Drug therapy in the elderly: what doctors believe and patients actually do

I. Barat,[1] F. Andreasen[2] & E. M. S. Damsgaard[1]

[1]*Center for Clinical Pharmacology, Department of Pharmacology, University of Aarhus and* [2]*Geriatric department C, Marselisborg Hospital, Aarhus University Hospital, Denmark*

Aims To examine the medication adherence among old persons living in their own homes, to assess their knowledge of their medication, and to indicate target areas for intervention.

Methods A cross-sectional study of data collected from randomly selected samples of 348 persons, aged 75 years recruited from a population-based register in the municipality of Aarhus, Denmark. Information on all drugs was collected from the subjects during a home visit, and their drug storage was examined. Information was collected from the general practitioners (GP). The measures of adherence were scores of agreements between the GPs' lists and the subjects' actual drug consumption.

Results We found disagreement between the drug information collected from the study population and from the GPs: concerning drugs in 22% of the study-population, concerning doses in 71%, and concerning regimens prescribed by the GP in 66%. Twenty-four percent stated that they did not always follow prescriptions. Most of the deviations from prescriptions were toward lower doses and less frequent drug intake. The drugs most often involved in deviations were hypnotics, analgesics, bronchodilators and diuretics. Sixty percent of the participants knew the purpose of medication, and 21% knew the consequences of omission of the drugs. Less than 6% of the subjects knew about the toxic risks, side-effects, or potential drug interactions. The participants' knowledge of the drugs was positively associated with their adherence. We found a correlation between an increased number of prescribed frequency of drug intake per day and deviation from the regimen ($r=0.25$, $P=0.01$). There was a positive association between nonadherence and the use of three or more drugs (odds ratio (OR) 2.5; 95% confidence interval (CI) 1.5,4.1), prescriptions from more than one doctor (OR 2.5; 95% CI 1.3,4.8), and probability of dementia (OR 9.0; 95% CI 1.1,72.5). Moreover compliance aids facilitated adherence (OR 4.4; 95% CI 1.6,12.3). Persons living alone were more prone to medication errors (OR 2.0; 95% CI 1.1,3.5).

Conclusions A differentiated evaluation of adherence by considering the drug, the dose, and the regimen separately produced quantifiable data concerning the subjects' medication habits. Non-adherence ranged from 20 to 70% depending on the measuring method. The participants' knowledge of the treatment was poor. Our results suggest that better information on medication and the use of compliance aids may prevent nonadherence. Special attention should be paid to persons receiving three or more drugs, living alone, receiving drugs from other doctors, and to persons with predementia symptoms, as they are at higher risk of nonadherence.

Keywords: aged, drug prescriptions, drug therapy, patient compliance, patient nonadherence

Correspondence: Dr Ishay Barat, Geriatric Department C, Marselisborg Hospital, Åarhus University Hospital, P.P. Orumsgade 11, 8000 Åarhus C, Denmark. Tel.: +45 89491991; Fax: +45 89491990; E-mail: i.b@dadlnet.dk

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Introduction

Medication adherence (the patients' use of the right drug in the correct dose at the right interval) is essential in the treatment of the elderly. Non-adherence may aggravate

health and lead to hospitalization [1-3] and to avoidable health-care expenditure [4]. Several studies have been conducted to shed light on this subject [1, 5–12]. Although there is an agreement on the frequency of nonadherence among elderly persons (26–59%) [13], conflicting reasons for medication nonadherence have been reported. An increased number of prescribed drugs is reported by some authors [1] to be associated with nonadherence [5, 8], while others report no association [6, 12]. Age and gender are reported to be correlated to nonadherence by some [7] and not to be by others [5]. The reports on mental conditions and nonadherence are conflicting [6, 8]. Some studies concentrate on one drug [7], few drugs [9], or all drugs possessed by the patients [1, 8]. Some studies compare the drugs possessed by the patient with records from general practitioners [14]. Other studies rely solely on the patients' ability to recall the drug [5]. The conflicting outcome of the previous studies may be explained by the different methods of assessing adherence. The individual elements of the non–adherence syndrome have not yet been determined simultaneously. Moreover, the patients' knowledge of their medication has not been included among the causes of nonadherence.

