Addiction

RESEARCH REPORT

doi:10.1111/j.1360-0443.2008.02421.x

Randomized controlled trial of a brief intervention for problematic prescription drug use in non-treatment-seeking patients

Anne Zahradnik[1], Christiane Otto[1], Brit Crackau[1], Ira Löhrmann[1], Gallus Bischof[1], Ulrich John[2] & Hans-Jürgen Rumpf[1]

Department of Psychiatry and Psychotherapy, University of Luebeck, Luebeck, Germany[1] and Ernst-Moritz Arndt University of Greifswald, Institute of Epidemiology and Social Medicine, Greifswald, Germany[2]

ABSTRACT

Aims Dependence on or problematic use of prescription drugs (PD) is estimated to be between 1 and 2% in the general population. In contrast, the proportion of substance-specific treatment in PD use disorders at 0.5% is comparatively low. With an estimated prevalence of 4.7%, PD-specific disorders are widespread in general hospitals compared to the general population. Brief intervention delivered in general hospitals might be useful to promote discontinuation or reduction of problematic prescription drug use. **Design** A randomized, controlled clinical trial. **Setting** Internal, surgical and gynaecological wards of a general and a university hospital. **Participants** One hundred and twenty-six patients fulfilling criteria for either regular use of PD (more than 60 days within the last 3 months) or dependence on or abuse of PD, respectively, were allocated randomly to two conditions. **Intervention** Subjects received two counselling sessions based on Motivational Interviewing plus an individualized written feedback (intervention group, IG) or a booklet on health behaviour (control group, CG). **Measurements** The outcome was measured as reduction (>25%) and discontinuation of PD intake in terms of defined daily dosages (DDD). **Findings** After 3 months, more participants in the IG reduced their DDD compared to the participants in the CG (51.8% versus 30%; $\chi^2 = 6.17$; $P = 0.017$). In the IG 17.9%, in the CG 8.6% discontinued use of PD ($\chi^2 = 2.42$; $P = 0.17$). **Conclusions** Brief intervention based on Motivational Interviewing is effective in reducing PD intake in non-treatment-seeking patients.

Keywords Brief intervention, discontinuation, Motivational Interviewing, prescription drugs, reduction.

Correspondence to: Anne Zahradnik, University of Luebeck, Department of Psychiatry and Psychotherapy, Research Group S:TEP (Substance Abuse: Treatment, Epidemiology and Prevention), Ratzeburger Allee 160, 23538 Luebeck, Germany. E-mail: anne.zahradnik@psychiatrie.uk-sh.de

Submitted 26 June 2008; initial review completed 11 September 2008; final version accepted 8 October 2008

INTRODUCTION

Dependence on prescription drugs (PD) is highly prevalent in a substantial number of individuals with estimations ranging between 0.5% and 4.4% in the general population ([1–4]; see Table 1).

Problematic use of PD is more frequent among general hospital in-patients (15.9–25.7% [5–8]) than among the general population (4.1–14.5% [9–11]). Dependence on PD among general hospital in-patients has been reported to be 4.7% [12]. However, a scientific consensus for confirmed criteria of dependence on PD has not yet been obtained [13,14]. Another concern in the discussion about taking and prescribing PD is an appropriate duration of intake: short-term use of benzodiazepines for individuals suffering from anxiety or insomnia is effective [15]. Long-term use of benzodiazepines (more than 4 weeks) is associated with impairment in long-term cognitive functioning [16], withdrawal and tolerance symptoms [17] and therapeutic dose dependence [18]. In chronic non-cancer pain the discussion about taking opioid analgesics over a longer period of time is still ongoing: there is no doubt about the effectiveness of opioids in acute pain [19], but long-term opioid treatment seems to be related to abnormal pain sensitivity, cognitive impairment and chronic obstipation [20].

In contrast to the high prevalence of dependence on PD, a report on out-patient addiction treatment facilities shows that only 0.8% of individuals treated revealed a diagnosis of dependence on PD [21]. This might indicate

Table 1 Epidemiology of problematic use of and dependence on prescription drugs (PD).

Author	*Year*	*Prevalence*	*Definition of problematic use*	*Country*	*Data background/setting*
General population					
Blanco *et al.* [1]	2007	0.5%	Non-medical prescription drug dependence	USA	National Epidemiologic Survey on Alcohol and Related Conditions (NESARC)
Goodwin & Hasin [2]	2002	0.5%	Self-perceived sedative dependence	USA	National Comorbidity Survey (NCS)
		7.1%	Non-prescribed sedative use		
Huang *et al.* [3]	2006		Non-medical PD use disorders:	USA	National Epidemiologic Survey on Alcohol and Related Conditions (NESARC)
		1.1%	Sedative use disorder		
		1.0%	Tranquillizer use disorder		
		1.4%	Opioid use disorder		
Neutel [9]	2005	4.1%	Benzodiazepine use	Canada	National Population Health Study (NPHS)
		2.0%	Long-term use of benzodiazepines		
Schuckit *et al.* [4]	2002	4.4%	Sedative dependence	USA	Collaborative Genetics Of Alcoholism (COGA)
		0.4%	Sedative misuse		
Roesner *et al.* [11]	2008	4.7%	Problematic prescription and over-the-counter drug use in the last 12 months	Germany	General population survey
Petitjean *et al.* [10]	2007	14.5%	Benzodiazepine prescribing in the last 12 months	Swiss	Community pharmacies
Health care institutions					
Fach *et al.* [12]	2007	4.7%	Prescription drug dependence	Germany	General hospital
Wancata *et al.* [5]	1998	15.9%	Anxiolytic or hypnotic use at admission	Austria	General hospital
Simoni-Wastila *et al.* [6]	2005	21.7%	Benzodiazepine prescribing in the last 12 months	USA	Medicare Current Beneficiary Survey (MCBS)
Lagnaoui *et al.* [7]	2001	23.6%	Benzodiazepine use at admission	France	General hospital population
Pélissolo *et al.* [8]	1999	25.7%	Daily anxiolytic and hypnotic use in the last 12 months	France	Internal medicine department

