

Proponen una Nueva Estrategia de Prescripción para Reducir el Consumo de Benzodiazepinas (especial para SIIC © Derechos reservados)

La prescripción mensual precedida de una consulta médica se asocia con la disminución del consumo de benzodiazepinas y ciclopirononas en el sector de atención primaria de la salud.



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Abstract

Background: The global consumption of benzodiazepines (BZ) and cyclopyrrolones (CP) is generally high. This article describes an effective strategy implemented to reduce consumption, while challenging practitioners' ingrained habits and prejudices in this field. **Design:** The rules implemented were such that a prescription for BZ and CP could only be issued for one month at a time, and only following consultation. The prescription of BZ and CP was introduced to 12 Danish medical practices, comprising 15 medical practitioners and a patient base of approximately 20 800 patients. **Findings:** Fifteen months after the implementation of the rules, consumption of BZ-anxiolytics were reduced by 44%, CP was reduced by 53% and BZ-hypnotics were reduced by 47% on average. Two General Practices were followed for a further 24 months, and the reduction attained here was 85%, 91% and 83% respectively. During the first three months, only 4 additional consultations per week per 1 000 patients were required, falling to two additional consultations after 15 months. **Conclusion:** It is recommended that these interventions be introduced into the primary care sector. The intervention does not require any major level of supplementary training. The findings of this study can also be of value for decision makers in health systems.

Key words

benzodiazepines, drug addiction, drug abuse, adverse effect, drug prescription, benzodiazepinas

Resumen

Antecedentes: El consumo global de benzodiazepinas (BZ) y de ciclopirononas (CP) es habitualmente alto a nivel mundial. Este artículo describe la implementación de una estrategia efectiva para reducir el consumo, además cuestiona los hábitos y prejuicios arraigados de los médicos generalistas en esta área. **Diseño:** Las reglas implementadas fueron que la prescripción de BZ y de CP podía ser solamente para el consumo mensual cada vez y luego de la consulta. Esta estrategia de prescripción de BZ y CP fue introducida en doce centros médicos daneses, que comprendían 15 médicos generales y una base de datos de 20 800 pacientes aproximadamente. **Hallazgos:** Luego de quince meses desde la implementación de las reglas, el consumo de ansiolíticos BZ se redujo en un 44%. Los CP disminuyeron 53% y las BZ-hipnóticas, en promedio, el 47%. Se realizó el seguimiento durante 24 meses más en dos centros y las reducciones logradas fueron 85%, 91% and 83%, respectivamente. Durante los primeros tres meses sólo se requirieron 4 consultas adicionales por semana por cada 1 000 pacientes, para luego caer a dos consultas adicionales luego de 15 meses. **Conclusiones:** Se recomienda que estas intervenciones sean introducidas en el sector de atención primaria. Esta intervención no requiere un mayor nivel de entrenamiento suplementario. Los hallazgos de este estudio también pueden ser valiosos para los responsables de la toma de decisiones en los sistemas de salud.

Palabras clave

adicción a las drogas

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Can the Consumption of Benzodiazepines and Cyclopyrrolones be Reduced in General Practice?

Introduction

Barbiturates, the precursors of benzodiazepines (BZ) were first introduced in 1903, and approximately 50 different derivatives were subsequently introduced and marketed to various degrees.¹ These products were characterized by their high misuse potential, small therapeutic index and high toxicity.

BZs were first synthesized in the 1950s and were introduced in 1960 by the pharmaceutical company Roche.^{1,2} The first marketed BZ was chlordiazepoxid, which was followed by a number of other products including the immensely successful Valium Roche (diazepam) in 1963 and subsequently by flunitrazepam in 1975.² BZ were introduced as successors for barbiturates, chloralhydrate and meprobamat, which had been the prevalent hypnotics and anxiolytics. From the 1960s and until the middle of the 1970, global consumption of BZ rose dramatically.

Subsequently, sales in many regions stagnated and declined. In the 1980s, the cyclopyrrolone (CP) group of drugs was introduced. There are clear advantages to both the BZ and CP groups of drugs, compared to the drugs previously available, specifically regarding decreased toxicity and increased therapeutic treatment range. The initial optimism, where it was believed that the perfect drug had been developed, has recently been replaced by a more realistic attitude, where it has been recognised that this group of drugs is associated with significant problems. The use of this group of drugs is associated with significant side effects, but although BZ and CP have come into disrepute in recent years, there is no reason to wish for a return to the older hypnotics and anxiolytics, which are far more toxic.

The over consumption of BZ and CP is a serious, global problem which has been the focus of much attention, although no unequivocal solution has yet been forthcoming.³ The attention paid to this issue has been professionally well-founded.³ In 2003 there were 355 000 users of BZ in Denmark, corresponding to 6.5% of the population, while approximately 225 000 were users of CP, corresponding to 4.1% of the population.^{4,5} In e.g. Norway the combined percent of consumers is reported to be 6.5% of the population, while in Spain and Ireland this figure is 18% and 25%, respectively.⁶ In many regions of the world, the consumption of BZ and CP is still excessively high.^{3,6,7} In Denmark it is estimated that approximately 2% of the population is addicted to these substances, corresponding to 100 000 individuals.^{8,9} A Danish investigation has revealed that every addicted patient subjects society to direct and indirect expenses in the region of 48 000 Euro per annum.¹⁰ This expense, as well as a problem of this magnitude has obviously attracted political interest.

