

# The Marketization of Depression: Prescribing SSRI Antidepressants to Women\*

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## Introduction

Prozac, Paxil, Zoloft, Effexor, Celexa, Remeron and Luvox. Most Canadians are aware of the new class of drugs called SSRIs (Selective Serotonin Reuptake Inhibitors) and related medications<sup>1</sup> prescribed for depression and other issues such as anxiety, panic, obsessive-compulsive, “pre-menstrual dysphoric” and “social anxiety” disorder. Since the first blockbuster SSRI, Prozac, arrived on the scene in 1988, SSRIs have become one of the most frequently prescribed classes of drugs in Canada and the world. The influence of SSRIs has become so widespread that they have shaped our language, culture and assumptions about sickness and health. We have been described as living in the “Age of Prozac”.

This paper looks at the impact of SSRI use among Canadian women and attempts to uncover the systemic reasons behind this widespread use. It reviews what is currently known about the benefits obtained and the harms caused by SSRIs, as well as both the definition and incidence of depression in women. The role of government regulation is addressed. Finally, the paper looks at alternative responses to women’s emotional distress.

In 2003, Canadians spent fifteen billion dollars on prescription drugs, an increase of 14.5% over 2002. Psychotropic drugs (drugs that affect the mind) were the *leading* driver of this increase and SSRIs are the major drug in this psychotropic drug class. To what degree are these enormous prescription drug expenditures appropriate or sustainable? Why aren’t proven *non-drug* alternatives that address the emotional distress of women, such as exercise, support, psychotherapy, and nutritional improvements, being supported, funded and prioritized by government?

At the time of writing, Health Canada is in the process of developing a national mental health strategy. Issues related to the use of SSRIs, their appropriateness, effectiveness, potential effects on health and the value of non-drug alternatives are of critical importance to Canadian women and need to be fully addressed in this strategy.

## The Age of Prozac

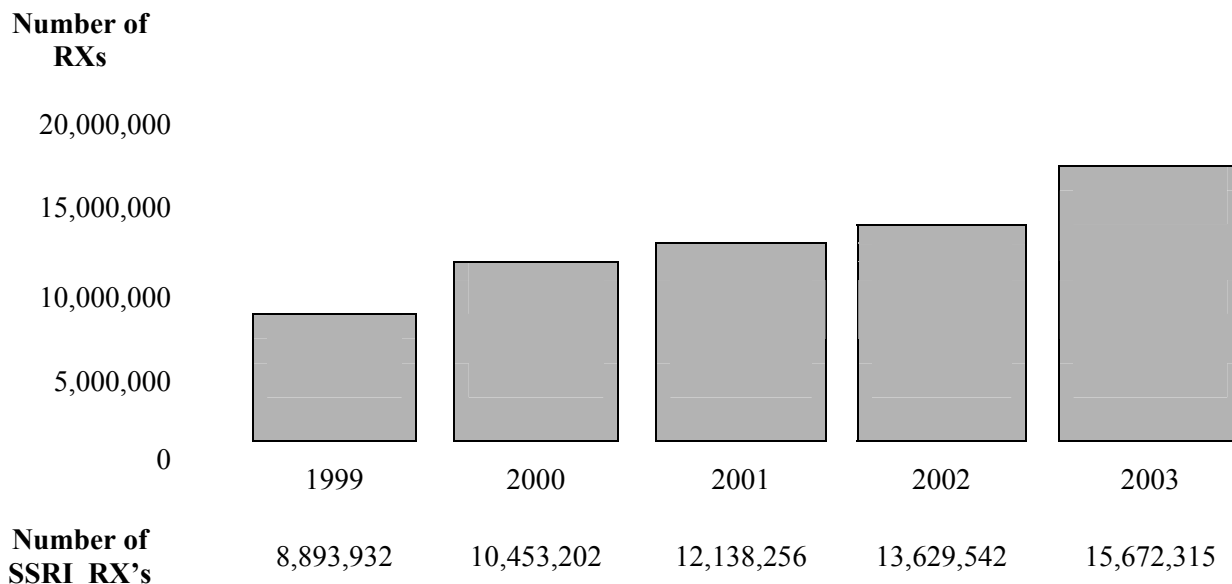
Between 1981 and 2000, total prescriptions for *all* antidepressants increased by 353% from 3.2 to 14.5 million.<sup>2</sup> SSRIs have gradually squeezed out older antidepressants, such as the tricyclics, so that they now comprise 81% of the depression drug market.<sup>3</sup>

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Between 1999 and 2003, the number of dispensed prescriptions for SSRIs in Canada grew by 80% to 15,672,315 prescriptions (Table 1).<sup>4</sup>

**Table 1: Estimated Number of SSRI Prescriptions Dispensed in Canada<sup>4</sup>**



Individual SSRIs, particularly those under patent protection, have shown enormous growth. Effexor, a dual-action SSRI introduced in 1998, recorded the highest increase in the total number of prescriptions (42.4%) of *any* prescription drug in Canada in 2002.<sup>5</sup>

SSRIs are also among the highest selling of all drugs in an industry that has been consistently ranked as one of the most profitable in the United States for the past twenty years. In 2003, Zoloft, an SSRI manufactured by Pfizer, was the tenth best selling drug in the world with sales of \$3.4 billion.<sup>6</sup>

Twice as many psychotropic drugs are prescribed for women as for men, and this holds true for the SSRI antidepressants.<sup>7</sup> Recent Pharmanet data from British Columbia indicate that almost one in five women (19%) in the province over the age of thirty received at least one prescription for SSRIs in the period between August 1, 2002 and July 30, 2003. Twenty-one percent of women in the age category 51-60 and 22% in the age category 81-90 received an SSRI prescription during this time.<sup>8</sup>

Sales of pharmaceuticals to Canadians in 2003 were estimated to be \$15 billion, an increase of 14.5% over sales in 2002. 2003 was the sixth successive year of annual increases in pharmaceutical sales exceeding 10%. The *leading* drug class driving the growth in sales (23.5%) was drugs affecting the nervous system, particularly the SSRIs and related drugs.<sup>9</sup>

In Ontario, Mamdani et al. found “tremendous cost implications” due to the shift from using older antidepressants to SSRIs. Total antidepressant drug costs were estimated to have risen 347% from 1993 to 2000. Eighty-eight percent of these additional drug costs were due to SSRI antidepressants.<sup>10</sup>

In the past fifteen years, the prevalence of depression appears to have soared. According to *The Economist*, 330 million people in the world are now said to be suffering from depression, a disease that it describes as affecting more people than either heart disease or AIDS. According to the World Health Organization, depression is projected to be the world's second most debilitating disease by 2020.<sup>11</sup> This dramatic increase in the prevalence of depression raises important questions. Is depression that is serious enough to be treated with psychiatric drugs really on the rise in the general population, or are other factors at play?