a gap between prevalence rates and treatment- seeking status of the population of individuals dependent on PD.

Effective treatments for dependence on PD are available. A recently published meta-analysis has found that brief interventions are effective strategies for reducing benzodiazepine consumption in pre-selected samples of benzodiazepine abusers, yielding an odds ratio (OR) of 2.8 in comparison with patients receiving usual care [22]. One approach to discontinue or reduce usage of benzodiazepines in mono-dependent individuals is abrupt or gradual taper-off, mainly with other cross-tolerant medications such as, for example, carbamazepine, propanolol or buspirone to alleviate withdrawal symptoms. Discontinuation rates for taper-off procedures range from 36% after 14 weeks [23] to 13% after 2 years in depressive individuals [24], but in both studies the effect was not controlled by an untreated group. In some programmes, the reduction or cessation of benzodiazepine use was the main objective; in others a reduction in anxiety and depression among patients was regarded as much more important than decreasing benzodiazepine use [25].

Psychological interventions such as cognitive–behavioural therapy (CBT) combined with a taper procedure have shown good results in clinical populations. In hypnotic-dependent individuals suffering from insomnia, discontinuation rates of 59% after 12 months [26] have been found. In anxiolytic-dependent individuals with a generalized anxiety disorder treated with CBT, a discontinuation rate of 64% was found after 12 months [27]. Reduction rates were not reported. A letter sent by the general practitioner, asking the patients to try to reduce or stop their PD medication and advising them that this should be carried out gradually, was followed by discontinuation rates ranging from 16% [28] to 24% [29,30] and reduction rates from 41% [31] to 49% [29]. One of the studies has found that in individuals intending to discontinue usage of benzodiazepines the effect of a single tailored letter intervention was 6.7 times higher compared to a general practitioner letter [30]. The approach of such a letter consists of individualized written feedback on the basis of, for example, readiness-to-change, self-efficacy or other psychological constructs related to

successful discontinuation of PD. Brief advice from the general practitioner led to a reduction rate of 43% after 6 months in subjects who took their benzodiazepines solely at night-time [32].

Taken together, studies have shown stable effects of brief interventions in individuals suffering from dependence on or misuse of PD. Limitations of the studies include the small sample size in clinical populations (e.g. $n = 76$ [26]; $n = 61$ [27]) and unclear or imprecise inclusion criteria (e.g. selection through the general practitioner [29,31]). Furthermore, a general comparison of these studies is difficult due to differences in withdrawal procedures/non-pharmacological interventions and patient characteristics.

In all trials which focused on problematic use of or dependence on PD, study participants were recruited by announcements or selected by their general practitioner. To date, no study has observed effects of brief psychological interventions in proactively recruited patients, i.e. every patient admitted is screened according to problematic use of PD. Because the proportions of in-patients with PD long-term use and dependence are elevated in general hospitals, a brief intervention delivered in this setting might be useful to promote discontinuation or reduction of PD. A pilot study of our research group within 45 individuals dependent on PD determined that about 60% were not motivated to change their medication intake. Particularly among substance-abusing individuals who do not intend to or are ambivalent about change, Motivational Interviewing (MI, [33]) proved to yield moderate effect sizes [34–36]. MI is a directive, client-centered counselling style for eliciting behaviour change by helping clients to explore and resolve ambivalence.

The aim of the current study is to evaluate the effectiveness of a brief motivational intervention in problematic use of or dependence on PD in a randomized controlled trial among general hospital patients who did not seek specialized treatment for their PD use. Our hypothesis was that an intervention based on MI would lead: (i) to a higher proportion of in-patients who discontinue and (ii) to a higher proportion of in-patients who reduce their consumption of PD by more than 25%.

METHODS

Sample

All patients aged 18–69 years and admitted recently to an internal, surgical or gynaecological ward of either a general hospital or a university hospital in the northern German city of Luebeck were asked to answer a screening questionnaire with regard to alcohol, nicotine and PD use. Screening questions were embedded in items on health, subjective wellbeing and socio-demographic characteristics. Data was collected on weekdays from 29 March 2006 to 29 June 2007.

Study participants were included if they had either consumed PD with addiction potential for more than 60 days in the last 3 months or fulfilled criteria for PD dependence or abuse according to DSM-IV. The study included drug groups according to the Anatomical Therapeutic Classification [37] of opioids (N02AA-AC, N02AE and N02AX), anxiolytics (N05BA-BC, N05BE), hypnotics and sedatives (N05CC-CF, N05CM) and caffeine (N06BC01).

