

Pre-randomization decisions and group stratification in a randomized controlled trial to improve prescribing

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ABSTRACT

Objective: To select and evaluate characteristics of primary care practice groups relevant for stratification prior to randomization.

Method: Structured telephone interviews and pre- and post-intervention prescription data.

Setting: Additional study in an RCT to rationalize prescribing in primary care, addressing groups of pharmacists and doctors. Representatives of 61 primary care practice groups in the Netherlands.

Main outcome measures: Identification and evaluation of primary care practice group characteristics related to changes in prescribing. These characteristics were evaluated by estimation of incidence rate ratios (Poisson regression).

Results: Of practice groups 40 representatives (66%) participated in our study. Three characteristics were found to be most relevant for stratification: the purpose of the practice groups (whether they participated in information exchange ($n = 14$) or binding consensus on pharmacotherapy ($n = 26$)), the use of a formulary (22 practice groups did and 18 groups did not) and the use of feedback data (22 groups did and 18 groups did not). These characteristics strongly modified the effect of the program on prescribing behaviour. While the overall effect of the program was to significantly reduce the prescribing of the targeted drugs, this change was not consistent in all strata.

Conclusion: Assessment of the characteristics of practice groups made it possible to define factors to be used for a stratified randomization of practice groups which in retrospect indeed modified the effect of an educational intervention directed to change prescribing. Such pre-randomization assessments can be a useful tool in interventions designed to improve practice patterns in groups of physicians.

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Introduction

In organizing an experimental intervention in natural populations, stratification prior to randomization offers an opportunity to prevent imbalance between treatment arms in factors that may strongly influence outcomes. Control of such variability can lower the occurrence of type-I errors and improve power for small trials. While it is important to define stratification factors that have a relevant effect on prognosis or treatment responsiveness, it is also important to avoid creating too many strata¹. Most literature on stratification strategies is based on interventions at an individual

(e.g., patient) level. Although educational interventions are often organized at a group level, there is little literature on the effect of stratification of groups within a group approach intervention^{2–6}. This study reports on the selection of characteristics of practice groups in an educational intervention designed to change prescribing.

The educational outreach intervention

We recently performed a three-armed randomized controlled trial among 190 primary care physicians and 36 pharmacists, organized into 21 practice groups. To examine the differences in a group approach educational intervention and an individual intervention, we organised a three-armed trial. The aim of the intervention was to reduce the prescribing of highly anticholinergic antidepressants in the elderly. In the first arm, individual primary care physicians and pharmacists were met twice, with a four-month interval, discussing the vulnerability of elderly for strongly anticholinergic agents. In the second arm of the RCT we approached primary care practice groups with the same information. The third arm was the control; professionals in this area were not contacted and did not receive any information from us related to the trial.

As GPs and pharmacists in the Netherlands are organised in study groups we chose to use characteristics of these groups for stratification prior to randomization. This publication describes the selection of relevant criteria and the analyses after the intervention of the relevance of the chosen criteria.

The primary care groups were randomized to compare the effect of individual educational visits and group visits versus no visits to reduce the prescribing of highly anticholinergic antidepressants in the elderly; the intervention has previously been described in detail⁷ (see also Figure 1).

Primary care practice groups

As the unit of randomization, pre-existing groups of physicians and pharmacists, who met regularly in the course of their practice to discuss and improve pharmacotherapy and patient management, were used. Peer review groups, study groups, pharmacotherapy consulting groups or primary care practice groups are a well-known phenomenon in the Netherlands. Primary care physicians and community pharmacists discuss issues in pharmacotherapy to rationalise pharmacotherapy. These meetings differ from journal clubs, as the intention is to work on consensus and to evaluate implementation. In the Netherlands, we observed that the group objectives can vary from unstructured information exchange to developing and agreeing on a binding formulary and evaluating it. This is also considered an evolutionary process of these groups. Some groups use prescription audit and feedback or a formulary to increase the effectiveness of the meetings. This type of interdisciplinary group is increasingly pop-

