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# Primary care

## Reducing prescribing of highly anticholinergic antidepressants for elderly people: randomised trial of group versus individual academic detailing

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### Abstract

**Objective** To compare the effect of individual educational visits versus group visits using academic detailing to discuss prescribing of highly anticholinergic antidepressants in elderly people.

**Design** Randomised controlled trial with three arms (individual visits, group visits, and a control arm).

**Setting** Southwest Netherlands.

**Participants** 190 general practitioners and 37 pharmacists organised in 21 peer review groups were studied using a database covering all prescriptions to people covered by national health insurance in the area (about 240 000).

**Intervention** All general practitioners and pharmacists in both intervention arms were offered two educational visits. For physicians in groups randomised to the individual visit arm, 43 of 70 general practitioners participated; in the group visit intervention arm, five of seven groups (41 of 52 general practitioners) participated.

**Main outcome measures** Numbers of elderly people ( $\geq 60$  years) with new prescriptions of highly anticholinergic antidepressants and less anticholinergic antidepressants.

**Results** An intention to treat analysis found a 26% reduction in the rate of starting highly anticholinergic antidepressants in elderly people (95% confidence interval -4% to 48%) in the individual intervention arm and 45% (8% to 67%) in the group intervention arm. The use of less anticholinergic antidepressants increased by 40% (6% to 83%) in the individual intervention arm and 29% (-7% to 79%) in the group intervention arm.

**Conclusions** Both the individual and the group visits decreased the use of highly anticholinergic antidepressants and increased the use of less anticholinergic antidepressant in elderly people. These approaches are practical means to improve prescribing by continuing medical education.

### Introduction

The need to improve rational prescribing is increasing, but many questions remain unanswered about how to achieve this goal.<sup>1-3</sup> Educational visits have been shown to modify professional behaviour.<sup>4,5</sup> They should

consist of repeated personal visits that include feedback, present clear recommendations that are relevant to practice, and anticipate any implementation problems.<sup>6-9</sup> Not all characteristics of effective visits have been identified.<sup>4, 10</sup>

Collaboration of doctors and pharmacists in regional groups is increasingly used to improve prescribing in several countries,<sup>1, 11-13</sup> and it can be a cost effective way to disseminate new knowledge and guidelines. This study was designed to evaluate the ability of academic detailing given to individuals and groups to influence prescribing patterns. We selected antidepressant drugs for elderly people as the focus for the study because analyses of dispensing data<sup>14</sup> and other studies<sup>15</sup> have shown that a substantial portion of patients aged over 60 are prescribed highly anticholinergic antidepressants despite their greater susceptibility to hazardous side effects such as dry mouth, blurred vision, constipation, urinary dysfunction, hypotension, tachycardia, and cognitive impairment.<sup>16-23</sup> We wanted to increase the awareness of the vulnerability of elderly people to anticholinergic side effects and decrease the prescribing of highly anticholinergic antidepressants (such as tertiary amine tricyclics) in this group while encouraging the use of less anticholinergic antidepressants such as secondary amines or selective serotonin reuptake inhibitors when indicated.

### Participants and methods

#### Study design

We conducted a randomised controlled trial to compare the effect of individual versus group educational visits on the prescribing of highly anticholinergic antidepressants in people aged 60 or over (fig 1). To organise the group visits we used an existing system of peer review groups that fosters collaboration between Dutch pharmacists and general practitioners. These groups of professionals practising in the same region meet regularly to discuss treatment, pharmacotherapy, and patient management. Similar initiatives exist in other countries and are known as quality circles, pharmacotherapy discussion groups, or pharmacotherapy consultation groups. The goals of these groups include exchanging information, advising on policy, agreement on guidelines, and using feedback methods to measure adherence to

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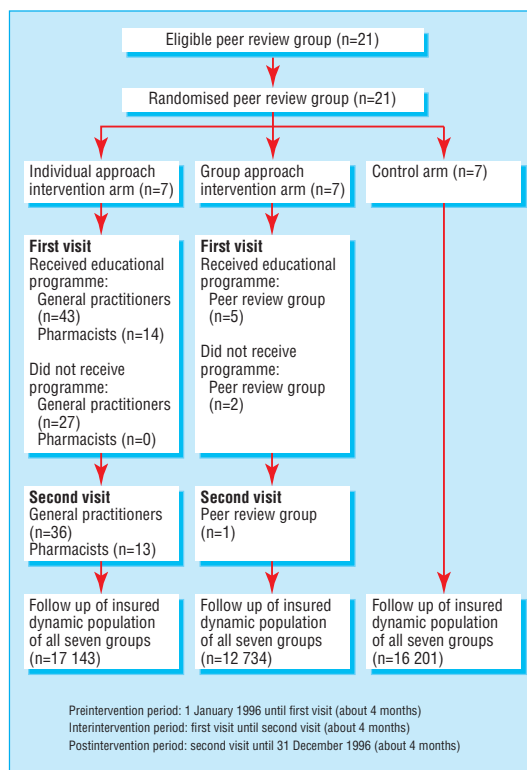