In 2003, the then Danish Minister for the Interior and Health, Lars Løkke Rasmussen, stated that a reduction of 50% of the total consumption should be implemented within 1-2 years, or measures including increased monitoring and statutory registration would be initiated.

In order to decrease consumption, a code of practice has been issued in the form of a circular. In England, for example, essentially the same rules apply as in Denmark. These state that the consumption of hypnotics and anxiolytics should be restricted to a period of no longer than a few weeks.¹¹⁻¹³ In Denmark, implementation of this initiative has been characterized by apathy, as practitioners have considered it impossible to live up to the requirements of the circular. Most practitioners have been dismissive, or have ignored the circulars. No effective method to implement a reduction has been introduced. The combined reduction in the consumption of BZ and CP in Denmark was 1.5% in 2004 and 3.5% in 2005.¹⁴

An interest in this field is professionally well-justified, as these substances have a limited duration of activity. The hypnotic effect diminishes after a few weeks adaptation, and the anxiolytics effect generally diminishes after a few months.^{3,15,16} These substances are strongly addictive with pronounced tolerance development, and risk leading to the development of both physical and psychological symptoms.^{3,15,16} In contrast, a very limited adaptation to the substances side-effect is observed, a factor which persists throughout the entire period of treatment.^{3,15,16} The most common side effects are impacts on the intellectual functions.^{3,15,16} This is especially true for older patients, who can experience pseudo dementia and a tendency to fall.¹⁷⁻¹⁹ Among older patients, the chances of sustaining a collum femoris fracture are increased by approximately 100%.¹⁷⁻¹⁹ Twenty percent die within the first year following the fracture. These drugs are considered to represent a danger for users of motor vehicles, and a study of elderly patients has shown a 2-5 times increase in the risk of traffic accidents.²⁰⁻²² This risk of traffic accidents is of the same magnitude as for those who operate motor vehicles under the influence of alcohol.²⁰⁻²²

Many patients are addicted to such a degree that they will experience abstinence symptoms upon attempting to reduce their consumption of these drugs.^{8,9,16,23-28} Abstinence symptoms include serious reactions, such as suicide impulses and abstinence cramps, as well as less serious reactions such as fear, unrest, increased dream activity, insomnia and melancholia.^{8,9,16,25-28} This may be the most important factor binding patients to their consumption of these drugs.^{23,24}

The so-called rebound effect may be observed during the gradual withdrawal of treatment, leading to an increased recurrence of the symptoms against which the drugs originally were prescribed, following the withdrawal.¹⁶

Efforts over the last eight years in the western part of Region Midtjylland have been focused on reducing the consumption in general practice of these drugs.^{8,9,25-28} Information and education seminars have been held.

Supervisory groups have been initiated, and counselling on the part of medical practitioners has been implemented, as well as psychotherapeutic counselling by specialist consultants. The Danish regional medical health officers have intensified their attempts to identify practitioners having patients with a large turnover of dependence-producing drugs. The practitioners in question have subsequently been asked to explain how they intend to reduce their use of dependence-producing drugs. The total reduction in dependence-producing drug consumption as a result of these joint efforts was four percent between 2003 and 2004. This reduction was more than twice the level of reduction reported for the rest of the country. Recently, the regional medical team decided to start an information campaign by visiting practitioners with the highest rates of ordination.

The means to achieve these reductions appear to be both resource-demanding and complicated. In most cases, implementation of these means requires extensive supplementary training for the average general practitioner as well as an extensive and time-consuming contribution from different authorities. It can be daunting to consider that 100 000 dependant patients should be treated in this manner. This would be the equivalent of approximately 30 dependant patients per medical practitioner in Denmark. However, these initiatives have undoubtedly benefited individuals, and have contributed to maintaining focus on the issues.

In 2004, two General Practises in the Danish village of Thyborøn used a few, simple methods to reduce the consumption of addictive medicine.^{8,9,25,26} The goal was to reduce the pattern of consumption in accordance with the official Danish requirements for a reduction of 50%, while at the same time updating patient treatment in

accordance with existing regulations, for the benefit of patients.¹¹ The primary experience derived from this intervention was that it was possible in the space of 15 months to reduce the consumption of BZ and CP by 50% and 75%, respectively. As a consequence of this initiative, the remainder of the municipal practitioners implemented the simple methodology.^{27,28} The results of the intervention for the municipality as a whole are presented in this publication, as well as the 3 1/4 year follow-up for the two initial, primary practices. In addition, an estimate of the age distribution among users, as well as changes within distribution groups is presented here.

