Manufacturing Addiction

The Over-Prescription of Benzodiazepines and Sleeping Pills to Women in Canada

The addictive nature of benzodiazepines and their profound effects on the brain and body have been known for over 40 years, yet these drugs are among the most widely prescribed in Canada and the world today. The over-prescription of benzodiazepines to women in Canada was first identified as a critical health care issue in the 1970s, yet it is estimated that 3 to 15% of any adult population is using and may be addicted to this class of drugs and of this group 60 to 65% are women. Physicians prescribe benzodiazepines (tranquilizers) and sleeping pills to help women cope with work or family stress, pre-menstrual syndrome, grief, and adjustment to life events such as childbirth and menopause, or for chronic illness and pain. Non-drug treatments for these circumstances and conditions are under-promoted and under-used.

Benzodiazepines impair cognitive functioning, memory and balance at therapeutic dose levels and because they are often prescribed to women for longer than the recommended time period (a maximum of two to four weeks), women are also at particular risk of involuntary addiction. The majority of those who take the drugs at recommended doses for more than one or two months will become dependent. Fifty to one hundred percent will experience difficulties withdrawing and recovering. Short-term use also puts women at risk of a variety of other health problems. Sleeping pills, while not technically benzodiazepines, act by the same mechanisms and have the same effects.

A comprehensive health policy and action plan is urgently needed to restrict benzodiazepines and sleeping pill use and to help those who are dependent. This paper outlines the pharmacology of benzodiazepines, prescribing rates and practices in Canada, the over-prescription to women, withdrawal and recovery from addiction, the socio-economic costs of addiction and associated health problems, and drug company advertising to women. Specific recommendations for health policy and programming conclude the paper.

It is estimated that 3 to 15% of any adult population is using and may be addicted to benzodiazepines. Of this group 60 to 65% are women.

What are Benzodiazepines?

The first benzodiazepines (commonly known as tranquilizers) were marketed in 1960. They were initially described as a safe, non-habit-forming substitute for barbiturates which, after many years of being prescribed, were found to be dangerously addictive. Only one year after benzodiazepines appeared on the market, the first report in the medical literature describing their addictive nature was published.[1]

Benzodiazepines are central nervous system depressants that act in complex ways on the neurotransmitter GABA (gamma-aminobutyric acid), which transmits messages from one brain cell to another. Directly or indirectly, benzodiazepines influence almost every brain function and ultimately most biological systems, including the central nervous, neuromuscular, endocrine and gastrointestinal.

About 16 benzodiazepines are available in Canada today. Among the most common are Ativan (lorazepam), Serax (oxazepam), Rivotril and Klonopin (clonazepam), Xanax (alprazolam) and Valium (diazepam). Sleeping pills (hypnotics) such as Ambien (zolpidem) and Imovane (zopiclone) are not technically benzodiazepines, but they act by the same mechanisms and have the same effects on the brain and body.

All benzodiazepines and sleeping pills are similar chemically but differ in potency (equivalent doses may vary as much as twenty-fold), and the speed at which they are metabolized. These pharmacological differences affect symptoms and are important considerations in designing an appropriate tapering protocol for addicted individuals.

Benzodiazepines have five short-term medical uses: anxiety relief (anxiolytic), sleep (hypnotic), muscle relaxant, anti-seizure (anti-convulsant) and pre-operative (amnesiac). They are sometimes inappropriately prescribed for depression, but they are themselves central nervous system depressants.

There is a consensus that benzodiazepines should not be prescribed on a regular or intermittent regular basis for more than two weeks of use, but longer-term prescribing, particularly to women, is common.

Prescribing Rates and Practices

For over 40 years it has been well known that benzodiazepines are highly addictive and have profound effects on the brain and body at therapeutic doses and if prescribed for more than several weeks.[2-7] Yet it is estimated that at least 3 to 15% of any adult population in the world is using prescribed benzodiazepines.[6] In 2000 there were 15,709,000 prescriptions of benzodiazepines filled by Canadian retail pharmacies, an increase of 12.8% since 1996.[8] Specific tranquilizers (e.g., Klonopin) showed an increase in prescribing rates of 57.5% for the same period. In British Columbia, psychotherapeutics (primarily tranquilizers and anti-depressants) made up the largest group of prescribed drugs (13.2%) in 2000.[9]

There is a consensus that benzodiazepines should not be prescribed on a regular or intermittent regular basis for more than two weeks of use,[2-5] but longer-term prescribing, particularly to women, is common.