Fig 1 Flow chart of study

guidelines.<sup>11-13</sup> Before the intervention these groups were surveyed on factors thought to be relevant for the intervention. We used the results of this survey to match groups according to their stated goals (binding consensus versus other goals) and their use of a formulary or feedback data (use of either versus neither), which created four blocks for randomisation. Groups for which information was not available were assigned to a fifth group.

We used block randomisation to assign all groups to one of three intervention arms. In the individual intervention arm each general practitioner was offered individual educational visits. In the group visit intervention arm the visit was offered to each peer review group as a whole. The control arm received no visits.

#### Research area and population

The research area (the South Holland islands) is part of the area covered by the health insurance company OZ zorgverzekeringen in the southwest Netherlands. This region is a mix of semirural and rural areas with a population of about 400 000, 60% of whom (240 000) are insured through OZ zorgverzekeringen.

The research population comprised all people aged 60 years old or over on 1 January 1996 (about 50 000 people) living in the southwest Netherlands health district and insured through OZ zorgverzekeringen. We performed a sample size calculation and found that seven peer review groups (with an average 2000 patients aged over 60 and 22 patients starting an anticholinergic antidepressant over one year) per treatment arm were enough to demonstrate with 80% power a significant ( $P < 0.05$ ) reduction of 30% in prescribing of anticholinergic antidepressants.

#### Databases

We measured prescribing of antidepressants using the reimbursement databases that pharmacists send to the health insurance company monthly. These contain information on all drugs dispensed to insured patients, including amount, dose, costs, and date of issue as well as information about the user's insurance number and birthday and the prescribers' code. All reimbursable drugs for the insured population are registered this way.<sup>14-24</sup> The box gives the classification of antidepressant drugs marketed in the Netherlands.

#### Intervention

The intervention was based on theories and experience usually referred to as social marketing or academic detailing.<sup>4-5-6-10</sup> It is a framework for dissemination and implementation of activities to improve prescribing. A combination of adult learning theories and the marketing experience of the pharmaceutical industry are directed at improving the rationality of prescribing.

All doctors and pharmacists from groups assigned to the individual visit intervention arm were individually contacted by telephone. They were told of the aim of the study (to improve antidepressant prescribing in elderly people and measure the effectiveness of an educational programme) and invited to participate in the programme. For those who agreed, an appointment was made for a 20 minute visit with the lead investigator (MvE), who is a doctor. This session emphasised the unique therapeutic difficulties of treating older people and the problems of anticholinergic side effects. Participants were given a leaflet containing

#### Classification of drugs used in study

##### Highly anticholinergic antidepressants

*Tricyclic derivatives*  
 Amitriptyline  
 Clomipramine  
 Doxepin  
 Imipramine  
 Maprotiline (polycyclic derivative)

##### Less or non-anticholinergic antidepressants

*Tricyclic derivatives*  
 Desipramine  
 Opipramol  
 Nortriptyline  
 Dosulepin  
 Dibenazepine  
 Trimipramine

*Selective serotonin reuptake inhibitors*  
 Sertraline  
 Fluoxetine  
 Fluvoxamine  
 Paroxetine

*Monoamine oxidase inhibitors*  
 Tranylcypromine  
 Moclobemide  
 Nialamide

*Others*  
 Trazodone  
 Venlafaxine  
 Mianserine  
 Mirtazapine

an evidence based summary of the most important information.

All sessions were based on a priority list for issues to be discussed. Depending on the length of the visit and the responses of the professionals, the following items were discussed (in order): altered pharmacodynamics and kinetics in elderly people,<sup>18, 19</sup> increased vulnerability of elderly people to side effects,<sup>20, 21</sup> the need to avoid anticholinergic antidepressants in elderly people,<sup>22</sup> and difficulties in diagnosing depression, especially in elderly people.<sup>17</sup> Participants were shown the overall data on prescribing of antidepressants in the past year to illustrate that most anticholinergic antidepressants are prescribed to people aged over 60.<sup>14</sup> The initial visits included no further comment on personal performance. At the end of each visit another appointment was made for about four months later. During the second visit a graph was provided showing personal performance and the proportion of prescriptions for anticholinergic antidepressant versus less anticholinergic antidepressants in three age categories: under 60, 60-70, and over 70 years old.

