late 1980s is that governments, pharmaceutical companies, hospitals, physicians and the public all want good news about treatments, whether drug or non-drug treatments. By the mid-1980s it had become impossible to write good news stories about the benzodiazepines. The benzodiazepines had been the big trees in the nervous disorder jungle, and felling these provided previously shaded plants with new opportunities to grow. The literature on the antidepressants blossoms from that point, even though drugs to treat depression had been available from the late 1950s. It would appear that this holds as true for the academic as for the lay media.

When a new literature emerges like this – for whatever reason – the coincidence of its claims with those of interested parties can significantly affect the rate of growth of the literature. In the case of psychotropic drugs, pharmaceutical companies provide an extremely efficient distribution system for scientific papers that suit their marketing interests. For example, I have in the past had enquiries from companies about the price of 5000, 10,000 and 20,000 reprints of a paper that I had written that happens to mention a particular drug; for non-commercially based research that doesn't feature a product, it would be very unusual to get more than 200–300 reprint requests.

In addition to supporting and distributing a literature, which companies have been doing since the 1950s, there are a number of other well-known factors that pharmaceutical companies can use to promote a change in cultures, some of which have operated for decades and others are more recent. From the 1950s, celebrity endorsement in advertisements and articles in the lay media have played an important role in the marketing of drugs. But more recently, a different form of celebrity endorsement and advertisement in the academic media has played an increasing role: pharmaceutical companies have commissioned rather than simply distributed scientific papers, as will be outlined later.

Another recent feature of the market place is the development of patient groups. Patient groups became part of the market development plans for new pharmaceutical agents in the 1990s, as companies realized that patients can often lobby more effectively for a new high-cost treatment than anyone else can. In the mid-1990s, it was common to find meetings

costing approximately US$1000 per day to attend, at which representatives from the major pharmaceutical companies offered lessons on how to set up patient groups. As the brochure for one such meeting put it:

> Carefully planned patient education campaigns are . . . becoming more widespread as pharmaceutical companies realise the benefits of added value services. At this two-day conference, you will discover how to successfully create targeted patient education campaigns which will establish your expertise in disease areas and increase company profile.

At the meeting I could '*experience* first hand demonstrations of successful campaigns and new educational techniques, *measure* the real business benefits of effective patient education, [and] *profit* from the experience of international disease management and pharmaceutical marketing experts' – amongst other things.[4]

Containing Negative Publicity: Silencing Critics

In addition to accentuating the positive, pharmaceutical companies have always been prepared to minimize the negative. This has meant providing responses from experts to counter adverse claims made by other experts. Whether well-founded or not there has always been a belief that journals carrying advertisements are at risk of losing this source of revenue if they carry papers detrimental to company interests (Braithwaite, 1986). Some recent instances of minimizing the negative that appear to go beyond what has previously been seen are outlined later.

In Spring 2000, the *Hastings Center Report* published five papers on Prozac (De Grazia, 2000; Edwards, 2000; Elliott, 2000; Healy, 2000; Kramer, 2000). Two argued that it was appropriate to restrict Prozac to treating proper clinical depression, while two argued that if Prozac helped people who might not appear to be classically depressed, but rather might seem to be alienated, this was a legitimate use of the drug. The fifth paper outlined the story covered here, that we have moved from an age of anxiety to an era of depression and we may move back in the near future. The interest in the Prozac story, accordingly, it was argued, lies in the abilities of pharmaceutical companies to manipulate consciousness, that a key feature in what happens is market share, and that in the interest of market share certain aspects of the data were not entering the public domain in a manner that would be appropriate for science. In response to this paper, Eli Lilly who, at the time as I understood it, were the biggest single funder of the Hastings Center withdrew their funding (Healy, 2002b).

In April 2000, the book *Prozac Backlash* appeared (Glenmullen, 2000). A series of reviews apparently authored by a number of senior figures in US psychiatry – Rothschild, Dunner, Greist, Ruben and Emslie – were sent to a number of media outlets shortly afterwards. These reviews have a consistent theme, which date back to Lilly's first defence of Prozac in 1990 against charges that it might provoke suicide in some patients, namely that Prozac is one of the most researched drugs in history and that the problems stem from the disease depression and not its treatment with

Prozac. The supposed real tragedy of books like *Prozac Backlash* is that patients who are at risk of committing suicide will be scared away from effective treatment and as a result will end up committing suicide.

These reviews went to Jamie Talan of Newsday in New York with a covering letter from Robert Schwadron of Chamberlain Communications, a public relations (PR) agency working for Lilly in New York. In his covering letter, Schwadron offers to arrange for interviews on this book with members of Eli Lilly as well as with 'independent researchers from the medical community'.

The Chamberlain logo features a target. It will come as no surprise therefore to find that Chamberlain had listed Dr Glenmullen as someone to manage. Chamberlain also appears to have targeted me. The views I have expressed in recent years are entirely consistent with views expressed in *The Antidepressant Era* (Healy, 1998), which was reviewed favourably by clinicians as well as investigators and others working with the pharmaceutical industry. Yet a few years later the same views were being described as controversial. I was receiving telephone calls from Canada, the USA, Japan and elsewhere to tell me that I was being described as trouble and was soon to be in trouble with US psychiatrists, who neither knew me nor had heard me talk. It remains a moot question as to whether this change of reception has had something to do with the attentions of PR agencies working with pharmaceutical companies. The only difference between 1998 and now is my involvement in a legal action as an expert for the plaintiffs. The clear involvement of PR agencies in some cases and the withdrawal of funds from a bioethical institution point to a qualitatively different scale of response to critics than hitherto.

