

Original Research

A Comparison of Benzodiazepine and Related Drug Use in Nova Scotia and Australia

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Objective: Benzodiazepines can be a problem if used for long periods, or in at-risk populations, such as the elderly. We compared the use of benzodiazepine and related prescription medicines in Nova Scotia and Australia.

Methods: The Nova Scotia Pharmacare Program and the Pharmaceutical Benefits Scheme in Australia were used to obtain dispensing data in comparable populations for all publicly subsidized benzodiazepines and related compounds. Usage was compared from 2000 to 2003, using the World Health Organization anatomical therapeutic chemical and defined daily dosage (DDD) system. We also determined differences in the types of benzodiazepines prescribed.

Results: The use of benzodiazepines increased at a steady but comparable rate in both areas. However, the use of benzodiazepines in Nova Scotia was more than double that of Australia in 2000 (123 and 48 DDD/1000 beneficiaries per day, respectively) through 2003 (138 and 57 DDD/1000 beneficiaries per day, respectively). Eight different benzodiazepines made up 90% of the drug use in Nova Scotia by contrast to only 4 different benzodiazepines in Australia.

Conclusions: Large differences exist between the type and rate of benzodiazepine prescribing in Nova Scotia and Australia, with Nova Scotia reporting more than twice as much use. Benzodiazepine use in both jurisdictions is increasing. The Canadian findings are especially concerning as benzodiazepine use in the Atlantic provinces has been reported to be less than other provinces. The variations between the 2 jurisdictions may be due to factors such as fewer benzodiazepines available in Australia, differences in prescriber, patient attitudes and behaviours, or different initiatives to influence benzodiazepine use.

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Clinical Implications

- Benzodiazepine use differed markedly between Nova Scotia and Australia, with use being more than twice as high in Nova Scotia.
- Increased use of benzodiazepines in Nova Scotia could be due to public subsidy of a wide range of these compounds, or other factors such as organizational influences and culture.
- Our findings show the need for greater awareness of the level and burden of benzodiazepine use in those aged 65 years and older, and the use of guidelines to improve prescribing.

Limitations

- Benzodiazepine comparative usage data were only for subsidized medicines, dispensed to individuals aged 65 years and older, and those who receive social security benefits.
- Only one Canadian province, Nova Scotia, was compared with Australia, as pharmaceutical subsidy is a provincial responsibility in Canada.
- Dispensing data are not linked to clinical outcomes, therefore it was difficult to determine any clinical reasons for higher use.

Key Words: benzodiazepine, usage, prescribing, Australia, Canada, Nova Scotia

The long-term use of benzodiazepines is concerning because of the risk of dependence, cognitive impairment, and falls and fractures.¹⁻⁴ Patients aged 65 years and older are particularly susceptible to the side effects of benzodiazepines.^{5,6} For instance, the use of benzodiazepines increases the risk of hip fracture in older individuals by at least 50%.⁵ Given the high morbidity and mortality of many of these side effects, the benefits of benzodiazepines for older individuals are unclear, especially as one-third of long-term users do not display psychiatric symptoms requiring benzodiazepines.⁷

There have been explicit guidelines on the inappropriateness of benzodiazepine prescription in older patients dating back to 1991. One example is Beers' criteria or list.⁸⁻¹⁰ This was originally developed for nursing home patients,⁸ but later modified to apply to all patients aged 65 years and older.^{9,10} It identified 20 medications that should be completely avoided, such as diazepam and chlorthalidone, and others where a specified dosage and duration should not be exceeded (for example, prescription of more than one month of a short-acting benzodiazepine).^{8,9}

In spite of this, epidemiologic data from Europe, Canada, Japan, and Australia indicate that rates of benzodiazepine use in the general population have remained steady at around 6%.¹¹⁻¹⁵ Further, in spite of their greater susceptibility to adverse effects, rates of long-term benzodiazepine use among those aged 65 years and older are actually reported to be higher than those of the general population (11% to 25%).¹⁶⁻¹⁸