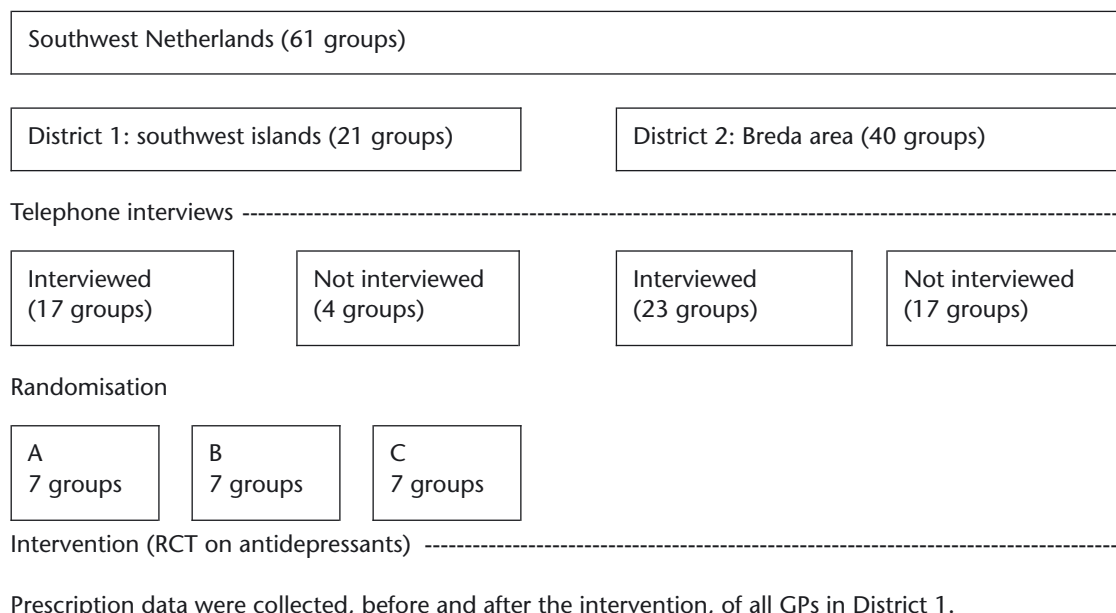


Figure 1 Trial flow chart.

ular in other countries as well⁸. For our trial we performed a stratified randomization of these primary care practice groups, based on the assumption that certain characteristics of these groups would modify the effect of the intervention on prescribing⁷.

Characteristics of professional groups that support dissemination of knowledge have been described by several authors^{9–15}. These can be divided into those concerning organizational structure, those on goals and consensus, and those on preparation and presentation. This paper describes the process of identification of these characteristics and how they modified the effect of the intervention (to reduce anticholinergic antidepressant use in the elderly).

Methods

Study design and participants

After a literature study on characteristics of practice groups, representatives of all practice groups in the working area of the health insurance company 'OZ zorgverzekeringen' in southwest Netherlands (61 practice groups, insured population approximately 600,000 persons) were contacted, to conduct a structured telephone interview.

Questionnaire

The questionnaire contained questions about characteristics of the primary care practice groups: the organizational structure, attitudes towards achieving consensus, and how topics to discuss were prepared and presented^{11, 12}.

Organizational structure

Most literature on practice groups is based on the paradigm that highly structured meetings will produce better results. A better structure facilitates problem-solving collaboration and improves the results of the meeting¹⁰. Structured cooperation results in more cooperation between members and leads to changes in drug therapy¹⁰. The minimal requirements of structural organization are generally considered to be:

group size between 5 and 15 professionals, frequency of meetings between 5 to 10 per year, duration of 90–120 minutes per meeting and good attendance rate. It also involves making commitments concerning the chairman, collaboration with other disciplines, preparation, agenda and minutes^{11, 12}.

Goals and consensus

Another important issue is a common goal and the intention of reaching consensus. This may seem easy; a major goal of these groups is to improve the quality of pharmacotherapy, but the interpretation and ambitions can be very different (from merely exchanging information to developing agreed prescribing consensus and testing adherence to guidelines). Practice groups are generally considered to evolve from information exchange towards more binding agreements,^{11, 12} and the goals of each are related to how long the practice group has been in existence¹⁴. The more binding the meetings and the agreements are, the more effective¹⁰. In our questionnaire we inquired as to the goals of the practice groups and about attitudes regarding consensus of prescribing.

Preparation and presentation

Style of presentation influences the outcome of meetings. The use of complaints, diagnoses and cases as topics appears to work better than theoretical lectures that cannot easily be implemented in practice^{11, 12}. The use of feedback data (prescription audit) or a formulary, are important aspects of preparation and presentation to achieve behavioural change. Questions on how groups actually prepared and presented meetings are summarised in Tables 1 to 3.

Stratification

Before the intervention study the stratification strategy was made based on findings from literature (see above) and distribution of these characteristics in our population (see Tables 1–3).