Materials and methods

The data was obtained from 12 general practices situated in Lemvig municipality, Denmark, comprising 15 medical practitioners with a total base during the period of approximately 20 800 patients. A single municipal practitioner was not involved in the project, and values from this practitioner are thus not included.

The first phase of the intervention was carried out in the Danish village of Thyborøn, and included two medical practices with a total of approximately 2 300 patients.^{8,9,25,26} In cooperation with the Medicine Unit of Ringkjøbing County and the County Medical Health Officer, the two practices agreed to work in accordance with the circular,¹¹ from the first of January, 2004. Due to geographical constraints, the intervention was initiated with patients living in Thyborøn village (approximately 2/3 of the patients) and from January 1, 2005 all patients from both practices were involved.

The remaining 10 practices in Lemvig municipality agreed to implement similar rules from the 1 April 2005. The intervention included N05BA (BZ anxiolytics e.g. oxazepam, diazepam, lorazepam, chlordiazepoxid and alprazolam), N05CF (CP hypnotics e.g. zopiclon, zaleplon and zolpidem) as well as N05CD (BZ hypnotics e.g. nitrazepam, flunitrazepam and triazolam). The ATC-group included all BZs and CPs available in Denmark with the exception of BZs for the treatment of epilepsy, such as clonazepam.

The internet site for the Institut for Rationelt Farmakoterapi (IRF) (www.Ordiprax.dk) was used to evaluate the consumption of BZ and CP, as data was freely available and covered the required material.²⁹

The material compiled by the IRF originates from data reported by pharmacies to the Drug Statistics Register of the Danish National board of Health covering the sale of prescription drugs. For each ordination, the practitioners identification code, the patients central person registration (CPR) number and the products specific product identification number are registered, where the latter comprises the products anatomical therapeutic chemical (ATC)-code, package size as well as the total number of defined daily doses (DDD) in the package.

Ordiprax is divided into two categories: regional data and practice data. Medical practice data comprises the individual practices prescriptions to own patients, redeemed at a Danish pharmacy, and is only visible to the regional Pharmaceutical Consultants and Medical Advisors via a special code.²⁹ Ordiprax data searches can be standardised for gender and age. The standardised DDD is an expression of the consumption which the individual practice would in theory have attained if all practices had the same gender and age distribution as the reference population (Denmark as a whole). The margin of error for Ordiprax data is less than four percent and has no effect on the conclusions derived from the results presented in this article.

The practitioners' intervention consisted of

- The elimination of telephone prescriptions for BZ and CP drugs.
- The issue of single prescriptions only, following consultation.
- The issue of medicine sufficient for a single month's consumption only.
- A discussion at each consultation regarding future treatment requirements as well as a possible phased reduction of treatments.

The rules are essentially in accordance with the Danish Health Authority's past and current regulative in this field.^{11,12} The fundamental principles for reduction are presented in Table 1. To support the intervention, a patient as well as staff guide and poster were prepared.

Table 1. The 10 most important, fundamental rules for the reduction in consumption of benzodiazepines and cyclopyrrolones.

Fundamental rules in benzodiazepine reduction:

- Adjust reduction rates individually.
- Proceed slowly; use a tablet doser or cutter if required.
- If abstinence symptoms arise, maintain current doses for a further month.
- Never increase doses.
- Benzodiazepines with short half lives are experientially most difficult to reduce.
- Possibly replace benzodiazepines with short half lives with products with long half lives (e.g. diazepam) over a period of months.
- Cyclopyrrolones can be reduced directly.
- A monthly reduction of 10-25% will be tolerated by most.
- Discontinue prescriptions when daily doses of e.g. Diazepam are reduced to ½ mg, or Zopiclon (Imovane) is reduced to ¼ of a 3,75mg tablet.
- Avoid alternative medications.

The patient guide in folded A4 format described

- The type of intervention.
- The reasoning behind the intervention.
- Effects and side-effect of the drugs.
- The preparations covered by the intervention.

The staff guide in folded A4 format described:

- The type of intervention.
- The reasoning behind the intervention.
- Administration of the first inquiry from the patient
- An explanation for the intervention, directed at the patient.

- A note in the journal.
 - Rules for the issue of the smallest packaging.
 - Rules for the issue of the next package only following consultation.
 - Rules for the allocation of consultations.
 - Which drugs were included
- The poster in A3 format described
- The reasoning behind the new rules.
 - The new rules.
 - Which drugs were included

A number of meetings were held in order to implement the intervention

1. A 2 1/2 hour meeting including a 2 hour Power Point lecture. The meeting was held to motivate participants in the project. The invited delegates were practitioners and pharmacists with staff.
2. A one hour afternoon meeting with practitioners where it was decided when and how the intervention would be implemented.
3. A two hour orientation was held for home care staff and other key personnel, such as the local psychiatrist.
4. Subsequently, a regional meeting was held, where results from the intervention were presented to practitioners. The press was informed about the intervention. This led to coverage of the project's purpose and scope in both local and national newspapers. In addition, the intervention was covered by local and national television. The press coverage contributed to an increased understanding on the part of the patients of the interventions purpose and scope, as well as the extent of the new regulations, including the fact that participation was compulsory as the intervention was in accordance with the circular in force at the time.¹¹ The coverage ensured that patients were well prepared for the intervention.

