# IS PSYCHIATRY FOR SALE?

# AN EXAMININATION OF THE INFLUENCE OF THE PHARMACEUTICAL INDUSTRY ON ACADEMIC AND PRACTICAL PSYCHIATRY.

BY

#### **JOANNA MONCRIEFF**

Published June 2003

This was prepared as a **MAUDSLEY DISCUSSION PAPER** and is available for £4 as a booklet from the Sarah Smith at the Institute of Psychiatry, de Crespigny Park, London SE5 8AF, tel 0207836 5454, e mail sarah.smith@iop.kcl.ac.uk

#### **SUMMARY**

Western society is consuming ever larger quantities of prescription drugs and many of these are for psychiatric complaints. Drugs are central to modern psychiatric practice and to much psychiatric thought about the nature and causation of mental disorders. Psychiatry has therefore become an important target for the large and powerful pharmaceutical industry. Drug companies direct lavish advertising and hospitality towards psychiatrists and provide funding for much medical education and some mental health service initiatives. The industry is now heavily involved in the organisation of research into psychiatric drugs and the dissemination of research findings. This raises questions about the scientific objectivity of this research and the extent to which the industry is able to shape the research agenda. Drug companies also provide funds for pro drug patient and carer groups and address advertising or disease promotion campaigns to the general public. They exert influence at a political level through lobbying and direct funding of political bodies including drug regulatory agencies.

This influence has helped to create and reinforce a narrow biological approach to the explanation and treatment of mental disorders and has led to the exclusion of alternative explanatory paradigms. The coercive function of psychiatry has been strengthened by promoting the idea that psychiatric disorders are akin to medical conditions and that they are amenable to technical solutions in the form of drugs. In addition,

alternative treatment approaches are neglected and it is likely that drugs are currently used for overly long periods and in excessive doses. The adverse effects of drugs are neglected.

Psychiatry provides fertile ground for pharmaceutical industry profits because it provides opportunities for expanding definitions of sickness to include more and more areas of social and personal difficulty. This paper gives examples of how the industry has been involved in promoting and expanding concepts such as depression, social phobia, attention deficit hyperactivity disorder and psychosis.

The current extent of drug company influence threatens the integrity of psychiatry and some suggestions are made about steps that could be taken to address this. The influence of the industry must be curbed for political reasons too. We are rapidly becoming a society that seeks a "pill for every ill;" one that looks for simplistic, technical solutions to complex social problems. This helps to divert attention away from the profound social and political changes that have occurred during the last few decades. Psychiatrists should not be colluding in this process.

#### **BACKGROUND**

#### The place of drug treatment in modern psychiatry

Drugs are the central focus of treatment in modern day psychiatry. The vast majority of psychiatric inpatients are prescribed at least one psychoactive drug and many are on several. The same is true for only a slightly smaller proportion of psychiatric outpatients and many more people are prescribed psychoactive drugs, especially antidepressants and benzodiazepines, in General Practice. Furthermore, most patients who are prescribed psychiatric drugs are told to take them for a period of months, and many are told that they will need to take them for many years or even for life. Psychiatric textbooks devote large sections to drug treatment and related aetiological theories and psychiatric journals are filled with results of drug trials and related brain research.

Almost all drugs in current use have been introduced into psychiatry since the 1950s. Although drug treatment was common before that time, with extensive use of barbiturates and other sedatives and some use of stimulants, it was rarely given much attention. This was because drugs were generally regarded as having only crude effects, usually acting as chemical forms of restraint (Braslow, 1997). However, from the 1950s, drug treatment came to be seen as important and glamorous. The drugs that were introduced from that time onwards came to be regarded as specific treatments for specific conditions and became the basis for speculations about the aetiology of mental illness (Moncrieff, 1999). A vast research into possible abnormalities in transmitter and receptor systems was spawned, epitomised by the dopamine theory of schizophrenia and the monoamine theory of depression.

The pharmaceutical industry undoubtedly played an important part in establishing drug treatment as central to psychiatry. It was involved from the beginning of the "psychopharmacological" era, for example with the huge marketing campaign that helped to introduce chlorpromazine (Thorazine) into America in the mid 1950s (Swazey, 1974). The industry has been described as the "ultimate force behind the adoption of new drugs such as chlorpromazine" and credited with transforming psychiatry into a genuine and modern medical specialism (Shorter, 1997).

#### **Recent developments**

Over the last ten to fifteen years psychiatric drugs have become much more widely prescribed and increasingly familiar to the general public. Drugs such as Prozac and Ritalin have become household names and books about them have become best sellers (Kramer, 1993). This is part of a more general increase in

consumption of all types of medicines, indicated by the fact that prescriptions issued increased by 56% between 1988 and 2001 in the United Kingdom. The average the number of annual prescriptions per head of population increased from 8 to 12 in the same period. However, increases in the use of psychotropic drugs have contributed disproportionately to this increase, with prescriptions of antidepressants rising by 173% in the ten years between 1991 and 2001 (Department of Health, 2002). The rise in cost has been even more marked since the majority of the increases in prescribing have been for expensive new classes of psychiatric drugs such as the Selective Serotonin Re-uptake Inhibitor (SSRI) antidepressants and the "atypical" antipsychotics. In the United States antidepressants are now the top selling class of prescription drug, with antipsychotics, anti-anxiety agents and stimulants all also ranking highly and/or showing rapidly increasing sales (National Institute of Health Care Management, 2002).

This increase in use of prescribed drugs has been achieved firstly by extending the boundaries of well recognised conditions like depression and psychosis. Secondly, lesser known disorders such as panic disorder and social phobia have been publicised, and thirdly, drug treatment has started to colonise areas where it was previously thought to be unhelpful such as substance misuse and personality disorder.

#### INFLUENCE OF THE PHARMACEUTICAL INDUSTRY

Over the 20<sup>th</sup> century pharmaceutical companies transformed themselves from small enterprises, often the offshoot of chemical companies, into some of the largest commercial concerns in the world. By the beginning of the 21<sup>st</sup> century they were making greater levels of profit than their counterparts in other commercial sectors (see Figure 1). In 2001, US pharmaceutical company profits averaged 18.5% of revenue compared with 2.2% for the rest of the Fortune 500 companies (Fortune magazine, April, 2002).

The Pharmaceutical industry exerts its influence at many different levels:

#### 1. The Medical Profession

The medical profession is the industry's primary target. Routine marketing strategies include the provision of "hospitality" which can vary from the provision of lunchtime refreshments for local meetings to the financing of meals in expensive restaurants or the provision of expenses paid trips to attractive foreign locations for company presentations. When psychiatrists refuse to see company representatives, they may persuade other members of the mental health team to accept hospitality. The provision of small gifts to doctors such as mugs, pens, books and diaries is also endemic. Drug company logos adorn many psychiatrists' offices and are encountered throughout psychiatric hospitals and wards.

Many medical educational events such as conferences now receive substantial income from commercial sources. In a recent article, respected American psychiatrist E. Fuller Torrey described the extravagant promotional methods employed at the 7<sup>th</sup> World Congress of Biological Psychiatry held in Berlin in 2001. Several drug companies constructed elaborate installations to attract delegates' attention. These included an artificial garden (Janssen-Cilag), a running stream (Lundbeck), a 40-foot rotating tower (Novartis) and a tent with costumed women offering fortune telling (Organon) (Torrey, 2002). The drug companies had also sponsored more than half of the conference delegates, paying for airfares, accommodation and entertainments and paid fees of between \$2000 and \$5000 to the speakers at the numerous industry sponsored symposia. In all, the conference was said to have cost the industry at least 10 million dollars (Torrey, 2002). This is not so extraordinary. The American Psychiatric Association and UK Royal College of Psychiatrists annual conferences have also come to resemble trade fairs due to the prominence of drug company stands.

