Canadian Centre on Substance Abuse
Centre canadien de lutte contre les toxicomanies
Partnership. Knowledge. Change.
Collaboration. Connaissance. Changement.

Evidence Exchange Network
Mental Health and Addictions

www.ccsa.ca • www.cclt.ca November 2014 Rapid Review

Effective Interventions to Manage Symptoms of Benzodiazepine Withdrawal in Seniors

Key Messages

- Effective interventions to manage withdrawal symptoms during benzodiazepine discontinuation in seniors should be tailored to their specific needs and consider concurrent medical problems, cognitive challenges such as dementia, and economic and social barriers to treatment and support.
- Minimal interventions aimed at changing prescribing practices, such as advising patients to discontinue benzodiazepines, can be an effective way to promote discontinuation. For example, gradual dose tapering is more effective than sudden discontinuation. Many effective interventions to manage withdrawal symptoms during benzodiazepine discontinuation were not specific to seniors and included psychological approaches, such as cognitive behaviour therapy.
- There is more research on interventions to promote the discontinuation of benzodiazepines than to manage withdrawal symptoms while discontinuing benzodiazepines.
- Psychological interventions, such as individual, group and family counselling, are more effective than providing alternative drug therapy alone.
- More research is needed on the use of psychological approaches as an alternative to prescribing benzodiazepines in seniors experiencing anxiety and insomnia.

Context

Patterns of Use

Benzodiazepines are a class of drugs commonly prescribed to adults for the short-term treatment of anxiety and insomnia (Voyer, Preville, Cohen, Berbiche, & Beland, 2010). In Canada, 3.3% to 9% of adults use a benzodiazepine (Esposito, Barbui, & Patten, 2009; Neutel, 2005). Among seniors, patterns of use are much higher. The Quebec Survey on the Health of Older Persons found that 25.4% of seniors who live in their homes (non-institutionalized seniors) used benzodiazepines (Voyer et al., 2010).

According to another Canadian survey (Esposito, et al., 2009), benzodiazepines are most frequently prescribed for:

- Sleep disorders (68.9%)
- Anxiety (35.8%)
- Depression (27.8%)
- Pain management (21.2%)

Individuals are more likely to use benzodiazepines if they are older, female, lower income, or widowed, separated or divorced and are experiencing poor physical or mental health (Cunningham, Hanley, & Morgan, 2010; Esposito et al., 2009; Luijendijk, Tiemeier, Hofman, Heeringa, & Stricker, 2008). A lack of training on prescribing benzodiazepines and lack of information on evidence-based alternative treatments for presenting symptoms (as listed above) also increases the likelihood a physician will prescribe this medication (Gould, Coulson, Patel, Highton-Williamson, & Howard, 2014).

Risk of Dependency

The risk of becoming dependent on a benzodiazepine varies according to the length of time it is used. Few users become dependent with less than three months of use. After more than a year of use, dependency rates are much higher, at 20% to 45% (New South Wales, Department of Health, 2008).

The prolonged use of benzodiazepines, especially among seniors, has a wide range of negative health effects that result in higher costs to the health system and to society as a whole (Voyer et al., 2010; Fang et al., 2009; Ruggiero, Lattanzio, Dell'Aquila, Gasperini, & Cherubini, 2009; Scott, Gray, Martin, Pillans, & Mitchell, 2013; Culberson & Ziska, 2008). Among seniors, long-term use of benzodiazepines can cause confusion, poor muscle co-ordination and increased risk of falls, hip fractures and car accidents (Culberson & Ziska, 2008; Clay, 2010).

Withdrawal Symptoms

The severity of withdrawal symptoms depends on various factors such as the type of benzodiazepine (if it is short acting or long acting), dose, length of treatment and if the drug is abruptly discontinued (Saunders & Yang, 2002; Conn et al., 2006).

- About 40% of patients who suddenly stop using a long-acting benzodiazepine (e.g., diazepam), after using it for six months or longer, experience withdrawal symptoms.
- Withdrawal symptoms typically start within two days with short-acting benzodiazepines and between two and 10 days with long-acting ones, but symptoms can start as late as three weeks (Saunders & Yang, 2002).
- The most common symptoms of benzodiazepine withdrawal include anxiety, depression, diarrhea, constipation, bloating, insomnia, irritability, muscle aches, poor concentration and memory, and restlessness.
- Some people also experience panic attacks and, occasionally, seizures and symptoms of psychosis such as hallucinations, delusions, disorganized thinking, or disorganized or abnormal motor behaviour (American Psychiatric Association, 2013; Scott et al., 2013; New South Wales, Department of Health, 2008).

