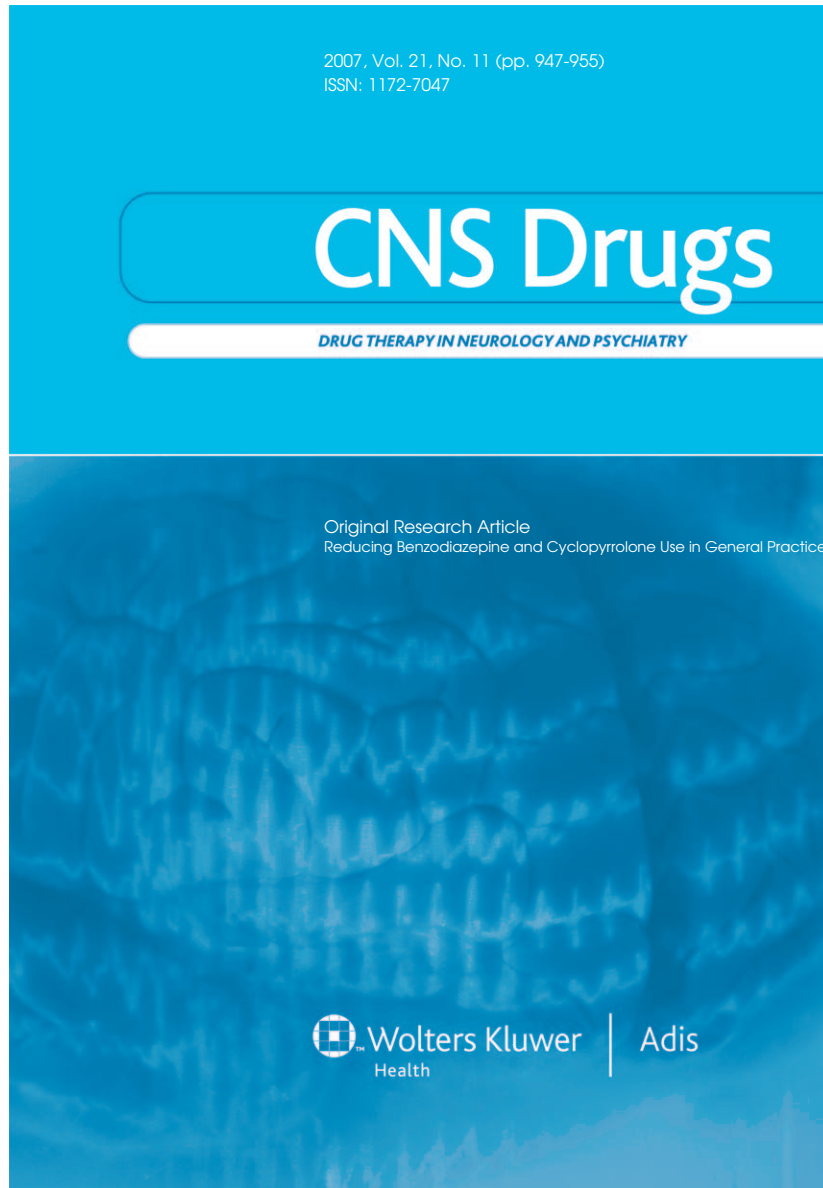


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An Approach to Reduce Benzodiazepine and Cyclopyrrolone Use in General Practice

A Study Based on a Danish Population

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Abstract

Background: The global use of benzodiazepines and cyclopyrrolones is generally high. The hypnotic and anxiolytic effects of these agents typically diminish after a period of weeks or months of continuous use. Patients may thus be caught in a trap where the usefulness of these substances is reduced and doses are consequentially escalated, and where a subsequent phased reduction in dose can be difficult. Although considerable resources have been expended on reducing the use of these agents, no unambiguous and effective method has been identified.

