

The effect of industry-independent drug information on the prescribing of benzodiazepines in general practice

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Abstract. In order to measure the effect of industry-independent information on the prescribing of benzodiazepines in general practice, 128 primary practitioners were randomly allocated to three intervention groups after stratification by year of graduation. One third of the participating physicians were forwarded written information about the indications and limitations of benzodiazepines, another third received both written and oral information, and the remaining third (the control group) obtained no information at all.

A comparison of the number of benzodiazepines prescribed per 100 patient contacts with prescription before and after the intervention showed an average decrease of 3% in the control group, of 14% in physicians who received only written information, and of 24% in physicians who were given additional oral information. Post hoc pairwise comparisons revealed a significant difference at the 1% level in the number of benzodiazepines prescribed between physicians who received both written and oral information and the control group.

A follow-up survey conducted 4 weeks after the intervention showed that the oral information campaign positively affected physicians' attitudes about the value of oral drug information from an industry-independent source.

Key words: Benzodiazepines, General Practice; industry-independent drug information, prescribing, intervention, primary care

Several experimental studies have shown the positive impact of independent drug information on the quality and quantity of drug prescribing in general practice. Shaffner et al. [1] found that a mailed brochure had no detectable effect, a drug educator had only a modest effect, and a physician visit produced a substantial reduction in the prescribing of three antibiotics contraindicated for office practice and oral cephalosporins. Similarly, Avorn et al.

[2] found no effect of the issuing of written materials on three excessively prescribed drug groups (cerebral and peripheral vasodilators, an oral cephalosporin, and propoxyphene), as opposed to the significant influence of an oral information procedure. However, in a second trial by the same authors [3], written information and 'guided' prescription forms produced a significant effect even after a short period of 4–8 weeks. The effectiveness of written material in the reduction of antibiotic prescription was also observed by Harvey et al. [4]. Ray et al. [5] found that a physician visit in combination with a brochure containing guidelines on withdrawal of benzodiazepines in chronic users could significantly reduce their prescription. Benzodiazepines are often the general practitioner's treatment of choice for problems of insomnia and anxiety, despite repeated statements in the literature about the negative implications of their prolonged prescribing [6–12]. A particular problem exists in Belgium, where the prevalence of chronic intake of benzodiazepines clearly exceeds that of short-term use [13].

In 1986, Cannoodt et al. [14] conducted a survey to study the determinants of drug prescribing habits of general practitioners, using case simulations and analyses of actual prescriptions. Both methods showed that the way in which physicians were informed about drugs was an important determinant of the quantity of prescriptions, regardless of other physician, practice or patient characteristics. Physicians who obtained information primarily from commercial sources prescribed more drugs than physicians who received the bulk of their information from industry-independent sources. An experimental study was designed to find out whether industry-independent information about the indications and limitations of benzodiazepines could significantly decrease their prescription rate, and whether physicians perceived such information as an acceptable alternative to drug information from commercial sources.

Subjects and methods

A random sample of 450 general practitioners was selected from a list of all physicians with a practice located in the Belgian provinces of East and West Flanders. They were invited by mail or by telephone to cooperate in a study about psychological problems in primary health care. Physicians who agreed to participate were stratified by year of graduation before allocation to three different intervention groups according to the method of random permutations: oral and written information about benzodiazepines (condition 1), written information about benzodiazepines (condition 2), no information (condition 3).

All participants were asked to record their drug prescriptions over a period of 12 weeks on special prescription forms provided by the researchers. The forms included information on the following topics: the patient's sex and age; description and nature of the complaint (chronic vs. new); relative importance of physical, personal and environmental/social factors to the origin of the complaint; first or repeat prescription; and duration of prescription.

Information was also collected on the following sociodemographic variables: physician's sex, year of graduation, university of graduation, size of practice (number of patient contacts during the registration period), perceived competition (estimated number of colleagues in the area), province where the practice was located. The physician's attitude towards drug information was operationalised in six variables: the number of medical representatives received in the last 4 weeks, commercial channels (brochures, representatives) used as sources of information on newly prescribed drugs, industry-independent channels (scientific literature, university, specialists, post-education) used as sources of information on newly prescribed drugs, reaction to brochures sent by pharmaceutical companies (from 'throwing away immediately' to 'keeping most of them'), estimated utility of commercial information (from 'totally unnecessary' to 'very useful') and estimated utility of independent information. The tendency to prescribe benzodiazepines was defined as the number of packages of benzodiazepines prescribed per 100 patient contacts with drug prescription. A restriction to contacts with drug prescription was chosen as the most reliable strategy, since these could be counted from the special prescription forms developed for the study.

