A REPORT ON THE USE OF PSYCHIATRIC MEDICATIONS
THEIR SAFETY AND EFFICACY

Providing a Detailed Meta-Analysis

A NON-PROFIT SUPPORT FOR THE MENTALLY ILL
• Research into the use of medications in the U.S. demonstrates that over 200,000 deaths are created within the hospital setting annually. Additionally over 2.1 million serious injuries take place. These occur from properly prescribed medications. Adverse Drug Reactions (ADRs) make these reactions between the fourth and sixth leading cause of death. In the year 2000 medication ADRs, drug related morbidity and mortality exceeded $177.4 billion in the ambulatory setting in the United States. The largest component of this total cost was associated with drug related hospitalizations. Since 1995, the cost of drug related problems have more than doubled.

• Data from numerous studies are demonstrating that clinical efficacy is not sufficient to warrant the risk of prescribing some of the most commonly used psychiatric medications.

• Extensive research shows that psychiatric medications are actually producing serious patient illness and hospitalizations.

• Relapse into hospital for a psychiatric patient is a common event in spite of continual medication maintenance treatment. Data shows a 5-year relapse rate to be well over 70% in spite of optimal pharmacological treatment.

• Of great concern is the growing evidence that many psychiatric medications raise the risk of cancer, addiction, and suicide. For instance, a woman taking certain psychiatric medications more than doubles her risk of ovarian cancer. Indeed, the use of one antidepressant Paxil (Paroxetine) is a greater risk factor for cancer than is smoking.

ADVERSE DRUG REACTIONS (ADRs)

In 1998 researchers at the University of Toronto reviewed adverse drug reactions (ADRs) in U.S. hospitals. Estimations using 1994 data showed that there were 106,000 fatalities and over 2.1 million serious complications requiring hospitalization due to ADRs. “The study excluded errors in drug administration, noncompliance, overdose, drug abuse, therapeutic failures, and possible ADRs.” These deaths or injuries resulted from properly prescribed medications. The researchers stated, “The incidence of serious and fatal ADRs in U.S. hospitals was found to be extremely high.” 106,000 people had fatal ADRs while hospitalized, “making these reactions between the fourth and sixth leading cause of death.”

In 1995 Johnson and Bootman published a study in the Archives of Internal Medicine in which they stated, “drug related morbidity and mortality was estimated to cost $76.6 billion in the ambulatory setting in the United States.”

Based on 1992 figures, these same investigators stated that “the number of admissions that was estimated from the model suggested that 28.8% of all hospital admissions were a result of drug – related morbidity and mortality…Our results indicate that drug – related morbidity and mortality should be considered one of the leading diseases in terms of resources consumed…The estimated number of deaths owing to ADRs (drug related problems) ranged from 79,159 to 198,815 deaths.”

A 2001 update to the 1995 Johnson – Bootman study completed by Ernst and Grizzle at the
University of Arizona, concluded that overall, the cost of U.S. drug related morbidity and mortality exceed $177.4 billion in the year 2000 with over 200,000 deaths created annually. The largest component of this total cost was associated with drug related hospitalizations. Since 1995, the cost of drug related problems have more than doubled “Strategies for preventing drug-related morbidity and mortality are urgently needed.”

The Institute of Medicine, a section of the prestigious National Academy of Sciences, reported in 1999 that as many as 98,000 people die every year in U.S. hospitals from medical errors. Many deaths are attributable to the use of medications. The report stimulated a swift response from Congress when the US President ordered congressional hearings into the matter.

Applying the above data to Canada, based on U.S. – Canadian population figures, approximately 20,000 deaths per annum occur from ADR’s at a cost of 17.7 billion dollars.

**IS CLINICAL EFFICACY A REALITY?**

In the past two years there have been a number of media stories on the extreme side effects of certain psychiatric medications. Providing a question as to efficacy is the 1998 report published in the APA Journal entitled “Listening to Prozac but Hearing Placebo”, the article details the meta-analysis of 19 drug studies. In short, the research showed that 75% of the “beneficial effect” of anti-depressant medication can be attributed to placebo effect.