In Denmark, it is estimated that there are approximately 100 000 benzodiazepine-dependent patients, constituting approximately 2% of the general population. The prescription of dependency-producing drugs (including benzodiazepine/cyclopyrrolone agents) in Denmark is regulated according to Danish directive CIR nr 12, introduced on 13 January 2003, which aimed for restrictions in the prescribing of benzodiazepine and cyclopyrrolone drugs while setting revised guidelines for the re-evaluation of these agents. However, by 2004, the use of these drugs had decreased by only 1.7%, far from the official objective of a 50% reduction.

This article describes an effective strategy implemented in general practice in Denmark to reduce the use of benzodiazepine and cyclopyrrolone agents, while at the same time challenging practitioners' ingrained habits and prejudices in this field.

Design: An intervention involving new regulations for the prescription of benzodiazepines and cyclopyrrolones was introduced to ten Danish medical practices, comprising 13 medical practitioners and a patient base of approximately 18 500 patients. The new intervention was essentially in accordance with the official Danish regulations, such that a prescription for benzodiazepines and cyclopyrrolones could only be issued for 1 month at a time, and only following consultation. Telephone prescriptions were eliminated. Use was monitored using the Danish registration system, Ordiprax, which monitors sales of prescription medicine. All users of benzodiazepines and cyclopyrrolones within the ten practices, with the exception of seriously psychiatrically and physically ill patients, were included.

Results: Fifteen months after the inception of the intervention, the use of cyclopyrrolones was reduced by 50.3%. Use of benzodiazepine-hypnotics was reduced by 46.5% and use of benzodiazepine-anxiolytics was reduced by 41.7%. The reorganisation of prescription patterns proved to be significantly easier than practitioners had expected. During the first 3 months, only 4.3 additional consultations per week per 1000 patients were required. Subsequently, this number fell to 2.1 additional consultations. The usual collaborative partners, such as psychiatrists, homecare services, hospitals and substance abuse units, were essentially not deployed. No serious side effects developed in patients in whom drug use was reduced.

Conclusion: The intervention was effective in reducing the use of benzodiazepine and cyclopyrrolone agents in general practices in a large municipality in Denmark. It is recommended that this intervention be introduced into the primary care sector, as it requires minimal effort on the part of the medical practitioner. The intervention is as simple as it is effective, and its implementation does not require any major level of supplementary training.

Introduction

The use of benzodiazepines and cyclopyrrolones is, in many global localities, too high.^[1,2] In Denmark, it is estimated that approximately 2% of the general population is dependent on these drugs, corresponding to 100 000 individuals.^[3,4] A Danish investigation has revealed that every dependent individual subjects society to direct and indirect expenses in the region of £ 48 000 per annum (1995 costs).^[5]

This cost, as well as the magnitude of the problem, has attracted political interest. In 2003, the Danish Minister for the Interior and Health, Lars Løkke Rasmussen, stated that a reduction of 50% in the use of benzodiazepines and cyclopyrrolones (use being defined as sales of prescription benzodiazepine and cyclopyrrolone drugs) should be achieved within 1–2 years, or measures including increased monitoring and statutory registration would be initiated. In order to reduce use, new regulations were issued in the form of circulars (essentially, the same regulations apply in England). These state that the use of hypnotics and anxiolytics should be restricted to a period of a few weeks.^[6,7] In Denmark, implementation of these regulations has been characterised by apathy, as practitioners considered it impossible to attain the requirements of

the circulars. Most practitioners have been dismissive of, or have ignored, the circulars. This led to the reduction in the total number of prescriptions in Denmark being as low as 1.7% in 2004, and approximately 5% in 2005.^[8]

An interest in this field is professionally well founded, as these drugs have a limited duration of activity. The hypnotic effect diminishes after a few weeks of continuous use, and the anxiolytic effect generally diminishes after a few months.^[9] These drugs are strongly addictive, with pronounced tolerance and a danger of patients developing both physical and psychological symptoms.^[2,9,10] In contrast, very limited adaptation to the adverse effects of the drugs is observed, a factor that persists throughout the entire period of treatment.^[3,4,9,10] This is especially true for older patients treated with these drugs, who can experience pseudo-dementia and a tendency to fall.^[10,11] Among older patients, the chances of sustaining a collum femoris fracture is increased by approximately 100% during treatment with benzodiazepines and cyclopyrrolones.^[12,13] Of such patients, 20% die within the first year following the fracture.^[12]