After a baseline registration period of 4 weeks, the intervention phase took place over the next 4 weeks. Three mailings were sent with 10-day intervals to physicians of the first and second condition. These mailings were developed in cooperation with professionals from the advertising business and had a layout similar to drug advertisements from pharmaceutical firms. Their content was derived from discussion between members of the research team, consultation of the existing literature on benzodiazepines and group discussions with general practitioners, psychiatrists and psychotherapists. The central message throughout the mailings was an appeal for the rational and short-term prescribing of benzodiazepines, which was summarised in a slogan at the end of the mailing. In addition, each mailing contained specific information on one of the following topics: (1) the limited effectiveness of long-term benzodiazepine use in patients with insomnia or anxiety (2) side effects of benzodiazepines on the cognitive and emotional functioning of patients (3) the importance of different forms of habituation and dependence associated with the use of benzodiazepines, and their possible share in the dynamics of chronic use. A young male general practitioner, who was trained by a team of medical and communication experts to take up his role as an independent medical representative, visited the physicians of the first condition in the 4-week intervention period. The content of his oral message was essentially the same as that of the written materials and he was prepared to answer questions from the physicians, such as the exact indications of benzodiazepines, alternatives to their prescription, feasibility of withdrawal in chronic users, etc. Drug prescriptions were followed up after the intervention phase for an additional 4 weeks.

At the end of the follow-up phase all physicians were asked to fill out a brief questionnaire to assess their awareness of the intervention, their knowledge and attitude in relation to benzodia-

Table 1. Sociodemographic characteristics of the study sample ($n = 128$) and the total population ($n = 2750$) of general practitioners of the Belgian provinces of East- and West-Flanders

	Population n (%)		Study sample n (%)		
		Total ($n = 128$)	Condition		
			1 ($n = 44$)	2 ($n = 43$)	3 ($n = 41$)
Province:					
East-Flanders	1485 (54%)	76 (58%)	26	26	24
West-Flanders	1265 (46%)	54 (42%)	19	18	17
Sex:					
Male	2420 (88%)	110 (85%)	38	36	36
Female	330 (12%)	18 (15%)	6	7	5
University of graduation:					
Gent	1210 (44%)	54 (43%)	21	19	14
Leuven	1320 (48%)	68 (52%)	22	20	26
Other	220 (8%)	6 (5%)	2	3	1
Year of graduation:					
Before '63	660 (24%)	14 (11%)	3	6	5
'63 - '75	715 (26%)	36 (28%)	13	11	12
'76 - '81	715 (26%)	38 (30%)	13	12	13
After '81	660 (24%)	40 (31%)	15	14	11

zepines, and their attitude concerning industry-independent drug information.

The data collected were analysed with two statistical procedures. Firstly, linear regression was used to determine significant predictors of the tendency to prescribe benzodiazepines and of the attitude towards industry-independent information. Predictors of the tendency to prescribe benzodiazepines were identified by two separate analyses: one with the block of physician and practice characteristics and one with the block of variables reflecting the physician's attitude towards drug information. Subsequently, all variables with a partial standardised regression coefficient significant at the 10% level were analysed together in a new linear regression analysis.

Secondly, the effect of industry-independent information was examined by a repeated measures analysis of variance, comparing the numbers of packages of benzodiazepines prescribed (per 100 patient contacts with prescription) before and after the intervention over the three experimental conditions. Duncan's multiple range tests were used for *post hoc* comparisons between conditions.