Prior to the introduction of SSRIs, depression was considered to affect only 100 people per million. Since the introduction of SSRIs, prevalence rates for depression are now considered to be in the range of 50,000 to 100,000 cases per million (a 500 to 1,000 fold increase).<sup>12</sup>

In Canada, depression is the fastest rising diagnosis made by office-based physicians. Visits for depression have almost doubled since 1994 and 66% of office visits for depression in 2004 were made by women. Eighty-one percent of physician visits for depression in 2004 resulted in a recommendation for an antidepressant, almost always an SSRI or a related drug.<sup>13</sup>

How can these increased rates of depression and prescribing of SSRI antidepressants to Canadian women be explained? Prior to the advent of SSRIs, depression was considered to be a self-limited phenomenon which was likely to resolve itself, without treatment, in *the vast majority of cases*. Now, according to researcher and author Charles Medawar, it is almost heresy to say that most episodes of depression are self-limited and will end without treatment. Drug intervention is seen to be so imperative that the failure to prescribe would be thought of as negligent, even perhaps legally indefensible.<sup>14</sup>

## **How Do SSRIs Work?**

SSRIs act on the chemical messenger (neurotransmitter) serotonin. Serotonin is widely distributed throughout the body and is found in very large concentrations in the walls of blood vessels, in blood platelets and in the brain. Serotonin acts on the peripheral nervous system (affecting vasoconstriction, platelet aggregation, intestinal peristalsis and other functions) and the central nervous system (affecting controlled behaviour, attention, cardio-respiratory function, aggression, sleep, appetite, motor and other functions).

Serotonin is normally released into the synapse (space) between the nerve cells and is either destroyed or reabsorbed back into the cell that released it. SSRIs block this reabsorption (re-uptake) causing more serotonin to accumulate in the synapse. Although many people receive long-term SSRI prescriptions, there have been no studies that assess the effects of blocking serotonin over months or years. Most of the forty-two clinical trials for Prozac, Paxil, Zoloft, Celexa, Serzone and Effexor lasted only six weeks.<sup>15</sup>

The stimulation of the serotonin system caused by SSRIs is a common feature of many psychiatric medications such as Ritalin and some street drugs, such as cocaine and Ecstasy.<sup>16</sup> Many of these drugs have a similar profile to the SSRIs, although stimulants such as Ritalin, Ecstasy and cocaine (and SSRI related drugs such as Effexor and Remeron), also boost additional neurotransmitters, such as dopamine and noradrenalin. A major effect of the stimulation of serotonin is an effect on mood. Many individuals can be over-stimulated by SSRIs and this accounts for the frequency of effects on the central nervous system, such as agitation, nervousness, mania, agitated depression or akathisia (a condition that involves an inability to sit

still, anxiety, restlessness and agitation). Agitated depression or akathisia have been associated with the increased risk of suicidal ideation (thoughts of suicide) and attempts by those taking SSRIs.<sup>17</sup>

Pharmaceutical companies have promoted the view that depression is actually a biochemical “disorder” caused by a chemical imbalance of serotonin in the brain. SSRIs have been marketed as “righting the balance” of a chemical that already exists in the body. The belief that depression is actually a “deficiency” disease, akin to diabetes, has been so aggressively promoted that it helps to explain why there is frequently an uncritical acceptance of the value of prescribing SSRIs, even for children.

There is no scientific evidence that there is a serotonin “imbalance” in people who are depressed, that they have a serotonin dysfunction or that they need serotonin drugs to operate normally. In the early 21<sup>st</sup> century, we still know very little about the complexities of brain function. There are trillions of synapses in the brain and hundreds of brain chemicals. Little is known about how these chemicals inter-relate or act on neurons, many of which are highly specialized.

## **Are SSRIs Effective?**

The value of any prescription drug must be calculated by weighing its potential benefits against its potential risks and capacity to harm. According to psychopharmacologist, researcher and author Dr. David Healy, the treatment effects of SSRIs are modest and the burden and costs of harm have never been defined.<sup>18</sup> Review of the data from published and unpublished clinical trials suggests that SSRIs have limited clinical significance.

In an analysis of efficacy data submitted to the US Food and Drug Administration (FDA) between 1987 and 1999 for the six most popular SSRIs, it was found that approximately 80% of the response to medication was duplicated in placebo groups. In the four pivotal trials for Prozac that were used to obtain FDA approval, 25% of the subjects in three of the trials had to be given a benzodiazepine tranquilliser (an addictive drug) to calm the agitation, akathisia, anxiety and mania caused by Prozac.<sup>19</sup>

In a re-analysis of clinical trial data related to SSRI antidepressant use by children in 2003, the British regulatory agency, the Medicines and Healthcare Products Regulatory Agency, announced an unacceptable risk-benefit ratio for all SSRIs except Prozac.<sup>20</sup>

Efforts to assess the effectiveness of SSRIs have been confounded by the unwillingness of drug companies to publish negative clinical trial results. The manufacturer of Paxil deliberately avoided publishing data that showed the drug was no better than a placebo in children because, in doing so, they would have risked the lucrative adult market. Unpublished data for Zoloft, Effexor and Celexa trials indicate that the risks, for children, of taking SSRIs outweigh the benefits.<sup>21</sup>

Drug companies are not obliged to publish the results of negative clinical trials, even if negative trials are in the majority. This means that the lay public and physicians do not have access to comprehensive information on risks or benefits. As well, drug companies design and fund most clinical trials themselves and the results of these trials are usually biased towards the positive.

For example, 90% of industry-funded placebo trials reported positive results from the use of SSRIs in children compared to 55.6% of non industry-funded studies.<sup>22</sup>

Clinical trials can also be manipulated in order to demonstrate more favourable results. For example, trial subjects who show a high response to placebo may be eliminated from a clinical trial and their experiences not documented. Harm resulting from a drug may be poorly recorded and researchers may rely on spontaneous reporting from subjects rather than on information gathered from comprehensive structured checklists. Trial subjects may be unaware that certain harmful effects can be caused by a drug they are taking and may be unlikely to report them.

Harmful effects resulting from drugs are frequently not examined in detail in clinical trials. For example, in some of the trials for SSRIs, the occurrence of suicidal ideation was assessed with only one question. In other cases, adverse effects were reported in the trial outcomes but were given more benign names. For example, the term “nervousness” was used to describe severe agitation experienced by trial subjects.

## **Harm Due to SSRIs**

Current literature indicates that adverse reactions to SSRIs are common, diverse and may be serious. Manufacturer’s information for Prozac indicates that the drug is associated with 242 different side effects, including 34 problems of the genital and urinary tract alone. A review of spontaneous adverse drug reaction reporting found that “during a ten-year period Prozac was associated with more hospitalizations, deaths or other serious adverse effects reported to the FDA than any other drug in America.”<sup>23</sup> Spigset found that the most common problems arising from SSRIs were neurological (22%), psychiatric (19.5%), gastrointestinal (18%) and dermatological (11.4%). Women experienced a higher rate of the most harmful effects from SSRIs than men.<sup>24</sup> Vanderkooy found that 10-32% of people taking Eflexor, Paxil and Zoloft experienced nervousness, agitation, tremor, dizziness, muscle spasms, headaches or sleep problems.<sup>25</sup>

SSRIs can and do elicit some of the same motor effects and long-term complications as the anti-psychotic drugs (those indicated for schizophrenia and psychoses), including EPS (extrapyramidal signs or abnormal movements) such as Parkinsonian syndrome, akathisia (inner agitation), dystonia (muscle spasm) and chronic dyskinesias (abnormal muscular movements or spasms). These reactions may affect all patients to some degree, can develop weeks or months after initiation of an SSRI and may continue after the drug is withdrawn.<sup>26</sup> Serotonin syndrome is also associated with SSRIs. It is a serious dose-related reaction that causes neuromuscular excitability, hyperthermia, altered muscle tone, mental status changes and autonomic instability. Left untreated, serotonin syndrome can lead to coma, seizures, high fever, metabolic acidosis, rhabdomyolysis, renal failure and death.<sup>27</sup>

