

Comparing patterns of long-term benzodiazepine use between a Dutch and a Swedish community

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SUMMARY

Background There is much concern about the widespread long-term use of benzodiazepines. Utilisation data can give a foundation for interventions for appropriate use.

Objective To compare long-term usage patterns of benzodiazepines in a Dutch and a Swedish community in different periods.

Methods Eight-year follow-up patterns of use were investigated with respect to the characteristics of those who continued use over the whole follow-up period. In the Dutch community of 13 500, the data of a cohort of 1358 benzodiazepine users were analysed during the years 1984–1991; in the Swedish community of 20 000 people, a cohort of 2038 benzodiazepine users was followed from 1976.

Results At the end of the follow-up period, 32.9% of the Dutch cohort and 33% of the Swedish cohort had continued use of benzodiazepines. The two overall survival curves showed similar patterns. Stratification for age, gender, previous versus initial use and heavy versus non-heavy use showed comparable proportions of patients continuing benzodiazepine use over time.

Conclusion The parallels in the results of two cohorts in different countries and different periods are striking and give support to the idea to stimulate interventions to reduce long-term benzodiazepine use. Copyright © 2002 John Wiley & Sons, Ltd.

KEY WORDS — benzodiazepines; longitudinal study; long-term use

INTRODUCTION

Long-term use of benzodiazepines has been an important pharmacoepidemiologic subject for many years.^{1–4} Although benzodiazepines are among the safest, most effective and most widely used drugs in the world, there is ample evidence that their long-term use is far from recommended therapy and a clear risk factor for dependence and abuse.^{5,6} Benzodiazepines are mostly indicated in the short-term treatment of anxiety disorders, muscle relaxation and insomnia.^{7–9} The literature abounds with articles dealing with interventions and strategies to reduce and control ben-

zodiazepine abuse.^{10,11} However, so far, only a few programmes have been shown to be effective in this respect in the long run. Moreover, regulation of benzodiazepine prescribing may induce unwanted alternative drug-taking behaviour. A report on the reduction of inappropriate prescribing of benzodiazepines by the New York State Department of Health showed that regulation was effective in reducing both the number of patients being prescribed benzodiazepines and the number of prescriptions given to those who remain on benzodiazepines.¹² However, prescriptions for agents like hydroxyzine, meprobamate, chloral hydrate and barbiturates were increasingly seen in the population studied.

In developing intervention strategies to enhance appropriate benzodiazepine prescribing, it is important to have in-depth insight into the patterns of long-term use and into the target groups that may benefit most

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from such programmes. From a cost-effectiveness point of view, it would make sense to focus on patients who continue usage of benzodiazepines for year after year without any evidence of appropriateness. Isacson found that age, prescriptions by other than the general practitioner and frequent daily use were associated with long-term use.⁴ In 1992, the same author wrote a paper on long-term use of benzodiazepines in a Swedish community.¹³ An important conclusion was that one out of three patients from the benzodiazepine cohort as identified in 1976 continued using these agents during all 8 years of follow-up. When considering those patients with a 'heavy' use of benzodiazepines in 1976, continuation throughout the whole follow-up period was found in approximately two out of three. Moreover, previous use of benzodiazepines before entering the study cohort was found to be a strong predictor of continued use during the follow-up period.

The objective of the present study was to evaluate long-term usage patterns of benzodiazepines in a similar Dutch small-town population and to compare the data with the work done earlier in the Swedish community. We were particularly interested in the comparison of the 8-year follow-up patterns of long-term use with respect to the characteristics of the 'survivors', i.e. those with continued benzodiazepine use over the whole period of follow-up.

It must be noted that interventions to enhance appropriate benzodiazepine use are dependent on the knowledge of a base-line situation in which no interventions are done. Therefore, we chose two older but qualified databases from a period without interventions.^{13,14} We compared results of two local databases in order to provide a more convincing basis for conclusions regarding usage characteristics.

METHODS AND MATERIALS

Study subjects and data collection

The setting of both studies was a geographically confined area with drug-exposure data for virtually the entire population. In both populations, the pharmacy systems were alike with patients being designated to a single pharmacy for all reimbursed prescription drugs. Attrition rates, reflecting the proportion of prescription drugs purchased elsewhere, were therefore very low. The pharmacy records provide accurate and complete study material. These pharmacy data cannot provide indications for use from the prescriber. However, indications for benzodiazepine use are limited (e.g. insomnia, anxiety). During the study

period, no important interventions were done by prescriber or pharmacist to improve or reduce the use.

The comparison data for the Swedish community were drawn from a previous study.¹³ Benzodiazepine exposure patterns in a general population of about 20 000 people were examined using data from a research registry on prescriptions. The community, called Tierp, can be characterised as rural with a relatively high proportion of elderly people. During the study period, all prescriptions were filled through two pharmacies. A cohort of all benzodiazepine users in 1976, aged 15–84 years, was identified and followed for 8 years with respect to continued benzodiazepine use.