Results

Of the 450 physicians contacted, 143 (32%) agreed to participate. Because 15 physicians didn't write down the date on their prescriptions in the baseline registration period, they were disregarded in the randomisation procedure. All of the remaining 128 physicians took part in the experiment. A comparison with the total population of general practitioners of East and West Flanders for province, sex, university of graduation, and year of graduation (Table 1) showed that the oldest age group was under-represented in the study sample ($\chi^2 = 9.9$, $P < 0.05$). Reasons for non-participation of older practitioners were that they were too busy or that they were discontinuing their practice. Forty-four physicians were assigned to condition one, 43 to condition two, and 41 to condition three. Sociodemographic characteristics per treatment group are presented in Table 1.

Table 2. Predictors of the tendency to prescribe benzodiazepines from linear regression analyses in general practitioners of East- and West-Flanders ($n = 128$)

Physician and practice characteristics			
Variable	β	T	Significance
Sex	-0.02	-0.20	NS
Year of graduation	-0.41	-4.49	***
University of Graduation	-0.05	-0.52	NS
Size of practice	0.10	1.08	NS
Perceived competition	0.06	0.85	NS
Province	-0.04	-0.43	NS
Physician's attitude about drug information			
Variable	β	T	Significance
Number of medical representatives received	0.16	1.70	*
Commercial channels as sources of information	0.10	0.76	NS
Industry-independent channels as sources of information	0.10	0.72	NS
Reaction to brochures from pharmaceutical companies	0.06	0.61	NS
Estimated utility of commercial information	0.17	1.78	*
Estimated utility of independent information	-0.08	-0.93	NS

* Significant at the 10 % level; ** significant at the 5 % level; *** significant at the 1 % level
 β , Standardised regression coefficient; T, t statistic; NS = not significant

Table 3. Mean number of packages of benzodiazepines prescribed per 100 patient contacts with prescription before and after the intervention for each treatment condition

Condition	n	Pre M (SD)	Post M (SD)
Oral and written information	44	14.1 (6.5)	10.8 (6.3)
Written information	43	13.0 (5.0)	11.2 (5.4)
No information	41	14.7 (5.5)	14.2 (5.6)

n Number of physicians in condition; Pre, before the intervention; Post, after the intervention; M (SD), mean number of benzodiazepines prescribed per 100 patient contacts with prescription (standard deviation)

The prescribing of benzodiazepines

The 128 practitioners who had complete registration records issued 6022 prescriptions for benzodiazepines during the baseline registration period of 4 weeks. On average, benzodiazepines were prescribed in 12.7 % of all patient contacts with prescription. In about 10 % of these contacts, at least one other psychotropic drug was issued, usually antidepressants (5.5 %) and neuroleptics (4.1 %). When data were converted into defined daily doses (DDD), a mean of 545 DDD's per 100 patient contacts with prescription was found. Altogether, 14.4 packages of benzodiazepines were issued per 100 contacts with prescription. There was considerable variability among physicians: about 60 % issued between 10 and 20 packages (per 100 patient contacts with prescriptions), and for about 90 % the number was somewhere between 5 and 25 packages. Only 15 % of all benzodiazepines were issued as a first prescription, the remaining 85 % being on repeat prescriptions. In 64 % of all prescriptions the duration of treatment with benzodiazepines was 1 year or more, in almost 10 % it exceeded 10 years. Seventy percent of all benzodiazepine prescriptions were for female patients, and 55 % involved patients who were over 60 years old.

Linear regression analyses were performed to determine significant predictors of the tendency to prescribe benzodiazepines in the period of baseline registration (Table 2). Of the block of physician and practice characteristics, only the year of graduation remained as a significant predictor, explaining 23 % of the variance in the dependent variable. The negative regression coefficient indicated that physicians who had graduated more recently prescribed less benzodiazepines. Significant predictors reflecting the attitude towards drug information were the number of commercial representatives received in the last 4 weeks and the estimated utility of commercial information. Year of graduation, number of commercial representatives received and estimated utility of commercial information together accounted for 26 % of the variation in the tendency to prescribe benzodiazepines. Only for the year of graduation and the estimated utility of commercial information were the partial regression coefficients significant at the 5 % level.

Effect of industry-independent information on the prescribing of benzodiazepines

The absolute reduction in the number of prescribed packages was highest in condition one (oral and written information) with a mean decrease of 24 % compared to the baseline (Table 3). A reduction of 14 % was found in physicians of condition two (written information) and of 3 % in the control group. An analysis of variance for repeated measures showed a significant pre-post decrease for the total sample ($F = 25.0$, $df = 1$, $P < 0.001$) and a significant interaction between pre-post scores and condition ($F = 4.7$, $df = 2$, $P < 0.05$), suggesting that the size of decrease differed between the experimental conditions.

