Does tailoring really make a difference? : the development and evaluation of tailored interventions aimed at benzodiazepine cessation

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CHAPTER 5

Long-term effectiveness of computer-generated tailored patient education on benzodiazepines: a randomized controlled trial

Chronic benzodiazepine use is highly prevalent and is associated with a variety of negative health consequences. The present study examined the long-term effectiveness of a tailored patient education intervention on benzodiazepine use. A randomized controlled trial was conducted comprising three arms, comparing (1) a single tailored intervention; (2) a multiple tailored intervention and (3) a general practitioner-letter. The post-test took place after twelve months. Five hundred and eight patients using benzodiazepines were recruited by their general practitioners and randomly assigned to one of the three groups. Two tailored interventions, the single tailored intervention (patients received one tailored letter) and the multiple tailored intervention (patients received three sequential tailored letters at intervals of one month), were compared to a short general practitioner-letter that modelled usual care. The tailored interventions not only provided different and more information than the general practitioner letter, they were also personalized and adapted to individual baseline characteristics. The information in both tailored interventions was the same, but in the multiple tailored intervention the information was provided to the participants spread over three occasions. In the multiple tailored intervention, the second and the third tailored letters were based on short and standardized telephone interviews. Measurements: Benzodiazepine cessation at post-test was the outcome measure.The results showed that participants receiving the tailored interventions were twice as likely to have quit benzodiazepine use compared to the general practitioner-letter. Particularly among participants with the intention to discontinue usage at baseline, both tailored interventions led to high percentages of those who actually discontinued usage (single tailored intervention 51.7%; multiple tailored intervention 35.6%; general practitioner-letter 14.5%). It was concluded that tailored patient education can be an effective tool for reducing benzodiazepine use, and can be implemented easily.

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Introduction

Benzodiazepines are one of the most frequently prescribed drugs. In 1998, approximately 11.6 million prescriptions for benzodiazepines were written in the Netherlands (1). In addition, other European and non-European countries, such as the United States, have to contend with widespread use of benzodiazepines (2). Benzodiazepines are only effective for the short-term treatment of insomnia and anxiety (3-7). Long-term use is not only non-effective, but is also associated with several negative side-effects such as addiction, cognitive decline, falls and accidents (8-16). Because of these problems, there is a strong desire to be able to control the use of benzodiazepines.

Two different treatment strategies are in circulation for decreasing the amount of benzodiazepines used (17). In minimal interventions, general practitioners may invite patients to discontinue their long-term benzodiazepine usage on their own by making them aware of the negative consequences of continued usage. Systematic discontinuation programs, on the other hand, are more intensive interventions in which patients discontinue their benzodiazepine doses gradually under the guidance of a general practitioner. Although both strategies have been shown to be effective (17), they are in many instances not offered to patients (18;19). As a result, patients are not given the opportunity to reduce their intake with the support of the general practitioner. This is partly due to the fact that general practitioners are subject to time constraints (20-23). It has also been suggested that the high levels of benzodiazepine intake are mainly the result of general practitioners failing to consider or feeling unable to suggest alternative strategies besides the continuation of benzodiazepines (20;24). It is, therefore, important to develop a tool which is feasible for general practitioners to use and more likely to be accepted by them, and which is at the same time effective in educating patients in order to reduce benzodiazepine intake.

Computer-tailored patient education could be such a tool. In other health behaviours, including addictive behaviours such as smoking, it has been shown that computerized tailored information can be more effective than no information and more effective than usual care (25-28). Computer-tailored information is directed at the individual by taking into account individual baseline characteristics. Tailored information, therefore, mimics the process of individual counselling and feedback, but the expertise of the counsellor is now documented in a computer program. In other words, this computerized patient education entails, on the one hand, individualization of information and, on the other hand, offers the possibility to apply it to large groups of patients. Once a computer system for tailored patient education is developed, the costs of large scale application are relatively low. It could, therefore, be an excellent tool in educating patients because it reduces the workload of the general practitioner and at the same time educates patients automatically.

The aim of this study was to test whether two different and newly developed computer-tailored interventions to educate patients were more effective than an existing patient education letter (the general practitioner-letter) in reducing benzodiazepine use. The intervention objectives of both

tailored interventions were based on the Social Cognitive Theory (29). In this comprehensive psychological theory, expectations of outcomes of a behaviour and perceptions of self-efficacy are the main determinants of behaviour, and these determinants therefore need to be changed in order to change a particular behaviour. Studies on psychosocial determinants of benzodiazepine use have indeed shown that outcome expectations and self-efficacy expectations are important predictors of benzodiazepine cessation (30). In addition, the information developed to change outcome and self-efficacy expectations was tailored to individual characteristics using the methodology of Dijkstra and De Vries (31). This means that individual data were fed into a computer system that composed a coherent letter that took into account several individual characteristics, such as name, gender, type of benzodiazepine used, outcome expectations and self-efficacy expectations.