Patients were not entered into the study if any of the following criteria were met: (i) use of an opioid analgesic due to any cancer disease, (ii) terminal disease, (iii) dependence on or misuse of illegal drugs, (iv) current treatment of associated substance abuse problems and (v) not having a telephone. The study protocol was approved by the University of Luebeck's ethics committee and written informed consent was obtained from all participants enrolled into the study.

Assessments

We used the following key question to assess prescription drug intake: 'Have you been taking prescription drugs like hypnotics, sedatives or analgesics regularly within the last four weeks?'. To screen for disorders related to PDs we used a questionnaire for prescription drug misuse (QPM, [38]) and the German version of the Severity of Dependence Scale (SDS, [39]), adapted for all relevant PD classes. The QPM was validated within three different groups of individuals: alcohol-dependent individuals with and without PD-related problems and people suffering from somatic illness without consuming PD. Discriminant validity was moderate with $r = 0.77$ and internal consistency was relatively high with $r = 0.94$. The items of the QPM were given as follows with a dichotomous answer format (yes/no):

1. Without medication, I have difficulties falling asleep.
2. To be on the safe side, I built up a small supply of medication.
3. If I did not take medication, I would be more content with myself.
4. At times, I would like to back out of it all.
5. There are situations which I am not able to handle without medication.
6. Others believe I have problems with medication.
7. At one time I want to stop taking medication, at another time I do not.
8. Because I suffer from pain, I often take medication.
9. I have eaten less in times of increased intake of medication.
10. I feel well even without medication.
11. Sometimes I was astonished at myself, when I thought about how many pills I had taken on a day.

12 I often feel more powerful with medication.

As cut-off values for a positive screening result, we chose 3 points for the QPM and 5 points for the SDS.

To diagnose a PD-related disorder we used Section E from the SCID-I (Structured Clinical Interview for DSM-IV Axis I Disorders [40]) and the computer-based version of the M-CIDI (Munchener Composite International Diagnostic Interview [41]), the German version of the CIDI [42], conducted by trained and supervised lay interviewers and psychologists. The M-CIDI was applied additionally to diagnose a comorbid disorder on Axis I with respect to the following: affective disorders, anxiety disorders, somatoform disorders and alcohol-related disorders.

Screening procedure

In total, 6042 patients were screened (refusal rate: 8.1%). Patients refusing the screening questionnaire ($n = 537$) were more often female ($\chi^2 = 6.85$; $P = 0.01$) and were older [mean age 56.36; standard deviation (SD) = 12.007 versus 52.17; SD = 14.11; $P < 0.001$]. Among all patients consenting to complete the screening questionnaire, 1090 (18%) were positive according to the QPM or SDS criteria. Of these, 826 patients (75.8%) had to be excluded, due mainly to the consumption of PD without addiction potential ($n = 680$; 62.4%). Of the remaining 410 patients, 112 refused to participate (27.3%) and 34 were discharged after screening. Of the remaining 264 individuals, 126 (47.7%) fulfilled the inclusion criteria. The majority of the 138 excluded patients were false positive (50.7%) due to low cut-off values of the screening questionnaires. There were no significant differences with respect to socio-demographic variables between patients refusing and patients participating in the study procedure after completing the screening questionnaire. Details are depicted in Figure 1.

Randomization and intervention

Study participants were randomized by ward to receive either an information booklet about PD generally (control group: CG) or two MI sessions (intervention group: IG). The first intervention took place in the hospital and was targeted to last 30–45 minutes; the second intervention, 4 weeks later, was conducted by telephone. We assessed core constructs of the Transtheoretical Model of behaviour change [43] and developed an individualized feedback letter, which was sent to study participants 8 weeks after the first intervention. When appropriate, strategies for improving self-efficacy and maintaining changes were included in the feedback letter. In each step of the intervention, we pointed out that it was necessary to discontinue or reduce the medication only with help from professionals, e.g. the general practitioner or a medical specialist.

Training of counsellors and supervision

All interventions were conducted by four psychologists with expertise in clinical treatment and research. They completed 2 weeks of training in MI (principles, basic techniques and practical exercises). Counselling sessions were audio-taped in participants consenting to this procedure and were coded for MI consistency by the other researchers. For supervision, staff met on a weekly basis. The use of the manual was checked and possible discrepancies were corrected. Quality control included the rating of MI consistency and advanced training over the whole period.

Follow-up

The follow-up interviews were scheduled after 3 months, with a mean interval between baseline assessment and follow-up interview of 98 days (SD = 23.2). Follow-up interviews were conducted between July and November 2007. A blinded personal interview was conducted by staff who had no contact with the patient prior to the outcome assessment that was conducted mainly by telephone. In cases of non-accessibility via telephone, participants were contacted personally at their homes. Of the baseline sample described above ($n = 126$), one individual (0.8%) had died. Of the remaining 125 participants, four (3.2%) were not attainable, three (2.4%) were too ill to answer the questions, one individual (0.8%) withdrew further participation and 117 (92.9%) were re-interviewed.

