PWS

Pharmacy World & Science

A journal dedicated to rational drug use

Supplement I

Supplement to Pharmacy World & Science,
Volume 17, Number 5, 22 September 1995

Abstracts of Papers and Posters

Drug Utilization Research and Pharmacoepidemiology Meeting

Utrecht (The Netherlands), 19 May 1995

Organized by the Section of Drug Utilization and Pharmacoepidemiology of the Dutch Society of Pharmaceutical Sciences (Sectie Geneesmiddelengebruiksonderzoek en Farmacoepidemiologie van de Nederlandse Vereniging voor Farmaceutische Wetenschappen)

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PRESCRIBING AUDIT: MORE THEN FEEDBACK OF PRESCRIPTION DATA

C.C.M. Veninga, P. Denig, F.M. Haaijer-Ruskamp

An educational programme aimed at improving the quality of treatment in primary health care is developed and tested. The programme is based on prescribing audit and peer discussion, as previous research has shown that this is a more successful combination for improving prescribing behaviour of physicians. Sofar, however, not much attention has been given to the format of the audit. We propose an approach which includes not only audit of the outcome of prescribing decisions, but also audit of the decision-making process itself. Our educational programme thus combines outcome feedback with process feedback, and offers introspection of what has been prescribed and which factors may have triggered optimal and suboptimal prescribing.

For the outcome feedback, prescription data are collected from pharmacies or health insurance companies. Criteria are set based on existing national guidelines for primary care. Feedback is presented to the physicians at patient level, i.e. data are shown of the number of their patients who have received a certain treatment (or combination of treatments). These data are then discussed in peer groups and a comparison is made between theory and practice.

To give insight in when and why treatments are chosen, a special method of feedback will be used oriented at the decision-making process of the physicians, so called clinical judgment analysis. This analysis makes use of series of patient cases that are presented to the physicians. For each case, the physician has to decide what to do. The cases vary in specific aspects, such as the age of the patient, severity and duration of complaints and previous treatment, to see how these aspects influence the physician's decision. These data are also discussed in the peer groups.

The educational programme has been developed for two clinical areas, i.e. the treatment of asthma and of uncomplicated urinary tract infections. The effect of the programme will be evaluated by looking at changes in the general practitioners' knowledge and attitudes, actual prescribing behaviour and patient outcomes. A pilot study is now being conducted in four local counselling groups of general practitioners and pharmacists. The effect of the programme will further be tested in a randomized controlled trial.

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100 DAYS INDIRECT REPEAT PRESCRIPTIONS

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Background. Many prescriptions are repeated without seeing the patient again. Is this practice acceptable?

Aim. Before the quality of the indirect repeat prescriptions by the different GPs can be assessed, we need to know more about the prescription process and what proportion are indirect repeat prescriptions.

Method. In 100 days all prescriptions for medicines of eight GPs (20.000 patients on the list) were marked as 'repeats' (repeated without direct contact between patient and doctor) or 'normal' (new or with face to face contact). These prescriptions were classified by ATC-groups and evaluated in two community pharmacies. Meanwhile the process from request to prescription was observed by an experienced receptionist.

Results. Of the 30.790 prescriptions 33% were repeats. Almost all repeats (93%) were requested by telephone. The repeats were written the same day, 61% by the GP and 39% by the receptionist. Most repeats (72%) were intended for continuous use. There were no registers or guidelines for the receptionists on how to handle repeats. The repeats did not take long to write and the patient's notes were not consulted. The amount of repeats varied with the ATC-group (sex hormones, psycholeptica and cardiac therapy were most indirect repeated). There was no difference between men and women and only a slight growth with the age of the patient. Large differences were found among GPs.

Conclusions. Repeats are one third of all prescriptions, most are for medicines intended for continuous use. The amount varies with the GP and with the ATC-group. The receptionist plays an important role in the process from request to prescription. Weak points are the lack of registers and guidelines.

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A HIGHER IMPACT OF DRUG FORMULARIES: DISCUSS THE CONTENTS WITH GPS

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Background: In September 1991, a drug formulary was introduced in the Groningen Province (the Netherlands). This year, the third edition of this formulary will be introduced. This led to a study of the impact of the Groninger Formulary.
Setting: A database is being maintained with pharmacy data from 12 pharmacotherapy discussion groups (19 pharmacies covering ±180,000 patients) in order to study the effectiveness of pharmacotherapy discussion meetings. This database was used to study the impact of the Groninger Formulary.