We divided peer review groups in those who only exchanged information and those who worked on a level of binding consensus (declared level of ambi-

Table 1 Characteristics of practice groups (n = 40) related to organizational structure

Questions	Average	SD	Min–max
Meeting since	4.5 yr	5.5	0.5–25
Number of members	9.9 persons	4.4	4–21
Attendance rate	85 %	18	60–100
Number of meetings per year	6.2	1.9	4–10
Duration per meeting	1.5 hours	0.6	0.5–3
	Yes (n)	(%)	
Is the practice group also the on-call group?	34	(85)	
Are the minutes discussed/ evaluated?	21	(53)	
Has a chairman been appointed?	31	(78)	
Is this a rotating position?	16	(41)	
Is there contact with other groups?	7	(18)	
Is there contact with hospital specialists?	13	(33)	
Are minutes being recorded?	25	(62.5)	
Is audiovisual support used?	27	(67.5)	
Is advertising material used?	6	(15)	
Are speakers invited?	10	(25.6)	

tion). The use of feedback data is needed to support evaluation of implementation and therefore seen as an important characteristic as well. Finally, we considered the use of a formulary as a relevant characteristic for the stratification strategy.

Analyses

After completion of the randomized trial, a Poisson regression model was used to estimate the number of patients who started anticholinergic antidepressants, using Incidence Rate Ratios (IRRs). We calculated the incidence of starters in the intervention arms versus starters in the control arm. These IRRs were estimated for six different subsets of the data by dichotomizing the whole data set three times (see Table 4). First, we stratified practice groups based on the stated objectives of the group. Secondly we stratified on the use of feedback data or not and finally on the presence or absence of using a formulary. In Egret, IRRs were estimated for each stratum after correcting for sex and baseline incidences, using baseline incidences as an offset variable.

Results

Response

Of the 61 practice group representatives that were contacted, 40 (66%) cooperated.

Questionnaire

Organizational structure

There was great variance in how long the groups had been in existence (0.5–25 years) and the number of members (4–21). There was less variation in the attendance rate (60–100%) and the number of meetings per year (4–10). Most practice groups were composed of physicians who shared on-call responsibilities (85%). Some groups had contact with other practice

groups (18%), invited speakers (26%) or had contact with hospital specialists (33%) (Table 1).

Goals and consensus

More than one answer could be provided for the question on goals. Eighty percent reported discussing current prescribing, 78% giving advice, and 65% making agreements on pharmacotherapy. Only 26% reported the testing of these agreements (Table 2).

Preparation and presentation

Lectures were the most popular format for meetings, followed by case discussion and the use of prescription data (Table 3). Twenty-two practice groups used feedback data. Sixteen groups reported to use both an existing formulary and feedback data.

Table 2 Characteristics of practice groups (n = 40) related to goals and consensus

Questions	Yes	
	n	(%)
Goals:		
To exchange information regarding pharmacotherapy	38	(95)
To discuss current prescribing	32	(80)
To give advice regarding pharmacotherapy	31	(78%)
To arrive at a consensus	26	(65)
Testing these agreements	10	(25.6)
Are the goals explicitly discussed?	32	(80)
Are personal prescribing attitudes discussed?	29	(73)
Are clear agreements made?	32	(80)

Table 3 Characteristics of practice groups (n = 40) related to preparation and presentation

Questions	Yes	
	N	(%)
Is the group working on a formulary?	9	(23)
Does the group use an existing GP formulary?	22	(55)
<i>What is being prepared/ presented?</i>		
Theoretical lecture / presentation	31	(78)
Case	23	(58)
Conceptual advice on first choice medication	15	(38)
Prescription feedback / numbers	22	(55)

Stratification

We sought to measure whether characteristics of practice groups, i.e., organization, goals and consensus and presentation, potentially influenced the effect of the educational intervention.

The results of the questionnaire showed that minimal requirements for structure as described in literature on these groups¹⁰⁻¹⁴ were fulfilled. We dichotomized the practice groups into those that did not go further than information exchange *versus* those that worked with binding consensus. All groups that indicated that the aim was to make agreements were considered to be in the category of binding consensus (26 practice groups). The rest were allocated to the category of information exchange.

Use of a formulary and the use of feedback data were two other characteristics warranting stratification. After distribution of practice groups into these strata, all but one stratum contained at least three practice groups (Table 4).