Statistical analyses

Data were analysed using SPSS for Windows, version 14.0. To check for comparability between groups at baseline assessment we used χ^2 statistics for categorical and dichotomous variables and the Mann–Whitney *U*-test for continuous variables. After evaluation of between-group baseline characteristics, the efficacy of the intervention was analysed. Outcome measures were analysed on the basis of intention-to-treat, assuming that the patient who could not be re-interviewed at follow-up did not change in outcome variables. As major outcome variables, the number of patients discontinued from baseline to 3-month follow-up, and the percentage of patients who achieved a clinically meaningful reduction were used. To avoid random fluctuation in PD use we chose a criterion according to Heather *et al.* [31], who defined a 'true reduction' as reducing medication by more than 25% compared to baseline. To allow comparisons within different classes of PD and related dosages, we calculated

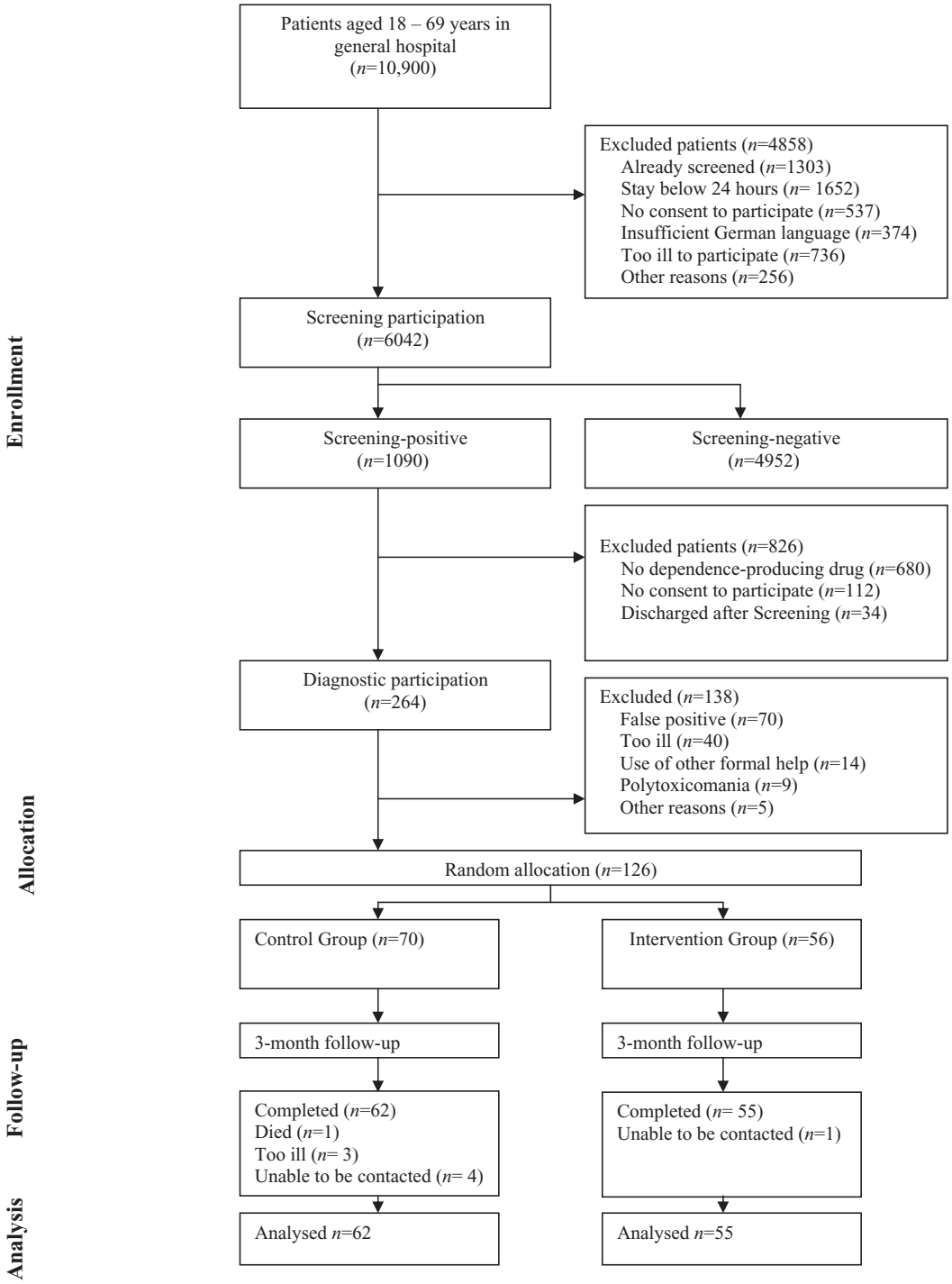

Figure 1 Recruitment of study participants in a general and a university hospital

the difference between defined daily dosage (DDD) of the baseline assessment and DDD of the follow-up assessment for each participant separately. A logistic regression was carried out to estimate the influence of intervention-confounding variables such as the DSM-IV diagnosis of dependence on/abuse of PD and substance group (analgesics containing opioids or caffeine, sedatives, hypnotics). Two-sided significance tests were used throughout.

Power

Originally the trial was powered with an expected discontinuation rate of 10% in the CG and 29% in the IG in a one-sided test and at a power of (1-b) = 0.80. To detect these statistically relevant effects we needed a sample size of 112. To protect against anticipated loss to follow-up of up to 10%, a targeted sample size of 125 was chosen.

Table 2 Baseline characteristics of control group (CG) and intervention group (IG).