Many patients will experience abstinence symptoms following attempts to gradually withdraw from these drugs.^[3,4,9,10] Occasionally, paradoxical effects such as anxiety, violent behaviour and hallucina-

tions may be observed.^[10] In addition, the so-called 'rebound effect' may be observed during the gradual withdrawal of treatment, characterised by an increased recurrence of the symptoms for which the drugs were originally prescribed.^[9]

In Ringkjøbing county, Denmark, efforts over the last 6 years have focused on reducing the use of these drugs in general practice.^[3,4] 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 use of dependence-producing drugs as a result of these joint efforts was 4% between 2003 and 2004. This reduction was more than twice the level of reduction reported for the rest of the country.

However, 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. It can be daunting to consider that 100 000 dependent patients, the equivalent of approximately 30 dependent patients per medical practitioner in Denmark, need to be treated in this manner. However, these initiatives have undoubtedly benefited individuals, and contributed to maintaining focus on the problem.

In 2004, using a few simple methods, two Danish general practice clinics in Thyborøn attempted to reduce the use of dependency-producing drugs.^[3,4] The objective was to change the consumption pattern in accordance with the official Danish requirements for a 50% reduction, while at the same time bringing patient treatment in accordance with the existing regulations for the benefit of the patients.^[7] The result of this initiative was a reduction in the use of cyclopyrrolones by 75% and benzodiazepines by 50% within a period of 15 months.

In the current study, the intervention used in Thyborøn was investigated in an expanded setting (multiple practices in a large municipality).^[3,4]

Materials and Methods

The data reported in this paper were obtained from ten general practices situated in Lemvig municipality, Denmark, comprising 13 medical practitioners with a total patient base during the study period of 18 513 patients. All practices took part in the intervention. As the project was not an experiment, but rather an observation of the effects arising when existing laws are followed, no application was made for the project to be approved by the Biomedical Research Ethics Committee.

In collaboration with the Public Health Department in Ringkjøbing Amt, the ten practices agreed to introduce the intervention from 1 April 2005. The intervention was based on a previous intervention implemented with considerable success in the Thyborøn practices,^[3,4] and carried out in cooperation with the regional medical officer. The intervention was carried out with the full support and cooperation of the involved practitioners, and was headed by the author of this paper in his capacity as Medical Advisor to the Medicine Team, Region Midtjylland.

The intervention included the drug groups N05CF (hypnotics from the cyclopyrrolone group, e.g. zopiclone, zolpidem and zaleplon), N05CD (hypnotics from the benzodiazepine group, e.g. nitrazepam, flunitrazepam and triazolam) as well as N05BA (anxiolytics from the benzodiazepine group, e.g. diazepam, alprazolam, oxazepam and lorazepam). The internet site of the Institute for Rational Pharmacotherapy (IRF; www.Ordiprax.dk) was used for evaluation of the extent of use of benzodiazepine/cyclopyrrolone drugs in the general practices in Lemvig and the effect of the intervention on this use, due to ease of access as well as a high degree of coverage of the required material.

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

prescription handled by the pharmacy, the prescribing physician's personal code, the patient's national registration number and the specific code regarding the drug in question, containing information covering the anatomical therapeutic chemical (ATC) code, package size and total daily defined doses (DDD) in the package, were registered.

Data on Ordiprax are divided into two categories: county data and medical practice data. Medical practice data comprises the individual practices prescriptions to their own patients, redeemed at a Danish pharmacy, and only visible to the practitioner and the county medical advisor via a specific code.^[14]

The practitioners' intervention consisted of: (i) the elimination of telephone prescriptions for benzodiazepine and cyclopyrrolone drugs; (ii) the issuing of single prescriptions only, following consultation; (iii) the prescription of medicine sufficient for a single month's use only; and (iv) discussion at each consultation regarding future treatment requirements as well as a possible phased reduction of treatments.