International comparisons can provide information on the influence of differing access to health care services and drug insurance programs, formulary policies, and practitioner and public education initiatives on drug use trends and consequences.¹⁹⁻²² For example, access to benzodiazepines and related drugs in Australia and the province of Nova Scotia differs significantly regarding both drug availability and reimbursement policies by public insurers, with only 4 agents having equivalent status (Table 1). Nova Scotia has more benzodiazepines and related drugs on the market than Australia and more agents eligible for open coverage by public insurance (14 and 5, respectively), but it is not known whether this difference has any effect on prescribing and use. The hypothesis to be tested was that use of benzodiazepines and related compounds, in those aged 65 years and older and those receiving social security payments, is similar in Nova Scotia and Australia.

Abbreviations used in this article

DDD	defined daily dosage
DU90%	drug usage 90%

Methods

Data Sources

In Canada, we used administrative claims databases from the Nova Scotia Pharmacare Program, which provided data on benzodiazepines dispensed to those eligible for a subsidy (seniors and social security beneficiaries, 80% of all Nova Scotians aged 65 years and older), except for those already with insurance, such as veterans and First Nations people. These seniors pay a yearly premium (ranging from Can\$215 in 2000 to Can\$336 in 2003) and a copayment of 33% of the total cost (to a maximum of Can\$30) for each prescription. Copayments are no longer required once the annual copayment total of Can\$350 has been reached. Community service beneficiaries paid either no copayment (for those with disabilities) or a Can\$5 fee for each prescription.

The Australian Pharmaceutical Benefits Scheme has a similar administrative database,²³ covering all Australian residents, with an equivalent population to the Nova Scotia Pharmacare population (seniors and social security beneficiaries, 75% of all Australians aged 65 years and older). The copayments were about Can\$3.50 for this type of beneficiary (concession) in 2003. Concession beneficiaries were those who receive social security payments (those with little or no income), and includes individuals aged 65 years and older and all women aged 62 years and older. Data on benzodiazepines and related drugs dispensed to Australian concession beneficiaries were obtained from the Australian Pharmaceutical Benefits Scheme database. Similarities between the 2 jurisdictions have allowed previous comparisons, for example, the use of statins.^{24,25}

The study had approval from the Dalhousie University ethics committee (2005-1052) in Halifax, Nova Scotia. As aggregated de-identified data were used for Australia, ethics committee approval was not required.

Comparing the Quantity of Use

We recorded the use of each individual benzodiazepine and related compounds, and total overall use each month, during a 4-year period from 2000 to 2003. Prescriptions were converted to DDDs.^{26,27} This standard measure represents the average maintenance dose for each day of a drug when used for its major indication. It overcomes difficulties in comparing prescriptions of different price, pack size, duration, and dose by relating all drug use to a standardized unit. We calculated the number of DDDs for each 1000 concession beneficiaries each day (DDD/1000 beneficiaries/day) to compare usage over time and place.²⁸ Mean annual data points were compared within and between each study site.

Table 1 Summary of benzodiazepines and their availability and (or) public reimbursement in Nova Scotia and Australia

Category, generic name	Marketed in Canada	Reimbursed in Nova Scotia	Marketed in Australia	Reimbursed in Australia
Benzodiazepines				
Alprazolam	Yes	Yes ^a	Yes	Yes
Bromazepam	Yes	Yes ^a	Yes	Only for veterans
Chlordiazepoxide	Yes	Yes	No	No
Clobazam	Yes	Yes ^a	Yes	No
Clonazepam	Yes	Yes	Yes	Only for epilepsy
Clorazepate	Yes	Yes ^a	No	No
Diazepam	Yes	Yes ^a	Yes	Yes
Flunitrazepam	No	No	Yes	Only for veterans
Flurazepam	Yes	No ^b	No	No
Lorazepam	Yes	Yes ^a	Yes	No
Midazolam	Yes	Yes ^c	Yes	No
Oxazepam	Yes	Yes	Yes	Yes
Nitrazepam	Yes	No ^b	Yes	Yes
Temazepam	Yes	Yes ^a	Yes	Yes
Triazolam	Yes	Yes ^a	Yes	No
Aldehydes and derivatives				
Chloral Hydrate	Yes	Yes	Yes	No
Benzodiazepine related drugs				
Zaleplon	Yes	No ^b	No	No
Zopiclone	Yes	Yes ^a	Yes	Only for veterans
Azaspirodecanedione derivative				
Buspirone	Yes	Yes ^a	Yes	Only for veterans
^a Partial subsidy				
^b Individual authorization only				
^c Special criteria exists				