It has been repeatedly shown that doctors prescribing practices are influenced by interaction with industry representatives and attendance at drug company sponsored events (Wazana, 2000). The fact that the

industry invested \$15.7 billion in marketing in 2000, and that in the United States there is about one drug rep per 15 doctors, also indicates the importance the industry attaches to its marketing activities (Shaunessy & Slawson, 1996, BMJ).

#### 2. Medical research

# **Organisation of research**

In the 1960s large clinical trials were funded by state funds through the NIMH in the United States and the MRC in the UK. At that time there was a belief that the commercial sector should play only a limited role (Healy, 2002). However, the industry now underwrites 70% of research into drug treatments (Bodenheimer, 2000). In addition most drug trials in United States are now conducted by commercial research organisations, called Contract Research Organisations. These organisations have emerged recently and hire out their services to drug companies. Thomas Bodenheimer describes a situation in which hundreds of commercial research organisations as well as academic medical centres and other independent non academic sites compete with each other for contracts to do industry funded research (Bodenheimer, 2000). Obviously if the studies do not achieve the desired results, the organisation may jeopardise future contracts. In addition, payment is usually awarded according to how many patients are entered into the trial, creating the incentive to stretch and expand diagnostic concepts. Evidence suggests that commercial research organisations conduct research more rapidly and more cheaply than academic medical centres (Commonwealth Fund, 1999). Bodenhemier (2000) concluded that "trials conducted in the commercial sector are heavily tipped towards industry interests."

Contract Research Organisations have argued that they are heavily regulated and have to follow internationally agreed Good Clinical Practice guidelines on the ethical and safe conduct of research (Beach, 2001). However, a few years ago, figures revealed by one audit company suggested that compliance with guidelines was frequently inadequate (Boyhachuk & Ball, 1999). Since audit results are not routinely published it is impossible to know whether this situation has improved or not. A recent audit of 17 Contract Research Organisations in Germany suggested quality was generally high but 31 cases of significant deviations from Good Clinical Practice guidelines were still found (Chase et al, 2001). In any case it may be difficult to detect the subtle influences that commercial pressures have upon the research process.

The case of Borison and Diamond, who were psychiatrists who set up a Contract Research Organisation in the United States, revealed the huge profits that can be made in this business. They were convicted of defrauding the University where they were employed. The investigation revealed not only their huge personal wealth, but also that large bonuses were paid to staff who enrolled the most patients and that patients were also offered cash inducements. Although Borison and Diamond were not indicted for research fraud, revelations about the operation of their business sheds a worrying light on the conduct of trials in the current highly competitive climate. Borison was, incidentally, principal investigator in two of the pivotal trials that led to approval of the atypical antipsychotic risperidone in the United States (see Whitaker, 2002, chap 11).

At an individual level, links between academic doctors and the industry are proliferating and include payment for speaking at conferences, consultancy fees, payment for sitting on advisory boards or boards of directors, and holding equity in a company (Boyd & Bero, 2000). A study of published papers found that 34% of primary authors had substantial financial interests in the work they published (Wadman, 1997). In psychiatry the situation may be even worse. In 2000, the New England Journal of Medicine did not have space to print all the financial interests of the authors of a paper on the antidepressant nefazadone and had great difficulty in identifying an academic psychiatrist to write an editorial on the subject who did not have financial ties with companies that make antidepressants (Angell, 2000).

It was also shown recently that 87% of authors of clinical practice guidelines had some interaction with the pharmaceutical industry, and 38% had served as consultants or employees of companies. Despite this, only 4.5% of guidelines contained any declaration of the personal financial interests of authors (Choudhry et al, 2002). This is a cause of concern since guidelines usually command professional respect and have a strong impact on practice.

# **Research findings**

Research findings can be effected both by the way a study is designed and by the way results are presented. The fact that drug firms now control most of the process of most clinical trials from design and implementation through to data analysis and publication is therefore a cause of concern for some commentators and researchers (Bodenheimer, 2000; Healy & Cattell, in press; Bero & Rennie, 1996).

The design of studies is a particular issue in psychiatry where disorders are highly variable and in most cases wax and wane, meaning it is easy to be deceived about the benefits of intervention. The history of psychiatry is full of treatments that were thought to be effective scientific treatments but turned out to be useless, not to mention harmful (for example see Whitaker, 2002, chapter 4, on the history of Insulin Coma Therapy). Although there is a consensus that psychiatric drugs including antidepressants, antipsychotics and mood stabilisers are effective and useful, problems with the design of studies means that questions remain about the reliability of some of the evidence base for this consensus. In antidepressant trials, problems such as the subjectivity of outcome measures and unblinding, have lead several authors to conclude that their efficacy is not firmly established (Antonnucio et al, 1999; Moncrieff, 2001). It has been suggested that the apparent benefits of atypical antipsychotics in relation to side effects were partly a result of comparison with high doses of standard drugs, which were popular at the time the atypicals were first introduced (Geddes et al, 2000). In addition, studies of long-term treatment have neglected the possibility that withdrawal related problems in people who stop drugs may inflate the apparent benefits of drugs such as lithium (Suppes et al, 1991) and antipsychotics (Baldessarini & Viguera, 1995).

The results of studies can be presented in a number of ways to give an exaggerated view of a drugs benefits (Bero & Rennie, 1996). These include failure to publish negative results, the use of multiple outcome measures, and selective presentation of ones that are positive, multiple publication of positive study results, and the exclusion of subjects from the analysis. For example, one review of psychotropic drug trials reported that hundreds of significance tests were conducted and that 50% of trials excluded subjects from the analysis (Hemminki, 1981).

These problems are not confined to studies conducted by the pharmaceutical industry, but it seems likely that commercial pressures may increase the risk of methodological biases and misleading reporting. In Bodenheimer's investigation 6 out of the 12 clinical investigators he interviewed reported cases in which publication of papers had been blocked, or the content of papers altered by a drug firm (Bodenheimer, 2000). Peter Breggin's analysis of FDA files claimed that several negative studies of fluoxetine (Prozac) were not published and that some published trials did not report negative outcomes (Breggin & Breggin, 1995). A recent review of company sponsored comparative drug trials for psychiatric disorders describes how various design and reporting modifications were apparent that appeared to serve the company's marketing objectives (Safer, 2002). The author describes instances of the use of inappropriate doses of comparator drugs, use of questionable definitions of outcome, the selection of major findings and end-points post hoc, the masking of unfavorable side effects, duplicate publication, emphasising favorable but not statistically significant differences, withholding unfavourable results and masking sponsorship.

Indirect evidence that drug company sponsorship effects trial quality is the finding that studies sponsored by drug companies are more likely to find evidence in favour of the sponsor's product than studies that do not

have commercial sponsorship. Research conducted in the 1980s found that 43% of trials that favoured a new therapy were sponsored compared with 13% that favoured the standard therapy or placebo (Davidson, 1986). A recent study found that authors' conclusions were more likely to be favourable towards an intervention where the study was fully funded by a for-profit organisation than where funding came from other sources (Kjaergard & Als-Nielson, 2002). Drug company sponsorship was associated with greater apparent benefit from the company's drug in trials of clozapine (Wahlbeck et al, 2000) and antidepressants (Freemantle et al, 2000).

## The research agenda

The extent of drug company funding for research and the interactions between academic personnel and the industry mean that much research activity is oriented towards drug treatments and related areas.

In addition, marketing strategies now include attempts to shape psychiatric thought through the academic arena. This is done by a strategy that is conceived long before a product is officially marketed and may involve the promotion of disease concepts and their frequency. A recent guide to pharmaceutical marketing suggests the need to "create dissatisfaction in the market," "establish a need," and "create a desire". A portfolio of articles which promote the disease concept in question and/or the company's product is constructed for the medical audience. The articles will often be written by a medical writing or education agency and then academic authors will be approached to become authors, a practice known as "ghost writing." Medical "opinion leaders" are also identified and cultivated as part of this strategy to act as "product champions" (Pharmaceutical Marketing, 2002).