To support the intervention, a guide and poster were prepared for the benefit of patients and staff (i.e. nurses and secretaries employed in the general practices). The patient guide, in folded A4 format, described the type of intervention, the drugs included, the reasoning behind the implementation of the intervention, and information on the therapeutic effects and adverse effects of the drugs.

The staff guide, also in folded A4 format, described the type of intervention; the drugs included; the reasoning behind the implementation of the intervention; guidelines for the initial consultation (where the intervention is explained to the patient, and the consultation is registered in the patient's journal); rules for the initial prescription of the drugs (initial prescription of the smallest available package size prior to consultation, and subsequent prescriptions only on the basis of personal consultation); and rules for the allocation of compulsory consultations prior to the ordination of prescriptions. A poster in A3 format described the reasoning be-

hind the intervention, the intervention itself and which drugs were included.

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

- a 2.5-hour meeting, including a 2-hour Power Point lecture. The meeting was held to motivate participants in the project. The invited delegates were practitioners as well as pharmacists with staff;
- a 1-hour afternoon meeting with practitioners, where it was decided when and how the intervention would be implemented;
- a 2-hour briefing session primarily aimed at the homecare services as well as other key persons, such as the local psychiatrist.

The press was informed about the intervention, and the author of this paper contributed with an article printed in the local newspaper in March 2005, covering the reason for, and scope of, the intervention. In addition, a front-page story in the regional newspaper was devoted to the intervention, elucidating patient benefits and emphasising that the rules outlined in the intervention were mandatory. The public information campaign contributed to increasing patient understanding of the intervention, and ensured that patients were well prepared prior to the implementation of the intervention.

All patients in the ten general practices who were receiving benzodiazepines or cyclopyrrolones were included, with the exception of patients with severe physical or psychiatric disorders. The number of patients excluded from the intervention was exceedingly small, and would not contribute significantly to the overall conclusions drawn in this study. In fact, the inclusion of these patients could have contributed to a further decrease in the prescription of benzodiazepine and cyclopyrrolone drugs. The term 'severe physical disorder' covered patients with a terminal disease, or patients whose disease characteristics were such that the prescription of medical drugs was primarily performed by a specialist unit. 'Severe psychiatric disorders' generally covered illnesses that were 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 in Ringkjøbing Amt, as well as the local medical association in Ringkjøbing Amt, had no objections to the increase in consultations arising from this study.

For all cases, the effect of the intervention on prescriptions was determined as follows. The total DDD for every 1000 of the physicians' patients per quarter for the second quarter of 2006 was compared to the average DDD for every 1000 of the physicians' patients for the last three quarters of 2004 and the first quarter of 2005. Accordingly, the effect of

the intervention on prescriptions was registered over a period of 1 year and 3 months. When calculating the effect of the intervention within the county, consideration was given to the fact that each practice had a different number of registered patients. In order to compare results on a national basis, data were standardised with respect to gender and age.

A questionnaire was sent out upon completion of the observation period. The questions were phrased in such a way as to elucidate the impact of the intervention on patients, practitioners and secondary health services (i.e. hospitals and specialists). A visual analogue scale (VAS) of 1–10 was used to determine the workload impact, where 1 indicated the least possible workload impact and 10 indicated