Of some drugs or drug groups (e.g. ofloxacin, macrolides, mucolytics), prescribing was studied in three regions: Groningen Province (region A), a region with another drug formulary (region B), and a region without any drug formulary (region C). Subsequently, prescribing within region A was audited to study differences in prescribing between GPs who had, and GPs who had not discussed the formulary in pharmacotherapy discussion meetings.
Results: of the macrolides, the incidence of prescribing of the 'drug of choice', erythromycin, was significantly higher in region A (73 per 100 prescriptions, n=666) than in the other regions (45 and 45 per 100 prescriptions in region B (n=380) and region C (n=381), respectively). Stratification by pharmacotherapy discussion group showed that this effect is mainly attributable to GPs who discussed the macrolides during pharmacotherapy discussion meetings. For the other drugs, a significant impact of the drug formulary could only be found after stratification by pharmacotherapy discussion group.
Conclusion: For a drug formulary, to be more effective, the contents of this formulary have to be discussed with GPs.

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HEALTH INSURANCE DATABASES DRUG THERAPY ENABLING (HIDDEN): PRESCRIPTION DATABASES IN QUALITY ASSESSMENT AND QUALITY IMPROVEMENT.

M.E.C. van Eijk A.de Boer Th.J.E.van Hemert A.J.Porsius

Health Insurance companies collect an enormous amount of health care data. Prescribing data are provided by pharmacists for reimbursement of costs of pharmaceutical care and are a potential source for research in health care and health care management.

At the Health Insurance company OZ which is situated in the Southwest of the Netherlands an initiative was started to enable research with prescription data. The final goal is to provide feedback to pharmacotherapy consulting groups (=FTO's) and to study the effect on drug prescribing.

These data are gathered according to a defined structure. The KNMP and the VNZ have agreed about the lay-out that all reimbursement-(prescription)data should have. Each record in the database is one prescription item. Potentially data are available on medication histories and demographic data per patient and prescriber and pharmacist characteristics.
Our first aim was to evaluate the completeness and accuracy of the available date of 240,000 patients.
From January 1993 on reimbursement data are available in the defined structure.

Our findings were as follows:

		1993
records that can be matched with the KNMP Taxe:		96,0 %
(not in KNMP Taxe due to *pharmacy made product* 3,8 %)		
records with an ATC code		91,4 %
Incomplete information on prescriber	ca.	1,5 %
Incomplete information on patient	<	1,0 %

On average in 1993 over 90 % of the records were accessible for research.

Procedures are now being developed to increase the percentage of usefull records.

Summary:
When using reimbursementdata for the accessing the quality of pharmacotherapy, considerable effort has to be done to test the quality of the data used. Several procedures have to be developed to improve the quality of the data.

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1) can be due to pharmacy made preparations or local codes

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PHARMACOTHERAPY DISCUSSION MEETINGS IN THE NETHERLANDS

Corinne S. de Vries[1], Johan A. van der Horn[2], Antonius G.M. Steerneman[2], Lolkje T.W. de Jong-van den Berg[1].

Background: In the Netherlands, pharmacists and general practitioners (GPs) participate in pharmacotherapy discussion meetings. The objective of these meetings is to improve prescribing, dispensing and pharmacotherapy for the individual patient. The meetings take place at a local level, on a one- or two-monthly basis.
Setting: an intervention study is being carried out with respect to the effectiveness of pharmacotherapy discussion meetings. To this end, a database is being maintained with pharmacy data from 12 pharmacotherapy discussion groups (19 pharmacies; 100,317 patients). A case-study has been carried out in one pharmacotherapy discussion group that had a meeting about antihistamines. A longitudinal study of prescribing behaviour of the participating GPs (n=12) and a control group (n=18) has been carried out. Seasonal influences were taken into account. Regression lines were fitted to estimate differences in prescribing before and after the meeting.
Results: During the meeting, several guidelines for the prescribing of antihistamines were established. After the meeting, a significant increase of the incidence of the prescribing of 'drugs-of-choice' is demonstrated in the group of participating GPs ($p<0.005$). Significant differences existed between the participating GPs, however. In a similar longitudinal study of prescribing by GPs from the control group, no significant differences in prescribing behaviour before or after the date of the meeting could be demonstrated.
Conclusion: pharmacotherapy discussion meetings can be an effective way to improve pharmacotherapy. For optimum results, agreements about guidelines for prescribing and dispensing have to be made in a very clear and unequivocal way.