The development of “agitated depression” among some who use SSRIs is one of the reasons why SSRIs are associated with an increased risk of suicide.<sup>28</sup> Although denied for years by pharmaceutical companies, it is now accepted that there is at least a doubling of the relative risk of both suicide attempts and completed suicides for those on SSRIs when compared to older antidepressants or non-treatment. This risk may be 3.0 times or greater for primary care depression in low risk populations.<sup>29</sup> In March 2004, the US FDA issued a *Drug Advisory* stating that patients on SSRIs should be monitored for worsening of depression and suicidality. The

*Advisory* also identified adverse drug reactions from SSRIs such as anxiety, agitation, panic attacks, insomnia, irritability, hypomania and mania.<sup>30</sup>

Sexual dysfunction (lack of libido, orgasmic dysfunction and, in men, delayed ejaculation) is a common side effect of using SSRIs, although again there are few randomized control trials (RCTs) to establish specific frequency levels. Although pharmaceutical company information initially suggested rates of sexual dysfunction at the level of 5%, later studies have established prevalence rates of 30-70%.<sup>31</sup> There are concerns that not all sexual dysfunction may fully resolve after termination of treatment. Since SSRIs are prescribed more often for women, women are more frequently affected by SSRI-induced sexual dysfunction. Because SSRIs can also lead to a worsening of depression, paradoxical effects, emotional blunting or detachment, reduced emotional activity, memory loss and confusion, these effects, in conjunction with sexual dysfunction, can negatively affect intimate relationships.

SSRIs have many effects on the gastrointestinal (GI) system, including gastric pain, dry mouth, nausea, constipation, weight loss and weight gain, dyspepsia and vomiting.<sup>32</sup> SSRIs also increase the risk of upper GI bleeding. Their potential to have this effect is increased by the concurrent use of NSAIDs.<sup>33</sup>

It is known that psychotropic drugs, such as benzodiazepines (tranquillisers) and hypnotics (sleeping pills), contribute significantly to the prevalence of falls and fractures in the elderly.<sup>34</sup> A study by Liu et al. concludes that SSRIs contribute to falls and fractures in the same way as these other drugs.<sup>35</sup> This is a concern considering that data from BC indicate that almost a quarter of elderly women in 2003 received prescriptions for SSRIs. Fractures among the elderly present a significant cost burden to the health care system.

SSRIs also affect the cardiovascular system and may produce vasospasm in the presence of coronary artery disease, a common condition.<sup>36</sup>

On-going research shows that there is evidence that SSRIs can be harmful to pregnant women or their babies. Chambers found that there was a 15.5% incidence of more than three minor genetically related anomalies among infants of women exposed to Prozac during pregnancy.<sup>37</sup> Health Canada issued an *Advisory* on August 9, 2004 advising pregnant women taking SSRIs during the third trimester of pregnancy that their newborns may experience withdrawal problems. The *Advisory* states that newborns whose mothers took SSRIs during pregnancy have developed complications at birth requiring prolonged hospitalization, breathing support and tube feeding. Reported symptoms include feeding and/or breathing difficulties, seizures, muscular rigidity, jitteriness and constant crying. The symptoms may be due to “discontinuation effects” (withdrawal from the drug) or other effects of SSRIs.<sup>38</sup>

SSRIs have been found in breast milk. Whether or how drug exposure affects the neuro-behavioural development of babies has not been established.<sup>39</sup>

The use of SSRIs may also contribute to increased levels and costs of hospitalization. Sheffield et al. found that switching or augmenting SSRIs was significantly associated with hospitalization.<sup>40</sup>

## Are SSRIs Addictive?

The possibility that SSRIs could cause addiction or dependency and result in withdrawal symptoms or difficulty stopping the drugs was known during the testing phase of Prozac. Withdrawal symptoms from Prozac, however, are sometimes difficult to identify because they frequently appear hours or days after stopping or decreasing the dose. This is because of Prozac's long *half-life* in the body (speed at which the concentration of the drug in the blood stream drops off). A long half-life means that withdrawal symptoms can start hours or even days later, making it difficult for the patient or the health care provider to associate them with the drug.

Initially, drug companies vigorously denied the existence of withdrawal symptoms.<sup>41</sup> The makers of Paxil described the incidence of withdrawal effects as being .0001% until 2001. The pharmaceutical company and government-funded national "Defeat Depression" campaign in Britain (1992-97) consistently told the public that antidepressants were not addictive. Doctors were advised to tell their patients that withdrawal problems due to SSRI use were rare and invariably mild.<sup>42</sup>

As part of the strategy to deny or minimize dependence associated with SSRIs, pharmaceutical companies became involved in a concerted campaign to redefine the meaning of prescription drug dependency in the DSM-IV (Diagnostic and Statistical Manual of Mental Disorders). This new definition stated that physical dependency resulting from drug tolerance wasn't enough to describe "dependency". Instead a patient would also have to demonstrate "abusive" or drug-seeking behaviours. Because most patients taking prescription SSRIs are taking *prescribed* doses and are not abusing drugs, this definition implied that they could not possibly be addicted, even if they found it difficult or impossible to stop taking the drug because of withdrawal symptoms. According to Medawar, this new definition meant that "as if by law, and at a stroke, 'dependence' had again come to mean something like frank drug abuse. In line with tradition, dependence problems were pinned on users once again."<sup>43</sup> Both doctors and pharmaceutical companies promoted this new definition because it characterized dependence as something no competent doctor or prescribed drug could ever cause.

Ironically, it was Eli Lilly, the manufacturer of Prozac, which initially brought withdrawal effects into the public eye by bringing critical attention to the withdrawal symptoms caused by Paxil, a competitor's product. But Eli Lilly was also careful not to use the term "withdrawal symptoms" and instead substituted the more benign term, "discontinuation symptoms or effects." Drug company employees were told to avoid using terminology such as 'withdrawal' because it implied dependence.<sup>44</sup>

Research now indicates that 35 – 85% of people who abruptly stop taking SSRIs will develop one or more symptoms of withdrawal.<sup>45</sup> Withdrawal from short acting drugs, such as Paxil and Effexor, can begin in as little as a few hours after a missed or reduced dose. Withdrawal can produce dramatic changes in mood, including a worsening of depression, appetite changes, insomnia, electric shock sensations, agitation and many other symptoms. Because withdrawal symptoms often mimic the reason for which the drug was initially prescribed (for example, depression), patients and their doctors often feel that the patient has relapsed. Additional drugs or a higher dose may be prescribed for symptoms that are related to the drug itself.

Observational studies have not established how long the effects of withdrawal will continue.