The Issue

The literature indicates that the patterns and impacts of prescription drug use differ in seniors as compared with the general adult population (Substance Abuse and Mental Health Services Administration, 2006), yet little intervention research has been conducted with seniors. Findings suggest that:

- Seniors dealing with substance use problems need information on harm reduction, how to manage their medications and treatments that consider the effects of substance misuse on health, and cognitive and physical function (D'Agostino, Barry, Blow, & Podgorski, 2006; Brown et al., 2006, Lee, Mericle, Avalon, & Areán, 2009; Briggs, Magnus, Lassiter, Patterson, & Smith, 2011).

- Effective substance misuse interventions for seniors are supportive, adaptive, creative and non-confrontational. They address the factors that give rise to presenting symptoms, such as anxiety, chronic pain and insomnia, and seniors' ability to participate in treatment (e.g., financial, literacy and cognitive factors). Additionally, effective interventions will consider the social context of elderly individuals, which can include social isolation and exclusion as well as poor prescribing practices by physicians when addressing psychological distress in seniors (Briggs et al., 2011).

This rapid review attempts to answer the following question: What are the most effective interventions to help seniors (male and female) manage withdrawal symptoms, such as anxiety, when discontinuing benzodiazepines?

Approach

The published and grey literature was searched using a combination of terms (see Appendix A). The following Population of Interest, Intervention, Comparators and Outcome (PICO) criteria were used to determine the inclusion or exclusion of the articles retrieved:

Population of interest: Seniors (women and men), aged 65 and over, who are discontinuing benzodiazepines.

Interventions: Two types of interventions were considered:

1. Interventions to promote the discontinuation of benzodiazepine use;
2. Interventions to manage withdrawal symptoms when discontinuing benzodiazepines.

Comparators: Standard approaches, such as abrupt or gradual withdrawal alone, to assist with benzodiazepine discontinuation and/or withdrawal symptom management.

Outcome: Effective interventions to discontinue benzodiazepines; effective withdrawal symptom management.

Findings

Effective Interventions to Promote the Discontinuation of Benzodiazepines

Guidelines, reviews of interventions and research studies to support benzodiazepine discontinuation in long-term and primary care are readily available in the literature (Authier et al., 2009; Chang & Chan, 2010; Lader, Tylee, & Donaghue, 2009; Scott et al., 2013; Smith & Tett, 2010). These discontinuation protocols recommend that an initial assessment be carried out with the patient to determine whether it is a suitable time to stop, whether symptoms of depression, anxiety, long-term insomnia or any other medical problems are present and whether withdrawal can be appropriately managed in a primary care setting. Once the assessment is completed by a physician, a flexible withdrawal schedule (dose tapering) can then be negotiated with the patient (Culberson & Ziska, 2008; Scott et al., 2013).

Educational interventions such as a letter, self-help information or consultation with a physician can also effectively reduce the long-term use of benzodiazepines among seniors in primary care settings without adverse effects (Mugunthan, McGuire, & Clasziou, 2011; Lader et al., 2009; Salonoja, Salminen, Aarnio, Vahlberg, & Kivelä, 2010).

Evidence from two meta-analyses indicated that among adults (individuals aged 18 and over) with benzodiazepine dependence, gradual, supervised discontinuation is more effective than stopping suddenly (Voshaar, Couvée, Van Balkom, Mulder, & Zitman, 2006; Parr, Kavanagh, Cahill, Mitchell, &

Young, 2009). When combined with psychological interventions, such as cognitive-behavioural therapy (CBT), psychological counselling, relaxation training and psycho-education, gradual, supervised discontinuation is more effective than routine care or gradual discontinuation alone (Parr et al., 2009, Gould et al., 2014).