All in all, the tailored interventions were developed to be more effective than the general practitioner-letter by adding three elements. Firstly, the tailored interventions aimed at changing psychological factors defined by the Social Cognitive Theory, while the general practitioner-letter was developed to only inform and advice patients. Secondly, the content and formulations of the information in the tailored interventions were adapted to the individual, while the general practitioner-letter was the same for all patients. Thirdly, the tailored interventions included more information than the general practitioner-letter. It contained information on more different topics and on skills to cope with anxiety or sleep problems and information on how to discontinue benzodiazepine use.

Although the objectives of both tailored interventions and the extent of the tailoring were the same, in the multiple tailored intervention the information was divided over three letters and was sent to the participants at intervals of one month. The rationale for developing and testing two systems that differ mainly in the time interval in which the determinants are addressed lies in the observation that decision-making and behavioural change take place over time and require time in order to become effective. In the present multiple tailored letter intervention, this notion was operationalized simply by spreading the information over three occasions. The resulting hypotheses were as follows: 1) the tailored interventions are more effective than the general practitioner-letter, and 2) multiple tailored intervention is more effective than single tailored intervention.

Methods

Study design

A three-pronged randomized controlled trial was used, which compared: (1) a single tailored letter intervention; (2) a multiple tailored letter intervention and (3) a general practitioner-letter (Figure 1). The study protocol was approved by the Local Ethics Research Committees of Leiden University Medical Center.