Although SSRIs and other drugs are heavily prescribed by physicians, few physicians are aware of their adverse effects. Young and Currie found that 70% of physicians involved in a knowledge base survey said that they were unaware of antidepressant discontinuation events. Only 17% said they would caution patients about the possibility of symptoms.<sup>46</sup>

## **Why Are More SSRIs Prescribed for Women Than for Men?**

Research indicates that women in North America and Europe have twice as many psychotropic drugs prescribed for them as men. Women use health services more than men and may be more likely to make visits to their doctors for psychological reasons. They are also more likely to be given a drug prescription and, starting at age 20, use more medications of all types than men. As people get older, more of them use prescription psychotropic drugs; but the ratio of female to male use remains the same.<sup>47</sup>

Women are more likely to be affected by physiological factors that lead to their using the medical system more than men. This may result in women being frequently diagnosed with medical problems, such as depression or anxiety, that are commonly addressed by prescribing psychotropic drugs such as SSRIs. Cooperstock found that women are more likely than men to describe their problems in psychological or social terms and are, therefore, more likely to be diagnosed with psychoneurosis, anxiety or other instabilities.<sup>48</sup> Simoni-Wastila et al. found that office visits by women are more likely to result in psychotropic prescriptions than office visits by men, even after controlling for diagnosis, demographic variables, insurance status and speciality.<sup>49</sup>

A range of other factors may also have an influence on why more psychotropic drugs are prescribed for women.<sup>50</sup>

- Women experience more discrete physiological events than men (e.g., menstruation, pregnancy, lactation and menopause) that bring them into contact with the health care system. Many of these natural life events have been medicalized by pharmaceutical companies and labelled as disorders requiring drug treatment (e.g., menopause defined as a deficiency state).
- Women are more prone to chronic diseases such as arthritis, which brings them into more frequent contact with the health care system.
- Women visit doctors more often for non-somatic complaints such as depression or anxiety.
- Women may experience increased stress from multiple and changing roles, from lack of time for rest and play, from the loss of extended family support, or from single parenthood, all of which may be expressed as physical or psychological complaints.
- Women suffer more frequently from poverty or impoverished situations (e.g., substandard housing, limited pensions) that may be associated with depression or health problems.
- Women often work in jobs with high stress (e.g., as nurses, teachers and social workers). Morrisette found that 15% of professional working women were using psychotropic drugs to deal with pressures from work, problems at work, and stress, anxiety and tiredness.<sup>51</sup>
- Women are often victims of intimate/family violence, including childhood sexual abuse, which may result in anxiety or depression in adulthood.
- Men may handle feelings of distress outside of the medical system (for example, through alcohol consumption).



The 2003 Canadian Women's Health Surveillance Report reflects many of these findings. The report found that predictive factors for depression among women were: previous depressive episodes, feelings of being out of control or overwhelmed, chronic health problems, traumatic events in childhood or young adulthood, lack of emotional support and a low sense of mastery. Women who are lone parents and women who have chronic pain were more likely to experience depression.<sup>52</sup>

Other factors also account for women receiving more prescriptions for SSRI antidepressants than men. For over fifty years, pharmaceutical companies have promoted the concept that emotional distress experienced by women in reaction to normal or traumatic life events is actually a "biological disorder" requiring treatment by potent drugs.

### **The Growth of Biological Psychiatry**

According to Jonathan Metzl, a professor of Psychiatry and Women's Studies, Miltown (meprobamate), a muscle relaxant with sedative properties, was introduced in the 1950s as the first "wonder drug" to be aimed directly at women. It introduced the notion of chemical (drug) treatment for outpatient "neurosis" and paralleled the shift that was taking place in treatment from psychoanalysis to biological psychiatry (from "blaming the mother to blaming the brain"). Miltown became wildly popular; by 1956 it and other tranquilisers were taken by one in twenty Americans.<sup>53</sup>

A review of leading newsmagazines and women's magazines from the 1950s and 1960s found that articles and advice columns explained how, thanks to psychopharmacology, women's "emotional problems could be cured simply by visiting a doctor, obtaining a prescription and taking a pill." These problems ranged from "a wife's frigidity, to a bride's uncertainty, to a wife's infertility."<sup>54</sup>

Books like *Recognizing the Depressed Patient* (1961), which encouraged the diagnosis of depression in the general population by the general practitioner, rather than primarily by psychiatrists in hospitals, were also promoted by pharmaceutical companies, thereby significantly expanding the base of potential prescribers. The pharmaceutical company Merck bought 50,000 copies and distributed the book world-wide.<sup>55</sup>

The arrival of "biological (or chemically based) psychiatry" and the targeting of women helped set the stage for the marketing of a succession of psychotropic drugs, including benzodiazepines and later, the SSRIs. The marketing and promotion of SSRIs has intensified with the increase in the economic power and deregulation of the drug industry.

### **Pharmaceutical Companies and the Bottom Line**

Pharmaceutical companies are among the largest and most profitable multinational companies in the world. In 2002, global sales topped \$400 billion.<sup>56</sup> Like all other corporations, pharmaceutical companies are driven primarily by the need to increase profits, firstly, by retaining and expanding market share and, secondly, by keeping drug prices high. Every activity undertaken by drug companies, including political lobbying, efforts to protect patents,

publication of clinical trial results, and promotion of drugs to doctors and consumers, is driven by these economic imperatives.

It is now estimated that, in order to sustain *average* industry growth, a typical large pharmaceutical company needs 5-7 significant *new* products (new chemical entities or NCEs) each year. Since the introduction of antibiotics, drug innovation has decreased to such a degree that most companies can only bring two new NCEs to market annually. The lack of innovation, coupled with a demand for profits, has led to a large-scale structural reorganization of the pharmaceutical industry. This has included market acquisitions and consolidations, a focus on the development of multiple “me-too” drugs (basically copies of older drugs that offer no real advantage over older or related drugs) and the “gradual shift of core business away from the unpredictable and increasingly expensive task of creating drugs towards the steadier business of marketing them.”<sup>57</sup>

Reliance on high profit “blockbuster” drugs has now become an economic necessity for the pharmaceutical industry. Blockbusters accounted for 6% of the pharmaceutical market in 1991; this percentage rose to 45% by 2001. In 2001, SSRI antidepressants accounted for 10% of all blockbusters. The top five SSRIs each earned between \$1 billion and \$3 billion a year, despite there being very little difference among them.<sup>58</sup>

## **Selling the Theory of Depression**

In order to sell a product, drug companies need to convince people that they need it. Prior to the introduction of SSRIs, there was the perception that the “depression market” was limited. There was uncertainty about what “depression” was, and prevalence rates of severe depression were considered to be low and primarily restricted to longer-term hospitalized patients. Experts believed that depression was one of the psychiatric conditions with the *best* prognosis for recovery, with or without treatment. When drug companies were initially approached with discoveries of potential antidepressants in the 1950s, they showed little interest because they believed that the market potential at the time was simply not there.<sup>59</sup> Most people with mental distress were classified as anxious and efforts were spent promoting the major and minor tranquilisers.

As global marketing and the deregulation of industry expanded in the 1980s, the marketing potential for antidepressants was reassessed. Depression began to be promoted by pharmaceutical companies as a chemical “deficiency state”. The message delivered to doctors and consumers was that depressed people *needed* SSRI antidepressants to elevate their “depleted serotonin levels”, just as diabetics require insulin. This was an explanation anybody could understand.