Benzodiazepines and Women in Canada

In the 1970s Dr. Ruth Cooperstock and her colleagues reported that Canadian women are prescribed benzodiazepines at twice the rate of Canadian men.[7,10,11] Recent data suggest that not only are women more likely to be prescribed benzo-

diazepines compared to men,[12] but women are also more likely to be prescribed benzodiazepines for longer periods of time.[13]

When women present to their doctor with comparable symptoms as men, they are more likely to be prescribed benzodiazepines.[14] Women are also more likely than men to be prescribed benzodiazepines and sleeping pills for non-medical reasons such as coping with grief or stress. They are also prescribed these drugs when adjusting to natural processes such as childbirth and menopause.[15] According to Health Canada's Women's Health Strategy "For many years, women's health advocates have stated that women and their health concerns are too often over-medicalized … because the health sector has difficulty distinguishing between natural processes and sickness" in women.[16] "Natural reproductive processes such as menses, pregnancy, childbirth and menopause may cause pain and discomfort and interfere with life events. When coupled with other sources of stress, they can bring about physical and mental distress unique to women."[16] Because of the multiple roles carried by many women in Canada and the "double workday" of paid labour and domestic work that many perform, the work stress index of women in the 20 to 44 age group is much higher than that of men.[17] Other conditions such as poverty, which affect women disproportionately as compared to men,[18] also make women particularly vulnerable to anxiety, depression and sleep problems for which they may be prescribed benzodiazepines or sleeping pills.

Women are more likely than men to be prescribed benzodiazepines and sleeping pills for non-medical reasons such as coping with grief or stress.

Benzodiazepine dependence is a serious problem among elderly women. Canadian and international studies indicate that 20 to 50% of all women over 60 may be prescribed benzodiazepines or sleeping pills and that long-term use increases with age.[12,13,19] Long-term care facilities, which have a higher proportion of female residents, also have high levels of benzodiazepine prescription rates. Elderly patients with other prescriptions who have been hospitalized previously are more likely to be prescribed benzodiazepines.[20] These drugs are a common cause of confusion, cognitive decline and dementia.[21-23]

Long-term benzodiazepine use has also been linked to increased risk of falls and hip and femur fractures among the elderly.[2,24-28] In 2001 in British Columbia, about 3,100 seniors were hospitalized for a broken hip; two thirds of these seniors were women.[25] A preliminary analysis of new epidemiological findings from B.C. PharmaCare data, hospital separations, and mortality and morbidity data shows a strong association between falls in elderly women and prescriptions for anxiolytics, sedatives and hypnotics, of which 90% are benzodiazepines.[25] The report, from the Office of the Provincial Health Officer, states that "withdrawal of the medication can be very difficult…. More effort must be made to ensure that fewer elderly patients are prescribed these drugs in the first place."[25]

In pregnant women, benzodiazepines can cross the placenta and, taken in therapeutic doses, can cause complications among the newborn, including floppy infant syndrome, failure to suckle and withdrawal symptoms.[29] There is some evidence that maternal use may impair fetal growth and retard brain development which may cause children to be prone to a spectrum of learning and emotional difficulties later in life.[30]

In 2000, one in three status Aboriginal women over 40 in western Canada were prescribed benzodiazepines.[31] The number receiving benzodiazepines through Health Canada's Non-Insured Health Benefits increased by 25% in just four years (1996-2000).[32]

The data on status Aboriginal people show that Aboriginal women are almost twice as likely to receive benzodiazepine prescriptions as Aboriginal men. According to B.C.'s Provincial Health Officer, Dr. Perry Kendall, benzodiazepines may be used to numb patients to the physical and mental pain of poverty and harsh reality.[31] In another study of Aboriginal prescription drug use in Canada, 48% of those accessing addiction treatment services used prescription drugs inappropriately and of these 74% used benzodiazepines. Over 60% were poly-prescription drug users.[32]

New data from B.C. confirm the link between benzodiazepine use and an increased rate of falls and fractures. Falls among elderly women in B.C. accounted for $131 million of health care costs in 1998 alone.