Comparable patterns of deployment of experts to silence critics, setting up patient groups/activist groups, and opposing those who question a corporate platform have in recent years become a feature of the corporate response across a wide range of areas from pharmaceuticals to environmental movements (Rampton & Stauber, 2001). A November 2000 front cover of *Forbes* magazine suggests that corporations see themselves as living in a world of corporate saboteurs, who have wrecked Monsanto and now have their sights on the US pharmaceutical companies. This does not seem to be a world that encourages debate. Perception management on this scale may have some justification in something like the oil business, but is more difficult to justify in a scientific field such as therapeutics, especially where the therapeutics involve inherently ambiguous problem areas.

Authoring Papers

A 1999 email said:

> Dear David I am delighted you are able to participate in our satellite symposium. . . . In order to reduce your workload to a minimum we have had our ghost-writers produce a first draft based on your published work. I attach it here. . . .

The attached paper was a recognizably Healy piece, complete with Healy references saying the kinds of things that I often say. Many people who think they know my work would probably be hard pressed to pick it out as a fake.

However, I had already mapped out what it was I wanted to write, and I sent a draft paper back to the company running the symposium. They were happy with the contents, but made it clear that there were some commercially important points in the previous manuscript and that they would arrange for someone else to author this. The paper I authored finally appeared in a journal supplement (Healy, 1999) sitting beside the paper that had been authored for me – with, as far as I could make out, only one change in the original ghost-written paper, the name of the author.[5]

Recently the *Lancet* in an editorial questioned how tainted medicine has become (*Lancet*, 2002a).[6] One of the examples of the taints mentioned was the publication of an article by Thase et al. (2001) on the merits of venlafaxine (Effexor).[7] This paper by Thase et al. forms the basis for a campaign by Wyeth to try and persuade prescribers that, while SSRI antidepressants may get a certain proportion of people better, venlafaxine, Wyeth's drug, will push people beyond better to well. The clinical trial data behind this claim were due to be presented at a meeting held in Laguna Beach (CA, USA) in Spring 2001.

The Laguna Beach meeting was one to which a large number of clinical researchers were invited. It came complete with travel and accommodation expenses and honoraria, and participants at the meeting had the opportunity to have their contributions written for them. The organizers of the meeting were keen to have input from me and a colleague on a topic related to the Thase material. A 2001 email communication brought an already written paper, and made it clear that I was free to edit the paper in any way I chose.

Rather than reject this draft, as an experiment, I edited it in two ways. One was to point to the fact that clinical trial data from mirtazapine, a product directly competing with Wyeth's venlafaxine, appeared to give a message that was very different to the message that Wyeth were hoping to put across. The second alteration was to point out that there was considerable evidence from clinical trials and healthy volunteer populations that personality types may in fact predict suitability to selective agents such as the SSRIs. The same can be expected to hold true for venlafaxine, in which case if patients are not suited to venlafaxine it might in fact make them suicidal (see Table 1).

Despite having been told that I was free to edit the original paper in whatever way I chose, by return of email there was an objection to the mention of mirtazapine. I did not attend the Laguna Beach meeting. The next time I saw this paper was when it had already been sent to the journal, which was going to publish the proceedings of the symposium. The final paper had been revised extensively. The reference to the fact that failing to match venlafaxine to patients could lead to problems including suicidality

was missing. A new ending stated the current best treatment was with venlafaxine. I objected and removed my name from the paper.[8] This chain of events gives the lie to pharmaceutical company justifications of ghost-writing of this type, which is that the notional authors of these papers check them closely and sign off on them.[9]

TABLE 1
Incidence of suicides and suicide attempts in antidepressant clinical trials drawn from Food and Drug Administration licence applications

Investigational drug	Patients (*N*)	Suicides (*N*)	Suicide attempts (*N*)	Suicides and attempts (% of patients)
Sertraline	2053	2	7	0.44
Active comparator	595	0	1	0.17
Placebo	786	0	2	0.25
Placebo run in		0	3	
Paroxetine	2963	5	40	1.52
Active comparator	1151	3	12	1.30
Placebo	554	0	3	0.54
Placebo run in		2	2	
Nefazodone	3496	9	12	0.60
Active comparator	958	0	6	0.63
Placebo	875	0	1	0.11
Mirtazapine	2425	8	29	1.53
Active comparator	977	2	5	0.72
Placebo	494	0	3	0.61
Bupropion	1942	3	–	
Placebo	370	0	–	
Citalopram	4168	8	91	2.38
Placebo	691	1	10	1.59
Fluoxetine	1427	1	12	0.91
Placebo	370	0	0	0.00
Placebo run in		1	0	
Venlafaxine	3082	7	36	1.40
Placebo	739	1	2	0.41
All investigational drugs	21,556	43	232	1.28
All SSRI	13,693	23	186	1.53
Active comparator	3681	5	24	0.79
Total placebo	4879	2	21	0.47
SSRI trial placebo	3140	2	15	0.57

Notes: Companies lodging their data with the Food and Drug Administration have coded data on suicidal acts in the placebo run in (washout) period under placebo. Coding under placebo minimizes the apparent problem. Comparing investigational drugs to placebo (excluding bupropion on the basis of missing data), using a Mantel–Haenszel procedure, the odds ratio of a suicidal act on new antidepressants compared to placebo is 2.4 (95% confidence interval 1.6, 3.7). The odds ratio for completed suicides compared to placebo is 4.62 (95% confidence interval 1.126, 18.953; $P = 0.031$).