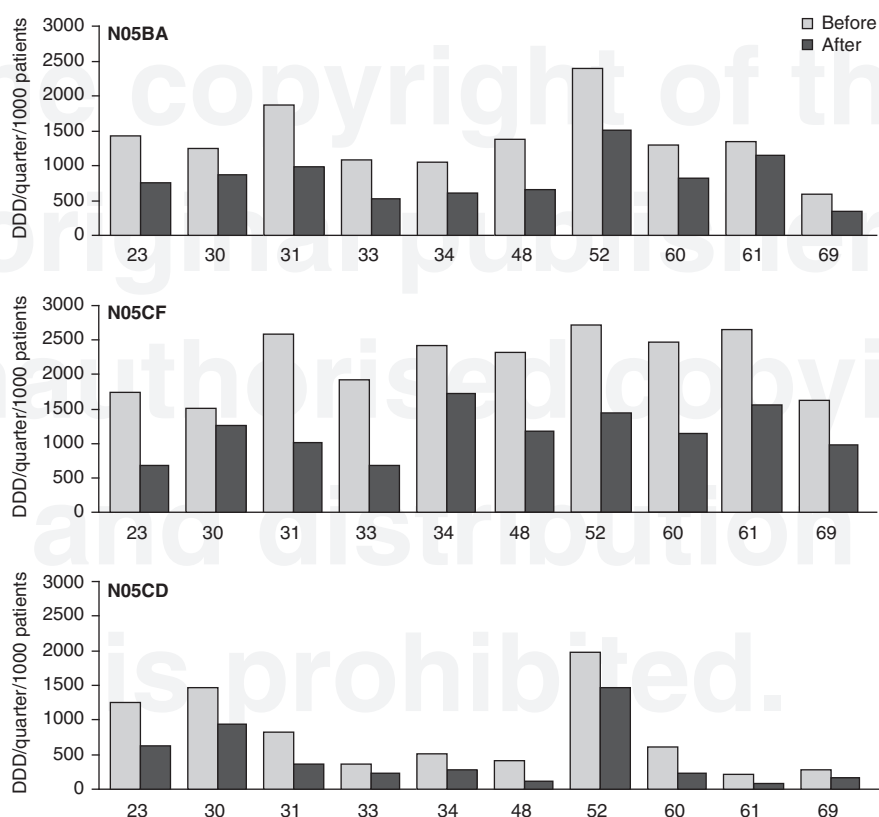


Fig. 1. Graphs showing the reduction in prescriptions of anxiolytics (N05BA) and hypnotics (N05CF and N05CD) for individual practices. On the x-axis, practices are identified by a double-digit code, while the y-axis represents the daily defined doses (DDD) per quarter per thousand registered patients. Data were standardised with respect to gender and age. The first column indicates the average prescription rate in the four quarters prior to the intervention (before), while the second column indicates the prescription rate in the fifth quarter after the intervention (after).

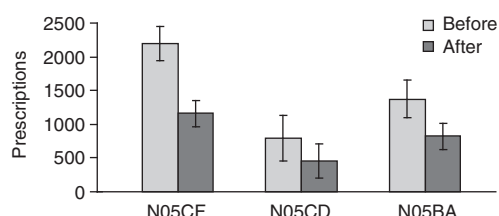


Fig. 2. Development in the number of prescriptions issued by ten Danish practices before and after initiation of the measures for the reduction of benzodiazepines (N05CD, N05BA) and cyclopyrrolones (N05CF). Data compiled before the intervention are derived from prescriptions that are quarterly averages for the period April 2004 to April 2005; data for prescriptions issued after the initiation of the intervention are for the second quarter of 2006. All compilations are derived from the data presented in figure 1. Error bars denote the 95% confidence interval of the means.

the worst possible workload impact. Furthermore, the questionnaire addressed issues related to the extent of patient relocation to other practices, as well as the level of official complaints regarding, for example, malpractice or negligence.

Means, as well as weighted (with respect to the number of patients in each practice) means, for the use of benzodiazepine/cyclopyrrolone drugs in the general practices in Lemvig municipality were calculated. Differences between means were calculated using a two-tailed t-test for two samples with equal variances, where equality in variance was determined using the F-test, or by using a single factor analysis of variance (ANOVA) for more than two means.

Results

Following the intervention, a clear reduction in the prescription of anxiolytics (N05BA) and hypnotics (N05CF and N05CD) was apparent for all practices participating in the project (figure 1). The overall numerical reduction was significant for anxiolytics, N05BA and the hypnotics group N05CF (figure 2). No significant difference was found for the average percent reduction between the three drug classes (figure 3).