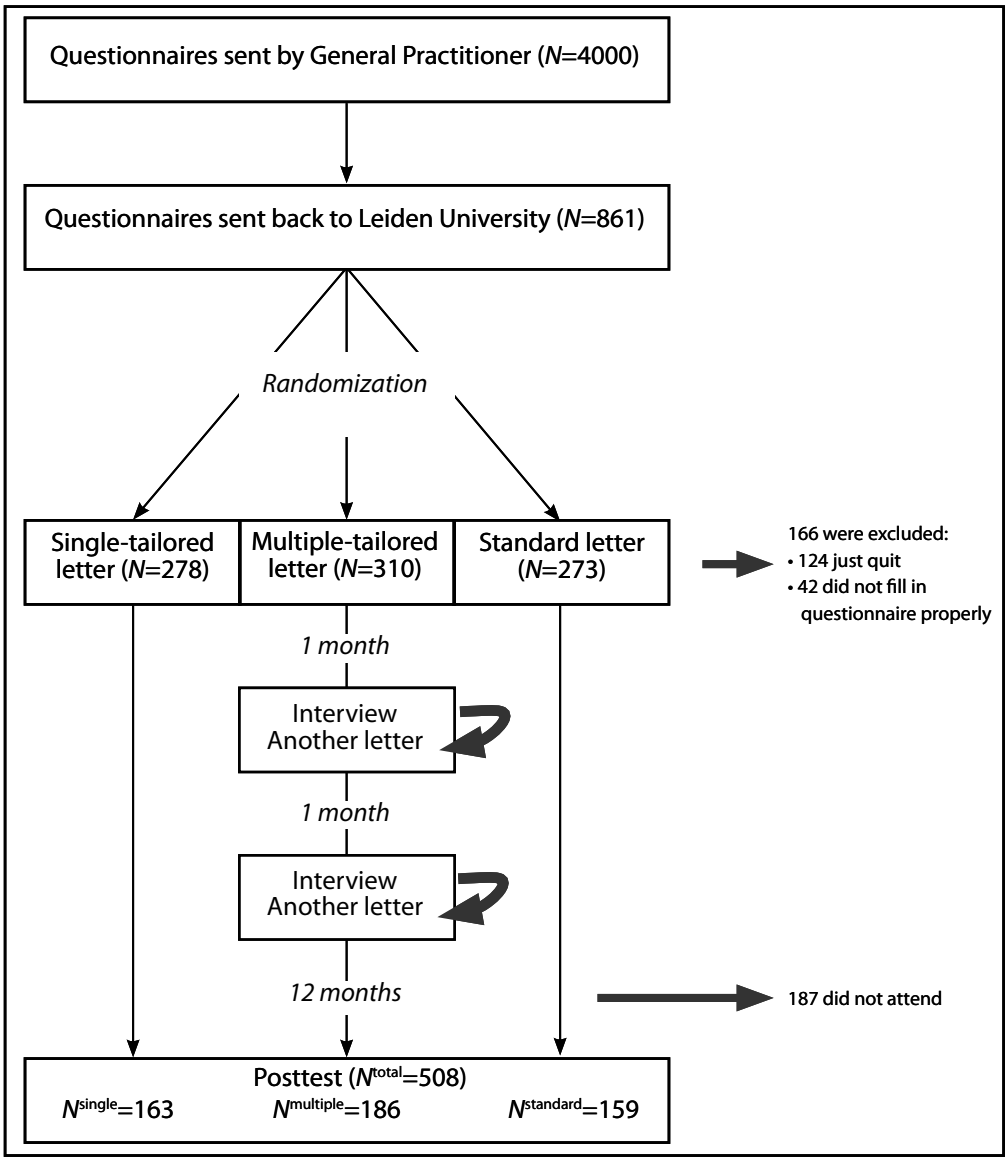

Figure 1 Flow diagram

Recruitment

Chronic benzodiazepine users were recruited via thirty general practitioners throughout the Netherlands. The general practitioners were originally randomly selected from an electronic version of the Dutch telephone directory and received €200 compensation for their participation. The general practitioners were phoned and asked how many chronic benzodiazepine users they had in their patient database. Five general practitioners declined participation on behalf of certain of their patients. The reported reasons for declining

were that patients had severe co-morbidity or psychosocial problems. As a consequence, an estimated fifty patients were excluded.

The general practitioners' assistants forwarded packages to their chronic benzodiazepine users. The packages contained, firstly, an informed consent form. Secondly, they contained one A4 sheet of information in which the procedure was explained. Thirdly, a pre-test questionnaire was added in order to produce the (first) tailored letter. Lastly, a prepaid envelope was added so that the patient could return the informed consent form and the questionnaire to the researcher. Four thousand packages were sent to patients using benzodiazepines. The patients who returned the pre-test questionnaires were randomly assigned to one of the three conditions. The data on the participants in the tailored interventions were imported into the computer program, which produced the tailored letters. All letters were sent to the participants within one week. The additional two subsequent letters in the multiple tailored intervention were each based on a separate individual assessment through a standardized telephone interview of a maximum of ten minutes. The post-test questionnaire was sent out after twelve months.

The tailored intervention

Both tailored interventions were developed on the basis of the methodology offered by Dijkstra and De Vries (31). Each letter was based on an individual assessment. The individual data were fed into a computer program in which an individually tailored letter was composed on the basis of rules about what information would be appropriate to include given a specific response on the individual assessment.

Each letter started with an introduction explaining the goal and the rationale of the information. Subsequently, the three main determinants of discontinuing usage were addressed. The information was designed to: 1) increase the perceptions of the positive outcome expectations of discontinuing benzodiazepine use (for example, it was argued that patients may function better cognitively and may evaluate themselves more positively); 2) lower the perceptions of the positive outcome expectations of the use of benzodiazepines (this was done by explaining the development of tolerance and a possible placebo effect), and 3) increase self-efficacy expectations with regard to discontinuing usage (this was done by offering several skills to reach abstinence, such as making a plan to cut down benzodiazepine use and by offering alternatives in order to cope with worrying thoughts).

The single tailored letter intervention consisted of one letter of 5 to 6 pages of information (approximately 1200 words) in which all of these three psychological determinants were addressed in the above order of presentation. The multiple tailored letter intervention consisted of three letters of about 3 pages each (approximately 400 words), sent at intervals of one month. In the multiple tailored intervention, the first tailored letter was designed to increase the perceptions of the positive outcome expectations of discontinuing benzodiazepine usage and to lower the perceptions of the positive outcome expectations of the use of benzodiazepines. The second tailored letter was designed to increase self-efficacy expectations with regard to discontinuing usage, while the content of the third letter provided more

skills for discontinuing usage, or provided a summary of the information in the first two letters, depending on the individual needs detected in the third assessment. In addition, in the introduction of the second and third letter, participants were provided with progress feedback: individual changes in benzodiazepine use were mentioned.

The tailoring included the three working mechanisms that have the potential to be effective; personalization, feedback and adaptation. Personalization was applied by starting with the participant's surname (e.g., "Dear ms. Brown,') and by mentioning twice in the text the type of benzodiazepine that the individual used. Feedback was provided on statements made by patients in the individual assessment. For example: "You think that benzodiazepines really help you to get a good night's sleep." Adaptation was used, for example, by taking into account the self-reported indication for the use of benzodiazepines when tolerance was addressed and persuasive arguments were provided.

The general practitioner-letter

The results of the two tailored letters were compared to the results of an existing letter that general practitioners in the Netherlands can use to inform their patients about benzodiazepine (the general practitioner-letter for benzodiazepine discontinuation) (32). This letter was the same for all patients and it only pinpointed the disadvantages of benzodiazepine use (such as the chance of becoming addicted) and they contained a short advice on how to discontinue benzodiazepine use. The letter consisted of approximately 200 words. Gorgels and others (33) demonstrated that this letter caused a reduction of 24% (versus 5% in the non-intervention group) in the first six months.