Inclusion criteria

All patients from the 12 practices who were users of BZ or CP were included, with the exception of patients suffering from severe physical or psychiatric disorders. The number of patients excluded from the intervention is small, and will not significantly affect the general conclusions obtained as a result of this study. In fact, these patients would contribute to an additional reduction, if it were possible to subtract the excluded patient's consumption of BZ and CP.

The term severe physical disorder covered patients suffering from a terminal disease, or patients where disease characteristics were such that the prescription of medical drugs was primarily performed by a specialist unit. Severe psychiatric disorders generally covered patients whose treatment was being monitored by a psychiatrist. Patients receiving high doses, as well as patients with prior failed drug reduction histories were not automatically excluded, unless they otherwise fulfilled the exclusion criteria.

The treatment of patients excluded from this study was not changed as a result of this project.

The Danish National Health Service as well as the local medical association in Ringkjøbing County had no objections to the increase in consultations arising from this study.

Units

The reduction in prescriptions was described in the same manner: for the practices covered by first phase of the intervention (practice 01 and practice 02, Thyborøn village), the total DDD (defined daily doses) for every 1 000 of the practitioners own patients per quarter calculated after the first quarter of 2005 is compared to the average DDD for every 1 000 of the practitioners own patients for the four quarters of 2003. For the remaining ten practices, the total DDD for every 1 000 of the practitioners own patients per quarter for the second quarter of 2006 is compared to the average DDD for every 1 000 of the practitioners own patients for the last three quarters of 2004 as well as the first quarter of 2005. Accordingly, the reduction in prescriptions was registered over a period of one year and three months for all practices. When calculating average declines per practitioner, the fact that a single practice comprised two practitioners while another practice comprised three practitioners was taken into account. These practices were weighted accordingly when calculations were carried out. In order to compare our results on a national basis, data was standardized with respect to gender and age.

A questionnaire was sent out upon completion of the observation period. Questions were phrased in a way which permitted the elucidation of the burden of the intervention on patients and practitioners, as well as the secondary treatment system. In addition, it has been our aim to evaluate the frequency of change of practitioner by patients, as well as the amount of patient complaints. A number of questions were evaluated using a visual analog scale (VAS) from 1-10, where 1 was the least problematic and 10 was the most problematic imaginable scenario.

In order to calculate the combined reduction for practice 01 and 02, results are combined and the results from 2003 are compared with the three final quarters of 2006 as well as the first quarter of 2007. The 3 1/4 year period was chosen due to the fact that a practitioner who did not partake in the intervention retired in the second quarter of 2007. As a result of this, practice 01 took over approximately 300 patients, and practice 02 took over about 800 patients who had not been included in the intervention. Accordingly, subsequent results would be irrelevant in the context of this study.

A number of consumption groups were constructed for practice 01 and 02, defining five levels of consumption of BZ and CP (Figure 1). Patients participating in the intervention were distributed into the five groups, both before and after the intervention. The distribution of patients prior to the intervention is based on their combined consumption of BZ and CP in 2003. The allocation following the intervention was carried out on the basis of practitioners' estimates 2 1/2 years later, with the second quarter of 2006 as the initial source of data (multiplied by four to obtain an estimated annual consumption). Only patients associated with the practices during the first 2 1/2 year period are included, as it has not been possible to gain access to subsequent data in this field.

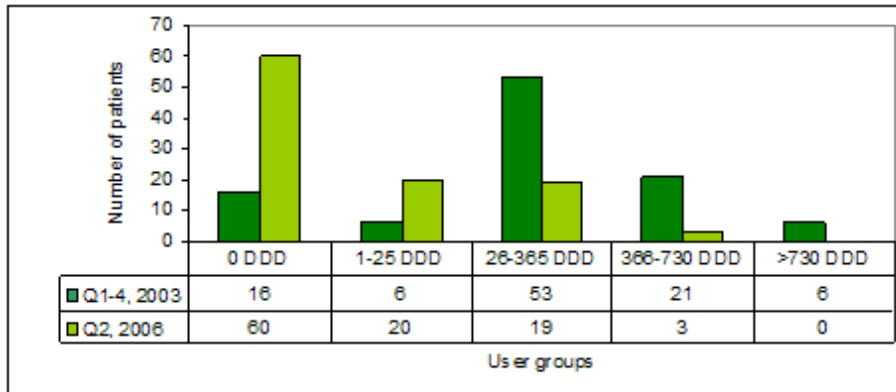


Figure 1. Distribution grouping of patients' total consumption of benzodiazepines and cyclopyrrolones, in defined daily doses (DDD) per year, for patients from the first two practices (practices 01 and 02) covered by the intervention. Only patients associated with the practices for the first 2½ years of the intervention are included (n=102). The dark columns indicate the distribution prior to the interventions; the light columns indicate distribution 2½ years after introduction of the intervention.