Authoring Papers: Current Medical Directions

Since the 1980s a majority of major pharmaceutical companies have outsourced their medical writing to medical-writing agencies (Healy, 2003b). Companies also began setting up satellite symposia in conjunction with formerly scientific meetings. Journals began to publish the proceedings of such satellite symposia in supplements. As this happened concerns grew about the prevalence of ghost-writing of medical papers such as that outlined earlier. Until quite recently the assumption has been that ghost-writing has been confined to review papers, appearing primarily in journal supplements or in obscure journals.

The idea that medical-writing agencies would restrict themselves to the margins of therapeutics does not tally with the mission statement for Current Medical Directions (CMD), a medical information company set up in New York in 1990, 'to deliver scientifically accurate information strategically developed for specific target audiences' (<www.cmdconnect.com>). This agency writes up studies, review papers, abstracts, journal supplements, product monographs, expert commentaries and textbook chapters. It conducts meta-analyses, and organizes journal supplements, satellite symposia and consensus conferences, and even constitutes advisory boards for its clients. In all this the company 'strives to exceed the expectations of our clients and to assist them in achieving their strategic objectives'.

In 1998 CMD was coordinating papers on Zoloft (sertraline) for Pfizer. As part of a legal action against Pfizer, I was given a document on a non-confidential basis that laid out a series of papers being coordinated by CMD. This document lists the progress of papers on Zoloft at the start of 1999. It details 85 papers being worked on, of which 55 had appeared by early 2001. As might be expected, the CMD papers exclusively cover areas of marketing concern for Pfizer. They are clinical trials or reviews on clinical conditions for which Pfizer had a marketing licence for Zoloft or in which they were seeking one.

PTSD was one of the conditions for which Pfizer was seeking a licence. In the case of the set of papers on PTSD, the document appears to indicate that the first draft of two papers on PTSD had already been prepared, even though the authors' names were listed 'TBD [to be determined]' (Current Medical Directions, 1999).[10] There is no way to know exactly who wrote the papers on PTSD, but the document appears to indicate that the agency actually doing the writing in the case of the PTSD papers was an agency called Paladin. The document furthermore indicates that the *New England Journal of Medicine* and the *Journal of the American Medical Association* (*JAMA*) were the target journals. The papers actually appeared in *JAMA* and the *Archives of General Psychiatry.*

Whatever the actual authorship of these papers, the CMD document defines a set of papers, and it is possible to compare CMD papers on Zoloft with non-CMD papers on Zoloft from the same period. We have done so by comparing CMD and non-CMD papers systematically in three

areas (Healy & Cattell, 2003). First, we searched out all CMD and non-CMD papers, and established the number of Medline citations for each author of these papers. Second, we established the impact factor of all journals in which all papers appeared. Third, we determined the subsequent citation rate of all papers.

A comparison reveals that the papers on Zoloft coordinated by CMD appear in the journals with the highest impact factors in the field, including *JAMA*, *American Journal of Psychiatry*, *Archives of General Psychiatry*, *British Medical Journal*, and others. The authors on CMD papers are among the most highly Medline-cited authors in the field, with upwards of 200 other Medline listed papers per author. The CMD authors have a citation rate three times greater than that of non-CMD authors. The CMD papers appear in journals with an impact factor three times greater than that of the journals in which non-CMD papers appear. As of mid-2002, the mean citation rate for the CMD papers published in 1998 was 20.2 (95% confidence intervals 13.4, 27.0) while that of the non-CMD papers published in 1998 was 3.7 (95% confidence intervals 3.3, 8.1). Finally, 100% of the CMD papers report favourable results for Zoloft, whereas only 44% of the non-CMD papers report favourable results.

An analysis of this document appears to establish that ghost-writing is no longer something happening only in peripheral journals, affecting only review papers. It happens in the most prestigious journals in therapeutics, and it probably happens preferentially for papers reporting randomized trials and other data-driven papers.

An analysis of the published CMD papers reveals some other important points. There are significant discrepancies between at least some of the CMD set of papers and the raw data underlying these papers. For instance, the CMD set of papers contains six papers in which Zoloft has been given in trials to children with OCD or depression. One of these papers published in *JAMA* mentions one child becoming suicidal. The other five papers make no mention of suicidality as a potential hazard of Zoloft given to children. One of these five papers in fact states that the authors are reporting on the side effects that had occurred at a 10% rate or more (Alderman et al., 1998). However, it is clear from internal company documents[11] that of the 44 children who were depressed and went on Zoloft in this series of trials four (9%) made suicidal acts.

In another paper, published in the *British Medical Journal*, Malt et al. (1999) report a study in which sertraline was compared with mianserin and placebo. Early drafts of the paper mention that there had been one suicide and three suicide attempts on sertraline, one suicide attempt on mianserin and no suicide attempts of any sort on placebo. The final version does not mention any of these adverse effects.