Effects on the Individual of Benzodiazepines at Prescribed Dosage Levels

Apart from the effects noted above, at normal prescribed levels benzodiazepines and sleeping pills also impair and compromise a wide range of basic skills that are necessary for coping with the intellectual and psychological demands of everyday living. They impair memory and reasoning, produce forgetfulness and disrupt the process of memory retrieval, affect flexibility of thoughts and motor control, eye/hand coordination, mental reaction, information processing, vigilance and focus.[4,5] These attributes lead to the increased rate of falls and fractures among the elderly described above, and an association with increased morbidity and mortality from car accidents.[33,34] A single dose of diazepam (Valium) has been shown to affect neuromuscular processing related to balance control.[35]

Long-term (more than several months) benzodiazepine use can cause or aggravate depression, memory impairment, emotional blunting and can precipitate suicidal tendencies. When prescribed for trauma they may delay shock and grief, which surface only after cessation of use. Agoraphobia and other phobias are common outcomes of longer-term benzodiazepine use.[2-4,36,37] Benzodiazepines sometimes cause paradoxical excitement, anxiety, hallucinations and rage. Cases of wife assault, baby battering and homicide have also been attributed to these drugs.[2,3,37]

Effects on the Individual of Tolerance and Addiction

The vast majority of those who take benzodiazepines on a regular or regular intermittent basis will become addicted, probably within a few months, although the exact time is highly individual and impossible to predict.[1] Tolerance to the hypnotic (sleep) effects of benzodiazepines and sleeping pills may occur within seven days.[3] As tolerance develops the body makes compensatory changes in the GABA and benzodiazepine receptors. Symptoms of tolerance are identical to drug withdrawal symptoms, but occur while a woman is *taking* the drug and include numerous physical and psychological symptoms such as increased anxiety/panic, severe insomnia, muscle pain and stiffness, digestive problems, heart and lung problems, depression, headaches, suicidal ideation, rage and agoraphobia.[2-5,37]

Drug-related tolerance withdrawal symptoms are frequently not identified by physicians or patients, leading to intensive diagnostic explorations or medical interventions. A lack of understanding of the symptoms of tolerance withdrawal often results in the addition of other prescription drugs, (for example, anti-depressants or anti-psychotics), with increased side effects, leading to further involvement of women in the health or mental health systems.[2,3,10,37]

A significant number of women who withdraw from benzodiazepines, from whatever method, face a lengthy period of withdrawal and recovery consisting of dozens of intense and varied symptoms that come and go for weeks or months in a cyclic fashion. Seizures commonly occur in sudden withdrawal from high doses. There is also evidence of a protracted period of withdrawal in some people that manifests in persisting motor, muscular, cognitive, insomniac, gastric or other symptoms.[2-4,37,38]

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Withdrawal and Recovery from Benzodiazepine Addiction

Many health care professionals are unaware of the physical signs of benzodiazepine dependency, of how addiction can occur and the time required for symptoms to develop. They are also unaware of the safest and most effective tapering methods. This contributes to the low rate of successful withdrawal from benzodiazepines – in most cases, 10 to 30%.[3,37] There is also little information available to physicians on the duration and normal course of recovery (post taper), which may last up to 18 months or beyond. This contributes to the practice of prescribing other psychiatric drugs to patients who are experiencing on-going recovery symptoms.[2,3,22,37]

A phased in substitution of a long half-life benzodiazepine (Valium), followed by small drug reductions at regular intervals has been proven to be the most successful method for withdrawing from benzodiazepines and sleeping pills. Withdrawal

success rates as high as 90% have been achieved using this method even among elderly long-term users.[2,22]

It is important to note that some patients may need support for up to one year post-withdrawal. In some cases short-term hospital residential care may be required for women who are experiencing extreme withdrawal symptoms, are suicidal or who have limited support. Families also require specific information and support to assist them with their caregiving role.

Socio-economic Costs of Prescribed Benzodiazepines

Prescription drugs, of which psychiatric drugs are a significant class, increasingly represent a cost burden to the Canadian health care system. From 1985 to 1998 prescription drug expenditures increased by 226.5%.[38] From 1997, prescription drugs have become second only to hospitals in overall Canadian health expenditures.[38] Many benzodiazepine users are prescribed additional drugs. Apart from the cost to society, women and the elderly are most affected by rising drug costs.

Since many benzodiazepine users have chronic mental and physical health problems resulting from prescription drug side effects, they are intensive users of the health care system.