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PRIVACY IN RELATION TO POSTMARKETING SURVEILLANCE STUDIES

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Objectives - To study the perceptions of patients regarding privacy in relation to the performance of postmarketing surveillance studies.
Design - A population-based cross-sectional study (survey).
Setting - Out of a source population of 1030 pharmacists a random sample of 30 (2,9%) was taken. 28 (93%) of them co-operated with the investigation. Pharmacists were visited for one day each in their pharmacy during which visit their patients were enquired with a closed questionnaire.
Subjects - On the day of the visit, a random sample of patients was asked wether they had filled prescriptions for their own use. Out of a total of 1277 patients in the 28 pharmacies, 849 (66,5%) used the filled prescriptions themselves. Of these 849, 669 patients (78,8%) co-operated and completed a questionnaire with questions pertaining to their perceptions and viewpoints of privacy in relation to reporting of adverse drug reactions (ADR) and postmarketing surveillance studies.
Results - Ninety-four percent of respondents had no objection against the reporting of ADR to the Inspectorate for Health Care by their medical practioner or pharmacist. In a multivariate analysis the following cofactors were positively associated with the reporting of ADR in a significant way: Visiting the pharmacist fewer than five times a year ($p<0,05$), regarding the computerisation of pharmacy as non-threatening to privacy ($p<0,01$) and full employment ($p<0,05$). Seventy-seven percent of respondents did not object to the use of their medical data, even if these data were not anonymous, as long as the data were kept strictly confidential. Most patient were of the opinion that such data could be used without asking permission. Males would more readily give their permission than females ($p<0,05$).
Conclusions - Most repondents did not have objections to the use of their medical data for postmarketing surveillance studies. The large majority of patients did not object to the reporting of ADR to the Inspectorate for Healh Care.

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TOWARDS AN INDICATION-RELATED MEDICATION DATABASE IN PRIMARY HEALTH CARE

E.Th.J. Peters, F.M. Haaijer-Ruskamp, G.Th. van der Werf

The feasibility of constructing an indication-related medication database in primary health care is assessed. A 'simple' method to establish such a database is the registration of indication-related medication by the General Practitioner (GP). However, in the Netherlands most GPs who make active use of computerized medical records only register indications and/or prescriptions separately and it is not expected that, in the near future, GPs will register indication-related medication. Therefore in this project it is studied whether indication data registered in general practices can be reliably linked to medication data from health insurance claims which are routinely collected from pharmacy records. This is evaluated in a sample of 12 GPs covering about 20,000 patients. The GPs work together in the Registration Network Groningen (RNG) and since 1989 they all use the same software. The GPs of the RNG register both medication and indication. The data can be retrieved in 3 different files; the 'morbidity-file' where the events of a face-to-face contact between GP and patient are registered, the 'problem-file' which represents chronic health problems and the 'medication-file' where the RNG registers medication and the indication. The first 2 files are used to link the diagnose to the medication claims. The medication-file is used to validate this linkage. The linkage is done first at the patient level with the unique coded (sickfund) insurance number and secondly at the level of the prescription using date of prescribing/dispensing as an extra linkage criterium. However, this results in unsolvable linkages since 1 patient can have comorbidity and can present these to the GP at 1 date so that it is unclear which indication is related to the medication. For instance for antimicrobial drugs (Anatomical Therapeutic Chemical (ATC) group J) and heart/vascular drugs (ATC-group C) the percentage unsolvable linkages was 68% and 72%. Two methods to reduce the unsovable linkages were examined:
1) before linkage; the use of another linkage criterium i.e. the theoretical logical relation between dispensed medication and diagnosis. It should be stressed that regular update of the theoretical logical relation is required because, in practice, indications can change.
2) after linkage; acceptance of an indication for a medication only if the frequency of the indication exceeds a certain minimum
Preliminary results show that both methods reduce the percentage unsovable linkages significantly (method 1: ATC-group J to 16%, ATC-group C to 19%, method 2; ATC-group J to 10%, ATC-group C to 28%) and can be used in the linkage process.