You’ve got a lowering of some brain chemical and treatment will restore you to normal. Many who might have resisted a prescription for Valium shrugged and took Prozac – what could be wrong with restoring things to normal?<sup>60</sup>

The growing interest in SSRIs also coincided with increasingly negative reports about benzodiazepines and their potential for addiction. Benzodiazepines were the most prescribed psychotropic drugs at the time and SSRIs were initially promoted as being a safer, non-addictive alternative. Ironically, despite a forty-year history of documented adverse effects and

dependence/addiction problems, benzodiazepines continue to be prescribed to Canadian women on a regular basis to this day.

Pharmaceutical companies continued to promote the serotonin deficiency theory long after it had been dismissed by science. In addition to being the basis of an effective promotional campaign, the serotonin theory had other benefits. According to Medawar,

The serotonin hypothesis made depression seem more “normal” by reducing the “stigma” of mental illness ... it relieved patients of blame and responsibility, ... and scotched the possibility of being dependent on the drug.<sup>61</sup>

## **Redefining Depression and Expanding the Market**

Along with promoting the “serotonin deficiency theory”, drug manufacturers embarked on strategies to expand the market for depression by extending the meaning of depression to include *all* forms of “dysphoria” or sadness, and by expanding the use of SSRIs for a range of new “disorders” that drug companies helped to influence or define.

According to Edward Shorter, a professor in the history of medicine and author of *A History of Psychiatry*, the boundaries of what is now said to be depression have been expanded “relentlessly outward”. Although major intractable depression has been familiar for centuries (and usually applied to longer-term hospitalized patients), depression “in the vocabulary of post-1960’s psychiatry has become tantamount to dysphoria, meaning unhappiness, in combination with loss of appetite and difficulty sleeping.”<sup>62</sup> According to Arthur Kleinman, a psychiatry professor at Harvard and the co-author of *Culture and Depression*, “There is no question in my mind that severe clinical depression is a real disease... But mild depression is a totally different kettle of fish. It allows us to re-label as depression an enormous number of things.”<sup>63</sup>

In a feature article for the New York Times, author Kathryn Schultz shows how, in a short time, an entire society can be manipulated by the pharmaceutical industry to redefine its concepts of sickness and health. She notes that there was not even a term for mild depression in Japan until the pharmaceutical company Meiji Seika Kaisha began to promote the SSRI Depromel in 1999. According to Japanese psychiatrist Tooru Takahashi, melancholia, sensitivity and fragility were not negative things in a Japanese context. “It never occurred to us to try to remove them, because it never occurred to us that they were bad.”

Because direct-to-consumer advertising is banned in Japan, pharmaceutical companies relied on aggressive “public education campaigns” to spread the word about the highly prevalent new “disorder” called “kokoro no kaze”. Drug company representatives visited doctors on average twice a week to promote the prescription of SSRIs for symptoms like “heavy head, stiff shoulders, sleep problems, backache, tiredness, laziness and poor appetite.” According to the product manager for Paxil:

People (in Japan) didn’t know they were suffering from a disease. We felt it was important to reach out to them. The message was that ... depression can be cured by medicine.

Within five years, profits from SSRIs in Japan soared. From 1998 to 2003, SSRI sales in Japan quintupled and GlaxoSmithKline alone saw its sales of Paxil increase from (US\$) 108 million in 2001 to \$298 million in 2003.

According to Arthur Kleinman, the Japanese example has ominous implications. The ability of large corporations to “recast moods as medical problems” is one of the most powerful aspects of globalization and Japan has been at its leading edge.<sup>64</sup>

Simplistic screening tools that screen for, or appear to diagnose, depression have been one of the methods used to expand the boundaries of depression. High depression prevalence rates drawn from simplified screening or diagnostic checklists are used to demonstrate to the public, health care providers and funders that depression is common in the general population and that it is seriously under-treated.

Popular diagnostic tests, such as the self-administered Prime-MD (originally developed with funding from the drug company Pfizer) and the 12-question SPHERE (funded by Bristol-Myers-Squibb), are widely used and promoted in many health care and less formal settings. They are frequently used in drug-sponsored “information” campaigns and administered by mental health organizations or patient groups.

Family practitioners (who prescribe the vast majority of SSRIs) play an important role in this net-widening function. The developer of SPHERE, who received funding from the pharmaceutical industry, recommends that *everyone* visiting a doctor for any reason should be “tested” for a mental disorder, such as depression, even if they show no symptoms at the time of the visit. In an application of the SPHERE test, six out of ten patients visiting a doctor for non-psychological symptoms were classified as having a mental disorder.<sup>65</sup>

Because most general practitioners find the numerous case finding and screening questionnaires for depression too cumbersome and time consuming for routine use, Arroll recommends the use of a pre-test for depression consisting of only the following two questions:

- *During the past month have you often been bothered by feeling down, depressed or hopeless?*
- *During the past month have you often been bothered by little interest or pleasure in doing things?*<sup>66</sup>

Depression screening tests are administered widely in clinical settings that have been targeted by pharmaceutical companies. For example, the Edinburgh Postnatal Depression Scale (EPDS) is used to assess women during the postpartum period and is based on the assumption that, without screening, many women with postnatal depression will go undetected. According to Oates, the range of false positives from this test ranges from 30 to 70%. The author notes that, even when well used, it is designed to pick up minor depression that would benefit from extra time with a health visitor (“listening visit”), but the lack of counselling resources and skills results in many women with postnatal depression receiving antidepressants rather than non-drug assistance.<sup>67</sup>

The Change You Deserve

Are these symptoms of depression interfering with your life?

- Not involved with family and friends the way you used to be?
- Low on energy?
- Not motivated to do the things you once looked forward to doing?
- Not feeling as good as you used to?

If you're experiencing symptoms of depression and you're not where you want to be, talk to your doctor about your treatment options.

Depression Checklist Used by the Makers of Effexor.

“National Depression Screening Days”, held across Canada and in the US, provide depression screening in various settings such as community mental health clinics and government offices. Funding for these screening days is provided by Eli Lilly and Co., Forest Laboratories, GlaxoSmithKline, Pfizer Inc. and Wyeth. According to Edward Shorter, the American Psychiatric Association jubilates over “depression records set” by National Depression Screening Days every year.<sup>68</sup>

National health observance days held in Canada, such as Childhood Depression Awareness Day, National Anxiety Disorders Screening Day, Mental Health Month, National Suicide Awareness Week and National Trauma Awareness Month, also provide opportunities for drug companies, or their patient-group representatives, to get their key messages across: that depression is highly prevalent and is seriously under-treated.

Drug companies also target vulnerable groups and health professionals to promote these messages. For example, Wyeth sponsors forums on college campuses called “Depression in College: Real World and Real Issues” which feature doctors, psychologists and celebrities who talk to student populations about depression and the need to expand treatment.<sup>69</sup>

The trend towards widespread and involuntary screening for depression is assuming ominous proportions. President George W. Bush’s New Freedom Commission on Mental Health has proposed comprehensive “mental-illness” screening for all Americans. Screening would take place in schools and during doctor’s visits. According to Sheldon Richman, if this proposal is carried out, no child or adult would be safe from intrusive probing by “experts” backed by drug companies who believe that mental illness is woefully under-diagnosed and, therefore, that many millions of people ought to be taking powerful and expensive prescription drugs.<sup>70</sup>

## **Exaggerating the Risks**

As well as describing depression as being widespread in the general population and woefully under-treated, pharmaceutical companies actively promote the view that the costs of *not* treating depression are alarming.