Another cost associated with benzodiazepine use is injury resulting from falls among the elderly. A study of the economic burden of unintentional injury in British Columbia noted that in 1998, $180 million was spent caring for injuries in seniors over 65 who had fallen.[39] Falls among elderly women accounted for 73% of these costs, or $131 million. Setting a target in B.C. of a 20% reduction in hospitalization rates for falls among the elderly would lead to 1,400 fewer hospital stays.[39] The overall savings could amount to $25 million a year in health care costs and 350 fewer elderly people disabled. Stopping the over-prescription of benzodiazepines to elderly women could help achieve these goals.

Other socio-economic costs of benzodiazepines are extensive, although more difficult to quantify. They consist of costs related to automobile accidents; increased fatalities due to suicides and overdoses; policing costs related to aggressive behaviour, shoplifting and spousal assault; individual costs related to unemployment, sick leave and career loss; and costs to social programs that provide disability payments and social assistance. Since many benzodiazepine users have chronic mental and physical health problems resulting from prescription drug side effects, they are frequent and intensive users of the health care system. Further research is needed to determine the extent of these costs to the individual and society.

Marketing of Prescription Drugs to Women

Psychotherapeutic drugs (primarily anti-depressants, benzodiazepines and anti-psychotics) are among the most profitable for drug companies. In drug company advertising, women are a heavily targeted "market". For example, in direct-to-consumer advertising (DTCA) of drugs on television and in magazines in the

U.S., it has been found that women are targeted more than twice as often as men in sex-specific ads and the volume of DTCA is highest in women's magazines.[40] Prescription drugs advertised directly to consumers are now the largest and fastest selling medications in the U.S.. This has resulted in more prescription drug use among women.[40] As these ads easily make their way across the border, women in Canada face additional pressure to view life events and natural physiologic processes as medical conditions for which medication is needed.

The marketing of psychotherapeutic drugs for "off label" uses (for purposes other than those approved by Health Canada) has also become aggressive. In order to make informed choices about the use of prescription drugs, women and the general public need to be given full information about drugs, including their approved uses and all of the risks involved in taking them, from their physicians, from objective drug insert information and from the Health Protection Branch of Health Canada. As direct-to-consumer ads have been shown to be a poor source of information about prescription drugs,[40] it is important that federal legislation in Canada be strengthened to protect women from DTCA.

Policy Recommendations

Despite the effects of benzodiazepines and sleeping pills on women, families and society in Canada, no comprehensive policy or intervention strategy exists to address this serious health issue. Significant gaps and limitations must be dealt with in the development of a strategic response.

1. There is a consensus that benzodiazepines and sleeping pills should not be prescribed on a regular or intermittent regular basis for more than two weeks of use. However, no specific Canadian guidelines exist to govern prescribing or to ensure that women are prescribed these drugs for the appropriate reasons or time period. There are also no procedures to track high-prescribing physicians or protocols to address this issue.
   - Health Canada must establish Clinical Practice Guidelines on the use and prescribing of benzodiazepines and sleeping pills, with directives to physicians and other health care providers. The guidelines should limit prescriptions of benzodiazepines to no more than two weeks of constant or intermittent regular use and discourage benzodiazepine and sleeping pill prescriptions at the first office visit.
   - Health Canada should encourage all provinces and territories, in collaboration with colleges of physicians and surgeons and colleges of pharmacists, to use computer networks to link on-line point of sale systems in provincial pharmacies and databases in emergency departments, colleges of pharma-

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cists and doctors' offices to track high-prescribing doctors. B.C. PharmaNet in British Columbia is an example of a secure computer network that could be used to serve this purpose.[41]

- Health Canada, in collaboration with colleges of physicians and surgeons, should develop protocols to monitor, evaluate and discipline high-prescribing physicians who have been identified by database tracking or other methods.

2. Health care providers and addictions specialists are often unaware of or cannot identify characteristics of physical dependency and do not know how addiction can occur or the time required for symptoms to develop.

   - Provincial/territorial governments should develop and/or distribute information on the physical characteristics and signs of benzodiazepine dependency to health care professionals, addictions treatment staff and the general public.

Health care providers and addictions specialists often can't identify characteristics of physical dependency.

3. The rate of successful withdrawal from benzodiazepines is low in most cases. Contributing to this is physicians' lack of knowledge about withdrawal and tapering protocols.