Effective Interventions to Manage Withdrawal Symptoms

According to Lader and colleagues (2009), psychological interventions to manage withdrawal symptoms during benzodiazepine discontinuation have three objectives:

- To manage symptoms;
- To prevent relapse; and
- To treat, if present, the underlying disorder that led to the benzodiazepine prescription.

CBT is an effective addition to the gradual discontinuation of benzodiazepines in seniors experiencing symptoms of withdrawal, including anxiety and/or insomnia (Gorenstein et al., 2005; Wuthrich & Rapee, 2013; Gould, Coulson, & Howard, 2012; Baillargeon et al., 2003). Evidence-based psychological interventions to manage symptoms when discontinuing benzodiazepines are available at the National Institute for Health and Care Excellence (NICE) website; however, these interventions are not specific to seniors.

A Cochrane review is currently underway to assess psychosocial interventions such as CBT for individuals experiencing benzodiazepine dependency. Although it is not looking specifically at seniors, its results will provide further information on this topic (Darker, Sweeney, Barry, & Farrell, 2012).

Limitations

Due to time constraints, our rapid review might have unintentionally missed some evidence relevant to this topic. The search results could have also been affected by the lack of consensus in the collected works about:

- How to define “senior” (60 and over or 65 and over);
- How to diagnose and define substance misuse or dependency;
- Whether diagnostic criteria for benzodiazepine dependence need to be adapted for seniors (Voyer et al., 2010).

Other challenges in identifying interventions included:

- Limited interventions and studies that targeted seniors as a population group;
- No unique or commonly accepted search term for “withdrawal” (the search terms used for this rapid review were “withdrawal” and “discontinuation”; it might be worthwhile for future reviews to include the term “cessation”);
- More research has been conducted on interventions to promote the discontinuation of benzodiazepines than on how to manage withdrawal symptoms.

Our review did not consider:

- Factors that can affect an intervention’s effectiveness (e.g., gender, age, severity of symptoms, income, ethnicity, etc.);

- Interactions between mental illness, other conditions and substance use/misuse (seniors are a varied group of individuals, so it is important that researchers undertaking future explorations into this question keep concurrent disorders in mind (Lenze, 2003; Conn et al., 2006));
- Promising practices used by mental health and addictions agencies to help seniors manage symptoms when discontinuing benzodiazepines.

Discussion

Few studies were found that focused on "seniors" and "senior women," despite the high use of benzodiazepines in these population groups and therefore the greater risk of dependency. More research is needed on the effectiveness of targeted interventions to reduce withdrawal symptoms during benzodiazepine discontinuation for seniors, such as behaviour therapy, exercise and complementary or alternative treatments for symptoms of anxiety, sleep hygiene and melatonin interventions for chronic insomnia.

Future research in this area could focus on interventions to treat underlying symptoms in seniors, such as the management of symptoms without prescribing benzodiazepines. For example, studies were found that examined non-benzodiazepine treatments for insomnia (Bain, 2006; Cheuk, Yeung, Chung, & Wong, 2012). This review did not find research that addressed the effectiveness of gender-specific interventions for senior females or senior males. Since this is of interest to service providers, future studies should explore gender-specific interventions or outcomes.

Conclusions

Educational interventions for service providers and gradual supervised discontinuation combined with psychological interventions are effective approaches to promote the discontinuation of benzodiazepines and manage withdrawal symptoms. More gender-specific research is needed for seniors as well as research on alternatives to benzodiazepine prescription.

Acknowledgements

This report was prepared by Ilene Hyman, Tatyana Krimus and Rossana Coriandoli, with the Evidence Exchange Network (EENet), located at the Centre for Addiction and Mental Health (CAMH), Toronto.

References

American Psychiatric Association. (2013). Schizophrenia spectrum and other psychotic disorders. In *Diagnostic and statistical manual of mental disorders* (5th ed.). Arlington, VA: Author.

Authier, N., Balayssac, D., Sautereau, M., Zangarelli, A., Courty, P., Somogyi, A. A., . . . Eschalier, A. (2009). Benzodiazepine dependence: Focus on withdrawal syndrome. *Annales Pharmaceutiques Françaises*, *67*(6), 408–413.