In the individual practices, the use of cyclopyrrolones (N05CF) was reduced by between 16.4% and 64.5%, with an average reduction of 46.4%. The total reduction at the county level was 50.3%. Use rates were unevenly distributed between the individ-

ual practices. The highest use rates were 80% higher than the lowest use rates. It is not possible to conclude from the size of a practice whether a reduction is possible. For example, 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%.

The prescription of hypnotics of the benzodiazepine group (N05CD) was reduced in the individual practices by between 26.0% and 72.2%, with an average reduction of 48.6%. The total reduction at the county level was 46.5%. Again, prescription rates were unevenly distributed between the individual practices. The practices with the highest prescription rates had rates 9-fold greater than those practices with the lowest prescription 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.

The prescription of anxiolytics of the benzodiazepine group (N05BA) was reduced in the individual practices by between 15.6% and 52.9%, with an average reduction of 40.2%. The total reduction at the county level was 41.7%. Use rates were unevenly distributed between the individual practices. The practices with the highest prescription rates had rates approximately 4-fold greater than those practices with the lowest prescription rates. The greatest

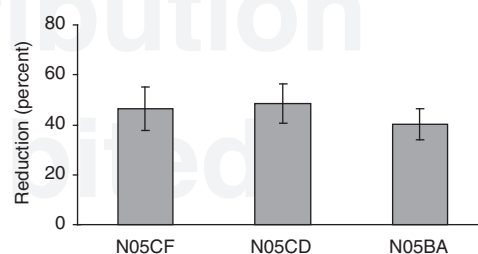


Fig. 3. Average reduction in prescriptions of benzodiazepines (N05CD, N05BA) and cyclopyrrolones (N05CF) issued by ten Danish practices. All compilations are derived from the data presented in figure 1. Error bars represent the 95% confidence interval of the means. Average values are not significantly different (single factor ANOVA, $p = 0.30$)

Table I. Results compiled on the basis of a circulated questionnaire. The first two results are based on a visual analogue scale (VAS) 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 county, or as a number per 1000 patients. All 13 practitioners involved in the intervention answered the questionnaire

Parameter	Value	Measurement	No. of practitioners answering the question
Expected workload impact of the intervention	6.0	VAS value	12
Actual workload impact of the intervention	3.6	VAS value	13
Initial consultations	4.3	Per 1000 registered patients	11
Final consultations	2.1	Per 1000 registered patients	11
Patients relocated as a consequence of the project	2	For entire county	13
Patients referred to psychiatrists	5	For entire county	13
Patients hospitalised in psychiatric wards	0	For entire county	13
Patients hospitalised in local hospitals	0	For entire county	13
Patients referred to outpatient treatment at the county's addiction unit	4	For entire county	13
Patients referred to homecare services	0.9	Per 1000 registered patients	13
Suicides or suicide attempts	0	For entire county	13
Patients referred for external cognitive-behavioural therapy	4	For entire county	13
Patients treated with cognitive-behavioural therapy by own practitioner	2.3	Per 1000 registered patients	13
Official complaints to Danish Public Health Service Complaints Board or to Chief Medical Officer	0	For entire county	13

numerical reduction was seen for the two practices having the highest prescription rates. The practice with the lowest prescription rate showed a reduction in prescriptions of 40.2%.

Additional results arising from the questionnaire are summarised in table I.

Few abstinence symptoms were reported; however, not all practices were equally systematic in their reporting of abstinence symptoms, with terms such as 'few' and 'many' being used. The specific symptoms reported were agitation, anxiety, insomnia, sweating, tremors and restlessness.

Discussion

For the original project carried out in Thyborøn,^[3,4] reductions in prescriptions were greater than those reported in the current study in the Lemvig municipality. This may be due to the fact that practitioners in Thyborøn were especially motivated, although the reduction of between 41.7% and 50.3% seen in the current study in an entire municipality over such a short period can in itself be considered extraordinary.