Comparing the Quality of Use

DU90% measures the number of medications that form 90% of prescribing for a particular drug class. Lower scores have been proposed to provide an indicator of the quality of drug prescribing.²¹ This is because a small range of medications for any drug class allows physicians to gain a greater knowledge of the available treatments.²¹ Prescribers, therefore, know more about benefits, risks, and dosage regimes, and may be less susceptible to industry promotion, if they only have to become familiar with a smaller number of compounds.²⁹ In this study, we calculated the number and volume of drugs that accounted for 90% of the total DDD/1000 beneficiaries/day for benzodiazepines and related compounds. The drugs were ranked from highest use to lowest use, as a percentage of the total DDD/1000 beneficiaries/day. The drugs that constitute 90% of total use are referred to as DU90%.

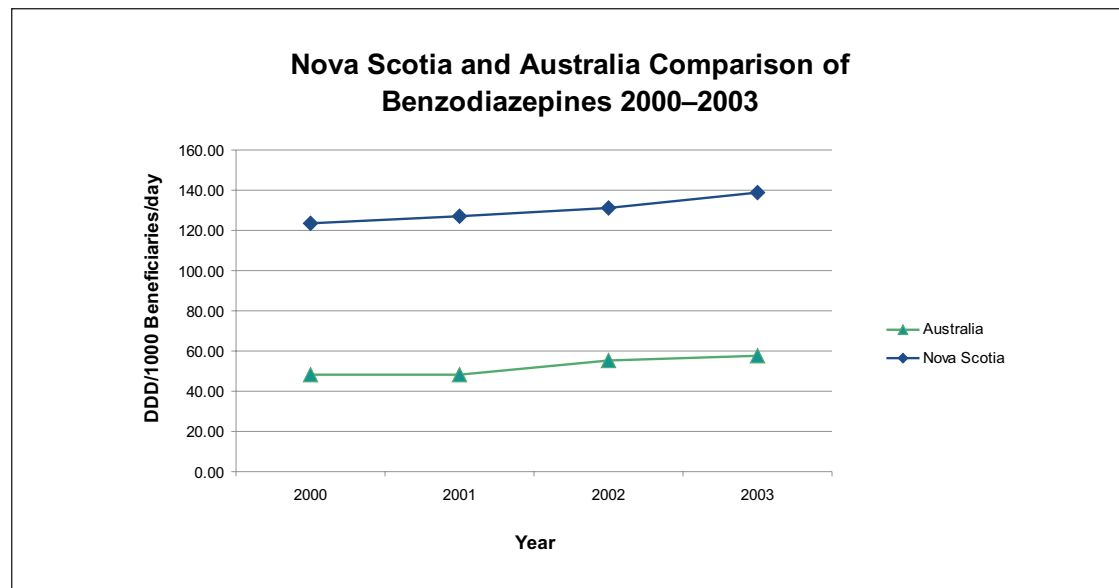
Data Analysis

We performed linear regressions and Student *t* tests to compare changes in the prescription of benzodiazepines and related compounds over time and jurisdiction (GraphPad Prism version 4.03, GraphPad Software, San Diego, California). Differences in the rate of increase were considered statistically significant at $P < 0.05$.