In order to determine whether the reduction in consumption is significant, results are analyzed using a two-tailed T-test for samples with unequal variance.

The intervention was an implementation of existing laws and was not categorised as an experiment, thus obviating the need for approval by the Danish Biomedical Research Ethics Committee.

The intervention was carried out with the full support and cooperation of all practitioners. The author of this article designed the primary phase of the intervention in cooperation with the other members of the Medicine Team, and the intervention was originally implemented in his general practice as well as a second practice. Later, when the intervention was expanded to include a further 10 general practices, the intervention was lead by the author in his capacity as Medical Advisor for Region Midtjylland.

Results

As a result of the intervention, a clear reduction in the consumption of anxiolytics (N05BA) and hypnotics (N05CF and N05CD) for all of the involved practices was observed (Figure 2).

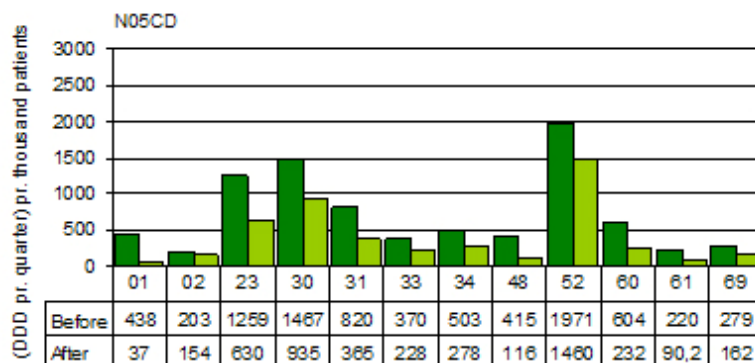
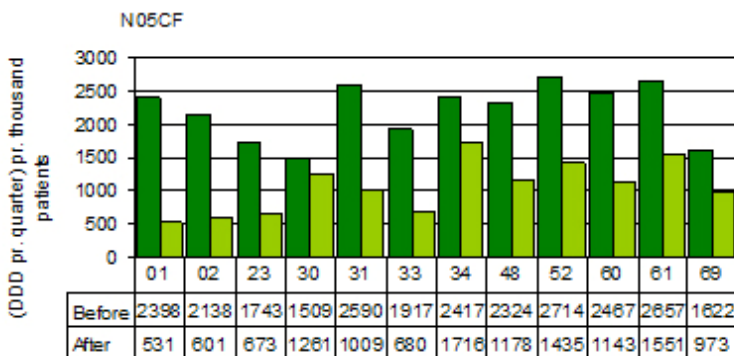
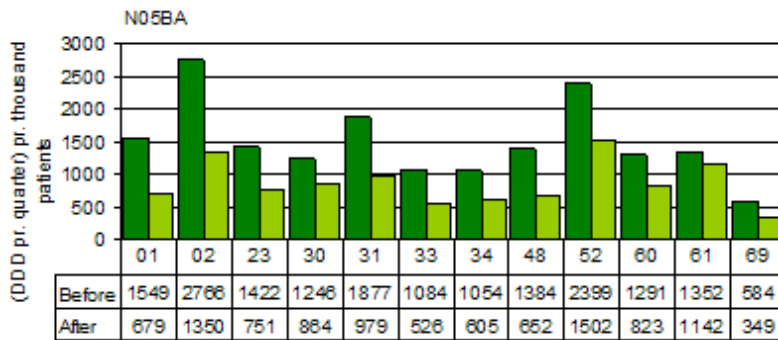


Figure 2. Graphs showing the reduction in prescriptions of anxiolytics (N05BA) and hypnotics (N05CF and N05CD) for individual practices. On the X-axis, practices are identified by a double-digit code, while the Y-axis represents the Daily Defined Doses (DDD) per quarter per thousand registered patients. Data was standardized with respect to gender and age. The first (dark) column indicates the average prescription rate in the four quarters prior to the intervention (Before), while the second (light) column indicates prescription rates after five quarters (After). The average reduction was 44% (N05BA), 53% (N05CF) and 47% (N05CD), respectively.

The consumption of anxiolytics of the BZ group (N05BA) was reduced in the individual practices by between 15.5% and 56.2%, with an average reduction of 42.5%. The total reduction at the municipality level was 43.6%. Consumption rates were unevenly distributed between the individual practices. The practices with the highest consumption rates had rates approximately four times greater than those of practices with the lowest consumption rates. The greatest numerical reduction was seen for the two practices having the highest consumption rates. The practice with the lowest consumption (practice 69) showed a reduction of 40.2%. In practice 01 and 48 the reductions were greatest, at 56.2% and 52.9%, respectively.