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REPORTING OF SUSPECTED ADVERSE REACTIONS TO DRUGS IN PRIMARY CARE

R. Hoek, B.H.Ch. Stricker, J.P. Ottervanger, J. van der Velden, A.J. Porsius.

Objectives: To asses the frequency and the kind of adverse drug reactions (ADR) which were presented in general practices with a source population of approximately 335,000 inhabitants in a three-month period.
Design: A descriptive study in a dynamic population
Setting: The 'Dutch National Survey of General Practice' as performed by the Netherlands Institute of Primary Health Care (NIVEL), encompassing 103 practices of 161 Dutch general practitioners (GP), in which from April 1st, 1987 through March 31st, 1988 all consultations, morbidity and other Health Care information were registered during four 3 months-periods.
Methods: Each consultation was registered by the GP by completing a registration-form. On this form, the GP had the possibility to register adverse reactions which were considered as drug-related by either the GP or the patient. All registration-forms with a notification of a possible ADR were studied in detail in order to verify whether they really consisted of adverse reactions and whether they contained more detailed information about the ADR.
Results: During the study period, of a total of 2891 patients (725 ♂, 2166 ♀) a possible ADR was reported. The average age of these patients was 44 years. The ADR were documentated on 3199 registration-forms containing 4436 adverse drug reactions of which 1184 were presented by males and 3252 by females. Allmost all (96,2%) ADR were already known. Of the 4436 adverse drug reactions, 213 (4,8%) were considered as serious. Extrapolated to the Dutch population of 15 million inhabitants, the number of patients seen with ADR in general practice may crudely be estimated at 519,000 per year. Of these 519,000 patients, 33,000 patients will have serious ADR.
Conclusions: Although adverse drug reactions are commonly encountered in general practice, the majority of these are known and not seriuos.

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THE DUTCH TELEPHONE MEDICINES INFORMATION SERVICE: AN ADDITIONAL SOURCE OF INFORMATION IN POSTMARKETING SURVEILLANCE

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Introduction: The 'Geneesmiddel-Infolijn' is an anonymous telephone medicines information service (TMIS) provided by the Royal Dutch Association for the Advancement of Pharmacy (KNMP) where the public can ask (free of charge) pharmacists all kinds of questions concerning pharmacotherapy. This project started in 1990, and is subsidized by the Dutch Ministry of Health and Welfare and the KNMP. The annual number of telephone calls is about 9,000. Previous studies showed that 20-35% of the questions concerned side-effects of drugs. Since March 1994 all TMIS questions are stored in a central database, developed by the Netherlands Pharmacovigilance Foundation LAREB.
Objective: A study was carried out to investigate wether the questions related to adverse drug reactions (ADRs) asked by patients at TMIS were related to other groups of drugs, in comparison with ADRs spontaneously reported by health professionals to the Netherlands Pharmacovigilance Foundation LAREB, and the expected frequency calculated on the basis of the number of prescriptions in the Netherlands.
Methods: A random sample of 1000 telephone questions in 1994 was analyzed, for questions predominantly concerning adverse drug reactions. These questions were divided in questions of a general nature (general ADR questions) and more specific and detailed questions (specific ADR questions). The latter possibly concerned a suspected ADR experienced by the phone-caller. The drugs associated to these specific ADR questions were classified according to the Anatomical Therapeutic Chemical (ATC) classification system. The frequency distribution of the medicines associated with TMIS specific ADR questions over the ATC codes was compared with a random sample of 1000 suspected ADRs classified in the same way reported in 1994 to LAREB, and the number of prescriptions in the Netherlands in 1992 as known from GIP-data.[1]
Results: In the sample of 1000 TMIS questions 344 (34%) questions predominantly concerned adverse reactions. 99 (10%) of these were general ADR questions. The remaining 245 (24%) questions were specific ADR questions. The frequency distribution of the associated drugs over the ATC codes in comparison with reported ADRs at LAREB and number of prescriptions are presented in table 1.

Table 1: Frequency distribution ATC codes and rate ratio (RR).

Therapeutic group	TMIS		LAREB		prescriptions	
	%	RR	%	RR	%	RR
antidepressants	20.0	10.0	6.9	3.5	2.0	1.0
benzodiazepines	10.6	0.9	3.0	0.3	11.4	1.0
sex hormones	6.9	1.2	3.9	0.7	5.7	1.0
analgesics	4.1	0.5	1.8	0.2	7.5	1.0
systemic antibacterials	3.7	0.7	10.9	2.0	5.4	1.0
other	54.7	0.8	73.5	1.1	68.0	1.0

Discussion: TMIS specific questions and ADRs reported to LAREB concentrate on different groups of drugs. TMIS was developed to deliver and not to collect information. However, in a number of the specific ADR questions the available data were suggestive that an adverse reaction had occurred, but since the data are anonymous there were no possibilities for follow-up or confirmation. Our study suggests that specific ADR questions asked at TMIS are of additional value in postmarketing surveillance.