Results

The number of Pharmacare beneficiaries in Nova Scotia ranged from a high of 169 000 in 2000 to a low of 155 000 in 2003 as Pharmacare became the insurer of last resort and dropped coverage for those with other insurance. The number of concession beneficiaries in Australia ranged from 4 800 000 in 2000 to 5 000 000 in 2003. The 2 populations were similar in terms of age and gender; 62% and 68% were

Figure 1 Overall use of all benzodiazepines among Pharmicare Program beneficiaries in Nova Scotia, and beneficiaries in Australia, from 2000 to 2003



aged 65 years or older in Nova Scotia and Australia, respectively, and the proportion of women were 58% and 56%. The prevalence of self-reported mental illness was 11.1% (95%CI, 9.5 to 12.8) in Nova Scotia,³⁰ and 10.5% in Australia.¹⁵

The use of benzodiazepines increased at a steady but comparable rate in both areas. However, the use of benzodiazepines in Nova Scotia was more than double that of Australia from 2000 to 2003 (Figure 1). The observed increases over this period were 15.5 (12.5%) and 9.2 (19%) DDD/1000 beneficiaries/day in Nova Scotia and Australia, respectively. The rate of increase did not differ between the jurisdictions ($P = 0.12$).

There was greater variety in benzodiazepine prescribing in Nova Scotia as indicated by DU90% (Figure 2). Eight different benzodiazepines made up 90% of the drug use in Nova Scotia, compared with 4 in Australia. In 2003, lorazepam was the most commonly used benzodiazepine in Nova Scotia (25%), whereas diazepam was most commonly used in Australia (33%). In total, 17 types of benzodiazepines and related drugs were used in Nova Scotia in 2003 (Figure 3), compared with 5 in Australia (Figure 4). The proportion of long half-life agents used in Australia—47% (diazepam and nitrazepam) was higher than in Nova Scotia—19% (diazepam, clorazepate, flurazepam, and nitrazepam).

Discussion

This is the first study to directly compare 2 jurisdictions using a standard methodology, and is particularly relevant at a time when Canada consolidates its National Pharmaceutical Strategy.^{31,32} We have shown that the use of benzodiazepines increased at a steady but comparable rate in both Australia and

Nova Scotia. Of most concern to Canadian prescribers was the finding that the use of benzodiazepines in Nova Scotia was more than double that of Australia from 2000 to 2003, even though the health systems in both countries have similar characteristics.^{25,33} This may be relevant to physicians elsewhere in Canada because the Atlantic region has, if anything, significantly lower benzodiazepine use than the rest of the nation.¹⁹ All this exists despite numerous initiatives to improve rational prescription including the use of clinical practice guidelines, electronic decision support tools, formularies, copayments, therapeutic and generic substitution policies, and education of doctors and pharmacists.^{24,34–37} Of particular concern is the continuing use of long-acting benzodiazepines that are contraindicated in the elderly.^{8,9} Our results from Australia and Canada confirm findings from the United States that benzodiazepines with longer half-lives such as diazepam and nitrazepam are some of the most common compounds prescribed.³⁸

Implications for Clinical Practice and Policy Change

Improving health status and reducing health care costs are major themes of health care policies worldwide. To achieve these goals, medicines need to be prescribed and used appropriately. For this reason, policies and guidelines for prescribing have been designed.^{32,39} Guidelines for benzodiazepines and related compounds, including the Beers' list,^{8–10} recommend that benzodiazepine use should be limited in the elderly to low dosages of a short- or medium-acting agent for no more than one month.^{8–10,40} However, the results of our study suggest these are not being implemented. Indeed, benzodiazepine use is increasing in this vulnerable population, and use in Nova Scotia is more than twice the use in Australia.