Measurements

In addition to demographic characteristics (age and gender), the type of benzodiazepine used, the dose and the indication for the use, the determinants were assessed in the pre-test questionnaire as follows:

Intention was measured using three items. An example of such an item was: 'How likely is it that you are going to stop within six months?', with a seven-point response scale from 'definitely not planning to do so' (1) to 'definitely planning to do so' (7)(α =.96). There were six items measuring positive outcome expectations (α =.80), such as: 'If I stopped taking benzodiazepines, I would be proud of myself.' The negative outcome expectations were measured by eight items (α = .88). An example of such an item was: 'If I did not use the medicine, I would suffer from a feeling of discomfort.' The answers could be given on a five-point scale from 'I totally disagree' (1) to 'I totally agree' (5). Self-efficacy expectations were assessed using eight items (α = .92). An example was: 'If you were to try to stop taking benzodiazepines, would you be capable of doing so if you had slept worse the night before?' on a seven-point scale from 'definitely not' (1) to 'definitely yes' (7).

The post-test measured benzodiazepine cessation with the question: 'Are you using benzodiazepines?' with two response options: No (0) and Yes

(1). The present study is a "low demand" study (34). This implies that the participants are under no social pressure to change their behaviour in either direction. In the letter inviting participation it was explicitly stated that it was not necessary to discontinue usage. Therefore, the above self-report was expected to be valid (34).

Statistical methods

A randomization analysis was conducted to check the comparability of the different conditions at baseline. This was done by chi-square statistics for categorical and dichotomous variables, while *t*-tests were used for continuous variables. An attrition analysis was conducted to see whether there were differences in baseline scores between the participants who remained in the study and those who withdrew at post-test. This was done by analyses of variance and chi-square. Finally, to check the effectiveness of the tailored letters, logistic regression analyses were conducted with benzodiazepine cessation at post-test as the dependent variable ('0'- did not quit and '1' – did quit) and condition as the independent variable. All comparisons between the intervention conditions were adjusted for age, gender and benzodiazepine dose (in diazepam equivalents).

Results

General

Of the packages which were sent to general practitioners, 861 pre-test questionnaires were returned (22%). These respondents were randomly assigned to one of the three conditions. Of these participants, 166 were excluded because they had just discontinued their benzodiazepine intake (n=124) or did not complete the questionnaire properly (n=42), leaving a total of 695 participants (81%), with 228 in the single tailored intervention, 256 in the multiple tailored intervention, and 211 in the non-tailored intervention. Of these 256 participants in the multiple-tailored intervention, 207 received a telephone interview (81 %) and the subsequent letter. Of these participants, 156 received another telephone interview as well as the third tailored letter (75 %). Only the participants who were approached with the telephone interview received the tailored letters. After twelve months, the post-test questionnaire was sent out to all the participants who received the first letter. Five hundred and eight participants returned the post-test questionnaire (response rate 73.1%), with 163 in the single-tailored intervention, 186 in the multiple-tailored intervention, and 159 in the non-tailored intervention (see also Figure 1).

Baseline characteristics

Looking at the characteristics, 68.1% were female and the mean age at pre-test was 62.3 years. In order to be able to compare benzodiazepine use, all medication dosages were transferred to an equivalent dose of diazepam using the conversion table of Zitman and Couvee (35). For participants taking more than one benzodiazepine, the dosages were summed up. The data showed that the mean usage of benzodiazepines was over eight years, with

an average of 49.3 milligrams of diazepam equivalents per week. 15.8% used more than one type of benzodiazepine. The most frequently used types of benzodiazepines were oxazepam (30.7%), temazepam (26.5%) and diazepam (10.7%). When looking at the baseline scores, most patients had no plans to discontinue usage (*M*=2.2). They also expected positive outcomes (*M*=2.9), as well as negative outcomes (*M*=2.3) for benzodiazepine cessation, and on average participants perceived their capability to discontinue usage as low (*M*=3.0) (see also Table 1).

Table 1 Baseline characteristics of the study participants (*N*=695) at baseline assessment in the three intervention conditions.