	CG (n = 70)	*IG (n = 56)*	*P-value*
Age (SD)	56.49 (11.24)	53.43 (11.9)	0.124
Women (%)	42 (60%)	36 (64.9%)	0.713
Married	41 (58.6%)	30 (53.6%)	0.592
Education			
<10 years	32 (48.5%)	24 (44.4%)	0.399
= 10 years	26 (39.4%)	21 (38.9%)	0.553
>10 years	8 (12.1%)	9 (16.7%)	0.326
Occupation			
Employed	10 (14.3%)	6 (10.7%)	0.748
Unemployed	9 (12.9%)	4 (7.1%)	0.383
Retired	42 (60%)	36 (64.3%)	0.713
Housewife	6 (8.6%)	6 (10.8%)	0.765
Axis I diagnosis	35 (50%)	24 (42.9%)	0.475
Affective disorder	17 (24.3%)	16 (28.6%)	0.684
Anxiety disorder	15 (21.4%)	11 (19.6%)	0.829
Somatoform disorder	9 (12.9%)	8 (14.3%)	1.000
Alcohol use disorder	7 (10%)	5 (8.9%)	1.000
Dependence on PD			
According to M-CIDI	14 (20.0%)	13 (23.2%)	0.669
According to SCID-I	25 (35.7%)	30 (53.6%)	0.049*
Misuse of PD			
According to M-CIDI	8 (11.4%)	9 (16.1%)	0.601
According to SCID-I	16 (22.9%)	6 (10.7%)	0.099
DDD (SD)	1.37 (1.41)	2.09 (3.30)	0.818
One PD	17 (24.3%)	16 (28.6%)	0.588

*P-value significant, $P < 0.05$; DDD: defined daily dosage; M-CIDI: Munchener Composite International Diagnostic Interview; SCID-I: Structured Clinical Interview for DSM-IV Axis I Disorders; PD: prescription drug; SD: standard deviation.

Table 3 Follow-up data in the intervention group (IG) and the control group (CG).

	All participants	*CG*	*IG*	*P-value*	*Effect size*
DDD difference[a] (SD)	0.26 (2.1)	0.12 (1.4)	0.42 (2.7)	0.08	0.14
Discontinuation[b] (%)	16 (12.7%)	6 (8.6%)	10 (17.9%)	0.17	0.28
Reduction >25%[b] (%)	50 (39.7%)	21 (30%)	29 (51.8%)	0.02*	0.45

[a]Difference: follow-up minus baseline, on the basis of 114 completed 3-month-follow-up data. [b]On the basis of an intention-to-treat-analysis. *P-value significant, $P < 0.05$; DDD: defined daily dosage; SD: standard deviation.

RESULTS

Baseline characteristics

In a first step, we compared IG and CG concerning baseline variables. Results are depicted in Table 2. No statistically significant differences were observed between the intervention and the control group except for dependence on PD, assessed with the SCID-I, which was higher in the IG ($P = 0.045$). In terms of socio-demographic variables, groups did not differ.

Of the final sample, 61.9% were female. Mean age was 55.13 years (SD = 11.59, range = 30–69), with 69% being aged 50 years or older. More than half were married (56.4%). The majority was retired (69.1%). The mean DDD was 1.68 (SD = 2.43) due to high-dose-dependent patients. Of the sample, 84.2% consumed medication of only one substance group: 71 individuals consumed analgesics containing opioids (55.6%) or caffeine (0.8%), 14 hypnotics (11.1%) and 21 sedatives (16.7%). Medication of more than one substance group was consumed by 20 individuals (15.8%).

Group differences at follow-up/efficacy of the intervention

Group differences at follow-up are displayed in Table 3. The difference of DDD of follow-up minus baseline measurement between groups did not reach significance,

although revealing a tendency (Mann–Whitney *U*-test: $U = 1238$; $P = 0.083$). In the IG, 16 patients (17.9%) discontinued their use of PD compared to six in the control group (8.6%), although this difference attained no statistical significance ($\chi^2 = 2.42$; $P = 0.17$). More than a third of patients (39%; $n = 50$) achieved a 'true reduction' in PD intake, including those who stopped completely. Significantly more patients in the IG than in the control group reduced their PD intake by more than 25% at 3-month follow-up (21 versus 29 patients; 30% versus 51.8%; $\chi^2 = 6.17$; $P = 0.017$).

Among the IG, we found a higher proportion of individuals with dependence on PD according to SCID-I than in the control group. The effect of the intervention remained stable after controlling for PD dependence in a logistic regression with respect to 'true reduction'. To control the effect of the intervention for different PD classes we conducted a logistic regression analysis with discontinuation and reduction as dependent variables and interaction terms (PD class × intervention) as independent variables. The following OR were obtained for reduction: hypnotics/sedatives × intervention with an OR of 3.1 [confidence interval (CI): 1.3–7.6 $P = 0.013$] and opioids × intervention with an OR of 2.8 (CI: 1.2–6.4; $P = 0.016$). The following OR were obtained for discontinuation: hypnotics/sedatives × intervention with an OR of 1.9 (CI: 0.6–5.9; $P = 0.29$) and opioids × intervention with an OR of 1.3 (CI: 0.4–4.2; $P = 0.64$). Calculated effect sizes yielded a small effect for discontinuation rate (ES = 0.28) and a moderate effect for reduction rate (ES = 0.45).