Evidence suggests this practice is not uncommon, with one study finding that 11% of articles in 6 major peer reviewed journals involved the use of ghost writers (Flanagin, 1998). A recent study of articles on the therapeutics of the antidepressant sertraline found that over half were produced by a medical information company employed by Pfizer Pharmaceuticals. These articles had higher citation rates and a higher profile within the medical literature than articles written independently (Healy & Cattel, in press).

Advertising in major academic journals provides another mechanism for influencing the message that reaches the public domain. Drug advertisements are now a prominent feature of major British and American psychiatric journals. A typical issue of the American Journal of Psychiatry consisting of about 200 pages of scientific content has around 35 pages of drug advertisements and a further 18 pages of adverts for drug company sponsored "educational" meetings (see for example May 2002 and Jan 2002). Issues of the British Journal of Psychiatry in 2002 had between 5 and 16 pages of advertisements for around 100 pages of scientific content.

In the 1960s a United States Congress investigation revealed that editors of some journals were allowing drug companies that were contributing advertising revenue, to advise rejection or alteration of articles that were unflattering to their products (Frank Ayd interveiwed in Healy, 1996). Recent cases involve papers concerning the dangers of the sleeping tablet Halcion (Ian Oswald, interviewed in Healy, 2000) and a paper reporting adverse effects of SSRIs (reported in Valenstein, 1998, chap 6, P191-2). Although many editors are making substantial efforts to make potential influences on research more transparent by requiring "conflict of interest" declarations by authors, it remains a concern that journals that receive a substantial amount of revenue from drug company advertising may be endangering their impartiality.

# 3) The Public and Patient Groups

In the United States and New Zealand, drug companies are permitted to advertise their products directly to consumers. Figure 2 shows that in the year 2000 alone, 2.5 billion dollars was spent on advertising

prescription drugs to consumers in the United States (Public Citizen, 2002). In 1999, it was estimated that the average American saw nine adverts for drugs every day (market research quoted in Mintzes, 2002). Non compliance with advertising standards and regulations is common. The Food and Drug Administration in the United States reported that 1 in 4 advertisements violated their regulations (Aitkin & Holt, 2000) and higher levels of non compliance have been reported from New Zealand (Medawar, 2001). The pharmaceutical industry has also been trying for some years now to introduce direct to consumer advertising into Europe (Medawar, 2001). In 2000, the then director of the Association of the British Pharmaceutical Industry described how "the ABPI battle plan is to employ ground troops in the form of patient support groups, sympathetic medical opinion and healthcare professionals....which will lead the debate on the informed patient issue. This will have the effect of weakening political, ideological and professional defences." (Pharmaceutical Marketing, 2000). After lobbying by industry and industry funded patient groups, the European Commission proposed some limited reduction in restrictions on advertising to consumers. Although the European Parliament overwhelmingly rejected these proposals, they have not been shelved and are now being considered by the European Council of Ministers (Medawar, personal communication, May 15<sup>th</sup> 2003).

There is no doubt that direct to consumer advertising leads to increased prescription of drugs. A recent survey showed that one in five Americans was prompted to call or visit their doctor to discuss an advertised drug (British Medical Journal, BMJ, News, 19<sup>th</sup> October, 2002). Mintzes et al (2002) showed that exposure to advertising lead patients to request more drugs, and that these requests were usually complied with despite doctors reservations about the appropriateness of the treatment. Drug company promotion to the public includes disease awareness campaigns that can be run in countries that do not permit direct to consumer advertising as well as those that do. Patient groups are recruited to give the campaign a human face and supply stories for the media. In some cases high profile celebrities have been included to help the campaigns reach prime time television audiences (BMJ News, 1<sup>st</sup> June, 2002).

Relationships with patient groups is another channel of influence for the industry. In some instances patient groups appear to have been set up by drug companies. The American magazine, Mother Jones found that the Social Anxiety Disorder Coalition, the Post Traumatic Stress Disorder Alliance and the National Mental Health Awareness Campaign operated out of public relations firms hired by drug companies. They appeared to have been set up for the purposes of disease awareness campaigns (Mother Jones, 2002). Two international groups are also linked to the industry and have been active in lobbying the European Commission to introduce direct to consumer advertising. IAPO (International Alliance of Patients Organisations) was founded and is funded by Pharmaceutical Partners for Better Healthcare, a consortium of about 30 companies, and GAMIAN (Global Alliance for Mental Illness Advocacy) was originally founded by Bristol Myers Squibb. Neither discloses its current sources of funding (Herxheimer, draft).

As well as setting up new groups, the industry is increasingly acting in co-operation with existing groups of patients and carers. In the mental health field it gives funding to groups that promote biological views of mental illness and drug treatments, including the National Alliance for the Mentally III (NAMI) and the National Mental Health Association in the United States and SANE and the Depression Alliance in the UK. It often gives funding for these organisations to run specific campaigns aimed at increasing the number of people seeking treatment. An example is the current CHADD (Children and Adults with Attention Deficit Disorder) campaign to extend diagnosis and drug treatment into under-served communities (see below).

#### 4. Political Institutions

John Abrahams (2002) has described the process whereby European and American drug regulatory agencies became more responsive to the needs of the pharmaceutical industry. This was achieved by increasing the

reliance of these agencies on funding from the industry through license applications, and reducing state support. As a consequence there has been a strong emphasis on reducing drug approval times. In the UK these have shrunk from 154 to 44 days since the changes came into force when the Medicines Control Agency was formed in 1989.

The industry is also increasing its influence over central government policy in the United Kingdom through recently established government bodies such as the Pharmaceutical Industry Competitiveness Task Force, the Industry Strategy group and partnerships with health service bodies. The National Institute for Mental Health England (NIMHE) and the pharmaceutical industry, represented by the Association of the British Pharmaceutical Industry (ABPI), recently announced a formal partnership. The first production of this partnership is a compendium describing collaborative projects around the country entitled "Meeting of Minds." These projects are diverse and include the publication of guidelines, audit packs, toolkits, websites, directories and funding additional personnel including a pharmacist and a primary care liaison worker (NIMHE & ABPI, 2002). Many of the projects undoubtedly contain valuable information and advice, but there must be a concern that projects such as the development of guidelines for the treatment of schizophrenia, and projects designed to improve recognition of depression in primary care might overemphasise the role of certain drug treatments. However, the main concern about these projects, and the NIMHE statement that it "expects that partnership with the industry will become routine in the development and implementation of mental health policy," is that incorporating the industry into the fabric of the health service in this way increases its influence enormously and may make it very difficult to identify and resist commercial pressures. There seems to be little acknowledgement that there might be conflicts of interest between the aims of industry and those of a public service.

In Scotland concerns have been raised about the level of financial interests of members of the newly established Scottish Medicines Consortium (Sunday Herald, 13<sup>th</sup> February, 2003). This body was set up to try to advise the Scottish Executive on National Health Service drug expenditure. More than half the members were revealed to have personal or non-personal (research grants) financial interests in the pharmaceutical industry.

The industry also seeks direct influence at a parliamentary level by employing political lobbyists and contributing large sums of money to political parties and campaigns. In the United States, there are more pharmaceutical industry lobbyists than Congress members. The lobby budget for 1999 and 2000, at 197 million dollars, was 50 million dollars larger than the drug industry's nearest rivals, the insurance and telecommunications industries. On top of this the industry makes generous contributions to election campaigns, mostly to Republican Party candidates (New York Times, 4<sup>th</sup> November, 2001).

#### ADVERSE EFFECTS ON PSYCHIATRY

So how does all this influence effect psychiatry and why should we be concerned about it? The alliance between psychiatry and the pharmaceutical industry has several important negative consequences. Firstly, it helps to reinforce a narrow biological conception of the nature of mental disorder. Secondly, it drives the expansion of this conception into more and more areas of everyday life. Thirdly, it is likely to play down the impact of the adverse effects of psychiatric drugs.

