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Agreement between the pharmacy medication history and patient interview for cardiovascular drugs: the Rotterdam elderly study

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Aims To study whether there is agreement between cardiovascular drugs presented at patient interview and pharmacy records in an elderly population.

Setting The Rotterdam Elderly Study, a prospective population based cohort study of people older than 55 years of age.

Methods We compared cardiovascular drug use as presented during patient interview with the computerized pharmacy medication history. Concordance of cardiovascular drug use in patient interview and pharmacy data was measured by merging the two data sets and assessed in two episodes: in a period of 6 months before patient interview and within the legend duration of each cardiovascular drug.

Results We found 2706 concordant pairs in a total of 3365 prescriptions (80.4%) in the merged data. There were 195 prescriptions presented at patient interview which had not been filled at the pharmacy, and 464 which had been filled but were not presented by the patient. The percentage of concordant pairs slightly increased to 80.6% (2275 of a total of 2824) for prescriptions of which the legend duration included the date of patient interview. The highest agreement was noted with β-adrenoceptor blocking agents with Kappa statistics of 0.97 for atenolol and metoprolol. The lowest Kappa statistic was found for organo-heparinoid, mainly as ointments against haemorrhoids (0.26).

Conclusion The agreement between patient interview and pharmacy records is good for prescription only drugs, and pharmacy records are a useful resource for pharmacoepidemiological studies on cardiovascular agents.

Keywords: cardiovascular drugs, pharmacy records, medication

Introduction

An exponential growth in the number of drugs available for treatment and prevention of disability and disease has occurred over the last 50 years [1]. A large number of relatively safe and effective drugs has been introduced into the medical market [2]. Since the usage of drugs has been rising, it is important to study their effects in large populations, i.e. pharmacoepidemiological research [3]. General contributions of pharmacoepidemiology are to solve issues on drug safety and to quantify drug effects and risk factors. Pharmacoepidemiology is important to get information that supplements that available from premarketing studies, to get better quantification of known adverse and beneficial effects and to provide data for pharmacoeconomics and drug utilization [3]. Rising drug costs and fiscal constraints in health care budgets have inspired a growing interest in pharmacoepidemiology, especially in elderly subjects with their risk factors for adverse reactions such as polypharmacy, deterioration in homeostatic mechanisms and altered pharmacokinetics and pharmacodynamics [4].

In pharmacoepidemiology, the accuracy of exposure assessment is important. Data on drug use may be obtained from the general practitioner's medical record, the pharmacy medication history, and from patient interview. Pharmacy records are usually considered as more complete resources for drug exposure than medical records, and they are often used to assess the completeness of medical records [5–11]. Little attention, however, has been paid to the nature of available information or accuracy of prescription databases used for pharmacoepidemiological research [1, 2].

The validity of drug exposure information is a concern in epidemiological studies of drug-disease relationships as even slight random misclassification of exposure may lead to non-valid risk estimations [11, 12]. Validity is often characterized by the degree of agreement between data collected by interview and prescribed therapies as documented in the medical record [5]. Although the literature uses the term 'validity' to describe the agreement between two sources of information, 'agreement' or 'concordance' is a more appropriate term to describe the comparison between drugs exposures provided by interview and medical records or pharmacy data, because even patient interview data are not a true gold standard for drug exposure, i.e. compliance. A previous study revealed that the overall proportion of concordance for estrogen use between patient interview and the medical record is 75% and between patient interview and the pharmacy record is 57% [13]. In a study similar but much smaller than ours,

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the sensitivity of pharmacy data as a proxy of drug presentation at interview varied from 50% to 91% [9].

In this report, we assessed the agreement between patient interview and the pharmacy record by studying whether filling data from the pharmacy were compatible with the drugs shown during the patient interview. Also, we studied whether this agreement varied with age, gender, and educational or socio-economic status. Cardiovascular drug prescriptions were used in this study because they are frequently prescribed in elderly people [4], and because they are used on a chronic basis that facilitates a relevant and more reliable comparison.

Methods

Setting

The Rotterdam Elderly Study (ERGO) study is a population based study of people 55 years of age and older living in the district Ommoord, Rotterdam, the Netherlands. This prospective cohort study was designed to investigate determinants of the occurrence and progression of chronic diseases in the elderly. The rationale and design of this study have been described elsewhere [14]. The cohort encompasses 7983 individuals. The large majority of patients fill their drugs at one large pharmacy that is fully computerized. Interview in this study was done by trained interviewers who also notified which drug canisters were presented by the patients to the question on current drug use.