The Dutch data came from a pharmacy serving Joure, a geographically concise area comprising a population of approximately 13 500 people in the north-west of the Netherlands.¹⁴ The population was comparable to the Dutch population with respect to age and gender distribution and socio-economic status. Data from all prescriptions of benzodiazepines dispensed at the local pharmacy to the above population during the years 1983–1991 were retrieved from automated pharmacy records.

Exposure definition

Use of benzodiazepines in a particular follow-up year was defined as having filled at least one prescription. Patients were categorised as 'initial use' when they had filled no benzodiazepine prescriptions in the preceding year. 'Heavy use' was defined by an age- and gender-specific percentile method, including all patients who obtained a number of prescriptions equal to or more than the value of the third quartile. Other details of this method have been described elsewhere.¹³

From the local authorities in both communities, population census data were acquired in order to adjust for population effects during the observation period. Patients who moved away or died were censored at the year of this event.

Data were analysed according to the principles of survival analysis (the Kaplan–Meier method) using SAS/SPSS statistical programmes.

RESULTS

In Table 1, the characteristics of the Dutch and Swedish benzodiazepine cohorts are listed. The Dutch cohort comprised 1358 patients, while the initial Swedish cohort included 2038 patients. The annual prevalence of benzodiazepine users in the initial year of use was 10.1% in Joure (1984) and 10.2% in Tierp (1976). The two cohorts were fairly similar with

Table 1. Baseline characteristics of the initial Dutch ($N=1358$) and Swedish ($N=2038$) cohorts

| | Dutch community (%) | Swedish community (%) |
|---------------|---------------------|-----------------------|
| Total | 100.0 | 100.0 |
| Men | 31.7 | 34.4 |
| Women | 63.3 | 65.6 |
| Age (years) | | |
| 15–34 | 14.1 | 8.3 |
| 35–44 | 14.7 | 10.1 |
| 45–54 | 16.8 | 14.1 |
| 55–64 | 15.6 | 23.0 |
| 65–74 | 20.1 | 26.8 |
| >74 | 18.7 | 18.0 |
| Initial use | 36.8 | 29.5 |
| Previous use | 63.2 | 70.5 |
| Non-heavy use | 72.6 | 66.9 |
| Heavy use | 26.4 | 33.1 |

respect to a number of baseline characteristics, although the Dutch population was younger with associated lower frequencies of previous and heavy use of benzodiazepines.

The overall proportion of the cohort left at the end of the 8 years of follow-up was 32.9% in Joure and 33% in Tierp. In Figure 1, the survival curves for the two cohorts are shown. Continuation of long-term use was associated with increasing age, previous versus new and heavy versus non-heavy use. Gender was only slightly associated with continued use throughout the 8-year follow-up period.

Comparison of the overall survival curve in Joure with that in Tierp (Figure 1) and comparison of the stratification for age, gender, previous and heavy use of benzodiazepines across the two communities

(Table 2) showed remarkably similar patterns of follow-up. There was no overall difference between the two cohorts, nor between men and women in the two communities. Only a few age groups showed significant differences in the proportions left at the end of the 8-year follow-up period, i.e. the categories 15–34, 55–64 and 65–74 years. Follow-up after both initial and previous use was comparable and the same was found for non-heavy users. The proportion of heavy users in the Dutch cohort was slightly higher than that in the Swedish community.

DISCUSSION

This study shows striking similarities in the patterns of long-term use of benzodiazepines between a Dutch and a Swedish community. When following benzodiazepine users over a period of 8 years, both populations showed that two out of three patients continue with benzodiazepine use in the first year of follow-up. At the end of the 8-year follow-up period, approximately one out of three patients from the initial cohorts was still receiving prescriptions for benzodiazepines. Stratification for age, gender, previous versus initial use in the first year and heavy versus non-heavy use in the first year revealed comparable proportions of patients continuing benzodiazepine use over time. Despite numerous medical, cultural and socio-economic differences (e.g. prescribing practice, disease behaviour, reimbursement regulations) between the Dutch and Swedish populations, the strong parallels in the 8-year follow-up patterns of both cohorts were remarkable.

Having once entered a cohort of benzodiazepine users, the probability of still being part of that cohort