Post hoc pairwise comparisons by Duncan's multiple range tests showed a significant difference at the 1 % level between the first condition and the control group. The

possibility that, after the intervention, physicians had replaced benzodiazepines by other psychotropic drugs (i.e. hypnotics, central stimulants, antidepressants and neuroleptics) was also considered. In none of the conditions was a significant increase in the prescribing of possible substitutes for benzodiazepines found. On the contrary, analyses of pre-post differences revealed a significant decrease ($P < 0.05$) in the prescription of antidepressants and neuroleptics for physicians of the experimental groups.

A linear regression analysis was conducted *a posteriori* to examine which factors promoted or hindered the effect of the intervention. The variable 'perceived competition' seemed important in that the effect of the intervention was significantly smaller at the 1% level in physicians who thought there were more other practitioners in the area. Moreover, the intervention was most effective in the province of West-Flanders.

Follow-up survey

A follow-up questionnaire could shed light on the extent to which the participating physicians took notice of the campaign. This obviously was 100% for the oral message, since all physicians of condition one received the medical representative and visits lasted on average more than an hour. These physicians generally labelled the conversation with the representative as a positive experience and a great majority (40 out of 44 physicians) said they wished to receive more independent representatives in the future. The written message reached only part of the target group. One in two physicians of the first two conditions could remember that exactly three mailings were sent; only one third could give an accurate description of at least one mailing. The slogan at the end of each mailing, which expressed the advice to prescribe benzodiazepines for limited periods only, was acknowledged by half the respondents. The majority of physicians described the contents of the mailings in positive terms.

Physicians were also asked to rank the various information sources of familiar drugs in order of importance. From these rankings, it was noted that physicians who had met the representative during the intervention phase had a far more positive attitude towards such a source of drug information than physicians who received mailings only, or no information at all ($\chi^2 = 15.45$, $P < 0.01$). No difference was found in the rank order of independent information through mailings between physicians who received the mailings and those who did not.

Discussion

Our experimental study confirmed findings from other studies in that benzodiazepines were primarily prescribed for female and older patients [15–20]. Besides age of physicians, the estimated utility of commercial information was a significant predictor of the tendency to prescribe benzodiazepines. Physicians who considered advertising and promotion from pharmaceutical firms to be more important also prescribed more benzodiazepines. This finding is

consistent with other studies about the determinants of the physician's tendency to prescribe drugs [21].

While mailings only moderately affected the physician's tendency to prescribe benzodiazepines, the additional information by an independent representative led to a considerable decrease in prescribing, a result that confirms findings from other studies [1, 2, 5].

Because of the low response rate to the study, some caution should be taken when generalising results to all practitioners of East- and West-Flanders. Perhaps the physicians who were willing to participate in a study about psychological problems in primary care were more aware of the problem of benzodiazepine prescription. Thus, the effect of the intervention can be somewhat overestimated.

Considerable effort was made in our trial to draw the physician's attention to the mailings, by involving advertising experts in their construction. In spite of this, the central message of the mailings only reached one in two physicians. It is possible that written information is only noticed if it involves a new topic (e.g., the introduction of a new drug). The duration of the intervention and the number of times the message is repeated are other factors to be considered in relation to the effectiveness of mailings.

On the other hand, the superior effect of the oral information strategy is probably due to factors inherent to the procedure. Personal contact with the physician allows for two-way communication, which is an important way of building a physician-specific presentation and increases the involvement of the physician in the interaction [22].

The short duration of the study could cast doubts on the durability of the intervention effect. However, Avorn et al. [2] found that the effect of their intervention persisted for at least 9 months after its start, and in the study of Ray et al. [23] it continued unabated until 2 years after the campaign. There has been little controlled research into the acceptability of noncommercial information by an independent representative. Our findings were encouraging, since physicians who had met the study representative appreciated the initiative. We believe that industry-independent information is a valuable additional education channel for general practitioners.

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