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

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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 counseling 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%; χ² = 6.17; P = 0.017). In the IG 17.9%, in the CG 8.6% discontinued use of PD (χ² = 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.

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...
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, propranolol 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

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

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Prevalence</th>
<th>Definition of problematic use</th>
<th>Country</th>
<th>Data background/setting</th>
</tr>
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<tbody>
<tr>
<td>General population</td>
<td></td>
<td></td>
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<tr>
<td>Blanco et al. [1]</td>
<td>2007</td>
<td>0.5%</td>
<td>Non-medical prescription drug dependence</td>
<td>USA</td>
<td>National Epidemiologic Survey on Alcohol and Related Conditions (NESARC)</td>
</tr>
<tr>
<td>Goodwin &amp; Hasin [2]</td>
<td>2002</td>
<td>0.5%</td>
<td>Self-perceived sedative dependence</td>
<td>USA</td>
<td>National Comorbidity Survey (NCS)</td>
</tr>
<tr>
<td>Huang et al. [3]</td>
<td>2006</td>
<td>7.1%</td>
<td>Non-prescribed sedative use</td>
<td>USA</td>
<td>National Epidemiologic Survey on Alcohol and Related Conditions (NESARC)</td>
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<tr>
<td></td>
<td></td>
<td>1.1%</td>
<td>Sedative use disorder</td>
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<td></td>
<td></td>
<td>1.0%</td>
<td>Tranquillizer use disorder</td>
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<td></td>
<td></td>
<td>1.4%</td>
<td>Opioid use disorder</td>
<td></td>
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<td>Neutel [9]</td>
<td>2005</td>
<td>4.1%</td>
<td>Benzodiazepine use</td>
<td>Canada</td>
<td>National Population Health Study (NPHS)</td>
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<td></td>
<td></td>
<td>2.0%</td>
<td>Long-term use of benzodiazepines</td>
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<tr>
<td>Schuckit et al. [4]</td>
<td>2002</td>
<td>4.4%</td>
<td>Sedative dependence</td>
<td>USA</td>
<td>Collaborative Genetics Of Alcoholism (COGA)</td>
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<td></td>
<td></td>
<td>0.4%</td>
<td>Sedative misuse</td>
<td></td>
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<tr>
<td>Roesner et al. [11]</td>
<td>2008</td>
<td>4.7%</td>
<td>Problematic prescription and over-the-counter drug use in the last 12 months</td>
<td>Germany</td>
<td>General population survey</td>
</tr>
<tr>
<td>Petitjean et al. [10]</td>
<td>2007</td>
<td>14.5%</td>
<td>Benzodiazepine prescribing in the last 12 months</td>
<td>Swiss</td>
<td>Community pharmacies</td>
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<td>Health care institutions</td>
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<tr>
<td>Fach et al. [12]</td>
<td>2007</td>
<td>4.7%</td>
<td>Prescription drug dependence</td>
<td>Germany</td>
<td>General hospital</td>
</tr>
<tr>
<td>Wancata et al. [5]</td>
<td>1998</td>
<td>15.9%</td>
<td>Anxiolytic or hypnotic use at admission</td>
<td>Austria</td>
<td>General hospital</td>
</tr>
<tr>
<td>Simoni-Wastila et al. [6]</td>
<td>2005</td>
<td>21.7%</td>
<td>Benzodiazepine prescribing in the last 12 months</td>
<td>USA</td>
<td>Medicare Current Beneficiary Survey (MCBS)</td>
</tr>
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<td>Lagnaoui et al. [7]</td>
<td>2001</td>
<td>23.6%</td>
<td>Benzodiazepine use at admission</td>
<td>France</td>
<td>General hospital population</td>
</tr>
<tr>
<td>Pélissolo et al. [8]</td>
<td>1999</td>
<td>25.7%</td>
<td>Daily anxiolytic and hypnotic use in the last 12 months</td>
<td>France</td>
<td>Internal medicine department</td>
</tr>
</tbody>
</table>
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.
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 (χ² = 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 χ² 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
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 $(1-\beta) = 0.80$. 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.
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%).

### Baseline characteristics

The difference of DDD of follow-up minus baseline measurement between groups did not reach significance.

### 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 \( \times \) intervention) as independent variables. The following OR were obtained for reduction: hypnotics/sedatives \( \times \) intervention with an OR of 3.1 [confidence interval (CI): 1.3–7.6 \( P = 0.013 \)] and opioids \( \times \) intervention with an OR of 2.8 (CI: 1.2–6.4; \( P = 0.016 \)). The following OR were obtained for discontinuation: hypnotics/sedatives \( \times \) intervention with an OR of 1.9 (CI: 0.6–5.9; \( P = 0.29 \)) and opioids \( \times \) 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–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.

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