To assess the agreement between patient interview and pharmacy data, we used the prescription database for cardiovascular drugs obtained from patient interview in the Rotterdam Elderly Study during the interview period between 1st June 1991 and 1st June 1993, and data from the pharmacy within 6 months before patient interview.

Exposure data

The Rotterdam Elderly Study provided an ERGO identification number, Anatomical Therapeutical Chemical (ATC) code for each drug presented at interview, date of interview, and patient characteristics such as age and education. The pharmacy data included the ERGO identification number, ATC code, date of prescribing, the amount of drug units given to patients, drug units taken by patients per day, daily dosages and other variables such as age and gender of the patient, and generic name of the drugs. Records with missing ATC-codes were excluded. The ATC-code for cardiovascular drugs consists of seven digits and is divided into eight groups, C01 (cardiac drugs), C02 (antihypertensive agents), C03 (diuretics), C04 (peripheral vasodilators), C05 (vasoprotective agents), C07 (beta blocking agents), C08 (selective calcium antagonists with direct heart effect) and C09 (angiotensin converting enzyme (ACE)-inhibitors).

Procedure

The two databases were merged according to the ERGO identification number. Overall concordance between patient interview and pharmacy records was calculated using the total number of prescriptions from both databases as a reference. Firstly, for each patient we assessed the concordance of interview data with the pharmacy data in a 6 months period before the date of the interview. Secondly, we then compared all prescriptions for which the interview date fell within the legend duration. This legend duration was defined as the period between the date of prescribing and the anticipated end date which was calculated by dividing the amount of drug units given to the patients by the prescribed daily dose per patient. In the results, we distinguished between two categories: concordant and discordant pairs. Concordant pairs are prescriptions of which the ATC code coincided in both ERGO and pharmacy data on a seven digits level, and pairs were discordant when this was not the case. The concordance between patient interview and pharmacy records was also assessed for the five first digits of the ATC code.

We were also interested in the description of the discordant pairs, how many prescriptions were presented during patient interview but not in pharmacy data and *vice versa*. For that reason we calculated the frequency of each ATC code in both patient interview and pharmacy data and identified the distinction between patient interview's ATC code and pharmacy ATC code. Besides overall concordance, kappa statistics were used to assess the agreement for the eleven most commonly notified drugs in both databases [15]. Univariate analysis using SPSS was performed for a description of patient characteristics (gender, age, education and income).

Results

Most of the 1682 patients in this study were female (64%). The highest number of patients was in the age group 65–74 years (36.3%). Education of the patients varied from primary school (40.9%), secondary school (46.7%), to college or university (9.2%). Income per month varied from below Dfl.1000 (23.5%) to more than Dfl.5.000 (2.1%) (Table 1). Atenolol, hydrochlorothiazide and K^+-sparing diuretics, digoxin, frusemide and metoprolol were among the five most commonly notified drugs in both pharmacy and patient interview data (Table 2).

After merging of the two databases, there were 3365 prescriptions of which there were 2706 concordant pairs (80.4%) and 659 discordant pairs (19.6%). If we only compare the prescriptions of which the interview date fell within the legend duration, the concordance percentage did not change much (80.6%). When restricted to the first five digits of the ATC code, the percentage of concordance between patient interview and pharmacy records further increased to 81.4% (Figure 1).

Regarding the discordant pairs, there were 464 drugs that were filled at the pharmacy but which were not presented during patient interview and 195 drugs presented during patient interview which were not filled at the pharmacy. When restricted to prescriptions in which the interview date fell within the legend duration, there were 154 drugs presented by the pharmacy but not during patient interview and 395 drugs *vice versa* (Table 3). Hence, the overall sensitivity of pharmacy data taking the patient interview as a gold standard was 93.3% for all prescriptions and 85.2% when restricted to the legend duration. Of all pharmacy prescriptions 85.4% were presented at interview date and

Table 1 Characteristics of the patients ($n = 1682$).

	Frequency (%)
Age (years)	
55–64	433 (25.7)
65–74	609 (36.3)
75–84	438 (26.0)
⩾85	202 (12.0)
Sex	
Female	1077 (64.0)
Male	605 (36.0)
Education	
1 Primary education	688 (40.9)
2 Secondary education	785 (46.7)
3 College or university	154 (9.2)
4 Other education	19 (1.1)
5 Missing	36 (2.1)
Income per capita per month (guilders)	
1 <1,000	396 (23.5)
2 1,000–2,000	714 (42.4)
3 2,000–3,000	327 (19.4)
4 3,000–4,000	182 (10.8)
5 4,000–5,000	29 (1.8)
6 >5,000	34 (2.1)

Table 2 Frequency of drugs in this study.