1 GeneesmiddelenInformatie Project (Drug Information Project). Amstelveen: Sick Fund Council, 1993.

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SPONTANEOUS REPORTING OF ADR IN BELGIUM AND IN THE NETHERLANDS: A COMPARISON BETWEEN TWO NATIONAL CENTRES

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Background: Voluntary reporting schemes have many advantages in detecting unknown adverse reactions to drugs (ADRs): they are cheap, are 'simple' to operate, can rapidly react to an alert, include the complete population of a country and are sources for pharmacoepidemiological studies. Comparison of reporting to different centres may give insight into the backgrounds of fundamental issues of spontaneous reporting schemes, such as types of reporters and (reasons for) underreporting.
Methods: Data were used from two national centres: the Belgian Centre for Monitoring of ADRs and the Netherlands Centre for Monitoring of ADR. Adjustments were made for differences in the number of inhabitants, physicians and pharmacists between the two countries.
Results: Belgium has a total population of approximately 10 million, and the Netherlands of approximately 15 million inhabitants. In 1993, the Belgium centre received 476 reports, whereas the Netherlands centre received 1585 reports. Adjusted for differences in population, the Netherlands centre received 2.2 times the number of ADR reports of the Belgian centre. The causality assessment of the Belgian centre was: certain 4.8%, probable 40.8%, possible 33.8%, unlikely 12.0%, and unclassified 8.6%, whereas the causality of the Dutch reports was: certain 2.5%, probable 30.3%, possible 43.8%, unlikely 4.2%, and unclassified 19.2%. In Belgium 64% of the reports were received from general practitioners, vs 55% in the Netherlands.
Conclusions: Underreporting is higher in Belgium compared to the Netherlands. Furthermore, there are differences in causality assessment: In the Netherlands relatively more reports are left unclassified. In the presentation, possible reasons for differences between the two centres will be discussed.

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HOW CAN ADVERSE DRUG REACTIONS (ADR) BE USED AS A SOURCE OF NEW INFORMATION FOR THE PROCESS OF DRUG DESIGN AND DEVELOPMENT.

Floor Rikken, Rein Vos

The field of medical and pharmaceutical sciences can be divided into many subdisciplines which are more or less related amongst each other. The resulting scientific literature of these subdisciplines has strong intra-subdisciplinary connections, but weak inter-subdisciplinary connections. This means that knowledge from the one subdiscipline is not always connected in the scientific research of another subdiscipline. This situation can be illustrated with the following example: An antidepressive drug is known to cause hypotension as an ADR. This knowledge is of potential interest for researchers developing an antihypertensive drug. However, at this moment there is no structural methodology to connect knowledge from one discipline to another. In this study we intend to contribute to innovation in the medical sciences by offering a theoretical model and the computational tools that provide a way to obtain new hypotheses from existing literature, by connecting knowledge from the different subdisciplines.

We have chosen ADRs as a starting point for the analysis. ADRs are knowledge about aspects of a drug which are considered to be unwanted or noxious. Furthermore this knowledge is context-dependent. A pharmacological ADR can only be described in combination with the drug and the indication. We think that this knowledge, connected to another context, can be a very useful trigger for innovative research.

Our case study is the angiotensin-converting enzyme inhibitors. One of the ADRs observed in the early years of Captopril, was proteinuria. Recently diabetic nephropathy has become an indication for Captopril. We try to reconstruct the development of this new indication through quantitative analysis of literature from the period 1978 to 1984. the resuls show that a connection between Captopril and diabetic nephropathy can actively be made, in which proteinuria serves as the connecting link.
We use this test case for further exploration and refinement of an automatic literature-based drug discovery system. The system can be used as a contributing tool in the process of drug innovation.

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HYPOGLYCAEMIA ASSOCIATED WITH THE USE OF ANGIOTENSIN CONVERTING ENZYME INHIBITORS

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The use of angiotensin converting enzyme (ACE) inhibitors has been associated with an increased insulin sensitivity in diabetic patients. Although such an effect could be of benefit when treating hypertension or congestive heart failure in diabetic patients, several reports underly the hypothesis that this mechanism might be responsible for precipitating severe hypoglycaemia. To test this hypothesis we performed a nested case-control study - using data of the Dutch PHARMO system (1986-1992) - among diabetic patients treated with either insulin or oral antidiabetics with hospitalisation for hypoglycaemia as the major outcome. Adjusted for a wide range of potentially confounding factors, hypoglycaemia was significantly associated with current use of ACE-inhibitors (OR: 2.8, 95% CI 1.4-5.7). Both among users of insulin and users of oral antidiabetics, the use of ACE-inhibitors was significantly associated with an increased risk for hospitalisation for hypoglycaemia (OR: 2.8, 95% CI: 1.2-6.4 and OR: 4.1, 95% CI: 1.4-12.2 respectively). Although ACE-inhibitors have several advantages over other antihypertensives among diabetic patients, the risk of developing hypoglaecemia should be considered. Further elaboration of the mechanism is needed as up to 13.8% of all hospitalisations for hypoglycaemia might be attributed to the use of ACE-inhibitors.