The aims of the present study were: (1) to assess the medication adherence in a randomly selected population of 75 year old persons living in their own homes in the municipality of Aarhus, (2) to evaluate their knowledge of their medicine and (3) to indicate targets of intervention by examining the relation between adherence and factors that may predict nonadherence. We used three different methods to assess adherence by comparing the participants' drugs, doses, and frequency of intake with the general practitioners' (GP) records. We assessed the participants' own evaluation of medication adherence. We examined the participants' knowledge of their medication and lastly, we examined whether knowledge of the medication among other factors may influence nonadherence.

Methods

Design of the study and the collection of data

The study was carried out in the municipality of Aarhus, Denmark, which on January 1, 1998 comprised 282 137 inhabitants of whom 1585 were 75 years old. The design of the study is described elsewhere [15]. Every fortnight a sample of 20 individuals was drawn from the Danish Population Register during the study period (August 1997 to February 1999) by a method developed by Damsgaard *et al.* [16]. A total of 793 persons was sampled (Figure 1).

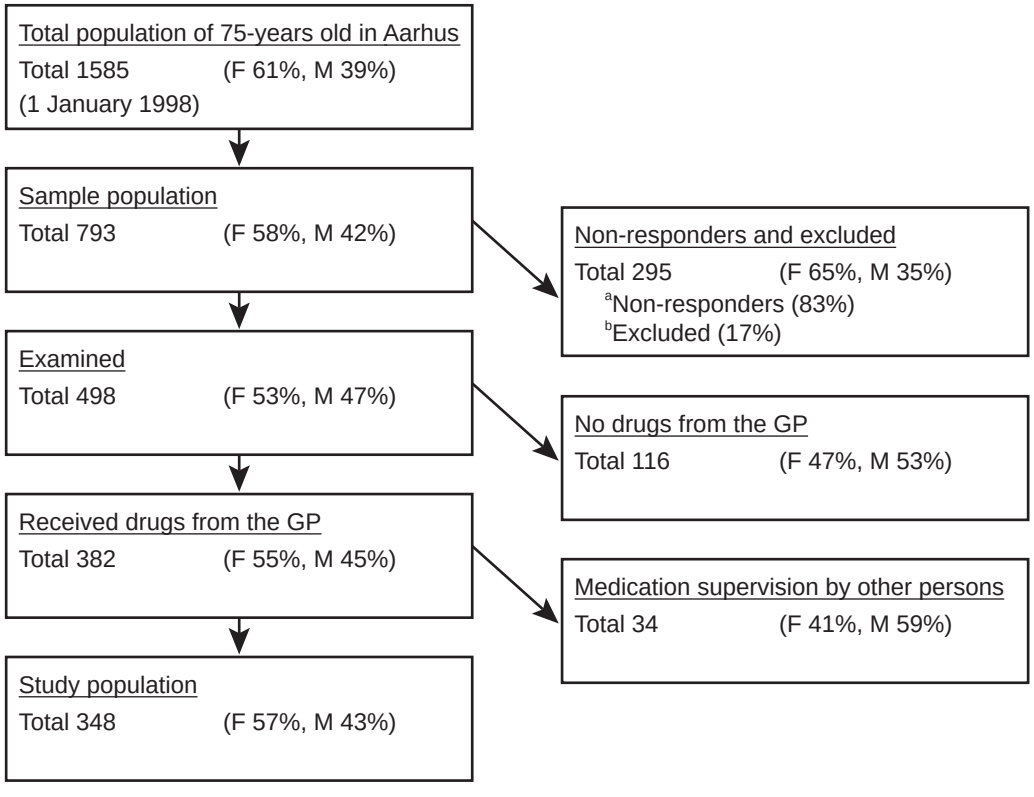

Figure 1 Selection of study population. (a) One half of the nonresponders were not interested in attending the study, one quarter did not wish to be examined, one fifth were frequently examined by the GP or an outpatient clinic and did not wish to undergo an extra examination, and the rest did not have time or did not give a reason. (b) One half of the excluded persons had dementia, one third were hospitalized, and the rest were either at homes for the aged or dead after the sample had been drawn.