For the group intervention arm, all group coordinators were contacted to ask permission to use one full meeting for the educational programme. The content of these presentations was essentially the same as in the individual contacts. At the end of the first visit, permission to use part of another meeting was requested. In this second meeting, a graph of accumulated prescribing in the group was shown and personal graphs were handed out. All contacts for both intervention arms were performed by MvE. The control arm was not contacted.

### Study outcome

The effectiveness of this intervention is best reflected in the choice of antidepressant for patients starting treatment. To define incident users of antidepressants, we used the prescription reimbursement records described above. For each prescription we calculated the number of days the prescription would cover, using the prescribed daily dose and the package size.<sup>14</sup> In this way, a time window of probable use was created. We assessed all antidepressant prescriptions from July 1995 onwards. If the patient had not previously been prescribed antidepressants or if the interval since the last prescription was over 180 days, the patient was considered an incident user.<sup>14</sup>

In the Netherlands all people with national health insurance are allocated to a general practitioner. We determined the periods before the educational visits, between the visits, and after the visits for each general practitioner in the region to allocate each incident patient to the right period for each general practitioner. In order to calculate incidence rates (number of incident users/1000 person years), the number of patient days per period was calculated to determine the denominator. For general practitioners in the control arm and those who declined to participate in the intervention arms we assigned average visit dates calculated from data on the doctors in the intervention arms who were visited. Incident use of highly anticholinergic antidepressants and less anticholinergic antidepressants was calculated for each general practitioner per period.

### Statistics

We used a Poisson regression model to estimate rate ratios of starting highly anticholinergic antidepressants and less anticholinergic antidepressants in elderly people in both intervention arms in relation to the control arm. The evaluation was done on an intention to treat basis in order not to overestimate the effect of the intervention by including only the most responsive doctors. Since randomisation was performed at a group level and correlated outcomes within a group can influence precision (95% confidence intervals),<sup>25</sup> we studied rate ratios with and without correction for correlated outcomes (exchangeable correlation matrix) using longitudinal data analysis (Spida). This did not materially influence outcome. Point estimates were virtually identical and 95% confidence intervals changed less than 3% (there was no change in significance of effects estimates).

Since it was not possible to correct for baseline rates with Spida, we used Egret, although in this program it is not possible to analyse correlated Poisson outcomes. In Egret, rate ratios were estimated after correcting for sex and baseline rates, with baseline rates as an offset variable. We estimated the effects of the first and second visits and of both visits together. The effects in each intervention arm and of both interventions together were also measured.

### Results

Overall, 190 general practitioners and 36 pharmacists were working in the research area. We visited 69% of the general practitioners and 100% of the pharmacists in the intervention arms (table 1). In the individual visit intervention arm, 86% of the professionals visited were visited twice. Our request for a second appointment after the first visit was always granted, but the second visit did not take place on seven occasions because the first possible date was after the closing date of the intervention. The average time spent per person was 14.6 minutes in the individual visit intervention arm. In the group intervention arm only one group was visited twice. Most groups first wanted to decide together whether and when they were going to join the programme. Well organised peer review groups had their agenda planned for the entire season, whereas

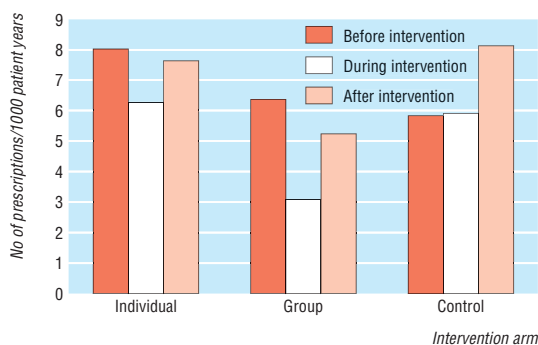
**Table 1** Baseline characteristics of general practitioners and pharmacists

	Intervention arms		Control arm
	Individual approach	Group approach	
No of groups	7	7	7
General practitioners:			
Total No (No of women)	70 (4)	52 (6)	68 (3)
No (%) visited	43 (61)	41 (79)	—
No visited twice	36	6 (from 1 group)	—
Average (range) visit time (min)	14.5 (5-30)	62.5 (15-105)*	—
Pharmacists:			
Total No (No of women)	14 (3)	9 (2)	13 (2)
No (%) visited	14 (100)	9 (100)	—
No visited twice	13	1	—
Average (range) visit time (min)	18.8 (7-30)	62.5 (15-105)*	—

\*8.3 hours per general practitioner or pharmacist.