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DETERMINANTS OF SUMATRIPTAN-INDUCED CHEST PAIN

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Background: There are several reports on serious cardiac adverse reactions including myocardial infarction attributed to the anti-migraineous drug sumatriptan. Chest pain is considered to be a relatively common adverse reaction to sumatriptan. We examined risk factors for chest pain following use of sumatriptan.

Design: Cohort study among sumatriptan users.

Patients and methods: The study is a part of a national cohort study on adverse reactions to sumatriptan, performed with assistance of drug dispensing general practitioners in The Netherlands. In this part of the study, all participating general practitioners had at least one patient with chest pain attributed to sumatriptan. 94% of the consumers of sumatriptan were visited at home for validation of the questionnaires, physical examination and collection of blood samples. 'Cases' were defined as consumers of sumatriptan who reported chest pain attributed to intake of sumatriptan. They were compared to consumers of sumatriptan with the same general practitioner, who did not report any type of chest pain or pressure after use of sumatriptan.

Results: The participating drug dispensing general practitioners in this part of the study, had dispensed sumatriptan to a total of 420 patients. Of these patients, 372 (89 %) responded to the questionnaires, of which 366 had indeed used sumatriptan. A total of 137 'cases' were identified. After multivariate analysis, low age, hypertension, general complaints of abdominal pain, and a family history of myocardial infarction were associated with an increased risk of chest pain attributed to sumatriptan.

Conclusions: Several determinants of chest pain attributed to sumatriptan were observed. The results may have consequences for both prescribing and understanding of the possible mechanism of this adverse reaction.

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BENZODIAZEPINES AND THE RISK OF FALLING LEADING TO FEMUR FRACTURES: DOSAGE MORE IMPORTANT THAN ELIMINATION HALF-LIFE

RMC Herings[1], BHCh Stricker[2], A de Boer[1], A Bakker[1], F Sturmans[3]

Background: The past decade the use of benzodiazepines has been identified as a major independent risk factor for accidental falls. We studied the role of dosing, timing, elimination half-life and type of benzodiazepine in relation to the occurrence of accidental falls leading to hospitalisation for femur fractures.

Methods: A 1:3 age, sex and pharmacy matched case-control study was performed using data from the Dutch PHARMO system (N=300,000). Cases included 493 patients (55+), newly admitted for a femur fracture resulting from an accidental fall (1986-1992). Relative risk estimates were calculated using conditional logistic regression analyses to control for the potential confounding effects of concomitant drug use and presence of a wide range of underlying diseases.

Results: Falls were significantly associated with current use of benzodiazepines OR=1.6, 95%CI: 1.2-2.1) and in particular with short half-life benzodiazepines (OR=1.5, 95%CI: 1.1-2.0), sudden dose increases (OR=3.4, 95%CI: 1.0-11.5) and concomitant use of several benzodiazepines (OR=2.5, 95%CI: 1.3-4.9). A strong dose-response relationship ($p<0.0001$), and dose-response relations among users of either short- or long half-life benzodiazepines, suggests that these increased risks are explained primarily by dose.

Conclusions: We conclude that benzodiazepines are a major, independent risk factors for falls leading to femur fracture and that the increased risk is probably explained by prescribing too high doses to the elderly.

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DIURETIC MISUSE AND COMPLICATIONS OF CONGESTIVE HEART FAILURE

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Introduction We sought to determine whether poor patient compliance plays an appreciable role in recurrent hospitalisations for congestive heart failure. We used the PHARMO system that links community pharmacy dispensing records to hospital admission and discharge data of 300,000 people.

Methods A case-control method was employed to assess whether evidence for poor compliance is a risk factor for recurrent hospitalisation for complications of CHF. We compared 174 patients with multiple admissions for CHF with matched controls with only one hospital admission.

Results After adjustment for cofactors, we found an increased risk for a second hospitalisation for CHF in patients with lack of refill of their loop diuretic therapy (OR [$CI_{95\%}$]: 2.0 [1.1-3.8]). We also found an increased risk in patients with a recent dosage change of loop diuretic therapy, both in lowered dosage (OR [$CI_{95\%}$]: 2.6 [1.2-5.7]) and in increased dosage (OR [$CI_{95\%}$]: 3.0 [1.6-5.8]).

Conclusions The two-fold risk we found may be an underestimation of the actual risk, because intervals between prescription refills cannot reveal occasional 'drug holidays' that, though they represent the omission of only a small percentage of prescribed doses, can still lead to acute fluid retention.

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DISCONTINUATION OF DIURETIC THERAPY IN GERIATRIC PATIENTS.