Subjects were invited by mail and telephone to participate. The subjects were visited at home for 2 h by one and the same nurse or physician for interview and medical, cognitive, and functional assessment. The participants were asked to present their drugs. Each item's name was registered. The pharmacy labels with dose instructions were not used in this study, as we wanted to focus on the patients' statement about the actual consumption. The subjects were asked about dose, frequency of use, and time of intake. It was noted whether or not the drug had been prescribed and by whom, whether the participants used compliance aids, and whether a family member or medical personal supervised the participants' medication. Compliance aids used included pill organizers and medication schemes. Drugs administrated by inhaler, eyedrops, or injections (insulin) are not suitable to pill organizers and are only noted on medication schemes. The subjects' knowledge of side-effects, toxic effects, consequence of omission, purpose of the therapy, and possible drug interactions was assessed. Moreover the subjects stated for each drug if it happened that they omitted one or used an extra dose, and how often this occurred. We used the Mini Mental State Examination (MMSE) [17] to assess cognitive status. Dementia was considered probably present when the score was below 24. The probability of depression was assessed by the Geriatric Depression Scale (GDS) [18] and was considered present if the score was higher than 6. Data on the living arrangement (alone, not alone), the number of years in school (<8 years, 8–10 years, >10 years) was noted. The use of alcohol was categorized according to the recommended maximal weekly consumption of 14 units for females and 21 for males [19] (no use, use not exceeding the recommended, use exceeding the recommended). The number of prescribed and over-the-counter (OTC) drugs used by each of the subjects was dichotomized to less than three drugs and three or more drugs. The participants' general practitioners (GP) were contacted by telephone and either interviewed or asked to mail information on all prescribed drugs used by the patients on the day of visit, and whether changes were made within the 6 months preceding the examination day. This information included the name of the drug, daily dose, daily regimen, and the purpose of treatment. In Denmark hospitals and specialists are required to inform the GPs on the treatment of their common patients. In the following, when the word prescribed is used, it refers to the information received from the GP. Anatomical Therapeutic Chemical (ATC) classification [20] was used to categorize drugs. The Regional Ethics Committee and the Danish State Registry Board approved the study, and all participants gave written informed consent.

The method of calculating adherence-scores

As others [21] we accepted 20% deviation from the information from the GP in order to compensate for possible inaccuracies in the GP's notes [6]. Calculation of adherence scores has been done by other authors [11, 22]. They calculated a ratio between a sum of adherence rates and the number of the drugs. We simplified the method considering adherence rates only as adherence (1) or nonadherence (0). For each participant we calculated three different adherence scores based on observations of the participants' actual use of drugs and information given by the general practitioner. OTC drugs, drugs prescribed 'as required', or after a changing scheme were excluded from the calculation.

1 The *drug score* was based on the ratio of the number of prescribed drugs used by the participants to the number of drugs prescribed by the GP. Drugs prescribed by other doctors than the patient's GP were not included. Ratios below 0.8 scored as deviating (0), above 0.8 as not deviating (1).

2 The *dose score* was based on daily doses that agreed with the GP's information. The following formula was used:

$$\text{Dose score} = \frac{d_1(a_1) + d_2(a_2) + d_3(a_3) + \ldots}{n}$$

where d_i is the drug used by the subjects (value 0 or 1), n is the number of drugs in the GP's record, and a_i is the dose-deviation-rate. Values of the dose-deviation-rate (deviation-rate calculated by dividing the patient actually used daily dose with the daily dose prescribed by the physician) outside an interval of 0.8–1.2 were scored as deviating (0), within as not deviating (1).

3 The *regimen score* was based on the adherence to the regimen prescribed for a particular drug (once daily, twice daily, etc.). The above mentioned formula was also used here, but a_i denoted the regimen deviation of the drug in question.

The participants self-evaluation of adherence

For each drug the participants stated whether the prescription was followed strictly or not. We considered nonadherence present when a dose was omitted or an extra dose was taken compared with the prescribed dose for at least one of the medications at least once every month.

The method of calculating a knowledge-score and evaluating-score

The knowledge of the drug side-effects, purpose of treatment, toxicity, consequence of omission, and possible

interaction with other drugs was assessed for each drug. The participants' answers were evaluated as correct, no knowledge, or wrong. Correct answers scored 1 point, while the other answers scored zero. The participants' knowledge of their medication was then calculated as the ratio of the number of points scored to the number of drugs used. We chose a cut-off point at the level of 0.75. We considered persons scoring a ratio of 0.75 and over as having good knowledge of their medication.