In summary, based on a published analysis of the CMD document, the following points can be made. First, up to 75% of the papers on randomized controlled trials on therapeutic agents appearing in major journals may now be ghost-written. Second, in terms of citation rates, the most cited papers in therapeutics are now likely to be ghost-written. Third, the

new methods of authorship appear to lead to an omission of negative data on the hazards of therapeutic agents.

Influence has always played a part in science. As Thomas Kuhn (1962) argued, dominant scientific paradigms often act to silence the dissent of critics rather than to stimulate critical thinking. However Kuhn never envisaged the possibility of a dominant paradigm emerging because a writing agency produced an apparent consensus by sprinkling a set of authoritative names on a group of papers.

Medicalization and the Marketing of Data

In response to media concerns about their free meals in the Waldorf and educational meetings in the Caribbean, clinicians say these 'freebies' do not influence them. Clinicians claim to be following the evidence. Both the media and clinicians see the free pens and posters and mugs, as well as meals and hotel rooms, as part of the marketing effort of a pharmaceutical company. But pharmaceutical companies see these trinkets and junkets as part of the gimmickry that stems from the sales department, a subdivision of marketing that comes into play primarily after the launch of a drug.

In contrast to the limited role of a sales division, marketing departments play a large role from the time of discovery of the drug, determining which clinical trials will be done for what therapeutic indications, and shaping, even as early as its point of the origin, the profile this new compound should have in terms of which journals the key papers on therapeutics with this new compound should appear in, and with which lead authors. The efforts of marketing departments extend beyond early development to include the support of scientific and educational symposia after launch, often aimed at selling not the drug so much as the condition this drug will treat. One result of this process is a significant number of papers on these drugs, such as the CMD papers. These effectively become infomercials in the form of scientific papers; influential because of that form.

The impact of this influence can be seen in the following development. Recently *Newsweek* ran a cover piece on teenage depression (*Newsweek*, 2002). Pfizer and GlaxoSmithKline have received or are seeking licences in a range of countries to treat nervous problems, such as depression in children or adolescents, with Zoloft and Paxil respectively. Clinicians did not in fact need company trials to treat children with Paxil or Zoloft, if this seemed to be clinically indicated, as such treatment could be based on an extrapolation from the adult data, as is done with anticonvulsants or antibiotics. However, in order to market Zoloft or Paxil to children, Pfizer and Glaxo must run a clinical trial that in some domain of measurement appears to demonstrate that their compound has positive effects.

Once in the market, companies can draw attention to the misery and discontent experienced by children and adolescents and can claim that this discontent can be mapped onto operational criteria for depression. The fact that adolescent misery can be mapped onto criteria for depression is

quite different from saying that these children have depression. Nevertheless as depression comes with risks, in particular the risk of suicide, pharmacotherapy can be sold not just as a possible treatment but as effectively mandated, in order to reduce such risks. This message is too important to leave in academic journals, hence papers in magazines such as *Newsweek*. While clinicians could always treat children with Zoloft and Paxil, before *Newsweek*, they would have been likely to reserve pharmacotherapy for more severely disturbed children, but post *Newsweek*, parents are much more inclined to seek out, and clinicians to prescribe, drug treatment for conditions that until recently were thought best managed by supportive interventions.

In this manner, a range of intimate childhood and adolescent experiences are at present being actively medicalized. Traditional medicalization is not inevitably tied to drug treatment, but in this case as with panic disorder, depression rather than its treatments is being sold. The trials of drug treatments, however, are central to the process. Treatment trials do not force medicalization per se, but at present within psychiatry apparent evidence of efficacy is taken to indicate that depression *should* be treated rather than that depression *can* be treated. As in other areas of psychiatry, the effects of treatment on selective outcome measures from clinical trials have become embodied in treatment algorithms and protocols drawn up by experts, many of whom have affiliations with pharmaceutical companies. Such protocols rank pharmacotherapy as a leading option for the management of nervousness in children and adolescents.

What is apparently missing from this process is any appreciation that, except in the case of treating patients moribund from conditions like heart attacks, where ordinarily there will be little disagreement on the need to intervene, treatment in medicine involves value judgements. Other effective treatments are commonly accepted on the basis that they eliminate the condition being treated. But in psychiatry, other than for the use of penicillin in general paralysis of the insane, there are no such treatments, and as a consequence treatment options ought to be contested.

This is not a matter of some intangible values being pitted against objective data, but rather a question of a disjunction between values and the role of data collection in pushing one set of values; this can be seen in the data from two of the major trials of antidepressants in children. In Glaxo's trials, while Paxil was marginally better than placebo on physician-based measures of outcome, there was a 5% suicidal act rate on Paxil, a measure arguably of greater interest to parents, compared with a 0% suicidal act on placebo (Keller et al., 2001). Despite this, physicians speaking for Glaxo exhort doctors to detect and treat depression on the basis that treatment will reduce risks of suicide. A second major trial, Pfizer's trials of Zoloft in depressed children, produced as we have seen a 9% suicide attempt rate on Zoloft, but the published literature gives no evidence for this.