#### I THE PROMOTION OF BIOLOGICAL PSYCHIATRY

#### **Explanatory paradigms in psychiatry**

Psychiatry as an institution has long been obsessed with identifying biological causes of mental disorders and with the narrow technical solutions that flow from such a paradigm (Moncrieff & Crawford, 2001). The pharmaceutical industry has helped to reinforce this approach by the promotion of drug treatments, funding biological research and by promoting claims that psychiatric disorders are caused by simplistic biological notions such "chemical imbalances." Although the Food and Drug Administration in the US prohibits such claims in advertisements that mention individual drugs, because they are not regarded as sufficiently established, they can be made in other promotional material. In 1995, the pharmaceutical industry provided funding for a campaign in the United States organised by the National Alliance for Research on Schizophrenia and Depression, entitled "Depression, a flaw in chemistry not character". This was an offshoot organisation formed by the National Alliance for the Mentally III (NAMI), and two other patient advocacy groups from the US, which also receive other financial support from the pharmaceutical industry. Advertisements in the national press and leaflets distributed as part of this campaign asserted that depression had been shown to be due to "an insufficient level of the neurotransmitter serotonin ....in the frontal lobes of the brain" (reproduced in Valenstein, 1998, chap 6, P 178). The pharmaceutical industry has also taken up this theme in its own promotional material. Eli Lily asserted that "like arthritis or diabetes, depression is a physical illness" (reproduced in Valenstein, 1996, chap 6, P 181).

The hegemony of biological psychiatry that now exists stifles other approaches to understanding the complex behaviours that constitute psychiatric conditions. It elevates quantitative positivist research methods, borrowed from the natural sciences. This approach depends on the notion that psychiatric conditions can be conceptualised as discrete entities occurring in individuals, which can be defined independently of their social context. Other philosophical and sociological approaches that seek to understand the meaning of psychiatric disorders at both an individual and social level are relegated to the fringes of psychiatric academia. The biological hegemony has consequences at a social and political level too. By locating the problem as a disease within an individual brain, biological psychiatry diverts attention away from the social and political conditions that help to determine how psychiatric disorders occur and how they are identified and defined (Conrad, 1992).

#### **Psychiatry and coercion**

The alliance between psychiatry and the drug industry also helps to strengthen the more coercive aspects of psychiatry. The coercion enshrined in much Mental Health legislation is justified on the basis that psychiatric conditions are discrete medical entities that respond to specific treatments. The planned extension of coercion into the community in the new Mental Health Bill for England and Wales is based on the simplistic idea that if patients would only comply with their drug treatment all would be well. However, it is acknowledged that a substantial proportion of patients with psychosis, for example, fail to make even an initial response to drugs and many more relapse despite ongoing drug treatment (Crow et al, 1986; Gilbert et al, 1995; Adams et al, 2001). Despite this reality, the dominance of drug treatment helps to create the impression that psychiatric conditions are easily treatable. This helps to justify coercion on medical grounds thus avoiding the scrutiny that would be entailed in legislation that was more transparently concerned with social control. I have argued elsewhere that it is the medicalisation of psychiatric legislation that has facilitated the expansion of coercion that is represented by the measures proposed in the new Mental Health Bill (Moncrieff, in press).

Foucault described psychiatry as "a moral tactic... overlaid by the myths of positivism." The modern psychiatrist wields an "authority he has borrowed from order, morality and the family" although from the 19<sup>th</sup> century onwards he "no longer quite knew what was the nature of the power he had inherited.." (Foucault, 1971, quotations P 274 to 276). This is what makes the marketing of psychiatric drugs into a force for social control and conformity. Personal or social problems are defined as diseases and the authority of psychiatry, backed by the financial muscle of the drug companies, is used to enforce this view. In the process we are

encouraged to radically alter our view of ourselves and the world. We are encouraged to aspire to narrow norms of behaviour and taught that anything else is not only undesirable but unnatural or diseased. We are encouraged to think that changes should be effected not by ourselves on our environment, but by technology on ourselves.

## **Effects on psychiatric practice**

Drugs so dominate psychiatric practice that it is not easy to develop alternative forms of treatment, even though some research suggests that patients with severe mental disorders may do well without them (Mosher, 1999; Lehtinen et al, 2000). In the UK, inpatient psychiatric units, in particular, have become more and more focused around drug treatment in recent years, with little else of therapeutic value on offer. One report found that 40% of inpatients had no social or recreational activities available to them and that occupational therapy and psychology services were very limited (Sainsbury Centre for Mental Health, 1998). Family therapy and Cognitive Behavioural Therapy have both been shown to be of value in the treatment of psychosis but they are rarely available in ordinary clinical practice in Britain.

Although there is increasing demand for counseling services and psychotherapy for the treatment of less severe mental disorders, this does not appear to represent a serious challenge to the medicalisation of such problems achieved by the widespread prescription of drugs. It appears to be rather another expression of an increasing demand for medical services that is encouraged by the marketing of drugs.

The pharmaceutical industry has supported the emphasis on long-term prescribing for psychiatric disorders and may also have encouraged the use of unnecessarily high doses of psychiatric drugs. Recent studies purporting to show the benefits of long-term treatment in a range of disorders including depression (Claxton et al, 2000), bulaemia (Romano et al, 2002) and obsessive compulsive disorder (Koran et al, 2002) were all supported by the pharmaceutical industry. Patients with chronic disorders often stabilise and many might benefit from attempts to reduce or stop medication (Gilbert et al, 1995). However, this can prove practically difficult in a culture that is so dependent on drug treatment. In a recent book, Jay S Cohen (2001) suggests that doses are tailored to make prescribing easier and inflate efficacy findings; he cites the fact that the recommended doses of one in five drugs is lowered years after the drugs are licensed. A review of the evidence on dose ranges for antipsychotics suggested that moderately low doses are preferable to the higher doses that are commonly used (Bollini et al, 1994).

#### II EXPANDING MENTAL DISORDERS

Psychiatric diagnoses are based on behaviours and mental experiences that are deemed to be abnormal or dysfunctional. They are notoriously difficult to define consistently and even the painstaking construction of standardised definitions, such as those first produced in the Diagnostic and Statistical Manual (DSM) version III, and subsequently revised in DSM IIIR and DSM IV, yield fairly poor reliability statistics (for a review of reliability studies see Kirk & Kutchins, 1999). Because there are no natural or physical boundaries to the definition of abnormality in relation to behaviour and mental experience, psychiatric disorders are particularly fluid and what counts as disorder is highly dependent on prevalent social norms and beliefs. Thus many commentators are concerned that the incorporation of more and more forms of ordinary difficulties, such as shyness and childhood behavioural problems under a psychiatric umbrella is an example of the encroaching and inappropriate medicalisation of everyday life (Moynihan et al, 2002; Double, 2002).

Examples of the expansion of psychiatric concepts include:

# **The promotion of Depression**

The promotion of depression is not new to psychiatry. In the 1950s, Merck, the company that had just launched the antidepressant amitriptyline, bought up and distributed 50,000 copies of a book, entitled "Recognising the Depressed Patient" by psychiatrist Frank Ayd, which suggested that depression was much more common than usually thought (Healy, 1997a). Then, from the late 1980s with the introduction of a new generation of antidepressants called SSRIs, interest in depression increased dramatically. The pharmaceutical industry and the medical profession joined forces in campaigns such as the Defeat Depression Campaign in the United Kingdom, which set out to increase the numbers of patients diagnosed with depression and treated with antidepressants in General Practice. In order to achieve this, the campaign tried to convince General Practitioners of the high prevalence of the condition and combat the general public's resistance to taking antidepressants. The campaign and associated literature claimed that depression affects 5% of the general population at any one time but also that up to a third of people might experience depression at some time in their lives (Paykell & Priest, 1992). It was also suggested that 20% of General Practice attenders might have some symptoms of depression and that around half of these might need treatment (Paykell & Priest, 1992).