Statistical analysis

Data were organized to fit the SPSS statistical package 8.0 (SPSS for Windows 8.0, SPSS Inc., Chicago). Logistic regression was used to evaluate the predictability of the factors that may determine nonadherence. This statistical method was also used to evaluate the association between adherence and the knowledge of the medications. Log-linear method was used to evaluate the relation between the different ATC groups and nonadherence. Spearman's correlation analysis and Pearson's chi-square analysis were used as mentioned in the text.

Results

The response rate was 63% (Figure 1). Females were underrepresented (expected 61% of the population, examined 53%). We have validated these data elsewhere [15] and found that the overall distribution of drugs among the participants was not significantly different from the distribution of drugs among the population of non-responders.

Three hundred and eighty-two participants received 1744 different prescribed drugs. Three hundred and ninety-three drugs (22%) used by 171 (55%) of the participants were not reported by the GP and could not be analysed in the formulas. Seventy-one percent of the drugs not reported by the GP were stated by the subjects to be prescribed by the GP, while other doctors prescribed the rest. The number of drugs that was listed by the GPs was 1351 (mean 3.5, range 1–14). Thirty-four participants (Figure 1) receiving 188 drugs (mean 5.5, range 1–13) had their medication supervised by family members or medical personals. The adherence in these cases did not differ significantly from the adherence of the population without supervision. However there was a trend towards a higher nonadherence, so we decided to omit the group with medication supervision from further analysis. The final number of participants included was 348 and the number of drugs 1163 (mean 3.3, range 1–14).

Drug deviations

Drug scores less than 0.8 occurred in 77 subjects (total 22%, males 21%, females 23%). We compared the drug-deviation of six major ATC drug categories (gastrointestinal drugs A, anticoagulant agents B, cardiovascular drugs C, musculoskeletal drugs M, CNS agents N, and respiratory drugs R) with each other (loglinear). There was no significant difference in deviation rate between the categories. The adherence in females did not differ from that in males within each ATC category.

Dose deviations

Dose scores indicating dose deviations were found in 71% (68% males, 73% females). Figure 2 illustrates the percentage deviation within each of the major drug categories.

The dose deviation rate was significantly higher in the musculoskeletal, the CNS, and the respiratory drug categories than in the gastrointestinal, the cardiovascular, and the anticoagulant categories (loglinear). Twenty-five percent of the deviating dose scores exceeded the doses prescribed (mean 2 times the prescribed dose; range 1.3–5 times) while the remaining 75% were lower (mean 0.3 of the prescribed dose; range 0.1–0.7). There was no significant difference between sexes. Fourteen percent of all the participants receiving low-dose aspirin, 12% receiving diuretics, 13% using nitrates, 14% receiving calcium antagonists, and 12% receiving nonsteroidal anti-inflammatory drugs used doses exceeding the prescribed. Fifty-eight percent of all subjects receiving hypnotics, 54% using nonsteroid anti-inflammatory drugs, and 46% receiving analgesics used lower doses than prescribed.

Regimen deviations

The treatment regimen ranged from once-every-third-month (cyanocobalamin) to six times a day (antiparkinson

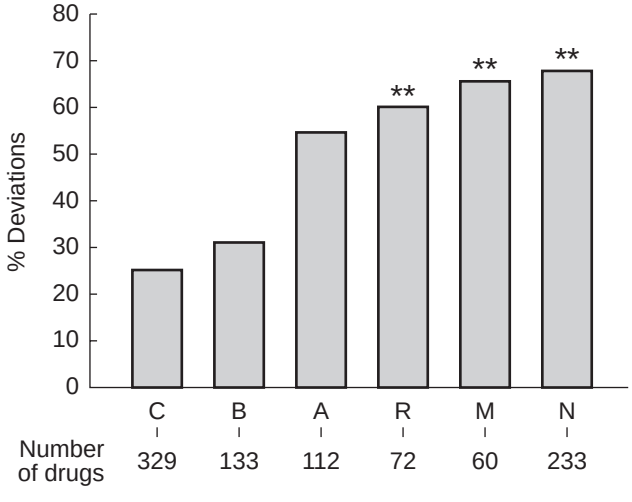

Figure 2 Percentage of dose deviations within six drug categories. The statistical significances of the differences between the expected and the observed values are indicated with stars. A gastrointestinal, B anticoagulants, C cardivascular, M musculoskeletal, N CNS, R respiratory. $**P<0.01$.