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Introduction: Approximately 25-40% of the elderly aged 65 years and older uses diuretics. This use increases further with age and is mostly longterm. Adverse effects of diuretics, in the elderly in particular include eldectrolyte disorders, dehydration, hypotensive episodes and incontinence. Small controlled studies suggest that discontinuation of diuretic therapy in the elderly is often possible.

Aim of study: To determine the frequency of discontinuation of diuretic therapy and its determinants in geriatric patients.

Methods: We retrospectively collected data on demographics, history, physical examination, diagnoses, and medications in all patients aged 75 years and older, seen at two geriatric departments (GAUZ, Nijmegen and GAAZ, Arnhem) in the years 1990 through 1993. Indications for diuretic use and reasons for discontinuation were recorded.

Results: The records of 1547 patients (459 men and 1088 women, median age 82 (range 75-102), were studied. 593 Patients (38%) were using diuretics. In 210 of these 593 diuretic therapy was discontinued (35%), in another 34 cases advise to stop was given. Resumation of diuretic therapy was reported in 48 of 210 stoppers (23%). Discontinuation was more often performed in inpatients (57% vs. 19%) and at the GAAZ (40% vs. 24%). Diuretics for unknown indications or hypostatic edema were discontinued more often than diuretics for heart failure or hypertension (48% and 41% vs. 29% and 33%). Reasons for discontinuation were doubts on the indication (45%) and adverse effects (43%).

Conclusion: Diuretic treatment was discontinued in 35% of this population of geriatric patients. Diuretic treatment was not only discontinued if prescribed for unknown reasons or unspecified edema but also in 29% of patients with heart failure and 33% of patients with hypertension. Doubts on indication and adverse effects were the main reasons for discontinuation.

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DRUG-DRUG INTERACTIONS IN MULTIPLE DRUG USERS—AGE IS NOT A RISK-FACTOR

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Introduction Interactions between drugs are a major source for complications in multiple drug users. The objective of this study is to provide prevalences of drug-drug interactions in patients with multiple drug use. Possible risk factors associated with the occurrence of drug-drug interactions will be studied, including age as a possible independ factor.

Methods Point prevalence of clinically important, potential drug-drug interactions were estimated in 4,737 patients using 4 or more drugs from different therapeutical categories. Patients with drug-drug interactions were compared to patients with no drug-drug interactions in a case-control design and possible risk factors were identified.

Results An overall of 17.3% of all patients showed one or more drug-drug interactions. After adjustment for the number of prescriptions and the number of different drug groups used, no increased risk in higher agegroups could be found. Interactions with cardiovascular drugs were most often seen.

Conclusions Patients, using drugs from multiple therapeutical categories, and showing cardiovascular disease have been shown to be at the highest risk for potential drug-drug interactions. Patients fitting this profile should be the prime target for reassessment of their medication.

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GENDER-DIFFERENCES IN SELF-REPORTED ANTIHYPERTENSIVE DRUG USE IN THE NETHERLANDS.

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Introduction: The Monitoring project on cardiovascular disease risk factors in The Netherlands has been carried out from 1987 to 1991 and examined over 36,000 men and women aged 20-59 years. In this project blood pressure, serum lipid levels, weight and height were assessed and people filled in a questionnaire about their health and use of medication. The objective of the current study is to describe gender-related differences in antihypertensive drug use.

Methods: Antihypertensive drug use was assessed by self-report of 546 hypertensive patiënts in 1987.
Hypertension was defined according to the WHO (1959) criteria; systolic blood pressure ≥ 160 mmHg and/or diastolic blood pressure ≥ 95 mmHg and/or antihypertensive medication.

Results: Prevalence of self-reported antihypertensive drug use was 55.1 (95% CI: 51.0 - 59.3) per 100 hypertensives, 60.9 (95% CI: 55.1 - 66.6) per 100 female hypertensives and 49.3 (95% CI: 43.3 - 55.2) per 100 male hypertensives. In the table the prevalence of self-reported anti-hypertensive drug use per 100 treated hypertensives by type of antihypertensive agent is shown. The relative risk is the ratio of the prevalence of drug use among treated female hypertensives and prevalence of drug use among treated male hypertensives.