Baillargeon, L., Landreville, P., Verreault, R., Beauchemin, J.P., Grégoire, J.P., & Morin, C.M. (2003). Discontinuation of benzodiazepines among older insomniac adults treated with cognitive-behavioural therapy combined with gradual tapering: a randomized trial. *Canadian Medical Association Journal*, *169*(10): 1015–1020.

Bain, K. T. (2006). Management of chronic insomnia in elderly persons. *American Journal of Geriatric Pharmacotherapy, 4*(2), 168–192.

Briggs, W. P., Magnus, V. A., Lassiter, P., Patterson, A., & Smith, L. (2011). Substance use, misuse, and abuse among older adults: implications for clinical mental health counselors. *Journal of Mental Health Counseling*, *33*(2): 112–128

Brown, S. A., Glasner-Edwards, S. V., Tate, S., McQuaid, J. R., Chalekian, J., & Granholm, E. (2006). Integrated cognitive behavioral therapy versus twelve-step facilitation therapy for substance-dependent adults with depressive disorders. *Journal of Psychoactive Drugs*, *38*, 449–460.

CAMH Healthy Aging Project (2008). *Improving our response to older adults with substance use, mental health and gambling problems: A guide for supervisors, managers and clinical staff*. Toronto, ON; Centre for Addiction and Mental Health.

Chang, C. B., & Chan, D. C. (2010). Comparison of published explicit criteria for potentially inappropriate medications in older adults. *Drugs and Aging, 27*(12), 947–957.

Cheuk Daniel, K. L., Yeung, W., Chung, K. F., & Wong, V. (2012). Acupuncture for insomnia. *Cochrane Database of Systematic Reviews,* July 18 (9): CD005472.

Clay, S. W. (2010). Treatment of addiction in the elderly. *Aging Health, 6*(2), 177–189.

Conn, D. K., Gibson, M., Feldman, S., Hirst, S., Leung, S., MacCourt, P., ... Mokry, J. (2006). National guidelines for seniors' mental health: The assessment and treatment of mental health issues in long-term care homes (focus on mood and behaviour symptoms). *Canadian Journal of Geriatrics, 9*(Suppl. 2), S59–S64.

Culberson, J. W., & Ziska, M. (2008). Prescription drug misuse/abuse in the elderly. *Geriatrics, 63*(9), 22–26, 31.

Cunningham, C. M., Hanley, G. E., & Morgan, S. (2010). Patterns in the use of benzodiazepines in British Columbia: Examining the impact of increasing research and guideline cautions against long-term use. *Health Policy, 97*(2-3), 122–129.

D'Agostino, C. S., Barry, K. L., Blow, F. C., & Podgorski, C. (2006). Community interventions for older adults with comorbid substance abuse: The Geriatric Addictions Program. *Journal of Dual Diagnosis, 2*, 31–45.

Darker, C. D., Sweeney, B. P., Barry, J. M., & Farrell, M. F. (2012). Psychosocial interventions for benzodiazepine harmful use, abuse or dependence. *Cochrane Database of Systematic Reviews*, Feb. 15 (2): CD009652.

Dijk, D.J., & Cajochen C. (1997). Melatonin and the circadian regulation of sleep initiation, consolidation, structure, and the sleep EEG. *Journal of Biological Rhythms, 12*(6), 627–635.

Esposito, E., Barbui, C., & Patten, S. B. (2009). Patterns of benzodiazepine use in a Canadian population sample. *Epidemiologia e psichiatria sociale, 18*(3), 248–254.

Fang, S. Y., Chen, C. Y., Chang, I. S., Wu, E. C., Chang, C. M., & Lin, K. M. (2009). Predictors of the incidence and discontinuation of long-term use of benzodiazepines: A population-based study. *Journal of Drug and Alcohol Dependence, 104*(1–2), 140–146.

Gorenstein, E. E., Kleber, M. S., Mohlman, J., DeJesus, M., Gorman, J. M., & Papp, L. A. (2005). Cognitive-behavioral therapy for management of anxiety and medication taper in older adults. *American Journal of Geriatric Psychiatry, 13*(10), 901–909.

Gould, R. L., Coulson, M. C., & Howard, R. J. (2012). Efficacy of cognitive behavioral therapy for anxiety disorders in older people: A meta-analysis and meta-regression of randomized controlled trials. *Journal of the American Geriatrics Society*, *60*(2), 218–229.