This recent scenario replays the process that brought SSRIs into the market place as antidepressants in the early 1990s. Around 1990, the

American Psychiatric Association and the British College of Psychiatrists launched 'defeat depression' campaigns. These were supported by money from pharmaceutical companies. The campaigns were extremely successful, and, as argued earlier, helped convert cases of Valium and Ativan to cases of Prozac and Paxil and Zoloft. A great part of the rhetoric of these campaigns stressed that the recognition of depression was extremely important so that this condition, which carried a high risk of suicide, could be treated effectively. Recognition and treatment would contribute to lowering national suicide rates.

Unbeknownst to the proponents of such campaigns, even if the detection of depression had been restricted to patients with classical cases of severe depression who are at risk of suicide, the central claim of these campaigns, namely that the detection of depression would lower suicide rates, was deeply problematic. Just as these campaigns began, data for suicides and suicidal acts from clinical trials of SSRI agents lodged with the Food and Drug Administration (FDA) in the USA demonstrated that SSRI antidepressants did not in principle lower suicide rates (Table 1). As of the early 1990s, the complete datasets lodged with the FDA, rather than the selected datasets commonly cited by pharmaceutical companies, revealed that there was a statistically significant increase in the risks of both suicides and suicidal acts for patients on these drugs (Healy, 2003a). Furthermore, it is now clear that the data lodged with the regulators are misleading on this very important issue. For example, the data on suicides and suicidal acts recorded under placebo in trials of Paxil indicate two suicides and six suicidal acts, when the true value may in fact be as low as one suicidal act on placebo. The remainder of the suicidal acts occurred during the run-in phase of trials, or sometimes in the case of SSRI trials, up to 1 year after the trial had ended. This pattern of data management appears common to most SSRI companies.

Other manoeuvres include, it would seem, outright suppression of data. Consider the data on suicidal acts with recently licensed antipsychotics lodged with the FDA (Table 2). It would appear from a published paper (Khan et al., 2001) that there are no data lodged with the FDA on non-lethal suicidal acts on olanzapine.[12] This is clearly not trivial, as the data on suicides for olanzapine suggest it has the highest rate of suicides in psychotropic trial history. The fact that these data are missing has been in the public domain since September 2001. During this time there has been no complaint from any scientific group and olanzapine has become the best-selling antipsychotic in North America and Western Europe. It would seem that he who controls the means of data production controls consciousness.

Aspects of the Sociology of Clinical Trials

The developments outlined here point to three issues in need of a detailed social analysis. First, there is the centrality now accorded clinical trials within the medical market place. Second is the emphasis on marketing

TABLE 2
Incidence of suicides and suicide attempts in antipsychotic clinical trials drawn from Food and Drug Administration licence applications (see Khan et al., 2001)

	Patients (*N*)	Suicides (*N*)	Suicide attempts (*N*)	All suicidal acts (%)
Risperidone	2607	9	43	2.00
Comparator	621	1	5	1.00
Placebo	195	0	1	0.50
Olanzapine	2500	12	?	?
Comparator	810	1	?	?
Placebo	236	0	?	?
Quetiapine	2523	1	4	0.20
Comparator	420	0	2	0.48
Placebo	206	0	0	0.00
Sertindole	2194	5	20	1.14
Comparator	632	0	2	0.32
Placebo	290	0	1	0.34
Ziprasidone	2993	6	?	
Comparator	951	1	?	
Placebo	424	0	?	
Total				
New antipsychotic	12,817	33	72	1.0
Comparator	3434	3	10	0.6
Placebo	1351	0	2	0.3

Notes: The data obtained by Khan et al. (2001) are supplemented here with data for suicidal acts on quetiapine provided by the company; in contrast to Khan's scrutiny of the Food and Drug Administration's (FDA) medical reviews for olanzapine, my scrutiny suggests that the true figure for suicides on placebo in these trials was 0; data from sertindole trials were provided by the Lundbeck pharmaceutical company; data on ziprasidone trials were taken from FDA medical reviews for ziprasidone obtainable from the FDA site. Analysing the data on suicides using an exact version Mantel–Haenszel procedure and a one-sided test for significance yields an odds ratio with a confidence interval of (1.0825, infinity), $P = 0.03955$, for new antipsychotics compared with placebo.

compounds by selling diseases and the risks associated with diseases. Third is the role of social institutions, such as the regulatory apparatus and institutional review boards, in containing problems that the drug development makes almost inevitable.

On the first issue, it is now commonly thought that clinical trials prove that treatments work. Philosophically, however, clinical trials are set up on the basis of a null hypothesis – namely that a putative treatment in fact does not differ from placebo. They were designed to stop therapeutic bandwagons. If the treatment appears to differ from placebo in these short-term trials (6–8 weeks) undertaken in conditions that may last months, years or decades, all that can be said is that the treatment does something,

and there is a basis for further research. This is not the same as saying that treatments work. To establish this would require studies that demonstrated long-term benefits and also controlled for hazards such as physical dependence that appeared on discontinuation.

Far from being treated as a basis for further research, the data resulting from clinical trials have now become the fuel of therapeutic bandwagons (Healy, 2001) and a factor contributing to globalization. A key to pharmaceutical globalization is the universality claimed for scientific methods. The results of trials conducted on what may be a small subset of volunteers recruited by advertisement are held to apply universally – in Japan as well as the USA, for children as well as adults, for all ethnic groups, ages and genders. This claim underpins transitions such as that from anxiety to depression, but it also leads to an extension of the psychopharmacological reach that can be seen in globalization. The same mechanisms that have been employed to transform the intimate experiences of many Westerners can be expected to lead to a homogenization of experiences on a global scale.