A July 5, 2002 study also published in the APA Journal by Kirsch et al. analyzed all of the data submitted to the U.S. Food and Drug Administration (FDA) for approval of the six most widely prescribed antidepressants between 1987 and 1999. More than half of the 47 studies found that patients on antidepressants improved no more than those on placebos, Kirsch says. “They should have told the American public about this. The drugs have been touted as much more effective than they are.”

Research is showing that a significant number of serious side effects creating hospitalization admissions and even death (e.g. depression, cardiac arrest, serotonin syndrome, fatal poisoning etc.) are produced by the medications themselves. Many studies have supported these findings.
The New England Journal of Medicine, released on April 17, 2003, indicated that **1 in 4 patients receiving a medication prescription would be injured by that prescription.** The study presented by Gandhi et al. revealed that the greatest source of injury was produced by the SSRI antidepressant type medications. "It is a problem that is common, in many cases the impact could be prevented or reduced, and it has a large impact on patients", said Tejal Gandhi an internist at Brigham and Women’s Hospital in Boston, a Harvard University Facility.

More than 200,000 Canadian school children take Ritalin (methylphenidate), yet the Canadian Medical Association Journal says the clinical trials of this drug have often been biased and poorly constructed. The Canadian article reviewed 62 randomized trials that involved a total of 2897 participants with a primary diagnosis of ADHD. The article stated, “However, these apparent beneficial effects are tempered by a strong indication of publication bias and the lack of robustness of the findings, especially those involving ADD features. **Methylphenidate also has an adverse event profile that requires consideration.**” In other words, these researchers believed that studies have tended to minimize the negative side effects of Ritalin.

Brain research carried out at John Hopkins University has shown that methamphetamine is toxic and damaging to both dopamine and serotonin brain neurons. In studies with laboratory rats, methamphetamine fed at 4 mg/day for only 3 days caused nerve fiber degeneration. Brain cells were permanently damaged by methamphetamine. Much more research is needed on the possible adverse effects of psychiatric medications on brain cells, especially in developing brains.

**RELAPSE IN SPITE OF MEDICATION**

Relapsing into a psychotic, depressive or bipolar episode while on medications is a common occurrence that leaves the patient crippled and despairing. Career, family, education etc. are put on hold while the patient works through the episode. Often, medication changes are initiated at this point, sometimes exacerbating the episode while the physicians attempt to bring a state of chemical balance into the patient’s life. For the safety of the patient, hospitalization often occurs at this point, creating an even greater burden for the already overtaxed medical system. In spite of the best of medications, this revolving door phenomenon occurs all too often.

Gitlin et. al. reported in bipolar patients that despite continual medication maintenance treatment, data “indicated a 5-year risk of relapse into mania or depression of 73%.” Of those who relapsed, two-thirds had multiple relapses. Relapse could not be attributed to inadequate medication. Even for those who did not relapse, the presence of significant mood symptoms was observed. “Even aggressive pharmacological maintenance treatment does not prevent relatively poor outcome in a significant number of bipolar patients.”

Licht et al. reported significant relapse in 148 patients using only lithium as a mood stabilizer, thirty-two (21.6%) patients were readmitted within two years with a new affective disorder episode.

In another relapse study, 15 patients with bipolar I disorder, who relapsed while on lithium despite positive initial response and adequate compliance, were treated by cognitive-behavioral methods in an open trial. In follow-up ranging from 2-9 years, 5 of the 15 patients (33%) experienced a new affective episode.

A study involving two groups of patients taking either risperidone or haloperidol showed that the risk of relapse of schizophrenia was 34% for the former and 60% for the latter. Many mentally disordered individuals travel a “revolving door”. Their episodes of relapse can be devastating, destroying their hopes for wellness, as well as their careers and family stability.