	Total	Single tailored letter intervention	Multiple tailored letter intervention	General practitioner-letter	*p*
Demographic variables					
Gender (female)	68.1%	67.9%	71.0%	65.2%	.41
Age (years) (mean (*SD*))	62.3 (14.2)	61.6 (14.0)	62.5 (14.8)	63.0 (13.6)	.61
Benzodiazepine usage:					
Duration of use (years)(mean (*SD*))	8.1 (10.6)	8.3 (11.1)	7.8 (9.8)	8.0 (11.1)	.88
Weekly dose in mg diazepam equivalent (mean (*SD*))	49.3 (70.8)	55.3 (66.6)	47.8 (86.9)	43.1 (50.9)	.19
Poly use: > 1 benzodiazepine	15.8%	18.4%	16.7%	11.6%	.13
Top 3:					.22
Oxazepam	30.7%	26.3%	27.7%	28.8%	
Temazepam	26.5%	22.3%	26.1%	23.1%	
Diazepam	10.7%	8.0%	9.5%	10.6%	
Diazepam: ≥70mg/week	26.2%	30.4%	22.5%	24.5%	.13
Indication					.15
Sleep	53.1%	57.5%	47.4%	55.6%	
Anxiety	25.1%	22.2%	28.5%	23.9%	
Physical	10.4%	10.9%	9.5%	11.7%	
Mental	11.3%	9.5%	14.6%	8.8%	
Cognitions:					
Intention to discontinue (mean (*SD*))	2.2 (1.9)	2.2 (1.9)	2.2 (2.0)	2.1 (1.9)	.75
Positive outcome expectation (mean (*SD*))	2.9 (1.2)	2.9 (1.3)	2.8 (1.3)	2.9 (1.2)	.96
Negative outcome expectation (mean (*SD*))	2.3 (1.2)	2.3 (1.2)	2.3 (1.2)	2.4 (1.3)	.53
Self-efficacy (mean (*SD*))	3.0 (1.5)	3.0 (1.5)	2.9 (1.5)	2.9 (1.5)	.57

Randomization and attrition

Randomization analyses showed that the participants in the conditions at pre-test did not differ among the different conditions for all baseline measurements listed in Table 1. The attrition analyses only showed that those who provided no or incomplete data at follow-up used a significantly higher weekly dose of diazepam equivalents ($F(694)=18.1$, $p=.00$).

Main analyses

The logistic regression analysis showed a significant main effect of condition ($\chi^2(6, N=475) = 48.43$; $p=.025$). In the single tailored intervention condition, 24.5% reported no longer using benzodiazepines, in the multiple tailored intervention condition the percentage was 23.7%, while in the general practitioner-letter condition the percentage of those who had discontinued use was 14.5%. The contrast between the single letter and the general practitioner-letter was significant ($p<.05$), while the difference between the multiple tailored letter and the general practitioner-letter approached significance ($p=.053$). There was no significant difference between the two tailored interventions.

Table 2 Percentage of benzodiazepine cessation per condition and the *OR* of the comparison of the two tailored interventions with the general practitioner-letter.

	%	*OR*	95% *C.I.*	*p*-value
Single tailored letter intervention	24.5%	2.3	1.21 – 4.24	.007
Multiple tailored letter intervention	23.7%	2.1	1.11 – 3.76	.01
General practitioner-letter	14.5%	1.0		

Moderating effects

Moderation analyses were conducted in order to test in whom the tailored interventions were most effective. The following were tested as potential moderators: age, gender, benzodiazepine dose, outcome expectations, self-efficacy expectations and the intention to discontinue the use of benzodiazepines. A logistic regression model was constructed for each of these potential moderators, including the covariates, the potential moderator (for continuous variables dichotomized by a median split), the factor condition and the interaction between the potential moderator and the factor condition. Only the interaction with pre-test intention to discontinue usage was significant ($\chi^2(8, N=485) = 61.45$, $p=.003$), signifying that the relative effects of the three interventions differed depending on whether participants were high or low on intention. Sixty-two percent ($n=289$) of the participants had no intention to discontinue usage (they had the lowest score on all three items that comprised the intention measure). Within this subgroup there was no main effect of condition and the percentages for the single tailored intervention, the multiple tailored intervention and the general practitioner-letter were 9.7 %, 15.2 %, and 14.1 %, respectively. However, among the remaining patients ($N=186$) - who had the intention of discontinuing usage - the main effect of condition was significant ($\chi^2(6, N=185) = 29.65$, $p=.000$). The percentages for the single tailored intervention, the multiple tailored intervention and the general practitioner-letter were 51.7%, 35.6%, and 14.5%, respectively. Contrasts showed that both tailored interventions were more effective than the general practitioner-letter ($p<.0001$). People who had received the single-tailored letter were 6.7 times more likely to have discontinued benzodiazepine use than those participants who received a general practitioner-letter. People who received the multiple-tailored letter were 3.8 times more likely to have discontinued the use of benzodiazepines than the general practitioner-letter (see Table 3). Although the percentage of

those who discontinued usage in both tailored intervention conditions differed by 15%, the difference was not significant.