Drug companies exaggerate the seriousness of depression in the general population by commonly quoting statistics that suggest 15% of people with depression have a lifetime risk of suicide (600 per 100,000 patient years). The inference is that this level of risk is associated with *anyone* who feels depressed and is not provided with treatment (such as an SSRI antidepressant). Dr. David Healy<sup>71</sup> notes that this 15% suicide risk estimate was drawn from a two-page 1970 paper, published in the British Journal of Psychiatry, which summarized studies in the German and Scandinavian literature of severely depressed *hospitalized* patients with chronic long-term depression *and* manic depression. Some of these patients may also have been exposed to the high risk, commonly used psychiatric drugs of this period.

Research for suicide rates in *primary* care depression shows variation from 0 to upper limits of 68 suicides per 100,000 person years for *all* affective disorders. As Charles Medawar notes, if suicide rates were really as high as suggested by pharmaceutical companies, then each family practitioner in the UK would have one patient per week commit suicide.<sup>72</sup>

In addition to exaggerating the likelihood of suicide resulting from depression experienced in the general (non-hospitalized) population, pharmaceutical companies have promoted the view that untreated depression results in enormous costs to society. For example, the national organization representing pharmaceutical companies in the US (PhRMA), along with the American Psychiatric Association, have developed a “depression calculator” to help employers in the workplace calculate the prevalence of depression and the financial benefits of assisting their employees who are battling depression.<sup>73</sup>

## Creating New Disorders

To expand market share and maximize profits, drug companies have expanded their scope outwards to include a variety of specific “new” disorders related to depression and anxiety. With the development of new disorders, such as social anxiety disorder, panic disorder, premenstrual dysphoric disorder and generalized anxiety disorder, pharmaceutical companies are also able to extend patent protection (exclusive rights to sell the drug for a period of years) for specific SSRIs. Patent extensions are enormously profitable for drug companies. According to Charles Medawar, GlaxoSmithKline won five patent extensions in the US for the SSRI Paxil between 1998 and 2001, extending the brand life for over five years. As a result, the company earned an additional \$1 billion per year.<sup>74</sup>

New disorders are often used to “reposition” an SSRI as it loses market share. GlaxoSmithKline had to reposition Paxil by promoting it for social anxiety and obsessive-compulsive disorder when another SSRI, Zoloft, became competitive. As a result of an aggressive promotional initiative, Social Anxiety Disorder quickly became America’s third most common mental illness. The promotional initiative was fronted by a coalition of non-profit patient and professional groups, but orchestrated by GlaxoSmithKline’s public relations agency. According to Dr. Marcia Angell, former Editor-in-Chief of the *New England Journal of Medicine* and author of *The Truth about the Drug Companies*, Paxil’s product director at the time stated that,

Every marketer’s dream is to find an unidentified or unknown market and develop it. That is what we were able to do with social anxiety disorder.<sup>75</sup>

Author and journalist Brendan Koerner, writing in *The Guardian* newspaper, outlines the strategy used by drug companies to market disease. The strategy is described as almost “mechanized” by Dr. Loren Mosher, a psychiatrist and former official at the National Institute of Health:

1. A focus is brought to a mild condition with a very large pool of potential sufferers (e.g., “premenstrual dysphoric disorder” or “generalized anxiety disorder”).
2. Pharmaceutical companies fund studies that prove the drug’s efficacy.
3. The FDA approves the drug based on a *limited* number of clinical trials that require proof only against placebos, not against other types of treatment.
4. Prominent doctors (often funded by drug companies) emphasize the seriousness and prevalence of the disorder in the popular press or in the medical literature.
5. Adverse drug reactions are minimized or not discussed in research publications or advertising.
6. Negative results from clinical trials are not published or made available.
7. Public relations companies are enlisted to promote the drug widely in the media. Statistics from corporate-funded studies are quoted to support the drug’s efficacy.

8. Patient groups are formed and funded to serve as the “public face” of the new disorder, supplying quotes and compelling personal stories for the media.<sup>76</sup>

The Diagnostic and Statistical Manual of Mental Disorders (DSM), a manual that defines and describes mental disorders, has also helped to expand the depression market. It is used worldwide and, throughout its history, has incorporated the dominant philosophy and cultural beliefs of the day. Psychoanalysts dominated the DSM naming committee for the first DSM in 1952, but by 1973 the DSM-III committee was made up of psychiatrists who believed in and promoted biological psychiatry, the theory that mental health problems result primarily from physical or pharmacological causes rather than life events or early life history. From this time, the number of identified mental disorders rapidly expanded. There were 106 mental disorders identified in DSM-I and over 350 in DSM-IV.<sup>77</sup>

Many new disorders have been identified with the involvement of pharmaceutical companies. For example, Dr. Paula Caplan, a psychologist and the author of several books on the DSM and methods used to define psychiatric disorders, notes that, in the late 1980s, influential DSM authors invented the alleged mental disorder now called “premenstrual dysphoric disorder” (PMDD) although there is no empirical proof that the “disorder” exists. From the beginning, the only recommended therapy for PMDD has been an SSRI, usually Prozac, even though premenstrual discomfort can be aided by diet, calcium supplements, exercise or group support. In June 1999, when Prozac’s patent was about to expire, its manufacturer, Eli Lilly, organized a roundtable of experts in the US to get PMDD approved – in order to extend Prozac’s patent life under the name Serafem. According to Caplan, the creation of Serafem extended Lilly’s patent on Prozac by seven years, thereby adding millions of dollars in profit.<sup>78</sup> Although the two drugs were the same, Serafem was sold at a higher price than Prozac.

## **Promoting SSRIs to Physicians**

Pharmaceutical companies spend two and a half times more on marketing and administration than on research and development, and this gap is growing. Between 1995 and 2000 the number of marketing staff working for US pharmaceutical companies increased by 60% while research staff declined by 29%.<sup>79</sup>

Physician promotion, which includes office and hospital-based promotion, provision of free samples and advertising in medical journals, makes up 85% of total promotional spending by pharmaceutical companies. Promotion to physicians increased 58% between 1996 and 2000.<sup>80</sup> It is estimated that pharmaceutical companies spend \$25,000 per year promoting drugs to each physician in the US (no comparable data is available in Canada).<sup>81</sup>

The provision of free drug samples to doctors helps to promote the over-use of SSRIs. In the US, during 2003, \$16.3 billion was spent providing free samples to physicians and hospitals. Another \$4 billion was spent on visits to doctor’s offices by drug company representatives.<sup>82</sup> In a systematic review of the influence of drug company gifts on doctors, psychiatrist and researcher Dr. Ashley Wazana concluded that “accepting samples was associated with awareness, preference and rapid prescription of a new drug and a positive attitude towards the pharmaceutical representatives.”<sup>83</sup>

According to Dr. David Healy, medical conventions such as those of the American Psychiatric Association have become promotional and marketing “circuses”, with pharmaceutical companies sponsoring limousine service, luxury hotel accommodations, meals, all registration and committee meetings, social events, publications, “special lectures”, and product samples. “Satellite symposia”, organized by pharmaceutical companies, are widely attended. Company-sponsored speakers use these platforms to speak uncritically about their own drugs. Many of these sessions are over-reported in the medical literature and give an inflated picture of the number and (positive) outcomes of clinical trials that have been held.<sup>84</sup>

Advertising in medical journals reinforces messages about drugs that are initially delivered through sales representatives. In a study of advertising in the American, British and Canadian Journals of Psychiatry, Munce et al. found that 57% of the psychotropic drug ads featured women; 67% of ads directed at the age groups 20-40 were for women as were 90% of the ads for the age group 81 plus.<sup>85</sup> Many of the psychotropic drug ads were misleading or unrealistic. All of the ads showing feeling states showed a progression from a negative to a positive state after drug treatment. The portrayals seen in the ads minimized the probability of treatment failure and troublesome adverse drug effects.