	Frequency (%)
Ten most commonly notified drugs in patient interview records:	
1 Atenolol	346 (10.3)
2 Hydrochlorothiazide + K^+-sparing diuretic	314 (9.5)
3 Digoxin	209 (6.2)
4 Frusemide	206 (6.1)
5 Metoprolol	194 (5.8)
6 Enalapril	155 (4.6)
7 Nitroglycerin	147 (4.4)
8 Nifedipine	126 (3.7)
9 Isosorbide mononitrate	125 (3.7)
10 Isosorbide dinitrate	106 (3.2)
Ten most commonly notified drugs in pharmacy records:	
1 Atenolol	360 (10.7)
2 Hydrochlorothiazide + K^+-sparing diuretic	340 (10.1)
3 Frusemide	224 (6.7)
4 Digoxin	217 (6.4)
5 Metoprolol	200 (5.9)
6 Enalapril	162 (4.8)
7 Nitroglycerin	156 (4.6)
8 Isosorbide mononitrate	141 (4.2)
9 Nifedipine	130 (3.9)
10 Epitizide + K^+-sparing diuretic	117 (3.5)

93.7% of prescriptions in the legend duration period were presented at the patient interview.

Table 4 shows that β-adrenoceptor blocking agents had the highest percentage of concordant pairs among cardiovascular drug groups in prescriptions within the legend duration (98.3%) whereas vasoprotective drugs had the lowest (35.3%). For all prescriptions, these percentages were 93.9 and 23.1 respectively. For all prescriptions, the highest proportion of concordant pairs was found in the group where the time interval between the prescription date and the interview date was <7 days (93.7%) and it showed that the longer the time interval was, the lower the percentage of concordance was (Table 5). For prescriptions within the legend duration, the proportions of concordant pairs for each time interval were almost similar.

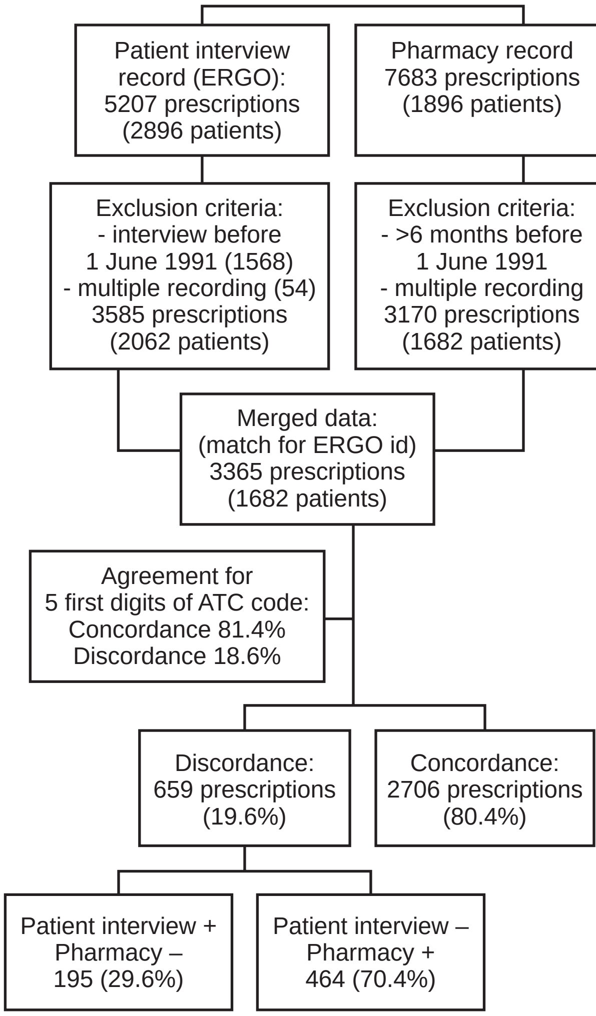

Figure 1 Scheme of the data set. All pharmacy record and patient interview.

Kappa statistics were calculated for the eleven most commonly mentioned drugs, and the vasoprotective drug organo-heparinoid as a comparison. The β-adrenoceptor blockers atenolol and metoprolol had the highest values (0.96 and 0.97, and 0.97 and 0.97 in the 6-months period and legend duration respectively). Organo-heparinoid (vasoprotective drug) had a low kappa, 0.26 and 0.27 in the 6-month period and legend duration respectively (Table 6). There were no significant differences in the level of agreement for age, gender, and educational or socio-economic status.