In the individual practices, the consumption of CP (N05CF) was reduced by between 16.4% and 77.9%, with an average of 51.2%. The total reduction at the municipality level was 53.2%. Consumption rates were unevenly distributed between the individual practices. There was no correlation between the level of consumption within a practice and the level of reduction achieved. Practice 31, which was among those practices with the highest prescription rates, was able to reduce prescriptions by 61%, while practice 23, which was among those with a low prescription rate, was similarly able to reduce prescriptions by 61%. In practice 01 and 02 the reductions were greatest, at 77.8% and 71.9%, respectively.

The consumption of hypnotics of the BZ group (N05CD) was reduced in the individual practices by between 24.1% and 91.6%, with an average reduction of 50.1%. The total reduction at the municipality level was 47.5%. Once again, consumption rates were unevenly distributed between the individual practices. The practices with the highest consumption rates had rates more than nine times greater than those of practices with the lowest consumption rates. The numerical reduction in prescriptions for the highest rated practice was of a magnitude equal to the total number of prescriptions for the two lowest rated practices, prior to the initiation of the intervention.

All 15 practitioners replied to the questionnaire, and the results are compiled in Table 2. The burden on the individual practitioners was minimal, with an additional 4.1 consultations per thousand registered patients at the inception of the intervention, falling to 2.1 additional consultations after 15 months.

Table 2. Results compiled on the basis of a circulated questionnaire. The first two results are based on a VAS (Visual Analogue Scale) of 1 (lowest) to 10 (highest) as a measure of workload impact. Subsequent results represent the impact relative to the number of patients in the entire municipality, or as number per 1000 patients. All of the 15 practitioners involved in the intervention answered the questionnaire.

Parameter	Value	Measurement	Number of practitioners answering the question
Expected workload impact of the intervention	6,2	VAS value	14
Actual workload impact of the intervention	3,3	VAS value	15
Initial consultations	4,1	Per 1000 registered patients	13
Final consultations	2,1	Per 1000 registered patients	13
Patients relocated as a consequence of the project	6	For entire county	15
Patients referred to psychiatrists.	6	For entire county	15
Patients hospitalised in psychiatric wards.	0		15
Patients hospitalised in local hospitals	0		15
Patients referred to outpatient treatment at the counties addiction unit	4	For entire county	15
Patients referred to homecare services	0,8	Per 1000 registered patients	15
Suicide or suicide attempts	0		15
Patients referred to external cognitive-behavioural therapy	4	For entire county	15
Patients treated with cognitive-behavioural therapy by own practitioner	1,9	Per 1000 registered patients	15
Official complaints to Danish Public Health Service Complaints Board, or to Chief Medical Officer	0		15

Only a few abstinence symptoms were reported, namely restlessness, fear, insomnia, sweating, tremors and agitation. No reports of serious abstinence symptoms such as suicide, suicide attempts or abstinence cramps were received. Not all practices were equally systematic when reporting abstinence symptoms, with terms such as "few" and "many" being used. According to the questionnaire, the additional burden to community nursing or the secondary treatment system was minimal or non-existent. No complaints were reported.

Consultation procedures

First telephone consultation: As a rule, these were carried out by staff. The new rules were described to the patients. The smallest package of the relevant drug was prescribed, and patients were encouraged to participate in a regular consultation prior to the ordination of their next prescription as telephone prescription was no longer possible.

First Consultation: This was probably the most important contact. Patients may have lain awake all night at the thought that their BZ and CP might be taken from them. They could be slightly aggressive. In addition, they were surprised that the new rules applied to them. They had typically received medication over a period of years, and could not do without it. They felt that they would become ill, and that their existence would collapse, if they did not receive medication. A significant part of the consultations consisted of reassuring patients that their medication would not immediately be taken from them. At the same time it was made clear that help would be available during the reduction period. After the first consultation, it was typically agreed that the patients would follow the scheduled dose. It was important to regain the patient's confidence. It was particularly important to uphold the rule regarding monthly consultations, even if it meant the practitioner came under considerable pressure.

Second Consultation: If the patient showed no, or only moderate, abstinence symptoms the actual reduction could be implemented. The reduction could be individually tailored, where a reduction of 10%-25% was a typical starting point. Practical issues with respect to package sizing and the possibility of dividing tablets could arise. Here it was possible to use a tablet-doser or cutter, available at pharmacies, which could divide a 3.75 mg zopiclon tablet or a 2 mg diazepam tablet into quarters, if required. Prescriptions were issued for a single month's consumption. If

greater amounts were prescribed, it was certain that patients would only return when the package was empty. In most cases it was an advantage to permit patients to order a new consultation at once.

Third Consultation: The reduction could now be continued, if the patient showed no or only moderate abstinence symptoms. If the opposite was the case, consumption was maintained at current levels for a further month. It was important that patients understood that although time was not an issue, the goal of a reduction should be maintained. No increase in medication was permitted. Once again the prescription was for a single month's consumption.

Fourth Consultation: The same as the third consultation, and so on.