DISCUSSION

This is the first study examining the efficacy of MI among non-treatment-seeking patients with dependence on or problematic use of PD in general hospital. Our initial hypotheses were that an intervention based on MI would lead to: (i) a higher rate of discontinuation; and (ii) a higher rate of reduction in consumption of PDs. The first hypothesis could not be confirmed: a trend towards more participants in the IG (17.9%) than in the control condition (8.6%) was revealed by the data. The second hypothesis was confirmed: 51.8% of the participants who achieved an intervention based upon MI reduced their consumption by more than 25%. In contrast, only 30% of the participants who achieved an information booklet reduced their consumption by more than 25%.

Findings concerning reduction rates confirm results from brief intervention studies, which used a letter sent by a general practitioner [29,31]. Discontinuation rates in our study correspond to those by Bashir *et al.* [32] in a brief intervention study. It must be kept in mind that recruitment of participants differs from the described procedure in our study. Interestingly, findings are also consistent with the effects of brief interventions in primary care populations with alcohol use disorders, showing an improvement of consumption rate of 56% [44].

Conclusions drawn from this study must be tempered by the following methodological limitations: (i) one of the screening questionnaires utilized (QPM) is an instrument which needs further validation. For this reason, we used a second well-validated screening-questionnaire, the SDS. (ii) The patients who refused the screening questionnaire were significantly older and were more often of female gender than patients who participated in the study. This could have led to a selection bias. Nevertheless, our study population is comparable with findings from epidemiological studies [2,9,11] in terms of gender (61.9%) and mean age (56.5 years). (iii) Of 410 potential study participants, 27.7% have refused further diagnostic procedure. This corresponds to other studies that found proportions of refusing patients from 33% [45] to 82.6% [22]. (iv) We included long-term users of PD as well as individuals who abuse or who were dependent on PD in the study. The reduction effect of the intervention remained stable after controlling for these two inclusion criteria in a logistic regression. (v) We excluded individuals who consumed illegal drugs such as heroin or cannabis. (vi) A small sample size could have masked statistical effects in participants stopping consumption of PDs. Calculated effect sizes concerning discontinuation rate (ES = 0.28) and 'true reduction' rate (ES = 0.45) tended to be small- to medium-sized. With the achieved reduction rate our sample is slightly underpowered, with (1-b) = 0.76. (vii) Participants in the IG showed a higher rate of dependence on PD according to SCID-I. However, the reduction effect of the intervention remained stable after controlling for dependence in a logistic regression analysis. (viii) As in the most brief intervention studies, our outcomes were based on self-reported data. One study, validating a patient's statement about the *status quo* of benzodiazepine consumption, found accordance with a patient's statement with biological tests in 95% of the cases [26].

The following strengths of the study ensure clinical representativeness: (i) participants were non-treatment-seeking. (ii) All PD with addiction potential were included in the study. (iii) All participants were diagnosed structurally with SCID-I and M-CIDI for detecting actual PD misuse or dependence. (iv) The current sample shows a higher rate of psychiatric comorbidity, because this often was an exclusion criterion in intervention studies. (v) All patients—irrespective of readiness to change—were included in the study. (vi) Although subject recruitment was difficult, once subjects were enrolled very few were

lost to follow-up (nine of 126; 7%). The higher proportion of dropouts in the control group might have been related to the lack of intervention. (vii) The OR of different substance groups suggest an intervention effect in each group, although this was found to be significant only among individuals who consumed hypnotics or opioid analgesics with respect to a 'true reduction'.

It should to be taken into account that in order to ensure the internal validity of the study, screening and interventions were conducted by study staff and exceeded brief intervention (e.g. brief advice) offered in primary care. Therefore, integrating interventions into routine care may need to consider further structural and organizational factors.

Despite limitations, this study has important clinical implications. By recruiting consecutive patients proactively, the entire population of interest could be reached and the intervention resulted in a 'true reduction'. The strength of such a brief motivational intervention lies in addressing of individual problems related to problematic PD use. Other factors influencing this brief intervention outcome, such as gender or psychiatric comorbidity, need to be investigated in future studies.

Trial registration

Please refer to this study by its ClinicalTrials.gov identifier: NCT00514839 (registered at 9 August 2007).

Declarations of interest

None.

Acknowledgements

This study is part of the German research network EARLINT (EARLy substance use INTervention) and is funded by the German Federal Ministry of Health. The present analysis is part of the MIMiK project (grant no. 15 02/68661). The authors wish to thank Christina Ahrens, Sabine Braun, Martina Sellnau and Andreas Schmücker for data collection, Anja Kreuzer for data entry, the medical and nursing staff of the SANA Hospital Luebeck (Professor T.-H. Hütteroth) and the departments of internal medicine (Professor H. Lehnert, Professor T. Wagner), surgery (Professor H.-P. Bruch) and gynaecology (Professor K. Dietrich, Professor D. Hornung) of the University Medical Center of Schleswig-Holstein for cooperation with the project, and especially the patients for their participation.