**Summary:**

Psychiatric medications do not overcome the risk for relapse which is very high for both affective disorders and psychosis.
SIDE EFFECTS - THE UNTOLD DANGER

Table 2 Below shows the top ten most commonly prescribed psychiatric medications in the U.S. for the year 2000. We will now review each one individually for side effects. The information in the following is somewhat limited. In other words the side effects presented by these medications are more extensive than indicated.

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Benzodiazapine Class of Medications

Benzodiazapine Addiction & Withdrawal:
In Canada the benzodiazapines are considered to be a controlled medication. The Canadian Compendium of Pharmaceuticals and Specialties (CPS) quotes the following side effects for the benzodiazapines:

**WARNINGS:** Benzodiazapines are not recommended for use in patients with a major depressive disorder or psychosis in which anxiety is not a prominent feature. **PRECAUTIONS:** Benzodiazapines may cause psychologic or physical dependence... Abrupt (or gradual reduction) of benzodiazapines may lead to symptoms such as anxiety, insomnia, irritability, gastrointestinal discomfort, anorexia, diaphoresis, photophobia, or increased sensitivity to noise. More severe symptoms may occur such as confusion, depersonalization, myoclonus, delirium, psychosis, or seizures.

Health Canada made the following statements in their report entitled “The Effects of Tranquillization: Benzodiazapine Use in Canada.”

- “The major indication of dependence is the development of withdrawal symptoms, which have been now clearly established at therapeutic dose levels.”
- “The high incidence of withdrawal symptoms suggests that a substantial minority of patients taking benzodiazapines chronically are pharmacologically dependent.”
- “One such carefully controlled study of withdrawal symptoms in patients who had been on low doses of benzodiazapines for a mean of 3.6 years, found between 27 and 45 percent evidencing clear withdrawal symptoms.”
- Babies have been born in an addicted state to mothers using benzodiazapines: “neonates born to drug-dependent women have shown withdrawal symptoms.”

Addiction of unborn and newly born children is a major phenomenon. Medication withdrawal syndromes have been observed increasingly in children with mothers using psychotropic medications. Research into babies suffering with Neonatal Withdrawal Syndrome report the following symptoms: continuous high-pitched cry, frantic sucking of fists, tremors, poor sucking response, sweating, and in some cases convulsions.

Cancer Risk from Benzodiazapine and Antidepressant Usage
Two studies have reported a positive association between antidepressant and benzodiazapine use and the development of cancer. Harlow and Cramer carried out a case control study of ovarian cancer incidence and obtained an adjusted risk ratio of 2.1, indicating that use of these medications for
more than 1-6 months resulted in more than doubling a woman’s risk of ovarian cancer. Among women who first used these drugs before age 50 years the odds ratio was 3.5. Among those who used them more than 10 years, the risk increased to 9.7.

Dalton and colleagues recently conducted a population-based study that followed for 7 years a total of 30,807 adult antidepressant users. They found an increased risk of non-Hodgkin’s lymphoma among subjects who received greater than 5 prescriptions.

Indiscriminate and Irresponsible Prescribing of Benzodiazepines by Medical Practitioners
Treatment guidelines in the U.K. recommend the use of benzodiazepines for a maximum of 4 weeks. In Canada and the U.S. it is common practice to prescribe these medications for years.

Health Canada guidelines recommend prescribing only for short term use: “continuous use should not exceed two weeks.”

“The costs of continued use of benzodiazepines require careful consideration. The concern with payment must extend beyond the price of prescriptions to the total cost to the health care system. Inappropriate prescribing may well keep individuals visiting physicians... for considerably longer than necessary.” Many studies have supported this position.