Clinical Practice Guidelines (CPGs) also play a major role in forming physician decisions about appropriate health care. CPGs are intended to present a synthesis of the evidence from clinical trials and recommendations of experts for the treatment of disorders like depression. They are widely published and adopted, are highly influential and may affect the practice of large numbers of physicians. In a review of North American and European CPGs for a variety of treatment areas, including depression, Choudhry et al. found that 87% of the authors had some form of interaction with the pharmaceutical industry. Almost 60% had relationships with companies whose drugs were considered in the guidelines. In the majority of cases, no conflict of interest declarations were made in the guidelines to indicate the possible bias of the authors.<sup>86</sup> Choudhry did not explore the impact of this bias on the content of the CPGs.

## **Changes in Physician Care and Funding of Care**

A substantial group of Canadians now lack their own family doctors or turn to walk-in clinics and emergency care for health assistance. Some of this care is impersonal and short term. In addition, general practitioners, who now prescribe 81% of the SSRIs, are frequently over-worked and may be unable to spend sufficient time with patients to discuss their emotional issues or distress in depth. For some doctors, SSRIs may appear to provide a quick solution for patient problems arising from normal life events such as bereavement, menopause, work stress, retirement or marital conflict.

In addition, payment for medical treatment under most medical/drug insurance plans may not cover more extensive counselling and cognitive therapy, but does cover visits which result in drug recommendations to treat depression. Research indicates that, in the US, psychiatric treatment has also become more oriented to medications. Olfson found that, in the US, between 1985 and 1995, visits to office-based psychiatrists became shorter, less often included psychotherapy and more often resulted in a prescription for medication. The number of visits that were ten minutes or less in length increased.<sup>87</sup> It is unclear whether the same trend exists in Canada.



## **Promoting SSRIs Directly to Consumers**

In 2000, GlaxoSmithKline spent \$91.8 million advertising the SSRI Paxil in the US, almost \$15 million more than Nike spent advertising its top brands of running shoes. This level of spending was associated with a \$355.6 million increase in sales between 1999 and 2000.<sup>88</sup>

The amount spent on direct-to-consumer advertising, or DTCA, has increased in the US from \$26.6 million in 1994<sup>89</sup> to nearly \$3.2 billion in 2003.<sup>90</sup> The increased spending on DTCA is primarily accounted for by television advertising. Although DTCA on Canadian television is illegal, with the exception of “reminder” or “help seeking ads”, most Canadians see explicit drug advertising on US television and in US periodicals on a regular basis.

DTCA has been dramatically successful in increasing the public recognition of specific drugs; this type of public awareness increased from 39% in 1993 to 91% in 2000. Research also indicates that about a third of those who see a drug ad talk to their doctor about the specific drug seen advertised; of those, 6-9% directly request the drug and, of these, 80-84% receive it. Market research, funded by pharmaceutical companies, reports a dramatic increase in patient requests for drug treatments for those conditions that have been specifically targeted by DTCA.<sup>91</sup>

Pharmaceutical company promotional efforts are highly responsive to “opportunities” created by the “marketplace”. After treatment for generalized anxiety disorder was approved, and shortly after September 11, 2001, Marcia Angell notes that GlaxoSmithKline launched an ambitious campaign promoting the use of Paxil.

Commercials showed images of the World Trade Centre towers collapsing. And who didn't feel anxious about that? But the implication was that even this perfectly appropriate (and, for most people, temporary) anxiety should be treated with drugs.<sup>92</sup>

## **Using Non-Profit and Patient Groups to Promote SSRIs**

Pharmaceutical companies are aware that the public, particularly older people, are sceptical of the claims made in advertising. By contrast, non-profit, community-based organizations are not only well known, but are given a high rating of trust by most people.

Furthermore, citizens prefer to support non-profit organizations and are likely to be positive about drug company campaigns associated with them. Consumers also believe that the products associated with non-profit organizations are safe and are fully endorsed by these organizations.<sup>93</sup>

For these reasons, pharmaceutical companies deliberately use non-profit organizations to: (1) increase sales of specific products, (2) increase their reputation as good corporate citizens, (3) build brand loyalties, (4) help in the differentiation of products, and (5) help develop relationships with potential customers.

Existing patient groups, or those specifically created by pharmaceutical companies, are commonly used to indirectly or directly promote SSRIs and other drugs. Most patient campaigns begin with “unrestricted educational grants” or other funding and are geared towards increasing recognition of the “disorder”. Eli Lilly, the manufacturer of Prozac, along with 17 other manufacturers of psychoactive drugs, provided millions of dollars to the National Alliance of the

Mentally Ill (NAMI), the biggest patient group in the US mental illness field. Soon NAMI was aggressively promoting the slogan “mind illnesses are brain illnesses” and recommending that treatment availability be expanded.<sup>94</sup> Patient groups are often used to increase sales by making “disorders” more widely known and to increase pressure on government or private health insurers to pay for drug treatment.<sup>95</sup>

Individual patients are also commonly used to reinforce advertising messages. According to Healy,

The promotion of a new antidepressant by the end of the 1990s commonly meant a patient on the speakers’ panel, even for a medical conference. At meetings open to the press, patient speakers were almost more important than medical experts. They could offer journalists a simplistic story of how the correction of low brain aminos by antidepressants put people right. By then this was a message few psycho-pharmacologists would have been happy to present.<sup>96</sup>

## **Lack of Government Regulation and Oversight as a Contributing Factor**

A lack of government regulation and oversight may contribute indirectly to high SSRI prescription levels. Health Canada does not require that the results of any clinical trials be made public. In the case of the SSRIs, negative clinical results were not publicized. This gives the public and health professionals an overly favourable view of the safety and efficacy of SSRIs.

Although direct-to-consumer advertising is illegal in Canada, Health Canada has, without public consultation or due process, changed the application of the law to permit “help-seeking” and reminder ads that direct consumers to seek help (from specific drug companies) if they are depressed. In addition, Canadians are constantly exposed to American television and advertising. Health Canada provides no regulatory control over this type of pharmaceutical advertising.

Because most clinical trials for SSRIs last only six weeks, an on-going, active (post-market) surveillance system is essential in order to identify potential harm caused by a drug after it has been approved and is being prescribed to the general population. Currently Health Canada funds and supports a very weak and passive post-market reporting system - the Canadian Adverse Drug Reaction (ADR) Monitoring Program. Under this program several regional ADR centres are funded with minimal budgets and staff allocations. There is no formal or accessible system through which the public can review adverse drug reactions reported by the public, health care providers and hospitals.