Discussion

In pharmacoepidemiology, drug exposure assessment depends on adequate registration of drug dispensing and on compliance by the patient [16]. Both items are important as even slight misclassification may have consequences for relative risk assessments [11, 12]. Although it is clear from this study that pharmacy filling data show a high agreement

Table 3 Drug use according to ERGO and pharmacy database.

	Presented by patient at interview	*Not presented by patient at interview*
All prescriptions (n = 3365)		
Present in pharmacy medication history	2706 (80.4%)	464 (13.8%)
Absent in pharmacy medication history	195 (5.8%)	
Prescriptions in the legend duration (n = 2824)		
Present in pharmacy medication history	2275 (80.6%)	154 (5.4%)
Absent in pharmacy medication history	395 (14%)	

Table 4 Overall concordance between patient interview and pharmacy records for each category of cardiovascular drugs (within legend duration).

	Concordance		*Discordance*		
Cardiovascular drugs	n	%	n	%	*Total*
Cardiac drugs	444	92.1	38	7.9	482
Antihypertensives	53	91.4	5	8.6	58
Diuretics	593	93.4	42	6.6	635
Peripheral vasodilators	41	95.3	2	4.7	43
Vasoprotective drugs	12	35.3	22	64.7	34
β-adrenoceptor blocking agent	616	98.3	11	1.7	637
Calcium antagonists	246	93.5	17	6.5	263
ACE inhibitors	260	93.9	17	6.1	277
Total	2265		154		2429

Table 5 Overall concordance and discordance regarding time interval between patient interview and prescription date (for all prescriptions; $n = 3365$).

Time	*Concordance*		*Discordance*		
interval	n	%	n	%	*Total*
<7 days	310	93.7	21	6.3	331
7–30 days	755	91.7	68	8.3	823
31–60 days	771	90.7	79	9.3	850
61–90 days	561	87.5	80	12.5	641
>90 days	309	58.9	216	41.1	525
Missing					195
					3365

Table 6 Agreement between patient interview and pharmacy records using Kappa statistics for eleven most commonly notified drugs and one vasoprotective agent.

	Kappa statistic	
Most commonly notified drugs	*6 months period*	*Legend duration*
Atenolol	0.96	0.97
Hydrochlorothiazide + K^+-sparing diuretic	0.91	0.91
Digoxin	0.96	0.95
Frusemide	0.90	0.86
Metoprolol	0.97	0.97
Enalapril	0.93	0.93
Nitroglycerin	0.53	0.31
Nifedipine	0.93	0.93
Isosorbide mononitrate	0.87	0.82
Isosorbide dinitrate	0.84	0.87
Epitizide + K^+-sparing diuretic	0.84	0.87
Organo-heparinoid	0.26	0.27

with the drugs presented by the patient, the latter does not prove that a patient is compliant. Even so, our figures are quite reassuring and in line with a similar study in a much smaller population [9]. At variance with that study, we were not able to calculate the specificity as the number of prescriptions *not* filled at the pharmacy and *not* presented at patient interview is meaningless and cannot be assessed. Management of pharmacotherapy by the pharmacist and the general practitioner can be a difficult task in elderly patients in whom chronic drug use is common, and self-reported drug use in elderly is not necessarily a gold standard [17]. There are still 154 prescriptions from the pharmacy record (in the legend duration) that were not presented at patient interview. There may be three reasons. Firstly, the prescriptions may have been filled out but thrown away without being used. Secondly, it may be due to overcompliance when the patient used too many pills and had nothing left at the patient interview. Thirdly, the patient may have forgotten to present the drug at the interview. There are four explanations for the drugs that were presented at patient interview but which had not been filled at the pharmacy. Firstly, the patient may have filled them at another pharmacy. Secondly, the patient may have been undercompliant and may present drugs of prescriptions that should have already been finished. Thirdly, the patient may have presented old cardiovascular drugs of prescriptions which were never finished. Fourthly, the vasoprotective agents (ATC-code C05) can be bought 'over the counter' which explains the high proportion of this group among the discordant pairs.

Pharmacoepidemiology requires information on patient characteristics (including age, sex, education, etc.) drug names, daily dosages, total drug units received by the patients for each prescription, duration, adverse reactions, prescriber, indication for treatment, and the underlying diseases of the patients. Unfortunately, there were no data about adverse reactions or benefit of the treatment and the diagnoses of the patients. Another crucial issue is the patient's actual intake, that is, their degree of compliance. Compliance is defined as a patient's behaviour in terms of taking prescribed medication, following diets, or executing recommended lifestyle changes [18]. Although this was not measured here, timely refills of chronically used agents such as cardiovascular drugs are probably a good proxy of compliance [9, 19].