Figure 2 DU90% for benzodiazepines and use of all benzodiazepines among Pharmicare Program beneficiaries in Nova Scotia, and beneficiaries in Australia, from 2000 to 2003

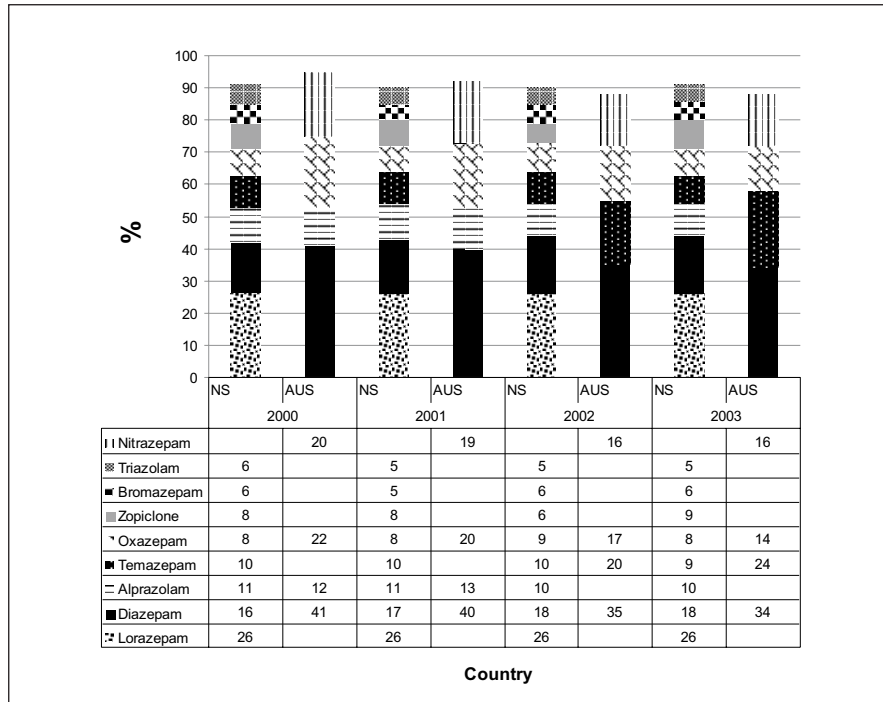


Figure 3 Proportion of each benzodiazepine and related compounds used by Nova Scotia Pharmicare Program beneficiaries in 2003, using DDDs

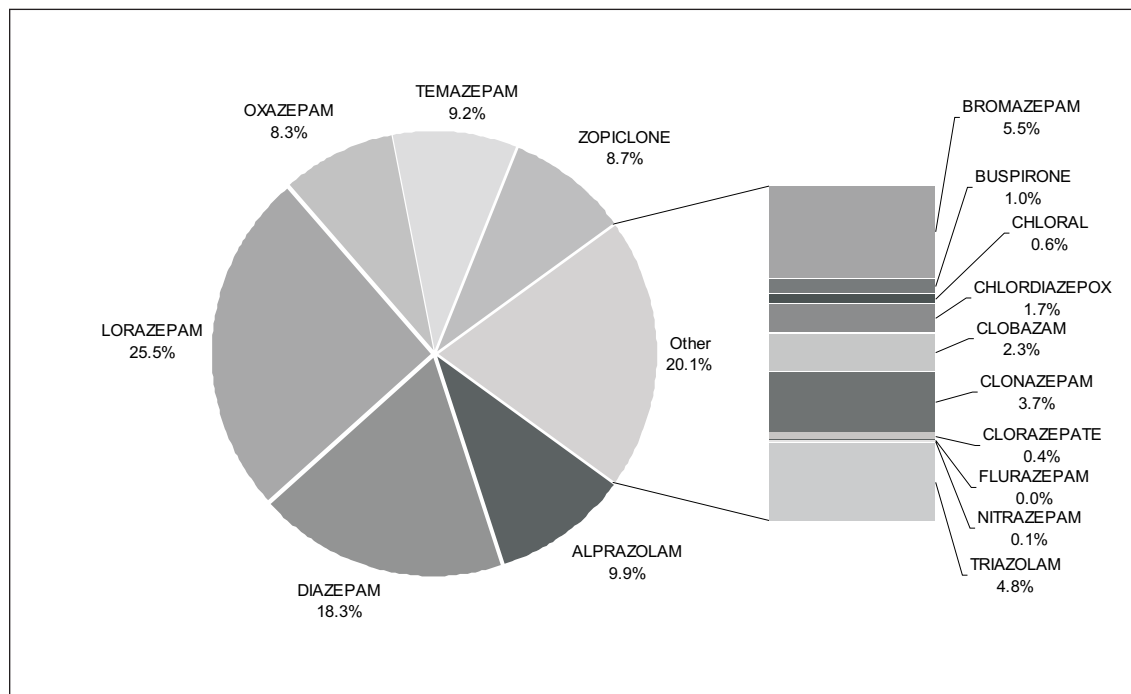
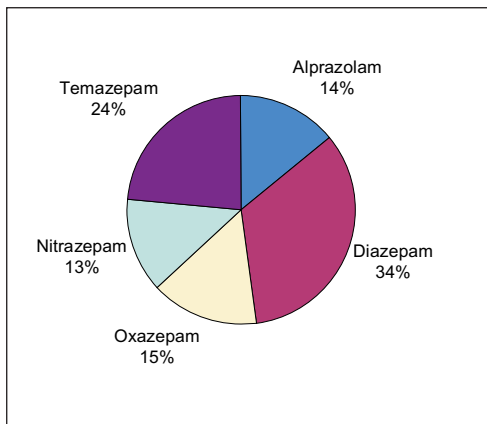