It is difficult to explain the differences in reduction between the individual practices, although ex-

planations may include differences in motivation among the individual practitioners. Data were standardised with respect to gender and age in order to compare the individual practices. All practices were able to implement a reduction in the prescription of all drug groups included in the project. Prescription rates for the individual practices varied greatly and in all probability reflect the individual practitioners' 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 individual prescribing practitioners who have the responsibility of prescribing these drugs to their patients.

The questionnaire used in this project is flawed by the fact that it was completed subsequent to the intervention itself, and the accuracy of the results may have been affected by the individual practitioners' memory. However, it is felt that the questionnaire provides a good indication of how few problems and complications there were with the project. Most of the treatments were carried out in general practice, and referral was only used to a limited degree. The practitioners' worst expecta-

tions were never realised, and implementation of the project was far easier than they had imagined. The requirement for extra services was limited, and no serious side effects in patients in whom drug use was reduced materialised.

An additional limitation of the present study is that the effect of the intervention on the prescribing of other drugs, such as SSRIs, was not assessed. This is a relevant issue that is currently being addressed by the author, and will be the subject of a subsequent paper.

The Danish Ordiprax system constitutes a solid basis for the direct surveillance and control of medical prescriptions, and the replication of this intervention will be greatly facilitated in countries with a similar level of organisation. Furthermore, if the intervention is to be introduced effectively a high level of collaboration among practitioners is necessary to eliminate 'doctor shopping'. It may be speculated that the intervention may not be easy to replicate in healthcare systems where patients pay doctors for prescriptions. However, it can be argued that the payment of prescriptions in itself can be a motivating factor in contributing to the reduction of the prescription of these drugs.

Many initiatives have been launched in order to reduce the consumption of benzodiazepines in general practice. A Norwegian study^[15] revealed a marked reduction in the consumption of benzodiazepines following the circulation of written brochures to patients being treated with benzodiazepines, as well as the initiation by practitioners of withdrawal therapies for individual patients. A similar Danish study^[16] combined the circulation of information to patients being treated with benzodiazepines with a questionnaire designed to encourage patients to reflect on their individual situations, their actual consumption and their expected future consumption, and a similar, marked reduction in the consumption of benzodiazepines was noted. A comprehensive English audit study^[17] revealed that a simple audit of the prescription of these drugs could lead to a fall of 16% in the number of consumers. In addition, an individually tailored treatment with a focus on the individual patients, comprising a course

of supervised benzodiazepine withdrawal, has been shown to be effective, although requiring considerable resources.^[18]

The present study contributes to the overall sum of knowledge in this field. In addition, this study differentiates itself from previous studies by the simplicity and low workload impact of the intervention. The patient is the centre of the intervention at all times, and no adjustments are made to prescriptions without the involvement of the patient. The monthly consultations are inspiring for both patient and practitioner, while contributing to drawing attention to problems related to the consumption of dependency-producing drugs.

As a result of this project, it is clear that the use of a few simple methods is able to bring prescription patterns in accordance with existing laws, for the benefit of patients. The knowledge required for any practitioner to implement a similar reduction in prescriptions can be attained during the course of a few hours, and is accessible through readily available literature, such as the references cited here.^[3,4,10] It is expected that the results of this intervention will be generally applicable, as similar rules have been implemented for approximately 125 practitioners in Ringkjøbing County, Denmark, representing a patient base of approximately 202 000 patients. Initial impressions have been positive, and final results are expected to be published in 2–3 years.

Conclusion

This study demonstrated that the intervention can bring about a reduction in the prescription of cyclopyrrolones and benzodiazepines of 40–50% in all practices. The intervention requires a minimum of supplementary training, as well as limited (although focused) effort on the part of practitioners. The extra time and effort required is minimal, and can be adapted for almost any practice.