Within psychiatry, the current evidence-based medicine bandwagon is as hegemonic as the Freudian paradigm ever was. The results from trials are incorporated into algorithms and protocols, which increasingly define a supposedly rational medicine. Criticisms of the system are not entertained if they offer sociological or qualitative analyses. Evidence-based medicine sees itself as building a value-free, timeless, ahistorical science. One of the current challenges facing the history and sociology of modern medicine is to outline the originating and sustaining factors for this belief system.

This is particularly important, as there is good evidence that treatment outcomes within mental health are deteriorating. While the absolute numbers of patients occupying beds in asylums through to the 1950s began to fall thereafter, the numbers of both voluntary and involuntary admissions per annum have been rising steadily since then in both Europe and North America. We have been able to quantify this increase in a study recently undertaken in North Wales, which systematically compared mental health service utilization over 100 years in a unique service delivery system, that because of population, financial and geographical constraints allows such comparisons to be made in a manner that should hold for services in both Europe and North America. In line with other data, this study demonstrated that we now compulsorily detain three times more patients than were detained before modern psychotropic drugs were first developed, we admit 15 times more patients than were admitted before the present psychotropic era began, and patients now on average spend more time in the course of a psychiatric career in a hospital than they did before modern drugs came on stream (Healy et al., 2001). In part this situation has arisen because as mentioned in the introduction, psychiatry also manages community nervousness in a way that was not the case until the 1950s. Based on these findings, there would seem to be a major disjunction between the results of short-term clinical trials and the longer-term effects of using treatments endorsed by such trials.

The second issue concerns the centrality of risk to modern marketing. Risk has become central to income generation for pharmaceutical companies. These companies at present need blockbuster drugs to survive – drugs that earn US$1.5 billion or more per year. Conventional medications simply won't do this. For some time it has been a matter of common knowledge that companies no longer develop drugs for real illnesses in less-developed countries, owing to the lack of return on such products. But what is less well known is that it is no longer economic for them to produce drugs for many major illnesses in the West, such as multiple sclerosis or epilepsy, unless these drugs can be sold off-licence for other indications.

The most reliable source of blockbuster revenues is from lifestyle drugs. Lifestyle means two things in this context. The first meaning is linked to the concept of reliability. From an industrial point of view, quality products are ones that are reliable in the way that Big Mac hamburgers are – they offer the same return every time. When drugs become quality products in this sense, companies appear happy to drop the medical or disease framework. In the case of Viagra, companies talk openly about lifestyle products for this reason as much as for its effects on sexual functioning. In this regard it is instructive to consider the evolution of plastic surgery into cosmetic surgery. Once reconstructive techniques became reliable, they left the domain of medical or plastic surgery and found a wider place in society as cosmetic surgery. (Of note perhaps is the fact that plastic surgery, like traditional medical approaches, aims at restoring individuals to their places in society. Cosmetic approaches in general make someone competitive within society.)

The second meaning of the notion of a lifestyle drug marries reliability and risk. For the past 20 years, the best-selling drugs in the market place have been drugs that act on risk factors for diseases, such as elevated blood pressure or elevated lipid levels, rather than on core diseases – strokes or heart attacks. There is a twofold appeal to pharmaceutical companies in treating risk factors. It is much easier to alter a risk factor reliably, such as elevated blood pressure or lipid levels, than it is to affect a disease process. Focusing on risk factors allows the development of products that meet industrial criteria for quality. For instance, antihypertensives reliably lower blood pressure. These quality products, however, may have little impact on the wider state of the health of the population.

In addition to providing a basis for developing quality products, populations carrying risk factors offer much larger markets than populations with diseases. If 1 per 100 has a disease but 10 per 100 carry a risk factor, conventional medical models will mandate the treatment of the one diseased individual, whereas the new emphasis on risk mandates the treatment of 10. Risk thresholds furthermore can be ratcheted down progressively, creating ever-larger markets. Finally, when it comes to treating risk factors, drugs that do so are often lifestyle agents in the further sense that many of these treatments act to reverse the effects of lifestyle options. Lipid-lowering drugs may effectively be acting to reverse the

effects of a diet chronically high in lipids. Antihypertensives may be acting to reverse the effects of a sedentary lifestyle laced with too much alcohol.

Within the current medical marketplace, the critical figures are those in which treatment is shown to have an effect on a risk factor. The clinical trial process feeds such figures into the market place. The problem for patients and physicians alike lies in the selection process that controls what figures appear in both the academic and lay markets. In addition to figures that might demonstrate a lowering of blood pressure, clinical trials can yield figures that tell us how many people need to be treated in order to save a life. Knowing that it might take 800 people to be treated with antihypertensives to save one life would influence many of us when it comes to contemplating whether to take a drug that might wipe out our sex-life or otherwise significantly impair our quality of life. The marketing of risk in the past 10 years, however, has made it difficult to persuade physicians that not treating a mild hypertension is completely different to not treating a fulminant pneumonia, and not intervening with a drug treatment for a person who could be conceived as being theoretically at risk of suicide is quite different to not intervening in the case of someone who has actually tried to commit suicide.