agents). Sixty-six percent of the participants (63% males, 69% females) had regimen scores indicating deviations from the regimens stated by the GPs. The associations between the regimen-deviations and the major drug categories (data not shown) were almost identical to the relation found for dose-deviations (Figure 2). No difference between the sexes was found. About 80% of the medicaments with regimen-deviations were used less frequently than suggested in the prescribed regimen. Fifty-eight percent of all subjects receiving hypnotics and 36% of participants using analgesics took these drugs less often than prescribed. We found a positive correlation between the prescribed frequency of intake and the regimen-deviations. The variables were treated as categorical and dichotomous, respectively ($r=0.25$; $P<0.001$).

Self-evaluation of adherence

Twenty-four percent (21% males, 26% females) of the participants admitted occasional deviation from the prescription. Most deviations were of omissions (80% of deviations). Five percent of all subjects using hypnotics and analgesics occasionally used higher doses than prescribed. Twelve percent of all the participants using cardiovascular agents, and 13% receiving respiratory drugs used lower doses than prescribed.

The participants' knowledge of their medication

Sixty percent (males 64%, females 57%) knew the purpose of treatment for at least 75% of their medications, and 21% (males 24%, females 19%) understood the consequences of omission of a drug or a dose. Only 4% had knowledge of side-effects, and 5% of the toxic risks. No one knew anything about the risk of drug interactions. We found no differences between sexes. The three adherence scores were correlated to both knowledge of the purpose of the treatment and to understanding of the consequences of omission (Table 1). The knowledge of the risk of toxicity was not correlated to adherence. The participants' self-evaluation of adherence was not correlated to knowledge of the medication. The knowledge of side-effects and the knowledge of the risk of toxicity were associated ($r=0.241$; $P<0.001$), so we omitted the knowledge of side-effects from the regression model.

Factors that may determine adherence

Table 2 summarizes tested association between relevant individual patient characteristics and adherence to prescribed therapy. We used logistic regression statistics, and included all parameters in the model. The parameters were dichotomous or ordinal, as all data were nonparametric. Self-evaluation of adherence (not shown in Table 2) was only correlated to 3 or more prescribed drugs used (OR 1.2; 95% CI 1.1,1.3; $P=0.004$). We found that the odds ratio of dose-deviations was about two times higher for persons living alone and the odds ratio of drug-deviations 2.5 times higher when more than one physician prescribed drugs. The probability of dementia increased the odds ratio of regimen deviations by a factor of 9. We found that the odds ratio of drug-deviations was 4.4 times lower when compliance aids were used. The use of three or more prescribed drugs was associated with a 1.2–2.5 times higher risk of nonadherence depending on which adherence score we looked at (drug-deviation, dose-deviation, regimen-deviation, or self-evaluation of adherence). A cut-off number of three or more drugs produced the most significant correlation to nonadherence. Gender, the number of years in school, probability of depression, number of OTC drugs used and the use of alcohol were not correlated to adherence.

Discussion

Validity of the data

We regarded the data received from the GP as complete. However, it is possible that the records of the GPs are not

Table 1 The association between participants' knowledge of the prescribed medication and the adherence to the prescribed drug therapy.

				Likelihood of adherence		
	Knowledge	n	*%*	*Drugs* OR (CI)	*Dose* OR (CI)	*Regimen* OR (CI)
The purpose of treatment	Yes	198	60	9.5 (4.5,19.8)***	1.8 (1.1,3.1)*	3.7 (2.2,6.2)***
	No	133	40			
The consequences of	Yes	70	21	12.3 (1.6,93.1)*	2.3 (1.3,4.2)***	1.8 (1.0,3.3)*
omission	No	261	79			
The risk of toxic effect	Yes	16	5	108.0 (0.0,911) NS	0.6 (0.2,1.9) NS	0.5 (0.2,1.6) NS
	No	315	95			

OR = Odds ratio. The OR is higher than 1 when adherence is associated with knowledge about the treatment. CI = 95% confidence interval. n = number of subjects. *$P<0.05$. ***$P<0.001$. NS $P>0.05$.