Figure 4 Proportion of each benzodiazepine and related compounds used by Australia beneficiaries in 2003, using DDDs



Prescriber-related factors contributing to this increase in use could include knowledge, confusion over differing psychotropic guidelines, difficulties in discontinuing an inappropriate medication started by a previous physician, multiple prescribers and pharmacies involved in the care of a patient, negative perceptions regarding aging, and cost issues.⁴¹ Patients may contribute to the problem by demanding an inappropriate medication. Finally, the inclusion or exclusion of specific medications in hospitals, health care plans, or provincial formularies may exacerbate the problem through the inclusion of excessive number of compounds for a given medication class.³⁸ Successful strategies to foster appropriate prescribing need to address all of these factors through educational and administrative approaches.³⁸

For physicians, these strategies include educational approaches such as one-on-one sessions and academic detailing. Education could be complemented by the use of personal formularies, where prescribers have a short personal list of drugs that are effective for, and tolerated by, the patients they treat.^{29,38} This technique can be easily taught to medical students through textbooks, national formularies, and guidelines.⁴² Evidence also suggests that most seniors can be gradually tapered off benzodiazepines, while avoiding negative effects of withdrawal.⁴³ Media campaigns and letters to patients can encourage them to gradually discontinue their benzodiazepine in partnership with their family physician.⁴⁴ Initiatives such as these can achieve 20% to 30% reductions in long-term benzodiazepine use.⁴⁵⁻⁴⁸

Our data also suggest an association between the number and range of benzodiazepines prescribed. Nova Scotia reimburses 17 benzodiazepines, while Australia only reimburses 5.

Administrative approaches could therefore include limits on the range of medications available for any particular drug

class, allowing physicians to gain greater knowledge of the medications they prescribe.²¹