It is difficult to demonstrate that the increased number of people taking antidepressants over the last decade has had any objective benefits. Long-term disability due to depressive disorders has been increasing over the same period (Moncrieff & Pommerleau, 2000). Although some authors, with extensive links to companies producing antidepressants, have claimed to show an association between increased use of antidepressants and lowered suicide rates (Hall et al, 2003), their own data has been shown to give the opposite results (Moncrieff, 2003). Others have noted that suicide rates have not fallen in line with increases in prescribing, and that rates of self harm have been increasing (van Praag, 2002). It has been suggested that the drug industry turned its attention to depression because of the disintegration of the market for benzodiazepines after the discovery of their addictive potential (Healy, 1999). Hence it seems that the escalating rates of use of antidepressants may have more to do with marketing imperatives than any benefits to mental health.

Recent interest in depressive disorders has focused on the extent of problems in the developing world and in children. A recent World Health Organisation (WHO) report suggests that 10% of women worldwide suffer from a depressive episode in every 12 month period (WHO, 2001). The American National Institute for Mental Health's new mood strategy prioritises the detection and treatment of depression in children (Costello et al, 2002). These moves potentially pave the way for massive expansion of antidepressant markets in the developing world and among children in the developed world. There are indeed already indications of increasing use of antidepressants, as well as other drugs, among children, including the very young (Zito et al, 2000).

#### The "Creation" of Social phobia

In 1998, the pharmaceutical giant SmithKline French applied to the FDA in the United States for a license to market its antidepressant, Paxil (paroxetine) as a treatment for Social Anxiety Disorder, or social phobia. Although there is a description of these conditions in the DSM and the WHO diagnostic classification systems, they were not previously regarded as amenable to drug treatments nor considered to be a significant public health problem. The pharmaceutical companies involved would argue that they were trying to raise awareness of a then little known and little treated, but potentially debilitating, disorder. In contrast, it has been suggested that the SmithKlineFrench campaign was prompted by the need to find a wider market than the market for depression, which was then dominated by two other antidepressants, Prozac and Zoloft (Mother Jones, 2002).

An investigation by Mother Jones magazine relates how in early 1999 Cohn & Wolfe, a PR firm working for SmithKline, started a campaign to persuade people that social anxiety disorder was a serious and common

disorder. Poster campaigns with slogans such as "Imagine being allergic to people" were conducted and video and radio news releases were created. Journalists were given a press pack stating that up to 13% of the population suffer from Social Anixety Disorder and that it is the third most common mental disorder after depression and alcoholism (Mother Jones, 2002). Cohn & Wolf also supplied journalists with eloquent patients and two Professors of psychiatry, both of whom worked as consultants to drug companies, including SmithKline, were featured on numerous television programmes. By May 1999, when the license for Paxil for Social Anxiety Disorder was approved by the FDA, there were hundreds of stories about the condition in the American media. A few months later, SmithKline launched advertisements promoting the use of Paxil for Social Anxiety Disorder, and by the end of the year it had become the United States second best selling SSRI with sales on a par with Prozac.

In Australia, Roche, makers of another new antidepressant moclobomide, launched a similar disease awareness campaign about social anxiety disorder, or social phobia. Moynihan et al (2002) have described how the promotion campaign seemed designed to "change the common perception of shyness from a personal difficulty to a psychiatric condition." A senior Roche official recently admitted that company promotion had exaggerated the prevalence of the condition (BMJ News, 13<sup>th</sup> April, 2002).

Pharmaceutical Marketing held up social phobia as an example of the importance of shaping public and medical opinion about disease concepts: "You may need to reinforce the actual existence of a disease and/or the value of treating it" (Pharmaceutical Marketing, 2002)

# Pathologising childhood and the marketing of stimulants

The pharmaceutical industry has helped to promote the idea of the "hyperactive child" since Ritalin, manufactured by Ciba pharmaceuticals (who merged with Sandoz to become Novartis), was approved for use in children in the 1950s. In an early study Schrag & Divoky (1975) catalogued Ciba's aggressive promotional tactics in the United States, including presentations to Parent Teacher Associations and other parent groups, at a time when direct to consumer advertising was illegal in the US.

There is currently an epidemic of stimulant use among school age and younger children. One survey in the United States in 1995 found that 30 to 40% of school children were taking stimulants (Runnheim, 1996). Prescription rates in the United Kingdom are also rising rapidly. Numbers of prescriptions increased by around 30% in 3 years between 1998 and 2001, and the cost of these prescriptions more than doubled (Department of Health, 2002). Although common stimulants are relatively cheap drugs, drug companies have recently been producing new and expensive preparations. This has fuelled huge growth in costs of stimulant prescribing. Stimulants showed the largest increase in financial sales, at 51%, between 2000 and 2001 of all classes of prescription drugs in the US (NIHCM, 2002).

The conditions for which these drugs are prescribed are now called Attention Deficit Hyperactivity Disorder (ADHD) or Attention Deficit Disorder (ADD). Despite the insistence of the advocates of a neurobiological approach in a recent "International Consensus Statement" (Barkley et al, 2002), the validity of the disorder is far from established. Critics have catalogued the wide variations in diagnostic practice and how definitions of the disorder have been widened to include more and more children over the last couple of decades (Timimi, 2002). Even the American National Institute of Health concluded that there was no evidence that ADHD was a biological brain disorder (National Institute of Health, 1998). Although trials demonstrate that stimulants have short term effects on concentration and attention, a recent Cochrane review found that there was little longer term research and questioned the overall value of using stimulant medication (Schachter et al, 2001). The publication of the International Consensus Statement (Barkley et al, 2002) is an explicit attempt to cut short debate on these issues and it is therefore of great concern that the authors were not required to divulge potential conflicts of interests.

The pharmaceutical companies have been actively involved in the promotional campaigns that have brought about this situation. In the United States they have achieved this partly in co-operation with CHADD (Children and Adults with Attention Deficit Disorder), which is predominantly a parent's organisation, set up in 1987. It is highly active in promoting biological views of the nature of ADD, and acceptance of drug treatment. Material produced by Novartis and CHADD promotes the idea that ADD is an established "neurobiological disability" and that stimulants work by "correcting for a neurochemical imbalance" (quoted in Breggin, 2001, chap 14, P225). CHADD also runs national "information" campaigns, and is currently organising a campaign to reach sections of the community that are currently "under-served" in terms of diagnosis and treatment of ADD (www.CHADD.org). It is also engaged in vigorously opposing any moves to restrict the prescribing of stimulants to children. In addition, it produces publications, supports research, lobbies national and local government and holds annual conventions and conferences. It currently receives around 20% of its funding from pharmaceutical companies (www.CHADD.org).

# The expansion of psychosis

The new or atypical antipsychotics have proved to be very profitable for the drug companies that produce them. In 2001 they were ranked 13<sup>th</sup> among the top selling drugs in the United States and their use had increased by 12.5% in one year (NIHCM, 2001). Their popularity has been unaffected by concerns about the validity of their research base (Geddes et al, 2000, see above).

Shortly after the introduction of the atypicals, various concepts about the early treatment and prevention of psychosis started to become fashionable, which are likely to result in increased rates of prescribing of these drugs. Early intervention is usually taken to mean early treatment for someone who has developed full-blown psychotic symptoms. Trials of preventive treatment involve "high risk" individuals, usually young people, who are defined by having a family history of schizophrenia, or having "attenuated" psychotic symptoms. There is obviously the potential for considerable overlap between the concepts of early intervention and prophylactic treatment, since they depend on judgements about what constitute full-blown psychotic symptoms and what do not. Both concepts suggest that the boundaries of when to initiate treatment for psychosis should be extended and should not depend on making a definitive diagnosis, or on the current degree of impairment of functioning. Both concepts are popular and fashionable, but contentious, and the strength of evidence on which they are based is disputed. Critics have argued that such programmes expose many people to the adverse effects of drugs who would never develop psychosis or schizophrenia, and that non drug treatments are neglected (Verdoux, 2002; Bentall & Morrison, 2002).