SSRI Class of Medications
2. Zoloft (Sertraline), 3. Prozac (Fluoxetine), 4. Paxil (Paroxetine)

Cancer Risks Associated With Paxil Usage
The American Journal of Epidemiology published two studies in 2000 by Cotterchio and colleagues which demonstrated that Paxil presented a 720% increase in risk of breast cancer in females. The Canadian Cancer Society website indicates that for heavy smokers there is a 400% increase in risk for cancer. In other words, Paxil use creates a greater risk factor for breast cancer than heavy smoking. With over 3,000,000 Canadian prescriptions for Paxil in the year 2000 this is major cause for concern.

SSRI's and Withdrawal Symptoms
On February 2, 2002 the British Medical Journal published an article entitled “Withdrawal from paroxetine can be severe, warns FDA”. The article outlined in detail how paroxetine (Paxil) creates dependence and withdrawal in a significant percentage of patients. “This drug has been promoted as safe and easy to discontinue,” said Charles Medawar, head of Social Audit. “The fact that it can cause intolerable withdrawal symptoms of this kind and lead to dependence is enormously important...” Dr. Peter Haddad, consultant psychiatrist for Salfords Mental Health Service NHS Trust, welcomed the FDA’s safety warning. He said, “Withdrawal side effects from antidepressants are far more common than many people realize.”

The FDA issued a warning about Paxil on December 14, 2001. “During Paxil marketing, there have been spontaneous reports of similar adverse events... upon the discontinuation of Paxil (particularly when abrupt), including the following: dizziness, sensory disturbances (e.g., paresthesias such as electric shock sensations), agitation, anxiety, nausea, and sweating. These events are generally self-limiting. Similar events have been reported for other selective serotonin reuptake inhibitors.”

The above FDA statement describes some of
the symptoms of protracted withdrawal. In some cases these symptoms can persist for a number of years.

Studies involving other SSRI’s including Luvox showed negative results in drug withdrawal. A group of French researchers reported severe withdrawal syndromes in 6 patients prescribed Effexor (Venlafaxine). There have been hundreds of studies published in the medical literature which demonstrate the significant symptoms that are produced when withdrawing from SSRI drug treatment. .

ABC News reported on May 24, 2001 that “up to 85% of patients who take these kinds of drugs (SSRIs) may have some type of symptom when they stop, studies say. According to recent research in the *Journal of Clinical Psychiatry*, as many as 70% of General Practitioners and 30% of psychiatrists do not know about the side effects of ending serotonin boosting drugs. Getting off these drugs properly is an issue that is underappreciated,” says Dr. Alexander Bodkin, director of the clinical psychopharmacology research program at Mclean Hospital. “These drugs are being prescribed without the full knowledge of how they should be monitored.”

As with the benzodiazepines, babies have been born in an addicted or toxic state to mothers using SSRIs.

**Akathisia from SSRIs**

Akathisia is a medication-induced disorder consisting of extreme restlessness, irritability and agitation. It is often associated with the withdrawal symptoms of insomnia, headaches, nervousness, anxiety, anorexia, tremors, weight loss, nausea, diarrhea and can be coupled with suicidal ideation, homicidal thoughts and or acts.

The number of people using psychotropic medication who suffer with Akathisia is significant. A study on Prozac reported in the *Journal of Clinical Psychiatry* estimated that the number of Prozac users who experience Akathisia is between 10 and 25%. There are numerous studies relating psychotropic medication-induced Akathisia with suicidal, homicidal, and violent behavior. As reported in a two-year study, Akathisia may create an inability to control impulses.

**SSRIs and Suicide**

Other researchers found that patients suffering Prozac-induced Akathisia became preoccupied with thoughts of suicide. Symptoms of agitation, panic, anxiety, mania and Akathisia can prompt suicidal or violent acts. Akathisia and associated extreme acts of violence have been reported with other categories of psychiatric medication. For instance, Haldol-induced Akathisia was reported in three patients who attacked other people or committed murder.