Table 2 The association between the subjects characteristics and the adherence to prescribed drug therapy.

				Likelihood of adherence		
				Drugs	Dose	Regimen
	Patient characteristics	n	%	OR (CI)	OR (CI)	OR (CI)
Gender	Males	150	43	1.5 (0.7–2.9) NS	0.7 (0.4–1.3) NS	0.8 (0.5–1.4) NS
	Females	198	57			
Living arrangement	Living with spouse	173	50	0.8 (0.4–1.6) NS	2.0 (1.1–3.5)*	1.3 (0.8–2.2) NS
	Living alone	175	50			
Number of years	More than 10 years	25	7	0.7 (0.5–1.1) NS	1.0 (0.7–1.5) NS	0.9 (0.6–1.3) NS
in school	8–10 years	111	32			
	7 years or less	212	61			
Number of prescribing	Only one	184	56	2.5 (1.3–4.8)**	1.0 (0.6–1.8) NS	1.2 (0.7–1.9) NS
physicians	More than one	145	44			
Dementia	No	327	96	3.0 (0.9–10.8) NS	3.3 (0.7–16.1) NS	9.0 (1.1–72.5)*
(MMSE <24)	Yes	15	4			
Depression	No	324	94	0.5 (0.1–2.6) NS	1.7 (0.5–5.6) NS	1.3 (0.4–3.6) NS
(GDS >6)	Yes	20	6			
User of compliance aids	Yes	61	18	4.4 (1.6–12.3)**	1.2 (0.6–2.4) NS	1.5 (0.8–2.8) NS
	No	287	82			
Number of drugs prescribed	Under 3	136	39	2.2 (1.2–4.1)*	2.3 (1.3–3.8)**	2.5 (1.5–4.1)**
	3 or more	212	61			
Number of OTC drugs	Under 3	125	36	1.3 (0.7–2.3) NS	1.3 (0.8–2.2) NS	1.4 (0.8–2.2) NS
	3 or more	223	64			
Alcohol consumption	None	166	48	0.6 (0.3–1.0) NS	0.8 (0.5–1.3) NS	0.9 (0.6–1.4) NS
	Not over the advisable[a]	166	48			
	Over the advisable[a]	16	4			

OR = Odds ratio. The OR is higher than 1 when adherence is associated with patient characteristics expected to facilitate adherence. CI = 95% confidence interval. [a]the advisable number of units weekly for males is 21 and for females 14 [19]. *$P<0.05$. **$P<0.01$. NS $P>0.05$.

always updated. It happens that other physicians change instructions without the GP's knowledge, and it may happen that changes made by the GP are not recorded. This could influence our results. To avoid such biases we included a safety margin of 20%.

The agreement between the participants' medication and the GPs' records

Omission of drugs occurred in a quarter of all the cases when the data received from the GPs were compared with the participants' medication. Gilchrist *et al.* [14] used a method similar to ours and found for 53% of the subjects disagreement between the practitioner and the patient. Glichrist *et al.* [14] also included both omitted drugs and drugs used by the patients and not listed by the GP, while we included only omitted drugs. We also found that 55% of the participants used prescribed drugs that the GPs were not aware Hof.

It is unclear why these drugs were not on the GP records. The participants stated that 71% of these drugs were prescribed by the GP, and it is expected that all prescribed drugs should figure on the GPs' records. An explanation may be that the GP records are not updated frequently enough. We were not able to trace the prescription of these drugs to the prescriber. Some of them may originate from specialists, out-patient-clinics, or hospital-departments.

In about three-quarters of the participants deviations from the prescribed doses were revealed. The general trend was to use lower doses than prescribed mostly from the CNS, the musculoskeletal, and the respiratory categories. It was remarkable that hypnotics and analgesics were most often used in fewer doses than prescribed. Most other reports on dose nonadherence are either database studies [7] or pill-count studies [9]. Large-scale database studies have often problems when changes in the doses occur during the observation period. Pill-counting studies often involve very small populations. The high frequency of dose-deviations may have two explanations. GPs may instruct their patients not to exceed a maximal dose while on the record they state the maximal dose. If this is the case, deviations express mismatch between instructions and records. It is also possible that the patients try to match the dose to the severity of the symptoms. In such cases deviations are based on the decision of the patients alone and may involve a risk of adverse drug reactions.