References

1. Blanco C., Alderson D., Ogburn E., Grant B. F., Nunes E. V., Hatzenbuehler M. L. *et al.* Changes in the prevalence of non-medical prescription drug use and drug use disorders in the United States: 1991–1992 and 2001–2002. *Drug Alcohol Depend* 2007; **90**: 252–60.
2. Goodwin R. D., Hasin D. S. Sedative use and misuse in the United States. *Addiction* 2002; **97**: 555–62.
3. Huang B., Dawson D. A., Stinson F. S., Hasin D. S., Ruan W. J., Saha T. D. *et al.* Prevalence, correlates, and comorbidity of nonmedical prescription drug use and drug use disorders in the United States: results of the national epidemiologic survey on alcohol and related conditions. *J Clin Psychiatry* 2006; **67**: 1062–73.
4. Schuckit M. A., Smith T. L., Kramer J., Danko G., Volpe F. R. The prevalence and clinical course of sedative–hypnotic abuse and dependence in a large cohort. *Am J Drug Alcohol Abuse* 2002; **28**: 73–90.
5. Wancata J., Benda N., Lesch O., Muller C. Use of anxiolytics and hypnotics in gynecological, surgical and medical departments of general hospitals. *Pharmacopsychiatry* 1998; **31**: 178–86.
6. Simoni-Wastila L., Zuckerman I. H., Singhal P. K., Briesacher B., Hsu V. D. National estimates of exposure to prescription drugs with addiction potential in community-dwelling elders. *Subst Abuse* 2005; **26**: 33–42.
7. Lagnaoui R., Moore N., Longy-Boursier M., Baumevieille M., Bégaud B. Benzodiazepine use in patients hospitalized in a department of internal medicine: frequency and clinical correlates. *Pharmacoepidemiol Drug Saf* 2001; **10**: 531–5.
8. Pélissolo A., Notides C., Lépine J.-P., Bisserbe J.-C. Anxiolytic and hypnotic use by general hospital inpatients. *Gen Hosp Psychiatry* 1999; **21**: 79–86.
9. Neutel C. I. The epidemiology of long-term benzodiazepine use. *Int Rev Psychiatry* 2005; **17**: 189–97.
10. Petitjean S., Ladewig D., Meier C. R., Amrein R., Wiesbeck G. A. Benzodiazepine prescribing to the Swiss adult population: results from a national survey of community pharmacies. *Int Clin Psychopharmacol* 2007; **22**: 292–8.
11. Rösner S., Steiner S., Kraus L. Gebrauch und Missbrauch von Medikamenten. Ergebnisse des Epidemiologischen Suchtsurvey 2006 [Use and misuse of prescription drugs. Results of the 2006 Epidemiological Survey of Substance Abuse]. *Sucht* 2008; **54**: S47–56.
12. Fach M., Bischof G., Schmidt C., Rumpf H. J. Prevalence of dependence on prescription drugs and associated mental disorders in a representative sample of general hospital patients. *Gen Hosp Psychiatry* 2007; **29**: 257–63.
13. Hughes J. R. Should criteria for drug dependence differ across drugs? *Addiction* 2006; **101**: 134–41.
14. Zandstra S. M., Furer J. W., Van De Lisdonk E. H., Van't H. M., Bor J. H., Van Weel C. *et al.* Different study criteria affect the prevalence of benzodiazepine use. *Soc Psychiatry Psychiatr Epidemiol* 2002; **37**: 139–44.
15. Rogers A., Pilgrim D., Brennan S., Sulaiman I., Watson G., Chew-Graham C. Prescribing benzodiazepines in general practice: a new view of an old problem. *Health (Lond)* 2007; **11**: 181–98.
16. Bierman E. J., Comijs H. C., Gundy C. M., Sonnenberg C., Jonker C., Beekman A. T. The effect of chronic benzodiazepine use on cognitive functioning in older persons: good, bad or indifferent? *Int J Geriatr Psychiatry* 2007; **22**: 1194–200.
17. Schweizer E., Rickels K. Benzodiazepine dependence and withdrawal: a review of the syndrome and its clinical management. *Acta Psychiatr Scand* Suppl 1998; **393**: 95–101.
18. Ashton H. The diagnosis and management of benzodiazepine dependence. *Curr Opin Psychiatry* 2005; **18**: 249–55.