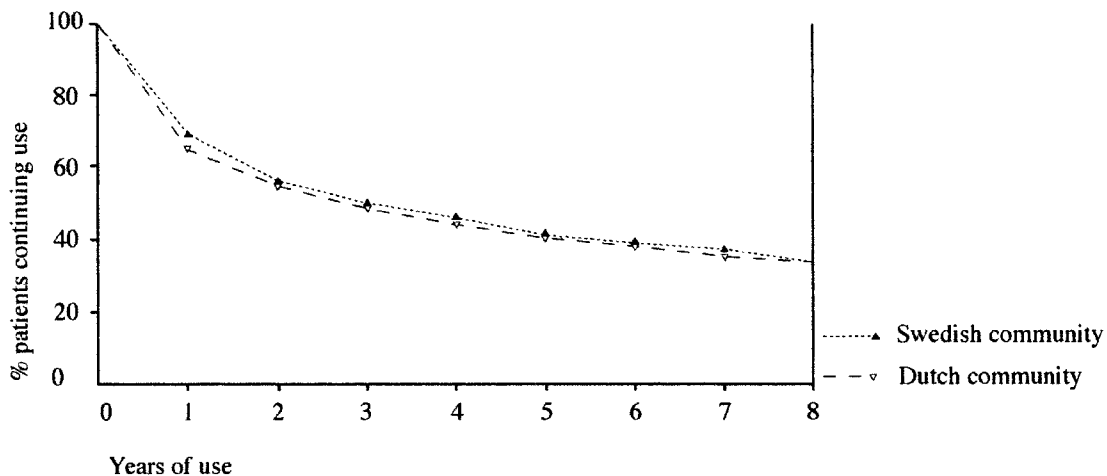


Figure 1. Proportion of users of continuing benzodiazepine use over 8 years

Table 2. Proportion of the cohorts left at the end of the 8-years follow-up period

| | Dutch community (%) | Swedish community (%) | Rate ratio (95% CI) |
|---------------|---------------------|-----------------------|---------------------|
| Total | 32.9 | 33.0 | 1.00 (0.91–1.10) |
| Men | 28.9 | 28.6 | 1.01 (0.84–1.22) |
| Women | 34.7 | 34.5 | 1.01 (0.90–1.13) |
| Age (years) | | | |
| 15–34 | 8.3 | 16.0 | 0.54 (0.30–0.95) |
| 35–44 | 21.8 | 18.6 | 1.17 (0.79–1.73) |
| 45–54 | 27.4 | 25.3 | 1.08 (0.81–1.44) |
| 55–64 | 42.1 | 33.5 | 1.26 (1.03–1.54) |
| 65–74 | 52.7 | 38.7 | 1.36 (1.16–1.58) |
| >74 | 36.3 | 45.4 | 0.80 (0.66–0.98) |
| Initial use | 11.2 | 10.6 | 1.05 (0.75–1.47) |
| Previous use | 45.4 | 41.5 | 1.09 (0.99–1.20) |
| Non-heavy use | 21.0 | 20.7 | 1.02 (0.87–1.19) |
| Heavy use | 63.4 | 56.3 | 1.13 (1.02–1.25) |

in the following years seems to be independent of where the population was studied. The proportions of elderly, previous and heavy users of benzodiazepines in the initial year are much more important determinants of long-term use. Gender has been found to be a significant factor in predicting benzodiazepine use in many studies.^{15,16} Our data show that having once started the use of benzodiazepines, gender is only a small factor in explaining the differences between males and females. As said before, roughly speaking, one out of three patients, both males and females, is still filling prescriptions in the 8th year after starting therapy. Several studies mentioned the relation between a poor physical health and benzodiazepine use in general. Interestingly, long-term use and a high number of prescriptions (e.g. heavy use) are not a factor associated with an impaired health status providing an argument in favour of restrictions on benzodiazepine prescribing.¹⁷

One could argue that the two study periods—1976–1984 in Sweden and 1984–1991 for the Dutch population—cannot be compared because of the time difference in observation. However, this makes the findings of this study even more remarkable. Neither the fact that two populations from different countries have been compared nor the two time frames of observation have resulted in dissimilar long-term usage patterns of benzodiazepines.

Drug utilisation studies have shown large regional and international variations in exposure to benzodiazepines.⁵ In the Scandinavian countries, the difference between Denmark (highest exposure) and Sweden (lowest exposure) is almost twofold.⁵ Moreover, there is ample evidence that utilisation of benzodiazepines is more prevalent among older age groups and females.¹⁸ Benzodiazepines continue to be prescribed

predominantly in the elderly, a group at considerable risk of side effects.¹⁹ Usually, over one-third of the patients taking benzodiazepines use other medicines as well.

We analysed data from two periods without important interventions regarding benzodiazepine use in order to provide a baseline description and an analysis which can be utilised as a point of departure in the discussion about interventions. Prescribers should continue to inform their patients about the side effects of benzodiazepines, the risk of dependence and the difficulties of withdrawal. In interpreting the finding that one out of three patients in both populations continued their benzodiazepine use year after year, repeated prescriptions are probably an important factor.²⁰ In the Swedish town Helsingborg, a large proportion of continuous benzodiazepine users has been associated with abundant repeated prescribing of these agents. About 40% of all benzodiazepine prescriptions were found to be repeat prescriptions.⁵ Erratic, indirect and repeated prescribing was an important determinant of irrational drug-taking behaviour.

In conclusion, this study shows that having once started the use of benzodiazepines, a more or less consistent follow-up pattern of continued use for long periods of time may be anticipated irrespective of professional standards, marketing and the like. In both communities studied, we found an annual prevalence of benzodiazepine use of one out of ten and a long-term use of one out of three of the benzodiazepine users. There is hardly any scientific evidence to justify these usage patterns. Further studies are needed to evaluate such follow-up patterns and their correlates with patient outcomes (dependence, chronic disease, quality of life and the like) in more detail.

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