Without a robust reporting system, most adverse drug reactions go unreported. It is estimated that fewer than 1% of physicians make ADR reports on drugs they prescribe. For example, as of October 1999, there were over 2,000 deaths by suicide associated with the SSRI Prozac, according to the US FDA’s Adverse Events Database. The FDA acknowledges that their database picks up only 1-10% of serious adverse events.<sup>97</sup>

## **The Implications of Marketing Depression and the Over-prescribing of SSRIs to Women**

The marketing of depression and the high incidence of SSRI prescribing means that more women experiencing minor symptoms of distress common to everyday living will be convinced that they have a mental disorder that requires treatment, and that the optimum treatment is medication, most frequently an SSRI. Because many doctors do not recognize the harm and addiction potential of SSRIs, women already taking these drugs may develop a range of problems and have more drugs prescribed to counter these drug-induced symptoms. Some studies have already noted that women who take SSRIs are more likely to be taking other psychotropic drugs like benzodiazepines (tranquillisers) and sleeping pills.

Psychotropic drug prescriptions are the major driver of increasing drug prescription expenditures. Because SSRIs are more costly than older psychotropic medications, they have already created pressures on public and private health plans. Unsustainable prescription drug costs will ultimately create pressures on health systems and insurers to reduce spending in other areas or to decrease benefits.

## **Responding Effectively to the Emotional Distress of Women**

One of the impacts of the dominance of biological psychiatry and the over-emphasis on treatment by antidepressants has been an erosion of funding for alternative non-drug options to address the emotional distress of women.

Cognitive or “talk” therapy, group or peer support, regular exercise, and nutritional changes have all been shown to reduce emotional distress, improve mood and decrease depressive symptoms. A number of studies have demonstrated the effectiveness of exercise in addressing symptoms. In a study exploring the effects of aerobic exercise and Zoloft on depression, Blumenthal et al. found that 16 weeks of treatment exercise was equivalent to medication in reducing major depression among older people.<sup>98</sup> Dr. Madhukar Trivedi, professor of psychiatry and director of a mood disorders program, found that participating in aerobic exercise for 30 minutes, three to five times a week, could dramatically reduce the symptoms of mild to moderate depression.<sup>99</sup> Non-drug alternatives do not expose patients to adverse drug reactions and are likely to have other health benefits. However, funding to promote these methods and to assess their outcomes has been meager. Community-based health services are limited. As a result, these strategies are under-valued, poorly promoted and under-utilized.

The “green prescription movement” may provide a sense of what an alternative, “non-drug” model to promote health could look like. In New Zealand, doctors can formally write a specific “green prescription” prescribing exercise and nutritional changes to help address health problems such as diabetes and cardiovascular disease. The patient is monitored and provided with concrete support (e.g., training support, access to gym or equipment) to meet his/her goals.<sup>100</sup> While not specific to depression, an expanded model of this type, supporting non-drug approaches, could be a useful strategy to help women cope with personal distress.

Much of the distress that women experience is related to their historical roles, sense of powerlessness and the demands of their multiple roles. The bio-chemical theory of depression, promoted by pharmaceutical companies, takes the onus away from societal institutions to

identify and *change* the factors that contribute to women's stress, sadness and worry. Emotional distress is often linked to poverty, violence, poor housing, past trauma, job stress, time stress, unpaid caregiving and lack of community support, all of which need to be addressed through public policy and broader social change. Strategies to address women's emotional distress would include a reduction of income inequities, improvements in wages, welfare and disability rates, addressing violence towards women and children, and implementing comprehensive home support and daycare programs.

The overall effect of the medicalization of depression and the promotion and over-prescription of SSRIs may be to disempower both women and society. As noted by Moynihan,

Death, pain and sadness are part of being human. All cultures have developed means to help people cope with all three. Indeed, health can even be defined as being successful in coping with these realities. Modern medicine has, unfortunately, destroyed these cultural and individual capacities, launching instead an inhuman attempt to defeat death, pain and sickness. It has sapped the will of the people to find their own way. People want to be taught, moved, treated or guided rather than to learn, to heal and to find their own way.<sup>101</sup>

*A series of recommendations related to this topic have been formulated by the Women & Health Protection Steering Committee and are appended.*

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## **Recommendations from Women & Health Protection on SSRIs**

### **1. Recommendations regarding the approval, monitoring, marketing and provision of SSRIs**

- i. Health Canada should make public the data from all clinical trials involving SSRI drugs, including all serious adverse events reported during the trials, as well as the comments of Health Canada reviewers about the data.
- ii. Health Canada should require clinical trials to include meaningful outcome measures and include all groups of patients with whom a drug will be used: specifically trials for antidepressants should include women aged 65 and older. The groups should be of sufficient size to permit sub-group analyses.
- iii. Health Canada should require that clinical trials extend over prolonged periods of time, to reflect the time period that patients will be taking antidepressants.
- iv. Health Canada should require clinical trials to include testing of SSRI dependency by extending trials to include a withdrawal phase.
- v. Health Canada should actively promote limiting use of SSRIs to indicated populations. Health Canada's passive approach, for example not granting a license to SSRIs for adolescents, has proven inadequate to limit SSRI use in this vulnerable population. Direct instruction not to prescribe is required.
- vi. Health Canada should require clinical trials of SSRIs to include treatment arms with effective, non-pharmacologic ways of treating depression.
- vii. Health Canada should require that all safety advisories be included with any SSRIs prescribed. Safety advisories should state how often different reactions occur. Safety warnings should be pre-cleared by Health Canada and an advisory group consisting of consumers and health care professionals.
- viii. Labelling of SSRIs should include specific information on withdrawal symptoms and effects.
- ix. Informational inserts provided with SSRIs should include information on alternative, non-pharmacologic approaches to the treatment of depression.

### **2. Recommendation regarding the federal Mental Health Strategy:**

- i. The "Second Report on Mental Health and Mental Illness in Canada" should include a gender-based analysis.
- ii. Time stress measurements by gender, collected by Statistics Canada, should be used as one of the mental health indicators.

### **3. Recommendations to federal health research funding bodies and provincial ministers of health:**

- i. The Canadian Institutes of Health Research should privilege the funding of research into non-pharmacologic ways of treating depression and ensure that the results of these trials are made publicly known.
- ii. The green prescription model, used in New Zealand, should be implemented by:
  - rewarding doctors who use this approach (with direct benefit to reducing costs to provincial drug formularies);
  - allocating resources for non-drug treatment models: primary care reform should include funding for counselling, body work and exercise;
  - improving community health services.

#### **4. Other recommendations:**

- i. Health Canada should fund independent consumer groups to provide information about depression and its treatment.
- ii. Health Canada should resist any pressure to broaden the definition and diagnosis of depression and instead encourage healthy debate on alternative methods of coping with day-to-day stress and promote broader systemic change to improve the conditions of people's lives.
- iii. There should be a significant increase in funding for Health Canada's post-marketing surveillance system. Health Canada should institute an active surveillance system rather than relying on reports of adverse drug reactions (ADRs). Safety warnings should include a message to consumers to report any ADRs either directly to Health Canada (with instructions about how to do so) or to their doctor or pharmacist.
- iv. Health Canada should not approve direct-to-consumer advertising (DTCA) and should ban "help seeking" and "reminder" ads, or severely restrict their content.

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