Final consultation: Patients were now at reduced doses, for example 0.5 mg diazepam or a quarter tablet zopiclon 3.75 mg. These doses were almost without effect, and the medication could now be discontinued without problems. Knowledge gained from this project show that it is important to maintain the monthly consultations, as these are a bearing element in the intervention. If this principle is not adhered to, one opens a possibility for discussion which can be fatiguing for the practitioner. It has also been discovered that it is expedient to prescribe medication for a single month at a time. It is important not to be swayed by arguments that it is cheaper and more expedient to prescribe larger packaging. Experience has shown that patients only attend consultations once the package is empty.

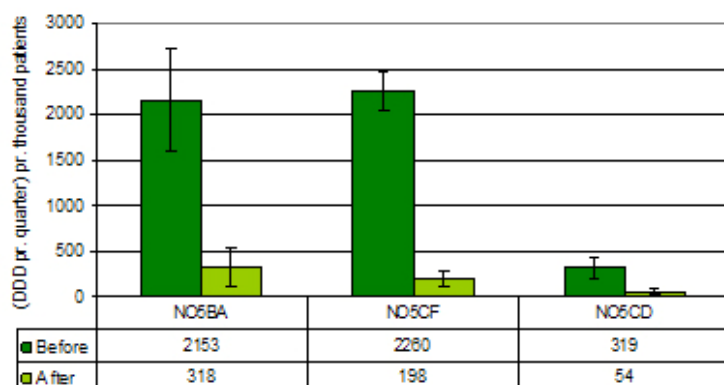


Figure 3. Development in the number of prescriptions issued by two medical practices, before and after the initiation of measures for the reduction of benzodiazepines (N05CD, N05BA) and a cyclopyrrolone (N05CF). Data compiled before the intervention "Before" are Daily Defined Doses (DDD) per quarter per thousand of the practitioners own patients, and describe prescription averages for the four quarters of 2003. "After" data describe prescription averages for the three final quarters of 2006 as well as the first quarter of 2007. Error bars denote the 95% confidence interval of the means. "Before" and "After" values are significantly different, ($P < 0.05$; two-tailed T-test for samples with unequal variance). The reduction over the 3 1/4 year duration of the intervention was 85% (N05BA), 91% (N05CF) and 83% (N05CD), respectively.

In practices 01 and 02 the intervention was followed for a period of 3 1/4 years. The reduction for N05BA was 85.2%, for N05CF 91.3% and for N05CD 83.1%, respectively (Figure 3). Age distribution among consumers was followed for the first 2 1/2 years in practises 01 and 02, and shows an accumulation in the age group 45-65 (Figure 4). It should be noted that the age groups are by no means standardised.

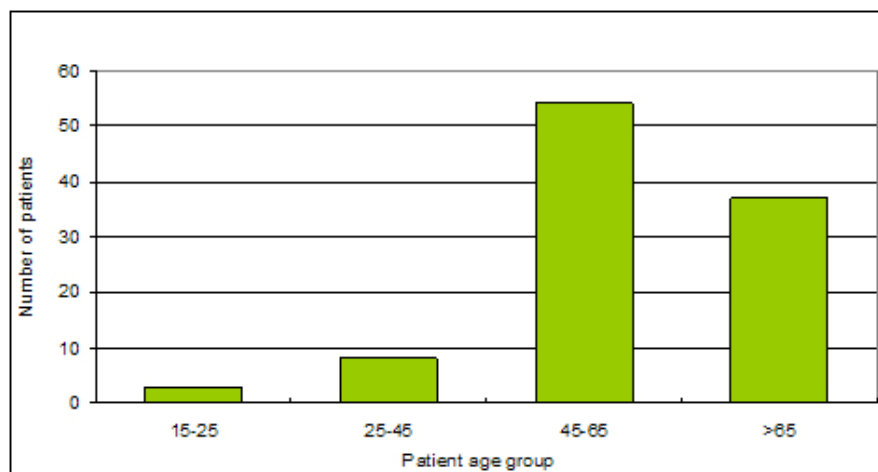


Figure 4. Patient-age grouping of benzodiazepine (N05CD, N05BA) and/or cyclopyrrolone (N05CF)-consuming patients, for patients in practices 01 and 02 (n=102). Only patients associated with the practices for the first 2 1/2 years of the intervention are included.

Discussion

The results reveal a reduction ranging from 43.6% to 53.2% in the consumption of BZ and CP for the whole municipality, over an extraordinarily short period of time. All practices were able to implement a reduction in the prescription of all drug groups included in the project. Consumption rates for the individual practices varied greatly and in all probability reflect the individual practitioner's attitude with respect to the prescription of these drugs. Prescription patterns can be traced several "practitioner generations" back in time, although this does not change the fact that it is the prescribing practitioners themselves who have the responsibility of prescribing these drugs to their patients.