**Table 2** Baseline characteristics of the population

	Intervention arm				Control arm	
	Individual visit		Group visit		Men	Women (%)
	Men	Women (%)	Men	Women (%)		
No of people aged:						
60-69	3399	4 144 (55)	2853	3367 (54)	3362	4026 (54)
70-79	2422	3 593 (60)	1809	2499 (58)	2410	3296 (58)
80-89	1035	2 041 (66)	650	1274 (66)	943	1736 (65)
90-96	133	376 (74)	84	198 (70)	114	314 (73)
Total	6989	10 154 (59)	5396	7338 (58)	6829	9372 (58)
Average age	70.5	72.2	69.8	71.3	70.3	71.84
Baseline rates of incident antidepressant use (/1000 person years):						
Highly anticholinergic antidepressants	8.02		6.36		5.82	
Less anticholinergic antidepressants	11.80		12.72		10.32	



**Fig 2** Rate of incident prescriptions of highly anticholinergic antidepressants in people aged ≥ 60 before, during, and after the educational intervention (intention to treat analysis)

other groups were glad to have one (or two) meetings organised by an academic researcher. This caused large differences between groups in contact time (from 15 minutes once to a full hour twice).

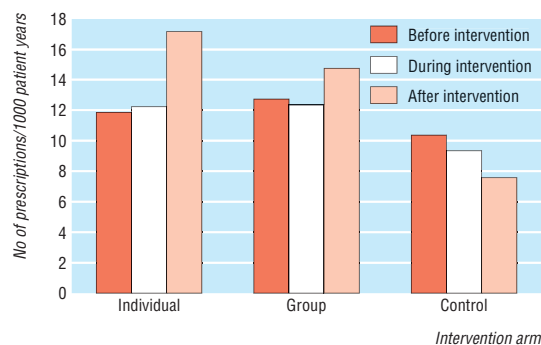
The total number of 60-96 year olds in the research area was 46 078, 58% of whom were women. Baseline incident use of highly anticholinergic antidepressants was lower than the incident use of less anticholinergic antidepressants (table 2). Baseline rates differed between treatment arms. In both intervention arms, incident use of highly anticholinergic antidepressants for patients aged ≥ 60 decreased during the study period, while in the control arm incident use increased (fig 2). Table 3 shows the rate ratios of incident prescriptions of anticholinergic antidepressants after correction for baseline rates and sex. All estimates

showed a reduction in the prescribing of highly anticholinergic antidepressants in the intervention arms compared with the control arm. This reduction was more than 30% after two visits in the individual visit arm and more than 40% in the group visit arm. This decrease was significant for the group approach and for the combined effect of both interventions.

In both intervention arms the incidence of prescribing less anticholinergic antidepressants for patients aged ≥ 60 years increased during the study period, while in the control arm the incidence decreased (fig 3). In the individual visit intervention arm, elderly patients were 100% more likely to start antidepressant treatment with a less anticholinergic antidepressant after the intervention (table 3). In the group visit intervention arm this figure was almost 70%.

### Discussion

We have shown that both individual visits and group visits can improve the clinical appropriateness of prescribing behaviour in an area of suboptimal prescribing—the treatment of depression in elderly people. Both interventions had a similar effect that was not seen in the control arm: elderly people starting antidepressant treatment were more likely to receive drugs that were less anticholinergic. The group visits significantly decreased the use of highly anticholinergic antidepressants and the individual visits significantly increased the use of less anticholinergic antidepressants in older patients. The combined effect of both intervention arms was also significant.