The third issue concerns the social institutions put in place to manage pharmaceutical companies. When faced with potential hazards like drug-induced suicidality, clinicians and consumers assume that if clinical trials with these drugs have been 'through the FDA', there cannot be anything fundamentally wrong. Regulatory bodies, however, essentially have only minimal audit functions. It is pharmaceutical companies that decide which trials should be conducted. And trials are conducted to fit the marketing requirements of the company, rather than being dictated by the effects of the drug. For example, SSRIs have greater effects on premature ejaculation than on depression. The decision to market these drugs as antidepressants is a business rather than a scientific decision.

Where once clinical trials were undertaken by independent universities, they are now conducted in settings and by notional investigators that suit pharmaceutical company interests (Healy, 2002a). The primary criterion for a successful study is the rapid completion of the trial. This is achieved by having a large patient through-flow. A new group of organizations, contract research organizations (CRO), have been set up to ensure this. It is now clear that some of these organizations have run trials that have included bogus patients, for which investigators and others have ended up in jail, and indeed that the trials conducted for a majority of the psychotropic drugs that appeared on the market since 1990 must be considered to be tainted in this way.[13] These CRO in addition now provide a privatized institution review board system that grants ethical approval to company studies (Lemmens & Freedman, 2000). The papers that stem from the data collected, tabulated and analysed by CRO are then written up by medical communications agencies working for pharmaceutical companies with some of the consequences outlined earlier.

There is therefore a rapidly shrinking degree of oversight of the drug development process. In this situation, compared with financial auditors, the one weapon the FDA has to prevent a pharmacological Enron happening is the fact that drugs are made available on prescription only. But where in the 1960s it might have been reasonable to think that many physicians, other perhaps than the recently de-institutionalized alienists, would have had the clout and inclination to grapple with the industry, this is not now the case. Clinicians are busy celebrating their adherence to the evidence provided by the marketing departments of pharmaceutical companies. None more so than psychiatrists.

The creation of medical paradigms creates demand for drugs. In creating demand, pharmaceutical companies may simply be exemplary modern corporations. J.K. Galbraith (1967) argues that in the latter half of the 20th century, corporations have downgraded efforts to make products to suit our needs, and are much more likely to aim at creating needs to suit the portfolio of products they have. In Bruno Latour's (1986) terms, it is more profitable to translate interests and then satisfy them than to satisfy pre-existing interests. Arguably, the availability of drugs on a prescription-only basis makes this creation of needs particularly simple in medicine, as so few hearts and minds need to be won.

Back to the Future

The challenge of establishing what is happening within mental health is of great importance especially in the wake of destruction of the World Trade Center. The discontents associated with globalization have been closely linked to the events of 9/11.

By the time of 9/11, Pfizer had obtained a licence for Zoloft for PTSD. Wyeth had also obtained a licence for venlafaxine (Effexor) for GAD, and GlaxoSmithKline were about get licences for Paxil for both GAD and PTSD. Articles began to appear in broadsheets and tabloids about the anxious times we live in. Some of these articles were full of references to these drugs and the companies that produced them and gave detailed operational criteria for GAD or PTSD. These articles may not have been written within the PR agencies of the different companies. It may simply be a case that the editors of newspapers realize that anxiety is in the air. Another example of pharmaceutical company money leveraging wider changes in consciousness.

At present up to US$100,000,000 is being spent per year selling the SSRI as anxiolytics or anxiolytic antidepressants. Wyeth has set up a campaign to teach general practitioners to recognize anxiety, worried apparently that they will no longer be able to do so. The Wyeth promotional material for Effexor contains two important commercial messages, which reappear in material for Pfizer's Zoloft and Glaxo's Paxil.

The first is that Paxil, Effexor, or Zoloft work to 'correct the chemical imbalance that causes the disorder'. This chemical imbalance is supposedly a lowering of serotonin, something that most people have thought happens

in the case of depression. There was never in fact any evidence for a lowering of serotonin levels in any nervous disorder, or indeed anything wrong with the serotonin systems in anyone affected with nerves or moods.

The second commercially important message is to 'talk to your doctor about non-habit forming Paxil today'. The other way that this is expressed is that anxiety can be treated with a benzodiazepine or with Paxil/Effexor/Zoloft. Benzodiazepines, however, cause dependence. The clear implication is that it will be easy to stop taking these SSRI.

These claims are being made even though withdrawal problems from Paxil were so clearly recognized in the mid-1990s that Lilly ran symposia on the issue and adverts telling clinicians that Prozac is less likely to cause withdrawal problems than Zoloft or Paxil. These claims are being made even though the rates at which withdrawal from and dependence on Paxil and related drugs have been reported to regulators and other bodies worldwide greatly exceed the rates for reporting either withdrawal from or dependence on benzodiazepines or, indeed, on therapeutically used opioids (Medawar, 1997; Medawar et al., 2003).[14] These claims are being made even though, 20 years ago, several years before Paxil was launched, the company in question had undertaken clinical trials on healthy volunteers that gave clear evidence of withdrawal problems, including one suicide.[15]

These developments see the closing of a circle. Paxil and other SSRI came on stream as antidepressants, in great part because of the withdrawal problems linked to the benzodiazepines. The business-designation of these drugs as antidepressants deflected concerns about their dependence-producing potential, which now seems as great as anything associated with earlier drugs.