Antihypertensive agent	Males	Females	RR [95% CI]
Diuretics	41.4	57.7	1.40 [1.10 - 1.78]
β-blockers	57.1	47.0	0.82 [0.66 - 1.02]
Calcium channel blockers	9.8	1.2	0.12 [0.03 - 0.53]
ACE-inhibitors	6.0	4.2	0.70 [0.26 - 1.88]
Central α-agonists	3.0	4.2	1.39 [0.41 - 4.63]
Combination products	5.3	8.3	1.58 [0.66 - 3.81]
Peripheral α-blockers	2.3	1.2	0.53 [0.09 - 3.11]
α/β-blockers	4.5	1.8	0.40 [0.10 - 1.55]
Direct vasodilators	2.3	3.0	1.32 [0.32 - 5.42]

Conclusion: In this cross-sectional survey on cardiovascular disease risk factors, among hypertensives more women than men reported antihypertensive drug use. More women than men reported use of diuretics and more men than women reported use of calcium channel blockers. For other antihypertensive agents no gender-related difference in self-reported drug use could be detected. To study gender-related differences and trends in therapy-choice and relations with risk factors, the results presented in this paper will be complemented with the data collected from 1988 to 1991.

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UNSTABLE THERAPY PATTERNS ASSOCIATED WITH A DECREASE IN QUALITY OF LIFE

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Introduction: Drugtherapy of dyspeptic symptoms in The Netherlands may be a reason for serious concern. Based on prevalence and incidence of symptoms, costs are two times higher than expected. We investigated patterns of antiulcer drug therapy as a possible indicator of quality of life.

Methods: In 10 pharmacies patients with drugtherapy for dyspeptic symptoms were asked to complete a questionnaire on dyspeptic symptoms and therapy patterns. Furthermore, the patients completed a 36-item general quality of life questionnaire (RAND-36, standardized Dutch version). A medicationscore was calculated (3-point scale, with higher score indicating more unstable therapy pattern) from their prescription drug history.

Results: In total 58 patients (27 men, 31 women, mean age 58 (±16) years with men younger than women) completed a questionnaire. Analysis of the RAND-36 showed that on all 9 domains (physical, emotional, and social) patients with dyspeptic symptoms scored considerably lower than expected from general population scores. No difference was found for gender; elderly scored better quality of life on emotional and lower on physical domains. Analysis of quality of life domains for medicationscore showed a clear decrease in quality of life with unstable therapy patterns, in particular for physical function (-22%), vitaly (-17%), general health perception (-20%), and pain (-29%).

Conclusion: Patients with dyspeptic symptoms reported considerable reduced quality of life. Unstable therapy patterns, in particular switching and comedication, were clear indicators of reduced quality of life. Analysis of prescription databases might, therefore, be a useful tool for both pharmacists and physicians to identify problems with antiulcer drugtherapy and reduced quality of life.

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ANTIDEPRESSIVES OR NOT
prescription patterns in relation to the indication

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The treatment of depression in primary care is high on the agenda. In the Netherlands in particular since the publication of the standard of the Dutch College of General Practitioners in 1994. But the same debate is going on in the UK. In this context it is important to know how GPs actually treated depression and prescribed antidepressives before the publication of the standard. Further developments can than be assessed in relation to such 'pre-standard' patterns. This question is approached by looking at 1. the treatment of depression; 2. the indications that are being used for antidepressives; and 3. the difference in indication for 'modern' antidepressives (SSRI's) and classical antidepressives (tricyclic agents).

Methods: Data are taken from a continuous registration network of 3 general practices with 12 GPs in the North of the Netherlands covering approximately 20000 patients; episodes of morbidity as well as indication (ICPC code) and medication (ATC-code) are being registered for every practice-patient contact (including tel and contacts with practice assistents). The data concern 1993.

Results: In total 286 patients with depression were identified, of whom 125 (44%) received an antidepressive (AD) at least once in 1993. In addition 279 patients received an AD for other indications. Of the 404 patients receiving an AD 125 (31%) did so for depression. Other indications were anxiety (19%) and other psychological problems and 21% for chronic pain. Overall 62% of the AD users received a classical AD. A wide variation was found between practices regarding all indicators studied; % depressive patients receiving AD (34-58%), % AD-users who have depression (19-58%) as well as the choice for a 'classical' AD (26-82%). Modern and classical AD differ significantly regarding the pattern of indications, the latter being used more often for chronic pain as well as other psychological problems. The results suggest a difference in treatment policy between the practices. one practice combining a relatively high use of AD for depressive patients with a relatively high use of AD for other indications, in particular so in case of the classical AD.

Conclusion: The results suggest that AD's have been used widely for other indications than depression for some time, mainly so the socalled 'classical' ADs. The SSRI's were in 1993 still primarily for the treatment of depression, although the first signs of a broadening indication were found also here. In view of these results the use of AD in pharmacoepidimiological studies as an indicator of depression (as has been done in earlier studies) is not possible.