The implementation of the following few and simple rules are recommended when prescribing benzodiazepine and cyclopyrrolone drugs:

- the elimination of telephone prescriptions;
- the issuing of single prescriptions only, following consultation;

- the prescription of medicine sufficient for a single month's use only;
- a discussion at each consultation regarding future treatment requirements as well as a possible phased reduction of treatments.

It is hoped that this will inspire colleagues within the field of general practice to implement these practicable rules as routine when prescribing benzodiazepines and cyclopyrrolones, as these initiatives have a noticeable effect on the level of use of these drugs.

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References

1. Ashton H, Golding JF. Tranquillisers: prevalence, predictors and possible consequences: data from a large United Kingdom survey. *Br J Addict* 1989; 84: 541-6
2. Srisurapanont M, Critchley J, Garner P, et al. Interventions to reduce benzodiazepine prescribing (protocol). *Cochrane Database Syst Rev* 2006; (2): CD005172
3. Jørgensen VRK, Toft BS, Fogh MS. Reducing the use of benzodiazepines and cyclopyrrolones in clinical practices [in Danish]. *Ugeskr Laeger* 2006; 168: 1636-40
4. Jørgensen VRK, Toft BS, Fogh MS. Reducing the use of benzodiazepines and cyclopyrrolones in clinical practices. *Pharm Pract* 2006; 4 (2): 74-8
5. Gyldmark M, Hansen EH. The social costs of dependency on psycho pharmaceuticals [in Danish]. *Lægemiddelforskning* 1997; 36-7
6. Chief Medical Officer's update 37. Benzodiazepines warning: patient safety [online]. Available from URL: <http://www.benzo.org.uk/cmo.htm> [Accessed 2007 Sep 16]
7. Communication regarding the prescription of addictive drugs. Directive CIR 12 from 13/01/2003. Copenhagen; Danish National Board of Health, 2003
8. Danish Medicines Agency. The consumption of benzodiazepines and benzodiazepine related drugs [online]. Available from URL: <http://www.dkma.dk/visUKLSArtikel.asp?artikelID=11644> [Accessed 2007 Sep 16]
9. Systematic review of the benzodiazepines. Guidelines for data sheets on diazepam, chlordiazepoxide, medazepam, clorazepate, lorazepam, oxazepam, temazepam, triazolam, nitrazepam, and flurazepam. Committee on the Review of Medicines. *BMJ* 1980; 280 (6218): 910-2
10. Ashton CH. Benzodiazepines: how they work and how to withdraw. The Ashton manual [online]. Available from URL: <http://www.benzo.org.uk/manual/index.htm> [Accessed 2007 Sep 11]
11. Allain H, Bentue-Ferrer D, Polard E, et al. Postural instability and consequent falls and hip fractures associated with use of hypnotics in the elderly: a comparative review. *Drugs Aging* 2005; 22: 749-65
12. Wang PS, Bohn RL, Glynn RJ, et al. Zolpidem use and hip fractures in older people. *J Am Geriatr Soc* 2001; 49: 1685-90
13. Cumming R, Le Couteur DG. Benzodiazepines and risk of hip fractures in older people. *CNS Drugs* 2003; 17: 825-37
14. Ordiprax: a tool for doctors and regions. Fact sheet from the Danish Medicines Agency [online]. Available from URL: <http://www.ordiprax.dk> [Accessed 2007 Sep 7]
15. Moulund G. A letter to benzodiazepine users: an efficient way to reduce the prescription [in Norwegian]. *Tidsskr Nor Laegeforen* 1997; 117: 3097-100
16. Andreassen CM, Errebo-Knudsen L, Kristensen KA. Patient information might reduce the use of benzodiazepines in general practice [in Danish]. *Ugeskr Laeger* 1989; 151 (45): 2968-70
17. Holden JD, Hughes IM, Tree A. Benzodiazepine prescribing and withdrawal for 3234 patients in 15 general practices. *Fam Pract* 1994; 11: 358-62
18. Ashton H. Benzodiazepine withdrawal: outcome in 50 patients. *Br J Addiction* 1987; 82: 665-71

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