The drug companies, notably the makers of new antipsychotics, have provided funding for conferences and journal supplements on Early Intervention and preventive treatment, and are also funding, or part funding drug trials involving treatment of young people judged to be at "high risk." The only completed and published randomised drug trial to date was small and not conducted double blind. Results showed small preventive effects that were not sustained over the follow up period. In addition, only 27% of the sample went on to develop a full blown psychosis and only 12% were diagnosed as having schizophrenia one year later (McGorry et al, 2002).

#### **Colonising and inventing other conditions**

I have illustrated only a selection of the expansion of psychiatric drug markets over the last decade or so. The marketing of drugs for other types of anxiety disorders such as panic disorder, generalised anxiety disorder and obsessive compulsive disorder and of drugs for alcohol problems, drug misuse, buleamia, post traumatic stress disorder, menstrual dysphoric disorder, compulsive shopping and intermittent explosive personality disorder, have helped to convince more and more people that they have a mental disorder that needs treatment. In the process, a market for drug treatments has been created in areas where they were formerly

not frequently used. The common factor is the identification of a diagnosis or concept that is constituted by behaviours and emotions that have a substantial overlap with normal experience. The condition is then inherently expandable, which allows the drug companies and their advocates to claim that they abhor the inappropriate over-prescribing of their drugs (Barrett, 2002), safe in the knowledge that this will almost certainly occur anyway.

#### III NEGLECT OF ADVERSE EFFECTS

Adverse effects of drugs represent a major public health problem with recent estimates indicating that 1.5 million Americans are hospitalised and 100,000 die each year, making drug related adverse effects one of the leading causes of death (Lazarou & Pomeranz, 1998). 51% of drugs of approved drugs have serious adverse effects that are not detected prior to approval (US General Accounting Office, 1990). It has been suggested that the system for monitoring adverse effects in the United States and elsewhere is wholly inadequate (Moore et al, 1998; Woods, 1999). For example, neither the Food and Drug Administration in America, nor the Medicines Control Agency in Britain, collect routine data on the prevalence and consequences of adverse effects.

It has long been known that patients with severe mental disorders have much reduced life expectancy, but there has been little attention until recently to the possibility that some of this risk may be associated with drug treatment. A recent study found that death rates in people on long-term treatment with commonly used antipsychotics were three to six times higher than patients taking medication for other non fatal medical conditions (Henessy et al, 2002). Lifestyle factors such as high rates of smoking are likely to account for a part of these high death rates, but the study appeared to confirm other evidence that suggests that antipsychotics can induce fatal cardiac arrythmias (Zarate & Patel, 2001). This propensity has been known about for many years, but drugs such as droperidol and thioridazine, which had been in widespread use for decades, have only recently been withdrawn due to their cardiotoxicity. There is also growing concern about the side effects of the newer atypical antipsychotics, especially their tendency to cause severe obesity and diabetes (Kero et al, 2002) and they have also been associated with adverse cardiac events (Hennessy et al, 2002).

Some companies have been accused of minimising the adverse effects of their products. Eminent psychopharmacologists claimed that drug companies attempted to impede publication of the adverse effects of Halcion and sulpiride (Ian Oswald and Pierre Simon interviewed in Healy, 2000). Bodenheimer (2000) also describes two cases in which companies have attempted to prevent the publication of papers about adverse effects. In the UK, solicitors for the Seroxat Users Group are currently considering whether to launch a lawsuit against GlaxoSmithKline for failing to warn patients about the discontinuation reactions experienced after stopping their best selling drug Seroxat (paroxetine).

#### CRITICISM OF THE INFLUENCE OF THE PHARMACEUTICAL INDUSTRY

Several sections of the general media have recently featured critical discussions of the relationship between medicine and the pharmaceutical industry, including British newspapers the Guardian and Scottish Herald and American magazines USA Today, Public Citizen and Mother Jones. Criticism has also come from major academic medical publications such as the New England Journal of Medicine (NEJM), the Journal of the American Medical Association (JAMA), the Lancet and the British Medical Journal (BMJ). The NEJM was so concerned about the extent of the influence of the industry that it published an editorial entitled "Is

academic medicine for sale?" (Angell, 2000).

Certain patient advocacy groups have taken a stand against the sponsorship of psychiatry. In July 2001, the user group Mad Pride organised a demonstration outside the annual Royal College of Psychiatrists conference in London about the level of commercial sponsorship underpinning the meeting. They were joined by members of the Critical Psychiatry Network, a group of UK based psychiatrists also concerned about the relationship between psychiatry and the drug industry.

Other web-based organisations have emerged to oppose corrupt marketing practices and their effects on medicine, including Social Audit in the United Kingdom (www.socialaudit.org.uk), No Free Lunch (www.nofreelunch.org) and Healthy Skepticism (www.healthyskepticism.org). No Free Lunch urges doctors to refuse drug company gifts and hospitality by taking a pledge. Healthy Skepticism is currently campaigning to stop direct to consumer advertising in New Zealand, and Social Audit is arguing against the relaxation of legislation preventing direct to consumer advertising in Europe. Consumer organisations including Health Which in the UK and Public Citizen in the US are also critical of the pharmaceutical industry's power and influence.

#### WHAT SHOULD PSYCHIATRISTS DO?

The current situation seems to many outsiders and some insiders to indicate that the pharmaceutical industry has a substantial influence on the theory and practice of psychiatry. It also appears that there may be a serious conflict for psychiatrists between satisfying the needs of patients and the wider community, and serving the interests of the corporations. Political pressure is rightly demanding that all institutions become more accountable and more transparent. In response the Royal College of Psychiatrists is initiating a review of its relationship with the pharmaceutical industry. It is drafting guidelines on the relationship between the College and the industry and on relationships between individuals and the industry (Paul Jessop, personal communication, March 2003).

I suggest that there are some further steps that should be taken to improve the integrity of psychiatry in the United Kingdom.

- The Royal College of Psychiatrists should publish in its accounts the exact amount of funding it receives each year from different pharmaceutical corporations.
- The Royal College of Psychiatrists should create and publish a register of member's interests that should be made publicly available.
- The Royal College should initiate a discussion among its members about the ethics of receiving drug company hospitality and discussions should also be initiated at a local level.
- Psychiatric institutions, including the Royal College, should stop accepting commercial sponsorship for educational events
- Full disclosure of interests should be required by all psychiatric journals and for conference presentations. Torrey (2002) provides an example of the latter: "prominently displayed next to the speakers lectern should be a sign reading 'For this talk Dr Smith is being paid \$3,500, business class air fare and four star accommodation by Eli Lilly and Company."

- Conflicting interests of authors of clinical guidelines should be reported and guideline committees should develop policies for managing these situations.
- Guidelines should be drawn up for research personnel, which should set limits on fees received from companies and should prohibit researchers from holding stock in companies whose drugs they are investigating (Torrey, 2002).
- Funding bodies should support research into treatment approaches that genuinely represent alternatives to a reliance on drugs.

#### **CONCLUSIONS**

As a society we are consuming more medicinal drugs than ever and a large proportion of these are for psychological conditions and complaints. This is making a major contribution to spiraling health costs and takes money away from other health services. Psychiatric practice is now firmly centered around drug treatment, and millions of other people, who have no contact with a psychiatrist, are receiving psychotropic drugs in General Practice. In recent years we have been encouraged to view more and more problems that were previously considered to be normal and manageable parts of the human condition as mental diseases that require treatment. The promotion of the idea of technical and professional solutions, the medical colonisation of everyday life, has profound consequences. At the individual level it seems likely to reduce personal coping strategies, to "gnaw away at our self confidence" (Payer, 1992). This is true in the area of mental health more than any other, since mental health involves our view of our own capabilities; the nature of our very selves. At the social level, the medicalisation of various problems obscures the effects of social changes that have taken place in the UK over the last couple of decades. For example, the retraction of the welfare state, increasing working hours, job insecurity and the dismantling of pension schemes have made life more difficult and more uncertain for many ordinary people. A society obsessed with its own navel is unlikely to be able to mount an effective challenge to these trends.