   - Provincial/territorial governments should develop and distribute information on the most effective protocols for tapering (e.g., long half-life benzodiazepine substitution), withdrawal and recovery to health care professionals, addictions treatment staff and the general public.
   - Guidelines should be developed for physicians and patients on the proper use of adjunctive drugs in withdrawal and on appropriate patient care, including the risks of specific medications.
   - Targeted information on tapering and recovery is particularly required by women who are prescribed benzodiazepines most often, including those experiencing difficult life events, Aboriginal women and seniors.

4. Tapering from benzodiazepines is often a lengthy process (two to twelve months) and patient support may be required for more than one year post-withdrawal. Care services to support tapering and withdrawal should incorporate an understanding of the unique needs of those who are involuntarily addicted.

   - Funding should be provided through provincial/federal government partnerships to support a continuum of care for those involuntarily addicted to benzodiazepines or sleeping pills. A significant proportion of these services

should be designed to meet the specific needs of women. Services should include:

- the establishment of community-based or ambulatory clinics specializing in benzodiazepine and sleeping pill tapering and peer support and counseling that are able to address the unique characteristics and needs of involuntary addicts;
- community-based residential facilities for those in withdrawal who are unable to cope with symptoms or are suicidal.

5. Not enough is known about the type and prevalence of benzodiazepine and sleeping pill prescribing, usage patterns among specific subpopulations, the personal and societal impacts and costs related to women and benzodiazepine use and addiction, the frequency and duration of use among elderly women, or the level of prescribing in health care settings such as long-term care facilities and Emergency Rooms.

   - The federal government should take an active role in facilitating and supporting research initiatives on benzodiazepine and sleeping pill use. All research should include a gender-based analysis.

6. In comparison with other drugs such as alcohol and heroin, the personal and societal costs associated with benzodiazepines and sleeping pills have had a limited profile among policy makers, government, health care and addictions treatment providers. This neglect has led to the lack of an effective, comprehensive strategy to address the issue.

   - The provincial and federal governments must take a leadership role in focusing attention on the over-prescription and involuntary addiction of women to benzodiazepines and sleeping pills through seminars and conferences and through the development of best practice guidelines.

7. Under Canadian law, drug companies are not required to provide comprehensive drug insert information to patients at the drug purchase point. Physicians receive most of their information about prescribing drugs directly from drug company representatives.

   - Women must be supported to make informed choices about the use of prescription drugs. General public and drug insert information must be accessible, comprehensive, accurate and objective (not controlled by drug companies). Physicians should be obliged to fully disclose all of the potential risks of prescription drugs.
   - Canada's Marketed Health Products Directorate should play a stronger role

Because benzodiazepines have such severe consequences for women, all research on this class of drugs should include a gender-based analysis.

in promoting consumer reporting of adverse drug effects, in disseminating accurate and comprehensive information about the risks of using benzodiazepines and sleeping pills, and in ensuring the Directorate is free from drug company influence.[42]

8. It has been shown that direct-to-consumer marketing of drugs in the U.S. has led to more prescription drug use among women. A U.S. survey showed that in most cases key medical or safety information was left out of these ads.[40]
   - Direct-to-consumer advertising must not be permitted in Canada. Current loopholes in the Food and Drugs Act need to be clarified and controlled. Monitoring, sanctions and fines should be used to address any violations under the Act.

9. Non-drug treatments and resources to enhance women's ability to cope with depression, anxiety, grief, stress, natural physiologic processes and difficult life events are under-promoted and under-used.
   - Health Canada and the provincial/territorial governments should provide funding and support to community-based organizations to explore and provide non-drug advice and options that support women's well-being and help women cope.

Direct-to-consumer advertising must not be permitted in Canada. Current loopholes in the Food and Drugs Act need to be clarified and controlled.

10. Opiates, barbiturates, benzodiazepines and sleeping pills were all initially described as safe and non-habit-forming drugs. Eventually all have been associated with serious personal and societal effects. A newer class of drugs, the Selective Serotonin Reuptake Inhibitor anti-depressants, is increasingly being associated with significant side effects such as sexual dysfunction, mania, suicide risk, gastric problems and long-term weight gain, in addition to tolerance withdrawal.
    - The federal government must provide a leadership role in identifying and publicizing the risk factors associated with all psychiatric drugs, including benzodiazepines, anti-depressants, sleeping pills and anti-psychotics.

By allowing the over-prescription and inappropriate use of benzodiazepines and sleeping pills to women in Canada, we are "manufacturing addiction" and contributing both to the suffering of women and their families and to escalating health care costs. The benefits of acting on this problem are many and clear. Action to address this problem is long overdue.

Notes

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