Among all cardiovascular drugs, β-adrenoceptor blocking agent drugs had the highest concordance whereas vasoprotective drugs had the lowest. This was also supported by the highest value of Kappa for atenolol and metoprolol and a low Kappa value for organo-heparinoid. This vasoprotective drug can be obtained 'over the counter' and is used as necessary. Hence, the low Kappa is not surprising and may largely be explained by the fact that the majority consisted of ointments against haemorrhoids. The low concordance for nitroglycerine was expected as this drug is used when needed. So many patients who filled a prescription 1 year earlier may still have these with them. The percentage of concordance for time intervals between patient interview and date of prescribing increased with shorter intervals (for all prescriptions). The level of agreement of both data bases was not influenced by patient characteristics such as gender, age, education or income. Further studies are needed to learn whether there is an association between certain other patient characterictics and the agreement between patient interview and pharmacy records.

In summary, it is well known that errors in measurement of either exposures or outcome can lead to biased estimates of measures of association in the analysis of epidemiologic studies, so that the validity of the data collected should be carefully noticed. We conclude that the agreement between patient interview and pharmacy records is good, and that pharmacy records are a useful resource for pharmacoepidemiological studies.

References

1 Tamblyn R, Lavoie G, Petrella L, *et al.* The use of prescription claims databases in pharmacoepidemiological research: the accuracy and comprehensiveness of the prescription claims database in Quebec. *J Clin Epidemiol* 1995; **48**: 999–1009.

2 Coons SJ, Sheahan SL, Martin SS, Hendricks J, Robbins CA, Johnson JA. Predictors of medication noncompliance in a sample of older adults. *Clin Ther* 1994; **16**: 110–117.

3 Strom BL. What is pharmacoepidemiology. *Pharmacoepidemiology 1994;* **2**: 1–13.

4 Walley T, Scott AK. Prescribing in the elderly. *Postgrad Med J* 1995; **71**: 466–471.

5 West SL, Strom BL, Freundlich B, *et al.* Completeness of prescription recording in outpatient medical records from a health maintenance organization. *J Clin Epidemiology* 1994; **47**: 165–171.

6 Strom BL, Carson JL, Halpern AC. Using a claims database to investigate drug-induced Stevens-Johnson syndrome. *Stat Med* 1991; **10**: 565–576.

7 Guess HA, West R, Strand LM, *et al.* Fatal upper gastrointestinal haemorrhage or perforation among users and non-users of nonsteroidal anti-inflammatory drugs in Saskatchewan. *J Clin Epidemiol* 1988; **41**: 35–45.

8 Christensen DB, Williams B, Goldberg HI, Martin DP, Engelberg R, LoGerfo JP. Comparison of prescription and medical records in reflecting patient antihypertensive drug therapy. *Ann Pharmacother* 1994; **28**: 99–104.

9 Lau HS, De Boer A, Beuning KS, Porsius AJ. Validation of pharmacy records in drug exposure assessment. *J Clin Epidemiol* 1997; **50**: 619–625.

10 Johnson RE, Vollmer WM. Comparing sources of drug data about the elderly. *J Am Geriatr Soc* 1991; **39**: 1079–1084.

11 Van Staa TP, Abenhaim L, Leufkens H. A study of the effects of exposure misclassification due to the time-window design in pharmacoepidemiologic studies. *J Clin Epidemiol* 1994; **47**: 183–189.

12 Rothman KJ. *Modern epidemiology*. 1986. Little, Brown & Co. Boston.

13 Harlow DS, Linet MS, Agreement between questionnaire data and medical records, the evidence for accuracy recall. *Am J Epidemiol* 1989; **129**: 233–248.

14 Determinants of disease and disability in the elderly: The Rotterdam Elderly Study. *Eur J Epidemiol* 1991; **7**: 403–422.

15 Landis JR, Koch GG. The measurement of observer agreement for categorical data. *Biometrics* 1977; 33: 159–174.

16 Heerdink ER, Leufkens HG, Koppedraaijer C, *et al.* Information on drug use in the elderly: a comparison of pharmacy, general-practitioner and patient data. *Pharm World Sci* 1995; **17**: 20–24.

17 Spiers MV, Kutzik DM. Self-reported memory of medication use by the elderly. *Am J of Health System Pharmacol* 1995; **52**: 985–990.

18 Hasford J. Compliance and the benefit/risk relationship of antihypertensive treatment. *J Cardiovasc Pharmacol* 1992; **20** (suppl. 6): S30–S34.

19 Heerdink ER. *Clustering of drug use in the elderly. Population based studies into prevalence and outcomes*. Doctoral Thesis. 9th October 1995, Utrecht University.

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