Table 3 Percentage of benzodiazepine cessation per condition for patients with a high intention and the *OR* of the comparison of the two tailored interventions with the non-tailored intervention

	%	*OR*	95% *C.I.*	*p*-value
Single tailoring	51.7%	6.7	2.58 – 17.50	.000
Multiple tailoring	35.6%	3.8	1.51 – 9.54	.005
General practitioner-letter	14.5%	1.0		

Analyses including withdrawals

Because attrition at post-test could be predicted by the weekly dose of diazepam equivalents, the present results could be influenced by selective withdrawals. One way to address this problem was to use the last known measurement (pre-test) for each participant who withdrew as a substitute for the post-test measurement and to repeat all analyses. This 'intention to treat analyses' (36) revealed that none of the results changed qualitatively. Only minor changes in *OR* and *p*-values emerged.

Discussion

The results of the present study showed that both tailored letters were more effective than the general practitioner-letter. Roughly, both tailored letters led to 10% more individuals discontinuing usage after twelve months. The difference between the tailored letters and the general practitioner-letter was particularly pronounced for participants with an intention to discontinue their benzodiazepine use: the single tailored letter led to an almost sevenfold likelihood (the multiple tailored letter an almost fourfold likelihood) of the patient having discontinued usage after twelve months compared to the general practitioner-letter. A positive intention to discontinue usage may be a measure of involvement in the topic of discontinuing benzodiazepine use and this may have led to more thorough reading (central processing) of the information, leading to larger differences among the conditions. In other words, people with a positive intention read the information so well that the differences became apparent.

In contrast, in participants with no intention to discontinue usage, the tailored letters were no more effective than the general practitioner-letter. These patients may have read the information only superficially and all three interventions may have been experienced as advocating something "they just are not motivated for." Apart from the lack of differences between the interventions, the cessation rate among this group was only 13%, compared to 34% in the participants with an intention to discontinue usage. The group of low intenders may comprise a "hard core" group of benzodiazepine users. This group may need more intensive guidance, directed at increasing the motivation to discontinue usage . Motivational interviewing in face-to-face counselling may be needed to start the process of change (37). One additional observation is that the effects of the general practitioner-letter were low and

independent of the intention to discontinue usage (14.1 % among patient with no intention and 14.5 % in patients with an intention). This suggests that this simple letter does not have the ingredients that can activate a patient's existing intention to discontinue usage.

The single tailored intervention and the multiple tailored intervention did not differ significantly, despite the fact that the latter intervention consisted of three assessments and three subsequent letters. The rationale of spreading the information over time was that the process of change takes time. That is, for the cognitions that underlie behaviour to change, people need to attend to and process information, and to integrate it in their existing views of, for example, the consequences of their current behaviour. Stage models, such as the Transtheoretical model (38) explicitly acknowledge this phenomenon and implicate that interventions should be matched to stage. However, the information in our multiple tailored intervention was spread over time but not matched to stage because, as yet, little is known about stages in benzodiazepine cessation. Instead, the three letters followed the simple rationale that, first, people to decide to change (first letter; weighing positive and negative outcome expectations) and after that they need to know how they can change (second letter; providing means to discontinue usage to increase self-efficacy). The third letter referred to both earlier letters. We must conclude that this particular way of integrating time in the delivery of the intervention did not prove to be more effective than the information it contained, as it did not perform better than delivering the information at once. On the other hand, it may also be caused by the fact that at least 20% of the patients in the multiple tailored intervention could not be reached for one of both telephone interviews and, therefore, did not receive the second or third tailored letter.

In the present study, a treatment package design was applied (39), meaning that each intervention contained several different potential change ingredients. This treatment package design is powerful because it provides effectiveness information of realistic interventions, including possible synergistic effects of working ingredients. The present study showed that compared to the existing general practitioner-letter, the effectiveness of a patient education "package" could be significantly increased by: 1) using a comprehensive psychological theory and targeting the factors specified by the theory; 2) tailoring the information to the individual and; 3) providing more information on more relevant topics including information on how to change. Only a dismantling design in which a separate test is carried out on each of the elements on which the tailored interventions differed from the general practitioner-letter can provide definite answers on why the tailored interventions were more effective.

The present study has at least two potential limitations. The first limitation is the selection of patients. The first and largest selection that may have occurred concerns the non-response to the initial invitation that was sent to the patients from the general practitioner's office. However, the participants who did return a usable pre-test questionnaire were largely comparable to the less selective sample recruited by Gorgels and others (33) on age (around 62 years), on proportion of female patients (around 70%) and on the top three

benzodiazepines (1. oxazepam; 2. temazepam; 3. diazepam). These figures at least suggest that no selection occurred on these basic variables. The second selection that may have occurred concerns the level of withdrawals during the trial. The attrition analysis showed that those who withdrew from the trial used a higher weekly dose of benzodiazepines. Thus, some selection was found. However, firstly, benzodiazepine dose was not a moderator of the effects of the interventions, meaning that the pattern of results was not influenced by the dose. Secondly, in all analyses, benzodiazepine dose was included as a covariate. In sum, although some selection may have taken place, we argue that it was small and, more importantly, had little influence on the comparative effectiveness of the interventions.