As of 1990, it was relatively clear that a post-SSRI generation of psychotropic drugs would be targeted at anxiety, and sold as anxiolytics. This simple switch of terminology – from tranquillizer to anxiolytic – was all it would take to allay the concerns of the public regarding the risks of dependence. No one would make the connection to Valium, Librium and Ativan even though these drugs were also anxiolytics. However, companies have been slow to bring out the next generation of drugs, and hence have needed to rebrand the SSRIs as anxiolytic antidepressants. In 1990, the SSRIs became antidepressants because it was thought unlikely that branding them as anxiolytics would work with academic psychiatrists. In 2002, it is clear that marketing departments have decided that rebranding SSRI drugs as anxiolytics, and avoiding use of the term tranquillizer, is all it takes to bring academic psychiatry onside.

This development offers some measure of the degree of control pharmaceutical company marketers now have over the consciousness of a profession. This paper has attempted to outline some of the mechanisms by which this control is achieved. These involve a set of relatively new departures within marketing, such that companies now sell diseases rather than just drugs. To do this, where they used celebrity endorsement before,

they turn to celebrity academics now. Where papers were placed in the lay media by PR companies before, academic papers are now increasingly written by medical writing agencies and placed in the leading journals in the field. Where company products were previously judged on the basis of independent research, and research publications were distributed by companies if they coincided with company interests, companies now design and conduct their own studies to produce indications that suit their commercial interests. Clinicians meanwhile continue to believe that they are not unduly influenced by pharmaceutical companies.

Notes

1. I base the frequency estimate here partly on personal clinical experience, but the fact that transformations like this were happening, 'mistakes', is attested to by Don Klein, the creator of the concept (see Klein, 1996).
2. The first series of Upjohn studies can be found in vol. 45 of *Archives of General Psychiatry* with an overview by G.L. Klerman (1988). An early critique of these studies can be found in Marks et al. (1989). A response to this critique came from Klerman et al. (1989). These studies were also published in *Journal of Psychiatric Research* 24 (supplement 1, 1990). A second series of Upjohn studies can be found in Klerman et al. (1992). Again these were critiqued by Marks et al. (1992), with a reply from Klerman (1992). A subsequent 'anti-Upjohn' study of interest can be found in Marks, et al. (1993b). This drew a response from investigators working with Upjohn (Spiegel et al., 1993) and a reply from Marks, et al. (1993a) and Marks, et al. (1993c). This series of exchanges offer a no-holds-barred set of comments on the merits of industry support of research.
3. As with the transformation of tension and stress into panic attacks, this claim is based in part on personal experience, but also on the data from drug sales, which given the crossover between sales of tranquillizers and antidepressants indicate that something like this must have been happening.
4. From a brochure for a meeting on Creating Targeted Patient Education Campaigns, organized by Institute for International Research (IIR) for London, 29–30 October 1996. As of 1996, the IIR described itself as the world's largest independent conference company and a leader in the provision of business information (see <iir-conferences.com>).
5. Papers available from the author on request.
6. See also responses in *Lancet* (2002b).
7. See also correspondence: 'Conflict of Interest and the *British Journal of Psychiatry*', *British Journal of Psychiatry* (2002) 180: 82–83.
8. All copies including the published paper in the *Journal of Psychiatry and Neuroscience* available from the author.
9. As Spilker of the Pharmaceutical Research and Manufacturers of America put it when the issue was raised in *The Washington Post*, 'Academic researchers participating in studies "are given every opportunity to review, make suggestions and sign off on manuscripts [and] except for some very, very rare exceptions ... [the process] is working very well"' (quoted in Okie, 2001: A1). In practice, as shown in the litigation surrounding Redux, senior figures are prepared to incorporate any changes suggested to them by companies or agencies and to sign off on papers without suggesting a single change of their own (Mundy, 2001).
10. This document is available on request from the author. See Lagnado (2003) for a response from a medical writer to these issues and analysis.
11. These figures are drawn from a public domain document available from the author: Pfizer Expert Report, 'Sertraline Hydrochloride for Obsessive Compulsive Disorder in Paediatric Patients' (approved 20 October 1997).

12. Data for suicides and suicidal acts for antipsychotics can be accessed from medical reviews posted on the FDA website: <www.fda.gov/cder/approval/index.htm>. My scrutiny of the records confirms that the data do not appear to be with the FDA. Requests to the company for the missing data have been rebuffed. Requests to the relevant departments of government in the UK have gone unanswered.
13. See Stecklow & Johannes (1997), Eichenwald & Kolata (1999a, 1999b) and Boseley (1999).
14. See <www.socialaudit.org> for a documentary record of the evolution of the issue. Adverse reactions lodged with the Adroit database in the UK, which are corroborated by the World Health Organization database.
15. This material was made available to me on a confidential basis as an expert witness in *Tobin v. SmithKline Beecham*, Case No. 00-CV-0025-BEA, heard in Cheyenne (WY, USA) starting 21 May 2001, and all that is available in the public domain is my testimony in this case, which returned a verdict against SmithKline. The transcript is available from the author on request.

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