Psychiatry and the pharmaceutical industry make a formidable combination. Modern psychiatry derives its legitimacy from the notion that mental disorders are equivalent to medical diseases and it is this that justifies the coercion of psychiatric patients. Drug treatments that are aimed at specific diagnoses help to endorse this view, and the industry has the financial capacity to ensure that this view becomes accepted and respectable. In turn, the authority of psychiatry enables it to define what is considered as mental disorder and what is appropriate treatment, thus creating markets and opportunities for the pharmaceutical industry.

The influence of the pharmaceutical industry over political processes and research is an example of what George Monbiot has termed the corporate take-over of Britain (Monbiot, 2000). The power of the pharmaceutical industry is particularly worrying, because the commercial incentive to promote disease and sell pills potentially changes our view of what it is to be human. Fortunately, there are signs of unease within the medical community about the degree and consequences of drug company influence. It is time for the psychiatric profession to reflect on its relationship with the pharmaceutical industry and attempt to reclaim its integrity.

#### **ACKNOWLEDGEMENTS**

I would like to thank Professor Robin Murray and Dr Peter Mansfield for their helpful comments on a previous draft of this paper, Madeline Moncrieff for legal advice and Michelle Blythe for her help in locating material.

#### REFERENCES

Abrahams J (2002) Making regulation responsive to commercial interests: streamlining drug industry watchdogs. British Medical Journal, 325, 1164-1167.

Adams CE, Fenton MK, Quraishi S, David AS (2001) Systematic meta-review of depot antipsychotic drugs for people with schizophrenia. British Journal of Psychiatry, 179, 290-299.

Aitkin M & Holt F (2000) A prescription for direct drug marketing. The McKinsey Quarterly, 22 March 2000, 82.

Angell M (2000) Is academic medicine for sale? New England Journal of Medicine, 342, 1516-1518.

Antonuccio DO, Danton WG, DeNelsky GY, et al (1999) Raising questions about antidepressants. Psychotherapy & Psychosomatics, 68, 3-14.

Baldessarini RJ & Viguera AC (1995) Neuroleptic withdrawal in schizophrenic patients. Archives of General Psychiatry, 52, 189-192.

Barkley RA, Cook Jr EH, Diamond A et al (2002) International consensus statement on ADHD, Clinical Child and Family Psychology review, 5, 89-91.

Barrett, J (2002) speaking on Woman's Hour, BBC Radio 4, September 5<sup>th</sup> 2002

Beach JE (2001) Clinical trials integrity: a CRO perspective. Accountability in Research, 8, 245-260.

Bentall RP & Morrison AP (2002) More harm than good: The case against using antipsychotic drugs to prevent severe mental illness. Journal of Mental Health, 11, 351-356.

Bero LA & Rennie D (1996) International Journal of Technology Assessment in Health Care, 12:2 209-237.

BMJ News, 13<sup>th</sup> April (2002). Drug firms hype disease as sales ploy, industry chief claims. British Medical Journal, 324, 867.

BMJ News, 1st June (2002) Celebrity selling. British Medical Journal News, 324, 1342.

BMJ News, 19<sup>th</sup> Oct (2002). A fifth of Americans contact their doctor as a result of drug advertising. British Medical Journal, 325, 854.

Bodenheimer T (2000) Uneasy alliance- clinical investigators and the pharmaceutical industry. New England Journal of Medicine, 342, 1539-1544.

Bohaychuk W, Ball G (1999) Conducting GCP Compliant Clinical Research. Chichester: John Wiley & Sons.

Bollini P, Pampallona S, Orza MJ, Adams ME, Chalmers TC (1994) Antipsychotic drugs: is more worse? A meta-analysis of the published randomized control trials. Psychological Medicine, 24, 307-316.

Boyd EA & Bero LA (2000) Assessing faculty financial relationships with industry. Journal of the American Medical Association, 284, 2209-2214.

Braslow J (1997) Mental Ills and Bodily Cures: psychiatric treatment in the first half of the twentieth century. Berkely, CA: University of California Press.

Breggin P (2001) Talking Back to Ritalin. Cambridge, MA: Perseus Publishing.

Breggin P & Breggin GR (1995) Talking Back to Prozac. New York: St Martin's Press.

Chase D, Gierend M, Letzel H, Ludwig S (2001) System audit of contract research organisations in Germany. International Journal of Pharmaceutical Medicine, 15, 191-193.

Choudhry NK, Stelfox HT, Allan D (2002) Relationships between authors of clinical practice guidelines and the pharmaceutical industry. Journal of the American Medical Association, 287, 612-617.

Claxton AJ, Li Z, McKendrick J (2000) Selective serotonin re-uptake inhibitor treatment in the UK: risk of relapse or recurrence of depression. British Journal of Psychiatry, 177, 163-168.

Cohen JS (2001) Overdose: the case against the drug companies. New york: Penguin Putnam Inc.

Commonwealth Fund (1999) From bench to bedside: preserving the research mission of academic health centres. New York: Commonwealth Fund.

Conrad P (1992) Medicalisation and social control. Annual Review of Sociology, 18, 209-232.

Costello EJ, Pine DS, Hammen C et al (2002) Development and natural history of mood disorders. Biological Psychiatry, 52, 529-542.

Crow TJ, Macmillan JF, Johnson AL, Johnstone EC (1986) A randomsied controlled trial of prophylactic neuroleptic treatment. British Journal of Psychiatry, 148, 120-127.

Davidson RA (1986) Source of funding and outcome of clinical trials. Journal of General Internal Medicine, 1, 155-158.

Department of Health (2002) Prescription Cost Analysis 2001. London: HMSO.

Double D (2002) The limits of psychiatry. British Medical Journal, 324, 900-904.

Flanagin A, Carey LA, Fontanarosa PB et al (1998) Prevalence of articles with honorary authors and ghost authors in peer reviewed medical journals. Journal of the American Medical Association, 280, 222-224.

Fortune magazine (2002), April issue, 2002.

Foucault M (1967) Madness and Civilisation. London: Tavistock

Freemantle N, Anderson IM, Young P (2000) Predictive value of pharmacological activity for the relative efficacy of antidepressant drugs: meta-regression analysis. British Journal of Psychiatry, 177, 292-302.

Geddes J, Freemantle N, Harrison P et al (2000) Atypical antipsychotic drugs in the treatment of schizophrenia: systematic review and meta-analysis. British Medical Journal, 321, 1371-1376.

Gilbert P,L, Harris MJ, McAdams LA, Jeste DV (1995) Neuroleptic withdrawal in schizophrneic patients. Archives of General Psychiatry, 52, 173-188.

Hall WD, Mant A, Mitchell PB, Rendle VA et al (2003) Association between antidepressant prescribing and ...freeuk.com/pharmaceuticalindustry.h...

suicide in Australia, 1991-2000: trend analysis. British Medical Journal, 326, 1008-1111.

Healy D (1997) The Antidepressant Era. Cambridge, MA: Harvard University Press.

Healy D (1996) The Psychopharmacologists vol 1. London: Arnold

Healy, D. (1999) The three faces of antidepressants. Journal of Nervous and Mental Disease, 187, 174-180.

Healy, D. (2000) The Psychopharmacologists vol 3. London: Arnold.

Healy D (2002) The Creation of Psychopharmacology. Cambridge, MA: Harvard University Press.

Healy D & Cattell D (in press) The interface between authorship, industry and science in the domain of therapeutics. British Journal of Psychiatry, in press.

Hemminki E (1981) Quality of reports of clinical trials submitted by the drug industry to Finnish and Swedish control authorities. European Journal of Clinical Pharmacology, 19, 157-165.

Hennessy S, Bilker WB, Knauss JS et al (2002) Cardiac arrest and ventricular arrhythmia in patients taking antipsychotic drugs: cohort study using administrative data. British Medical Journal, 325, 1070-1072.