In conclusion, the present findings show that a tailored intervention providing information on a broad range of topics and based on a comprehensive psychological theory can be a useful instrument to influence benzodiazepine use. A web-based version of the single tailored intervention with limited access (password provided to patients by the general-practitioner or psychiatrist) is now published on the internet. The strength of such minimal interventions lies in their broad reach. Because the method is easy and cheap to apply, many patients can be exposed to the information, and relevant effects can be achieved at population level.

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References

(1) Stichting Farmaceutische Kengetallen. Data & Feiten [Pharmaceutical Indicators Foundation. Data and facts]. 2005.

(2) Zandstra S.M., Furer J.W., Van de Lisdonk E.H., Van't Hof M., Bor J.H.J., Van Weel C. *et al*. Different study criteria affect the prevalence of benzodiazepine use. *Soc Psychiatry Psychiatr Epidemiol* 2002; 37: 139-44.

(3) College voor Zorgverzekeringen. Gebruik van benzodiazepinen 1993 - 1998 [Dutch college for health care insurance. Use of benzodiazepines 1993-1998]. 2000.

(4) Holbrook A.M., Cheng C., King D., Crowther R., Lotter A. Meta-analysis of benzodiazepine use in the treatment of insomnia. *CMAJ* 2000; 162: 225-33.

(5) Holbrook A.M., Cheng C., King D., Crowther R., Lotter A. The diagnosis and management of insomnia in clinical practice: a practical evidence-based approach. *CMAJ* 2000; 162: 216-20.

(6) Kupfer D.J., Reynolds C.F. Management of insomnia. *N Engl J Med* 1997; 336: 341-6.

(7) Lader M.H. Limitations on the use of benzodiazepines in anxiety and insomnia: are they justified? *Eur Neuropsychopharmacol* 2000; 9:S399-S405.

(8) Ashton H. The diagnosis and management of benzodiazepine dependence. *Curr Opin Psychiatry* 2006; 18: 249-55.

(9) Barker M.J., Greenwood K.M., Jackson M., Crowe S.F. Persistence of cognitive effects after withdrawal from long-term benzodiazepine use: a meta-analysis. *Arch Clin Neuropsychol* 2004; 19: 437-54.

(10) Gorgels W.J., Breteler M.H., Van de Lisdonk E.H., Oude Voshaar R.C., Mol A.J., Zitman F.G. Het langdurig gebruik van benzodiazepinen [Long-term use of benzodiazepines]. *Ned Tijdschr Geneeskd* 2001; 145: 1342-6.

(11) O'Connor K.P., Marchand A., Bélanger L., Mainguy N., Landry P., Savard P. *et al*. Psychological distress and adaptational problems associated with benzodiazepine withdrawal and outcome: A replication. *Addict Behav* 2004; 29: 583-93.

(12) Salzman C. Addiction to benzodiazepines. *Psychiatr Q* 1999; 69: 251-61.

(13) Schweizer E., Rickels K., De Martinis N., Case G., Garcia Espana F. The effect of personality on withdrawal severity and taper outcome in benzodiazepine-dependent patients. *Psych Med* 1998; 28: 713-20.

(14) Wan H., Koder T.J., Cho K., Park Y., Warburton E.C., Zhu X.O. *et al*. Benzodiazepine impairment of perirhinal cortical plasticity and recognition memory. *Eur J Neurosci* 2004; 20: 2214-24.

(15) Westra H.A., Stewart S.H., Teehan M., Johl K., Dozois D.J., Hill T. Benzodiazepine Use Associated With Decreased Memory for Psychoeducation Material in Cognitive Behavioral Therapy for Panic Disorder. *Cogn Ther Res* 2004; 28: 193.

(16) Kan C.C., Breteler M.H., Zitman F.G. High prevalence of benzodiazepine dependence in out-patient users, based on the DSM-III-R and ICD-10 criteria. *Acta Psychiatr Scand* 1997; 96: 85-93.

(17) Oude Voshaar R.C., Gorgels W.J.M.J., Mol A.J.J., Couvée J.E., Van Balkom A.J.L.M., Zitman F.G. Behandelmethoden om langdurig benzodiazepinegebruik te staken [Treatment modalities to discontinue long-term benzodiazepine use]. *Ned Tijdschr Geneeskd* 2001; 137: 1347-50.