**Fig 3** Rate of incident prescriptions of less anticholinergic antidepressants in people aged ≥ 60 before, during, and after the educational intervention (intention to treat analysis)

**Table 3** Rate ratios for incident prescriptions of highly anticholinergic antidepressants and less anticholinergic antidepressants in intervention groups compared with control group during and after educational intervention\*

	Individual visits		Group visits		Both intervention arms	
	Rate ratio (95% CI)	P value	Rate ratio (95% CI)	P value	Rate ratio (95% CI)	P value
Highly anticholinergic antidepressants:						
During intervention	0.77 (0.50 to 1.20)	0.248	0.48 (0.22 to 1.02)	0.057	0.70 (0.46 to 1.07)	0.098
After intervention	0.68 (0.39 to 1.18)	0.169	0.56 (0.28 to 1.15)	0.114	0.63 (0.38 to 1.07)	0.084
Both	0.74 (0.52 to 1.04)	0.082	0.55 (0.33 to 0.92)	0.023	0.69 (0.50 to 0.95)	0.022
Less anticholinergic antidepressants:						
During intervention	1.16 (0.83 to 1.61)	0.385	0.66 (0.43 to 1.01)	0.635	1.14 (0.84 to 1.56)	0.401
After intervention	2.02 (1.24 to 3.30)	0.005	1.66 (0.97 to 2.85)	0.066	1.87 (1.18 to 2.96)	0.008
Both	1.40 (1.06 to 1.83)	0.016	1.29 (0.93 to 1.79)	0.127	1.36 (1.05 to 1.75)	0.018

\*Intention to treat analyses. Rate ratios were corrected for sex and baseline rates of incident antidepressant prescriptions. The difference between the group and individual arm was not significant.

Reasons for non-participation were diverse. For the group intervention it was mainly a time problem. Most groups eventually agreed to participate, but in some cases the intervention period had already ended. For the individual visits reasons mentioned included shortage of time, a belief that the study should be initiated by the medical faculty rather than the faculty of pharmacy, and lack of motivation.

### Validity of results

The data reported probably represent a low estimate of the potential of this approach. Anticholinergic versus non-anticholinergic antidepressant prescribing was a topical issue during the study.<sup>26-29</sup> Although we focused our intervention on use of anticholinergic antidepressants in elderly people, this controversy might have diluted the effect.<sup>30</sup>

We think the observed changes over time are not due to a "regression to the mean" effect. The statistical analyses adjusted for the different baseline rates. In addition, regression to the mean usually occurs when a sample has been selected because it has an unusually high (or low) set of values for a given variable. The groups studied were not defined or chosen on this basis.

Tricyclic antidepressants are used for not only depression but other indications such as chronic pain syndromes. Their use for other indications may also have had a diluting effect on our intervention. The effectiveness of the intervention was probably also diluted by prescriptions initiated by psychiatrists or other specialists who were not part of the intervention because we allocated all incident cases to the general practitioner.

### Group and individual learning

We did not evaluate the long term effectiveness of our intervention. However, other studies have shown that repeated interventions are needed for sustained behavioural changes. Our approach should also be effective for other drug categories. In groups, two opposing processes can influence the effect of an outreach programme on prescribing. Groups can be more effective in accomplishing tasks,<sup>31</sup> and publicly announcing behavioural changes results in more commitment than private change. In this way, behavioural changes can be facilitated by the group approach. Psychological research into group behaviour has produced an inventory of factors that influence conformity with group standards.<sup>32</sup> Unanimity provides more pressure to conform, while privacy makes it easier not to. On the other hand, as there is rarely unanimity in medicine, more barriers against the new strategy might be expressed in a group than in a one-to-one setting. The implementation of new knowledge is facilitated by expressing and discussing how to overcome obstacles to its acceptance. This may occur more intensely in groups than in an individual learning setting. Further research in group learning processes among health professionals may give valuable information on factors that facilitate the dissemination and application of new knowledge about drug treatment.

Audit and feedback are becoming increasingly important to help professionals keep up with evolving knowledge and implement new findings. This study adds to our knowledge of educational programmes in

### What is already known on this topic

Pressure is increasing to make prescribing more rational

Educational visits have been found to be successful in modifying professional behaviour

### What this study adds

Academic detailing aimed at individuals and groups produced changes in prescribing behaviour compared with a control group

Education of general practice groups is likely to be a cost effective way of making prescribing more evidence based

daily practice. Group approaches are likely to be a useful and cost effective addition to the arsenal of academic detailing approaches used to improve evidence based prescribing.

We thank the general practitioners and pharmacists who participated in the study and OZ zorgverzekeringen and its employees for their continued assistance.

Contributors: MECvE initiated and coordinated the formulation of the primary study hypothesis, designed the protocol and was responsible for data collection, interpretation, analyses, and writing the paper. JA participated in the protocol design, interpretation of the data, and editing the paper. AJP initiated the research project, participated in the design of the study protocol, discussed core ideas and interpretation of the findings, and editing the paper. AdB participated in the design and execution of the study (particularly quality control) and statistical analyses and contributed to the paper. MECvE and AdB are guarantors for this study.

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Competing interests: None declared.

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