Gould, R. L., Coulson, M. C., Patel, N., Highton-Williamson, E., & Howard, R. J. (2014). Interventions for reducing benzodiazepine use in older people: Meta-analysis of randomised controlled trials. *The British Journal of Psychiatry, 204*(2), 98–107.

Heijden, K.B., Smits, M.G. & Gunning, B.W. (2006). Sleep hygiene and actigraphically evaluated sleep characteristics in children with ADHD and chronic sleep onset insomnia. *Journal of Sleep Research*, *15*(1), 55–62.

Lader, M., Tylee, A., & Donoghue, J. (2009). Withdrawing benzodiazepines in primary care. *CNS Drugs, 23*(1), 19–34.

Lee, H. S., Mericle, A. A., Ayalon, L., & Areán, P. A. (2009). Harm reduction among at-risk elderly drinkers: A site-specific analysis from the multi-site Primary Care Research in Substance Abuse and Mental Health for Elderly (PRISM-E) study. *International Journal of Geriatric Psychiatry*, *24*, 54-60.

Lenze, E. J. (2003). Comorbidity of depression and anxiety in the elderly. *Current Psychiatry Reports, 5*(1), 62–67.

Luijendijk, H. J., Tiemeier, H., Hofman, A., Heeringa, J., & Stricker, B. H. (2008). Determinants of chronic benzodiazepine use in the elderly: A longitudinal study. *British Journal of Clinical Pharmacology, 65*(4), 593–599.

Mugunthan, K., McGuire, T., & Glasziou, P. (2011). Minimal interventions to decrease long-term use of benzodiazepines in primary care: A systematic review and meta-analysis. *British Journal of General Practice, 61*(590), e573–e578**.**

Neutel, C. I. (2005). The epidemiology of long-term benzodiazepine use. *International Review of Psychiatry, 17*(3), 189–197.

New South Wales, Department of Health. (2008). *Drug and Alcohol Withdrawal Practice Guidelines*. North Sydney, NSW: Author. Retrieved Sept. 2014 from: http://www0.health.nsw.gov.au/policies/gl/2008/pdf/GL2008_011.pdf.

O'Grady, C. P., & Skinner, W.J.W. (2007). *A Family Guide to Concurrent Disorders*. Toronto, ON: Centre for Addiction and Mental Health.

Parr, J. M., Kavanagh, D. J., Cahill, L., Mitchell, G., & Young, R. (2009). Effectiveness of current treatment approaches for benzodiazepine discontinuation: A meta-analysis. *Addiction, 104*(1), 13–24.

Ruggiero, C., Lattanzio, F., Dell'Aquila, G., Gasperini, B., & Cherubini, A. (2009). Inappropriate drug prescriptions among older nursing home residents: The Italian perspective. *Drugs and Aging 26*(Suppl 1), 15–30.

Salonoja, M., Salminen, M., Aarnio, P., Vahlberg, T., & Kivelä, S. (2010). One-time counselling decreases the use of benzodiazepines and related drugs among community-dwelling older persons. *Age and Ageing, 39*(3), 313–319.

Saunders, J. & Yang, J. (2002). *Clinical Protocols for Detoxification in Hospitals and Detoxification Facilities*. Brisbane, Queensland: Royal Brisbane Hospital and the Prince Charles Hospital Health Service Districts.

Scott, I. A., Gray, L. C., Martin, J. H., Pillans, P. I., & Mitchell, C. A. (2013). Deciding when to stop: Towards evidence-based de-prescribing of drugs in older populations. *Evidence-Based Medicine, 18*(4), 121–124.

Smith, A. J., & Tett, S. E. (2010). Improving the use of benzodiazepines—is it possible? A non-systematic review of interventions tried in the last 20 years. *BMC Health Services Research*, *10*, 321–333.

Substance Abuse and Mental Health Services Administration. (2006). *Results from the 2005 national survey on drug use and health*. Rockville MD: Author.

Voshaar, R. C., Couvée, J. E., Van Balkom, A. J., Mulder, P. G., & Zitman, F. G. (2006). Strategies for discontinuing long-term benzodiazepine use: Meta-analysis. *British Journal of Psychiatry, 189*, 213–220.