Herxheimer A (draft) Relationships between the pharma industry and patients organisations. Draft paper prepared for British Medical Journal.

Huston P & Moher D (1996) Redundancy, disaggregation and the integrity of medical research. Lancet, 347, 1024-1026.

Kero CE, Fedder DO, L'Italien GJ et al (2002) Assessment of independent effect of olanzapine and risperidone on risk of diabetes among patients with schizophrenia: population based nested case- control study. British Medical Journal, 325, 243-247.

Kirk H & Kutchins SA (1999) Making us Crazy. London: Constable.

Kjaergard LL & Als-Nielson, B (2002) Association between authors competing interests and authors conclusions: epidemiological study of randomised clinical trials published in the BMJ. British Medical Journal, 325, 249-251.

Koran LM, Hakett E, Rubin A et al (2002) Efficacy of sertraline in the long-term treatment of obsessive compulsive disorder. American Journal of Psychiatry, 159, 88-95.

Kramer PD (1993) Listening to Prozac. New York: Viking.

Lazarou J, Pomeranz BH, Corey PN (1998) Incidence of adverse drug reactions in hospitalised patients: a meta-analysis of prospective studies. Journal of the American Medical Association, 279, 1200-1204.

Lehtinen V, Aaltonen J, Koffert T et al (2000) Two year outcome in first episode psychosis treated according to an integrated model. Is immediate neuroleptisation always needed? European Psychiatry, 15, 312-320.

McGorry PD, Yung AR, Phillips LJ et al (2002) Randomised controlled trial of interventions designed to reduce the risk of progression to first episode psychosis in a clinical sample with subthreshold symptoms.

Archives of General Psychiatry, 59, 921-928.

Medawar C (2001) Health, pharma and the EU. A briefing for members of the European Parliament on direct to consumer advertising. www.socialaudit.org.uk

Mintzes B (2002) Direct to consumer advertising is medicalising normal human experience. British medical journal, 324, 908-909.

Mintzes B, Barer ML, Kravitz RL et al (2002) Influence of direct to consumer advertising and patients requests on prescribing decisions: a two site cross sectional survey. British Medical Journal, 324, 278-279.

Monbiot G (2000) Captive State: the corporate takeover of Britain. London: Macmillan.

Moncrieff J (1999). An investigation into the precedents of modern psychiatry. History of Psychiatry, 10, 475-490.

Moncrieff J & Pommerleau, J. (2000) Trends in sickness benefits in Great Britain and the contribution of mental disorders. Journal of Public Health Medicine, 22, 59-67.

Moncrieff J (2001) Are antidepressants over-rated? A review of methodological problems in antidepressant trials. Journal of Nervous and Mental Disease, 189, 288-295.

Moncrieff J (2003) Misleading analysis. BMJ e correspondence at www.bmj.com/

Moncrieff (in press) The politics of a new mental health act. British Journal of Psychiatry.

Moore TJ, Psaty BM, Furberg CD (1998) Time to act on drug Safety. Journal of the American Medical Association, 279, 1571-1573.

Mosher L (1999) Soteria and other alternatives to acute psychiatric hospitalisation. Journal of Nervous and Mental Disease, 187, 142-149.

Mother Jones (2002) Disorders made to order. Mother Jones magazine July/August 2002. www.motherjones.com

Moynihan R, Heath I, Henry D (2002). Selling sickness: the pharmaceutical industry and disease mongering. British Medical Journal, 324, 886-891.

National Institute of health (1998) Consensus statement: diagnosis and treatment of attention deficit hyperactivity disorders. Rockville MD: National Institute of Mental Health.

National Institute for Health Care Management (2002). Prescription drug expenditures in 2001. www.nihcm.org.

National Institute for Mental Health England (NIMHE) & Association of the British Pharmaceutical Industry (ABPI) Partnership (2002). Meeting of Minds. <a href="https://www.nimhe.org.uk">www.nimhe.org.uk</a>

New York Times (2001) A muscular lobby tries to shape the nation's bioterror plan. New York Times, November 4<sup>th</sup> 2001.

Payer L (1992) Disease Mongers. New York: John Wiley.

Paykell ES & priest RG (1992) Recognition and management of depression in general practice: consensus statement. British Medical Journal, 305, 1198-1202.

Pharmaceutical Marketting (2000). The mark of Zorro. Pharmaceutical Marketing, May 2000. www.pmlive.com

Pharmaceutical Marketting (2002) Practical Guides: Medical Education parts I & II. Pharmaceutical Marketing, 2002. www.pmlive.com

Public Citizen (2002) America's other drug problem: a briefing book on the prescription drug debate. www.citizen.org/rxfacts.

Romano SJ, Halmi KA, Sarker NP et al (2002) A placebo controlled study of fluoxetine in continued treatment of bulimia nervosa after successful acute fluoxetine treatment. American Journal of Psychiatry, 159, 96-102.

Runnheim VA (1996) Medicating students with emotional and behavioural disorders and ADHD: a state survey. Behavioural Disorders, 21, 316-314.

Safer DJ (2002) Design and reporting modifications in industry sponsored comparative psychopharmacology trials. Journal of Nervous and Mental Disease, 190, 583-592.

Sainsbury Centre for Mental Health (1998) Acute problems. A survey of the quality of care in acute psychiatric wards. London: SCMH.

Schachter HM, Pham B, King J et al (2001) How efficacious and safe is short acting methylphenidate for the treatment of attention deficit disorder in children and adolescents? A meta-analysis. Canadian Medical Association journal, 165, 1475-1488.

Schrag P & Divoky D (1975) The Myth of the Hyperactive Child. New York: Pantheon.

Swazey J (1974) Chlorpromazine in Psychiatry. Cambridge, MA: Massachusetts Institute of Technology.

Shorter E (1997). A History of Psychiatry: from the age of the asylum to the age of prozac. New York: John Wiley & Sons.

Sunday Herald, Feb 23rd (2003) Fury at Holyrood's medicine panel as members reveal drug firm links.

Suppes T, Baldessarini RJ, Faedda GL (1991) Risk of recurrence following lithium discontinuation of lithium treatment in bipolar disorder. Archives of General Psychiatry, 48, 1082-1088.

Timimi S (2002) Pathological child psychiatry and the medicalisation of childhood. Hove, East Sussex: Brunner-Routledge.

Torrey EF (2002) The going rate on shrinks. The American Prospect, volume 13, issue 13, 2002. www.prospect.org.

United States General Accounting Office (1990) FDA drug review: post approval risks, 1976-85. Washington DC: US General Accounting Office; April 26, 1990.

Van Praag HM (2002) Why has the antidepressant era not shown a significant drop in suicide rates? Crisis, 23, 77-82.

Wadman M (1997) Study discloses financial interests behind papers. Nature, 385, 376.

Wahlbeck K, Tuunainen A, Gilbody S, Adams CE (2000) Influence of methodology on outcomes of randomised clozapine trials. Pharmacopsychiatry, 33, 54-59.

Wazana A (2000) Physicians and the pharmaceutical industry. Is a gift ever just a gift? Journal of the American Medical Association, 283, 373-380.

Whitaker R (2002) Mad in America. Cambridge, MA: Perseus Publishing.

Wood A. the safety of new medicines: the importance of asking the right questions. Journal of the American Medical Association, 281, 1753-1754.

World Health Organisation (2001) World Health Report, 2001. www.who.int/whr/2001

Valenstein E (1998) Blaming the Brain. The truth about drugs and mental health. New York: Free Press.

Verdoux H. (2001) Have the times come for early intervention in psychosis? Acta Psychiatrica Sandinavica, 103, 321-322.

Zarate CA Jr, Patel J (2001) Sudden cardiac death and antipsychotic drugs: do we know enough? Archives of General Psychiatry, 58, 1168-71.

Zito JM, Safer DJ, dos Reis S et al (2000) Trends in the prescribing of psychotropic to preschoolers. Journal of the American Medical Association, 283, 1025-30.