19. Ballantyne J. C., Laforge K. S. Opioid dependence and addiction during opioid treatment of chronic pain. *Pain* 2007; **129**: 235–55.
20. Eriksen J., Sjorgen P., Bruera E., Ekholm O., Rasmussen N. K. Critical issues on opioids in chronic non-cancer pain: an epidemological study. *Pain* 2006; **125**: 172–9.
21. Sonntag D., Bauer C., Hellwich A. K. Deutsche Suchthilfestatistik 2006 für ambulante Einrichtungen [German statistical report for 2006 on outpatient treatment facilities for substance-use disorders]. *Sucht* 2007; **53**: S7–41.
22. Voshaar R. C., Couvee J. E., Van Balkom A. J., Mulder P. G., Zitman F. G. Strategies for discontinuing long-term benzodiazepine use: meta-analysis. *Br J Psychiatry* 2006; **189**: 213–20.
23. Tyrer P., Ferguson B., Hallstrom C., Michie M., Tyrer S., Cooper S. *et al.* A controlled trial of dothiepin and placebo in treating benzodiazepine withdrawal symptoms. *Br J Psychiatry* 1996; **168**: 457–61.
24. Zitman F. G., Couvée J. E. Chronic benzodiazepine use in general practice patients with depression: an evaluation of controlled treatment and taper-off. *Br J Psychiatry* 2001; **178**: 317–24.
25. Denis C., Fatseas M., Lavie E., Auriacombe M. Pharmacological interventions for benzodiazepine mono-dependence management in outpatient settings. *Cochrane Database Syst Rev* 2006; **3**: CD005194.
26. Morin C. M., Bastien C., Guay B., Radouco-Thomas M., Leblanc J., Vallieres A. Randomized clinical trial of supervised tapering and cognitive behavior therapy to facilitate benzodiazepine discontinuation in older adults with chronic insomnia. *Am J Psychiatry* 2004; **161**: 332–42.
27. Gosselin P., Ladouceur R., Morin C. M., Dugas M. J., Baillargeon L. Benzodiazepine discontinuation among adults with GAD: a randomized trial of cognitive–behavioral therapy. *J Consult Clin Psychol* 2006; **74**: 908–19.
28. Gorgels W. J., Oude Voshaar R. C., Mol A. J., Van De Lisdonk E. H., Van Balkom A. J., Breteler M. H. *et al.* Predictors of discontinuation of benzodiazepine prescription after sending a letter to long-term benzodiazepine users in family practice. *Fam Pract* 2006; **23**: 65–72.
29. Cormack M. A., Sweeney K. G., Hughes-Jones H., Foot G. A. Evaluation of an easy, cost-effective strategy for cutting benzodiazepine use in general practice. *Br J Gen Pract* 1994; **44**: 5–8.
30. Ten Wolde G. B., Dijkstra A., Van Empelen P., Van Den Hout W., Neven A. K., Zitman F. Long-term effectiveness of computer-generated tailored patient education on benzodiazepines: a randomized controlled trial. *Addiction* 2008; **103**: 662–70.
31. Heather N., Bowie A., Ashton H., Mcavoy B., Spencer I., Brodie J. *et al.* Randomised controlled trial of two brief interventions against long-term benzodiazepine use: outcome of intervention. *Addict Res Theory* 2004; **12**: 141–54.
32. Bashir K., King M., Ashworth M. Controlled evaluation of brief intervention by general practitioners to reduce chronic use of benzodiazepines. *Br J Gen Pract* 1994; **44**: 408–12.
33. Miller W. R. Why do people change addictive behavior? The 1996 H. David Archibald Lecture. *Addiction* 1998; **93**: 163–72.
34. Hettema J., Steele J., Miller W. R. Motivational interviewing. *Annu Rev Clin Psychol* 2005; **1**: 91–111.
35. Rubak S., Sandbaek A., Lauritzen T., Christensen B. Motivational interviewing: a systematic review and meta-analysis. *Br J Gen Pract* 2005; **55**: 305–12.
36. Vasilaki E. I., Hosier S. G., Cox W. M. The efficacy of motivational interviewing as a brief intervention for excessive drinking: a meta-analytic review. *Alcohol Alcohol* 2006; **41**: 328–35.
37. Who Collaborating Centre for Drug Statistics Methodology. *About the ATC/DDD System*. Oslo, 2007. Available at: http://www.whocc.no/atcddd (accessed 6 June 2008).
38. Watzl H., Rist F., Höcker W., Miehle K. Entwicklung eines Fragebogens zur Erfassung von Medikamentenmissbrauch bei Suchtpatienten [Development of a questionnaire to assess prescription drug misuse in substance misusing patients]. In: Lieb H., editor. *Sucht und Psychosomatik: Beiträge des 3. Heidelberger Kongresses*. Bonn: Nagel; 1991, p. 123–39.
39. De Las Cuevas C., Sanz E. J., De La Fuente J. A., Padilla J., Berenguer J. C. The Severity of Dependence Scale (SDS) as screening test for benzodiazepine dependence: SDS validation study. *Addiction* 2000; **95**: 245–50.
40. Wittchen H. U., Wunderlich U., Gruschwitz S., Zaudig M. *SKID-I. Strukturiertes Klinisches Interview für DSM-IV. Achse I: Psychische Störungen [SCID-I. Structured Clinical Interview for DSM-IV, Axis I Disorders*]. Göttingen: Hogrefe; 1997.
41. Wittchen H.-U., Beloch E., Garczynski E., Holly A., Lachner G., Perkonigg A. *et al. Manual zum Munchener Composite International Diagnostic Interview (M-CIDI) (Version 2.0, 1/95) [Manual for the M-CIDI, version 2.0]*. Munchen: Max-Planck-Institut fur Psychiatrie, Klinisches Institut; 1995.
42. Robins L. N., Wing J., Wittchen H. U., Helzer J. E., Babor T. F., Burke J. *et al.* The Composite International Diagnostic Interview. An epidemiologic instrument suitable for use in conjunction with different diagnostic systems and in different cultures. *Arch Gen Psychiatry* 1988; **45**: 1069–77.
43. Prochaska J. O., Diclemente C. C., Norcross J. C. In search of how people change. Applications to addictive behaviors. *Am Psychol* 1992; **47**: 1102–14.
44. Kaner E. F., Beyer F., Dickinson H. O., Pienaar E., Campbell F., Schlesinger C. *et al.* Effectiveness of brief alcohol interventions in primary care populations. *Cochrane Database Syst Rev* 2007; **18**: CD004148.
45. Baillargeon L., Landreville P., Verreault R., Beauchemin J. P., Gregoire J. P., Morin C. M. Discontinuation of benzodiazepines among older insomniac adults treated with cognitive–behavioural therapy combined with gradual tapering: a randomized trial. *Can Med Assoc J* 2003; **169**: 1015–20.