Paxil (Seroxat) has been found to increase suicidal ideation and suicide in youth. “New expert advice recommends that the drug Seroxat (paroxetine) is not used to treat children and teenagers under the age of 18 years”, said Professor Alasdair Breckenridge, Chairman of the U.K. Medicines and Healthcare Products Regulatory Agency. “It has become clear that the benefits of Seroxat in children for the treatment of depressive illness do not outweigh these risks.” The British government has now prohibited sales of Paxil (Seroxat) for youth under the age of 18.

There have been a number of lawsuits involving medication and Akathisia. The following is an Associated Press release:

**CHEYENNE, Wyo.** (AP) June 6, 2001: “The manufacturer of the nation’s second-best-selling anti-depressant must pay $8 million to the relatives of a man who killed himself and three others after taking the drug Paxil, jurors said.

Jurors in U.S. District Court considering the wrongful death civil suit returned a verdict against SmithKline Beecham today. They received the case Tuesday afternoon. Relatives of Donald Schell, 60, claim the man, originally from Gillette, Wyo., took two Paxil tablets
before shooting his wife, their daughter, his granddaughter and himself to death on Feb. 13, 1998.”

Research published in the American Journal of Psychiatry supports the possibility that SSRI medications may induce suicidal ideation in some patients. The study, by Teicher and colleagues at Harvard Medical School, reported on six patients who were depressed but not suicidal before they started taking SSRI medication. Within a few weeks of taking the drug, the patients experienced “intense, violent suicidal preoccupation.”

Another important study involving children and adolescents and the use of Prozac demonstrated self destructive phenomena created by Akathisia.

Psychiatric medications in other categories:

6. Amitriptyline (Elavil)
Amitriptyline is a tricyclic antidepressant with many side effects, as demonstrated by the following:

“Depressed patients, particularly those with known manic-depressive illness, may experience a shift to mania or hypomania. Schizophrenic patients may develop increased symptoms of psychosis; patients with paranoid symptomatology may have an exaggeration of such symptoms. Tricyclic antidepressant drugs, including amitriptyline HCl, particularly when given in high doses, have been reported to produce arrhythmias, sinus tachycardia, and prolongation of the conduction time. Myocardial infarction and stroke have been reported with drugs of this class. After prolonged administration, abrupt cessation of treatment may produce nausea, headache, and malaise. Gradual dosage reduction has been reported to produce, within two weeks, transient symptoms including irritability, restlessness, and dream and sleep disturbance.”

In a recently published study on “The effects of tricyclic antidepressants on breast cancer risk” published in the British Journal of Cancer, a number of the tricyclics were implicated in raising the risk of breast cancer. Amitriptyline was an exception, and was not shown to increase cancer risk rate, while some of the other TCA’s (tricyclic antidepressants) did.

A number of studies have shown that tricyclic medications have induced manic episodes in patients suffering with various mental disorders.

7. Ambien (Zolpidem)
Ambien is commonly used as a sleep aid. Like the other top ten medications, it has a number of negative side effects. The following adverse events included in DSM-III-R criteria for uncomplicated sedative/hypnotic withdrawal were reported during U.S. clinical trials following placebo substitution occurring within 48 hours following last Zolpidem treatment: fatigue, nausea, flushing, lightheadedness, uncontrolled crying, emesis, stomach cramps, panic attack, nervousness, and abdominal discomfort. There have been adverse events reported such as delirium, nightmares and or mania being induced in patients using Zolpidem. Research is also showing that Zolpidem may create dependence in some patients.

8. Desyrel (Trazodone)
Trazodone is also used as a common sleep aid. Research has shown numerous negative events associated with Desyrel usage.

Summary
Hundreds of studies suggest that further research is needed on the safety of psychiatric medications. ADRs are a major cause of illness and death. The top ten most prescribed psychotropic medications exhibit serious and dangerous side effects. Addiction and withdrawal have become huge problems for many patients using psychotropic medications. The efficacy of these medications is also being questioned by many psychiatrists and especially by the patients using them.
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