Voyer, P., Preville, M., Cohen, D., Berbiche, D., & Beland, S. G. (2010). The prevalence of benzodiazepine dependence among community-dwelling older adult users in Quebec according to typical and atypical criteria. *Canadian Journal of Aging, 29*(2), 205–213.

Wuthrich, V. M., & Rapee, R. M. (2013). Randomised controlled trial of group cognitive behavioural therapy for comorbid anxiety and depression in older adults. *Behaviour Research and Therapy, 51*(12), 779–786.

Appendix A: Search Strategy

We analyzed a total of 64 peer-reviewed articles and eight non-academic articles. Articles were included in the review if they addressed the following topics:

- Benzodiazepine discontinuation
- Benzodiazepine withdrawal
- Seniors
- Symptom management

Additionally, articles were included if they provided background information on issues related to benzodiazepine use, dependency and treatment in seniors or in the general population.

To develop and test our electronic search strategies, we consulted a medical information specialist. We searched PubMed and the Cochrane Library on Wiley (including CENTRAL, Cochrane Database of Systematic Reviews, DARE, and HTA). All searches were performed on December 11, 2013. We focused only on articles in English published from 2008 to the present. We conducted our search of non-academic papers and reports on December 13, 2013, using the Canadian Agency for Drugs and Technologies in Health's *Grey Matters Light*.

We used a combination of controlled terms (e.g., "benzodiazepines," "health services for the aged," "substance withdrawal syndrome") and keywords ("diazepam," "elderly," "taper"). To ensure the results were consistent, we adjusted the keywords across the databases. Database searches were supplemented with manual searches of bibliographies of relevant items, which turned up additional references.

Finally, a Scopus 2000–2014 search using the additional key words "dependency," "psychosocial interventions," "therapy," and "counseling" was conducted and queries were sent to clinical experts at the Centre for Addictions and Mental Health (CAMH). This search used a wider timeframe so that it would not miss any relevant articles.

One highly relevant review article (Gould et al., 2014) was identified and added after the search was completed and the article was drafted.

Appendix B: Glossary of Terms

Alternative drug therapy: Pharmacological treatment approaches with medications, including: Propranolol, Buspirone, Carbamazepine, Trazodone, Flumazenil and Imipramine (Voshaar et al, 2006).

Concurrent disorders: A term used to refer to co-occurring addiction and mental health problems. It covers a wide array of combinations of problems, such as anxiety disorder and an alcohol problem, schizophrenia and cannabis dependence, borderline personality disorder and heroin dependence, and bipolar disorder and problem gambling.

Concurrent disorders are also sometimes called:

- Dual disorders;
- Dual diagnosis (however, in Ontario, this term is used when a person has an intellectual disability and a mental health problem);
- Co-occurring substance use and mental health problems.

These problems can co-occur in a variety of ways. They can be active at the same time or at different times, in the present or in the past, and their symptoms can vary in intensity and form over time (O'Grady & Skinner, 2007).

Discontinuing benzodiazepines: To stop use of benzodiazepines, whether gradually or abruptly (Lader et al., 2009).

Gradual dose tapering/dose tapering: To stop use of medication by degrees; to decrease; to diminish (Voshaar et al, 2006).

Melatonin interventions: Melatonin is a naturally occurring hormone in the body that aids with sleep. Melatonin can also be synthetically produced and used in therapeutic approaches to aid symptoms of insomnia during benzodiazepine discontinuation (Dijk, & Cajochen, 1997).

Minimal interventions: An approach that includes giving simple advice in the form of a letter or meeting to a large group of people, sometimes in addition with the provision of a self-help book (Voshaar et al, 2006).

Sleep hygiene: The controlling of all behavioural and environmental factors that precede sleep and that might interfere with sleep (Heijden, Smits, & Gunning, 2006).

ISBN 978-1-77178-216-6

Canadian Centre on Substance Abuse
Centre canadien de lutte contre les toxicomanies

The Canadian Centre on Substance Abuse changes lives by bringing people and knowledge together to reduce the harm of alcohol and other drugs on society. We partner with public, private and non-governmental organizations to improve the health and safety of Canadians.

CCSA activities and products are made possible through a financial contribution from Health Canada. The views of CCSA do not necessarily represent the views of the Government of Canada.