Limitations of This Study

This study used administrative databases designed for pharmacist payment rather than for drug usage studies, which lack clinical data related to patient characteristics and reason for use. Therefore these data need to be interpreted with care. The databases do not allow individual tracking of patients, therefore coprescribing with other medication, or doubling or tripling the dose on benzodiazepine use cannot be quantitated. The data indicated dispensed medication (rather than actual prescribed medicine or actual taken medicine), and so do not take into account primary noncompliance (medication prescribed but the prescription not filled) or non-compliance by the patient (medication prescribed and dispensed but not actually taken by the patient). The data are only available for subsidized medicines, dispensed to individuals aged 65 years and older, not otherwise insured, or receiving social benefits (and therefore entitled to subsidized medicines) in Nova Scotia, or dispensed to those receiving an old-age pension, or receiving social security benefits in Australia. The groups are essentially similar, in particular the proportion aged 65 years and older, but there may be some minor differences in the populations. We were only able to compare the Australian data with data from one Canadian province; we therefore do not know how generalizable the findings would be to other parts of Canada. The DDD methodology may not reflect the actual dosage taken, especially if the medication was not used regularly. The knowledge, skills, and attitudes about benzodiazepine prescribing among physicians and the beliefs and values among patients may also be different in Nova Scotia and Australia.

Conclusion

This study found major differences in the type and rate of benzodiazepine prescribing in Nova Scotia and Australia. Benzodiazepine use increased in both Nova Scotia and Australia during the period, with benzodiazepine usage being twice as high in Nova Scotia than Australia. Of particular concern was the continuing use of long-acting benzodiazepines, which are contraindicated in this age group.^{8,9} This study has suggested that the high use of benzodiazepines in Nova Scotia may be due to Nova Scotia having 12 more benzodiazepines (and related compounds) available than Australia. It may be possible to achieve a decrease in use by promoting the use of guidelines and enhancing awareness of the level and burden of benzodiazepine use, especially in those aged 65 years and older. The effects of different formulary policies of drug insurance programs, funding, beliefs and attitudes of patients and prescribers, and education therefore merit further investigation.

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Résumé : Une comparaison de l'utilisation de benzodiazépines et de médicaments connexes en Nouvelle-Écosse et en Australie

Objectif : Les benzodiazépines peuvent poser un problème si elles sont utilisées sur de longues périodes, ou par des populations à risque, comme les personnes âgées. Nous avons comparé l'utilisation de benzodiazépines et de médicaments sur ordonnance connexes en Nouvelle-Écosse et en Australie.

Méthodes : Le programme d'assurance-médicaments de la Nouvelle-Écosse et celui d'Australie (le Pharmaceutical Benefits Scheme) ont servi à obtenir les données sur les ordonnances dans des populations comparables pour toutes les benzodiazépines et tous les composés connexes subventionnés par l'État. L'utilisation a été comparée de 2000 à 2003, à l'aide des codes de classification anatomique thérapeutique chimique et du système de doses thérapeutiques quotidiennes (DTQ) de l'Organisation mondiale de la santé. Nous avons aussi déterminé les différences entre les types de benzodiazépines prescrites.

Résultats : L'utilisation de benzodiazépines a augmenté à un rythme régulier mais comparable dans les deux régions. Cependant, l'utilisation de benzodiazépines en Nouvelle-Écosse était plus que le double de celle de l'Australie en 2000 (123 et 48 DTQ/1000 bénéficiaires chaque jour, respectivement) jusqu'en 2003 (138 et 57 DTQ/1000 bénéficiaires chaque jour, respectivement). Huit différentes benzodiazépines constituaient 90 % de l'utilisation de médicaments en Nouvelle-Écosse, contrairement à seulement 4 différentes benzodiazépines en Australie.

Conclusions : De grandes différences existent entre le type et le taux des prescriptions de benzodiazépines en Nouvelle-Écosse et en Australie, la Nouvelle-Écosse déclarant plus que le double de l'utilisation. L'utilisation de benzodiazépines augmente dans les deux territoires. Les résultats canadiens sont particulièrement préoccupants car il a été signalé que l'utilisation de benzodiazépines était moindre dans les provinces atlantiques que dans les autres provinces. Les variations entre les 2 territoires peuvent être attribuables à des facteurs comme l'offre réduite de benzodiazépines en Australie, les différences chez les prescripteurs, les attitudes et le comportement des patients, ou les différentes initiatives influençant l'utilisation de benzodiazépines.