About two-thirds of our subjects followed other regimens than prescribed. The trend was to reduce the number of drug-intakes per day. Kruse [9] looked at the

deviation from regimens and found that persons receiving drugs twice a day make more errors than persons receiving drugs once a day. In our study the frequency of drug intake per day was significantly positively correlated to the regimen-deviations. This indicates that simplification of regimens is required when possible to meet the patient's ability to adhere.

About one quarter of the participants admitted occasional deviations from the prescription. Other studies relying solely on the subjects' own evaluation [5] found a similar value. Our data do not allow us to compare the subjects' self-evaluation of adherence with our other assessments of adherence. While self-evaluation is a measure of sporadic deviations from prescription, the other scores were intended to measure whether the subjects had made permanent change. However, it should be emphasized that this study is cross sectional and as such does not describe adherence over time.

Knowledge of the medication

Two-thirds of the subjects knew the purpose of the treatment, but only one fifth understood the consequences of omitting the medicine, and only 5% had knowledge of side-effects and toxic risks. This lack of knowledge was associated with nonadherence. Only one recent study [12] assessed the patients' comprehension of the purpose of medication showing that 72% of the answers were correct. Our findings seems to indicate that persons with little knowledge of the medication are likely to show risk of nonadherence. Better information may reduce nonadherence as shown by Espositos' intervention trial in 1995 [23].

Factors that may predict nonadherence

Multiple drug use was a powerful predictor of non-adherence according to all our assessment methods. This finding is in agreement with Coons *et al.* [5], Jackson *et al.* [8], and Col *et al.* [1] but in contradiction to Botelho & Dudrak [6], Monane *et al.* [7], and Blenkiron [12]. The other possible predictors gave different results on the three adherence scores. Subjects living alone had higher risk of dose-deviations. Other studies using methods such as pill-count, dose-deviations, and drug-deviations did not demonstrate association between living arrangements and adherence [5, 8, 12]. Persons living alone use the prescribed drugs but often have difficulties in following the prescribed dose. Two persons living together may support each other in remembering drugs and doses. We found that the risk of nonadherence increased when more than one physician were involved in the medication in agreement with Col *et al.* [1] and Monana *et al.* [7]. However our method was comparing drugs used with drugs prescribed, while Col *et al.* [1] relied on the patients' recall and Monana *et al.* [7] calculated omissions relying on database information. Our findings of nonadherence may be due to confusion or misunderstanding when different physicians give information.

The probability of dementia was associated to regimen-deviation but not to dose-deviation or drug-deviations. The nature of this finding is difficult to interpret. Other studies reported no association to dementia but they looked only upon deviations from the drugs [8] or doses [6, 10]. We believe that persons with impaired cognition (MMSE score <24) are at high risk of nonadherence. The use of compliance aids seems to reduce drug-deviation. The study of Park *et al.* [11] based on pill-counts showed similar results. In agreement with other studies we found that gender, education, and the probability of depression [6] were not associated with nonadherence. Furthermore, we found no correlation of adherence to the use of alcohol, self-evaluation of loneliness, or the number of OTC drugs used.

Conclusions

The evaluation of adherence by a differentiated method quantified the information on the medication habits of our population. We found that nonadherence occurred in 20–70% depending on whether we measured deviations of drugs, regimens or doses. Most deviations from prescriptions concerned symptomatic medication. The general trend was to reduce the amount of medication. The knowledge of the participants of their medication was poor. Comprehensive information about drugs of the elderly may increase the awareness about benefits and risks of the medicine and may improve adherence. No matter what scores of adherence we used, we found that the number of prescribed drugs is a very powerful predictor of nonadherence. The use of compliance aids may reduce nonadherence. Based on our findings we suggest that physicians carefully evaluate each drug prescribed in order to reduce the number of drugs and the number of drug-intakes per day. Special attention should be given to persons living alone, and persons with incipient dementia.

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