The questionnaire used in this project is flawed by the fact that it based on the practitioners memory, rather than on actual registration. However, it is felt that the questionnaire provides a good indication of how few problems and complications the project experienced. The practitioners' worst expectations were never realized, and implementation of the project was far easier than they had imagined. The requirement for extra services was limited, and no serious side-effects materialized.

Many methods have been used in an attempt to reduce the consumption of BZ. In a Norwegian study³⁰ a significant reduction was observed in a group of users following the dissemination of written information together with an offer of assisted reduction from their practitioners. In a corresponding Danish study,³¹ information pamphlets and a questionnaire were sent to individual consumers of BZ, in an attempt to make them reflect on their own situation and future consumption. This resulted in a significant decline in consumption. These findings are in accordance with an English study, where a 24% reduction was achieved merely by sending a letter to patients.^{32,33} In a simple audit study³⁴ regarding the prescription of BZ it was discovered that the number of consumers could be reduced by 16%. In addition, studies reveal that focused and individualised efforts give remarkably good results.³⁵

The intervention described by the present study is simple, and only requires a minimal effort on the part of the practitioner. The patient is at all times the focus of attention, and no changes are implemented without consulting the patient. The monthly consultation is inspiring for both the patient as well as the practitioner; and contributes by maintaining focus on the issues of addictive medicine.

With the guide of July 8, 2008, new regulations for the prescription of BZ and CP¹² were introduced in Denmark which, in similarity with previous guides¹¹ maintained that re-evaluations for the prescription of anxiolytics should take place after four weeks, while the prescription of hypnotics should be re-evaluated at least every two weeks. The most significant point in the new guide was that the regulation regarding personal attendance upon prescription could only be dispensed with in exceptional cases. Accordingly, the simple rules described here, now popularly known as the "Thyborøn model", had become part of a national intervention.

In the western part of Region Midtjylland, the introduction of the "Thyborøn model" to reduce BZ and CP consumption has been successfully carried out on a larger scale. The regulations were introduced to practitioners with a patient base of 365 000, representing an estimated patient population of 18 000 consumers of BZ and CP.²⁵ Impressions of this intervention were positive.

At present, no published results or information on whether an intervention of this nature can lead to increased prescriptions of other medications is available. However, similar studies could give cause for concern. In 1989 in New York, new rules were introduced requiring that prescriptions of BZ be copied in triplicate on special, serialised forms. At the same time, practitioners were required to acquire and purchase these prescription forms. The initiative reduced the consumption of BZ by 30%-60%.³⁶ Subsequently, an alarming increase in the prescription of alternative medication was observed. The article which describes this intervention³⁶ concludes "further evaluation must be carried out before similar programs are instituted elsewhere". In Denmark, alternatives to hypnotics and anxiolytics such as barbiturates (with the exception of Phenobarbital) and choralhydrate may normally not be prescribed by practitioners without special dispensation, and it may be more relevant to expect an increase in the prescription of antipsychotics and antidepressives. A future study will be focused on this issue.

Although each of the fundamental methods for reduction has its benefits and disadvantages, it is recommended that "cold turkey" reduction as well as reduction under hospitalization should be reserved for special circumstances. Neither specialist systems nor the hospital sector are able to deal with a problem of this magnitude. Accordingly, the issue must be dealt with within the primary sector. The resources of the health care system would soon be depleted, if the problem was indiscriminately transferred from the primary to the secondary sector.

Conclusion

The results presented here reveal that a halving of the consumption of BZ and CP can easily be carried out by all practices, and that an even greater reduction in all probability could be achieved by maintaining focus on the issues, and by not reverting to old prescription patterns. This will require a minimum of supplementary training, as well as a limited though focused effort on the part of practitioners. The extra time required is minimal, and can be adapted for almost any practice.

It is recommended that the following few and simple rules are implemented in general practice for the prescription of BZ and CP.

- The elimination of telephone prescriptions.
- Prescriptions limited to one month at a time.
- Issue of prescriptions only following consultation.
- Every month, the patient and the practitioner are to consider whether the actual level of consumption is appropriate, or whether withdrawal should be initiated.

The mounting of a poster in waiting rooms as well as the distribution of guidelines for the prescription of addictive medicine, together with press coverage, are efforts which also could contribute in a positive way to the success of similar projects.

At the same time it should be pointed out that the choice of alternative medication should be based on critical judgement. It is important that the prescription of these drugs should not merely be rerouted to other, more problematic medications, but rather that a genuine improvement in prescription strategy should be implemented through the monthly consultations.

It is the goal of this study to convince colleagues in general practice that it is easy and practicable to address these issues. It is recommended that these routines be applied upon prescribing BZ and CP, as these simple rules will have a significant effect on consumption. It is especially thought provoking when one discovers that 80%-90% of ones prescriptions of these potentially dangerous drugs are superfluous.

These findings could also be interesting for decision makers in health care systems who are preparing new

regulations for the prescription of BZ and CP. This is especially relevant when we see that the rules presented in this study have already been implemented at the national level through the Danish guide dated July 8, 2008.¹²

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