To evaluate the characteristics used for the stratified randomization, we compared the outcome of the educational intervention (number of patients who started anticholinergic antidepressants) for groups with and without these characteristics (Table 5). The

Table 4 Number of practice groups (n = 40) after distribution over selected characteristics of practice groups thought to be relevant for the effect of an educational intervention on prescribing behavior

Binding consensus	Use of feedback data	Use of existing formulary
Yes: 26	Yes: 17	Yes: 13 No: 4
	No: 9	Yes: 3 No: 6
No: 14	Yes: 5	Yes: 3 No: 2
	No: 9	Yes: 3 No: 6

Table 5 Incidence rate^a ratios (IRR)^b of anticholinergic antidepressants of the intervention arms (n = 14) versus the control arm (n = 7) within characteristics of practice groups which were used for the stratified randomization

Practice group characteristic	Yes/ No	IRR	95% C.I.
Level of binding consensus	Yes	1.36	0.73-2.53
	No*	0.26	0.12-0.55
Use of feedback data	Yes	0.64	0.34-1.22
	No	1.45	0.70-2.99
Use of existing formulary	Yes*	0.43	0.23-0.82
	No	1.66	0.73-3.77

^a The incidence rates (starters) of anticholinergic antidepressants in the intervention arms and control arm at baseline were 7.2/1000 person years and 5.8/1000 person years, respectively. After the intervention the incidence rates were 5.5/1000 person years and 7.0/1000 person years, respectively.

^b An IRR lower than 1 means that the prescribing of anticholinergic antidepressants in the intervention group compared to the control group was decreased.

* P < 0.05.

population of the educational program comprised 21 practice groups from one district. Our overall analysis showed that the intervention successfully improved prescribing (a reduction of anticholinergic antidepressants of 31%, 95% confidence interval 5-50%, P = 0.022)⁷ in the intervention arms.

The effect estimates demonstrated that all three characteristics modified the effect of the outreach program. The desired effect of the intervention was seen in groups using a formulary and those working with feedback data. The intervention was not effective in groups on a level of binding consensus.

Discussion

This study reports on the definition of characteristics of primary care practice groups hypothesized to be predictors of responsiveness to an educational intervention. Analysis identified which characteristics modified the effect of the intervention. Our results confirm the effect of the pre-specified group characteristics and the importance of distributing them evenly across the experimental arms. Further research will be needed to determine whether there are other characteristics, which have an important modifying effect on such interventions using groups of physicians as the unit of intervention and of randomization.

There is little literature describing the properties of practice groups that might facilitate goal achievement (improvement of quality of pharmacotherapy). More general theories on the diffusion of innovations conclude that diffusion is fundamentally a social process, and emphasize the importance of network interconnectedness (affiliation with a hospital, office-sharing and sociometrical position)¹⁶.

Some limitations to this approach should be considered. Response to the telephone interview was 66%. This may have caused response bias. Interviews were conducted with group representatives, who may have been more motivated and more enthusiastic about the

meetings than other group members. Because not all groups wanted to, or were able to cooperate with the prior inventory of characteristics of practice groups, the stratification was based on available information. For the trial we randomly assigned groups that had not been interviewed over the intervention arms.

We found that groups that focused on developing binding consensus were less receptive to our intervention strategy. An explanation may be that these groups take more time to change prescribing because they first have to reach a new consensus on the subject. The use of a formulary indicates an intention to rationalize prescribing, but it can also cause a different effect: there are already guidelines on the subject of intervention. This may make it more difficult to influence prescribing. Surprisingly, we observed that prescribing was most influenced in groups that did work with a formulary.

Experience with feedback data was relevant because it was part of the intervention strategy to change prescribing⁷, and also because of its central role in attempts to arrive at a consensus. Prescribing changed more with groups familiar with feedback data. Further research is needed to find out whether this is an important factor for groups to be optimally receptive to educational programs.

Methods of achieving quality improvement and change in clinical practice vary in their effectiveness. There is a large body of work examining the role of organizational factors that influence the implementation of new evidence¹⁷. This study does not take into account many other factors known to influence CPD/CME and the possible interactions known to be important in groups. This field is continuously evolving¹⁸. Our study reports about characteristics of primary care practice groups and their possible effects on an educational intervention.

Conclusion

These findings indicate that future educational interventions may benefit from the use of several tailored strategies depending on the characteristics of the practice groups targeted. Stratification is likely to be superior to simple randomization in such research, although other interventions or practice groups with other characteristics may require another set of factors for stratification.

Although many aspects of continuing medical education are not yet well understood, the use of stratified randomization can improve the analytic approach to an educational intervention where the level of intervention is a group of professionals. It will be important to further identify the characteristics that best predicts improvements in practice, by comparing groups in which prescribing altered *versus* groups in which this was not the case.

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Conflicts of interest

Part of the funding was MvE being employed at 'OZ Zorgverzekeringen' for the duration of the project. No other conflicts of interest.

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