(18) Terzano M.G., Ferini-Strambi L., Mondini S., Parrino L., Cirignotta F. Studio Morfeo 2: Survey on the management of insomnia by Italian general practitioners. *Sleep Med* 2006.

(19) Ten Wolde G.B. Nog veel ruimte voor verbetering - voorlichting over benzodiazepinen [A lot to improve - education on benzodiazepines]. *Pharm Weekblad* 2004; 139: 1494-6.

(20) Parr J.M., Kavanagh D.J., Young R.M., McCafferty K. Views of general practitioners and benzodiazepine users on benzodiazepines: A qualitative analysis. *Soc Sci Med* 2006; 62: 1237-49.

(21) Brook O., Van Hout H., Nieuwenhuyse H., Heerdink E. Impact of coaching by community pharmacists on drug attitude of depressive primary care patients and acceptability to patients; a randomized controlled trial. *Eur Neuropsychopharmacol* 2003; 13: 1-9.

(22) Kapur N., Appleton K., Neal R.D. Sources of job satisfaction and psychological distress in GPs and medical house officers. *Fam Pract* 2000; 16: 600-1.

(23) Commonwealth Fund / Harvard / Harris. The Commonwealth Fund 2000 International Health Policy Survey of Physicians. New York; 2000.

(24) Dempsey O.P., Moore H. Psychotropic prescribing for older people in residential care in the UK. Are guidelines being followed? *Primary Care Psychiatry* 2005; 10: 13-8.

(25) Brug J., Kok G., Van Breukelen G.J., Glanz K., Van Assema P. The impact of computer-tailored feedback and iterative feedback on fat, fruit, and vegetable intake. *Health Educ Behav* 1998; 25: 517-31.

(26) Kroeze W., Brug J., Werkman A. A systematic review of randomized trials on the effectiveness of computer-tailored education on physical activity and dietary behaviors. *Ann Behav Med* 2006; 31: 205-23.

(27) Oenema A., Tan F., Brug J. Short-Term Efficacy of a Web-Based Computer-Tailored Nutrition Intervention: Main Effects and Mediators. *Ann Behav Med* 2005; 29: 54-63.

(28) Dijkstra A., De Vries H., Roijackers J. Long-term effectiveness of computer-generated tailored feedback in smoking cessation. *Health Educ Res* 1998;13(2).

(29) Bandura A. Social foundations of thought and action: A social cognitive theory. Upper Saddle River, NJ, US: Prentice-Hall, Inc: 1986.

(30) Ten Wolde G.B., Dijkstra A., Van Empelen P., Knuistingh Neven A., Zitman F.G. Psychosocial determinants of benzodiazepine cessation. Submitted 2007.

(31) Dijkstra A., De Vries H. The development of computer-generated tailored interventions. *Patient Educ Couns* 2003; 36: 193-203.

(32) Oude Voshaar R., Van Balkom A., Mulder J., Breteler M., Gorgels W., Mol A. *et al.* Predictors of relapse after discontinuation of long-term benzodiazepine use by minimal intervention: a 2-year follow-up study. *Fam Pract* 2003; 20: 370-2.

(33) Gorgels W.J.M.J., Oude Voshaar R.C., Mol A.J.J., Van de Lisdonk E.H., Van Balkom A.J.L.M., Van den Hoogen H.J.M. *et al.* Discontinuation of long-term benzodiazepine use by sending a letter to users in family practice: a prospective controlled intervention study. *Drug Alcohol Depen* 2005; 78: 49-56.

(34) Velicer W.F., Prochaska J.O., Rossi J.S., Snow M.G. Assessing outcome in smoking cessation studies. *Psychol Bulletin* 1992; 111: 23-41

(35) Zitman F.G., Couvée J.E. Chronic benzodiazepine use in general practice patients with depression: an evaluation of controlled treatment and taper-off: report on behalf of the Dutch Chronic Benzodiazepine Working Group. *Br J Psychiatry* 2001; 178: 317-24.

(36) Heyting A., Tolboom J.T., Essers J.G. Statistical handling of drop-outs in longitudinal clinical trials. *Stat Med* 1993; 11: 2043-61.

(37) Miller W.R., Rollnick S. Motivational Interviewing. Guilford Press, New York; 1991.

(38) Prochaska J.O., DiClemente C.C., Norcross J.C. In search of how people change: Applications to addictive behaviors. *Americ Psychol* 1992; 47(9): 1102-1114

(39) Kazdin, A.E. The evaluation of Psychotherapy: research designs and methodology. In S.L. Garfield & A.E. Bergin (Eds.), *Handbook of Psychotherapy and Behavior Change*. 1986; New York: John Wiley & Sons