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The quality of drug utilization:

Can prescribing in general practice be changed by quality circles?

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Analysis of prescription patterns of hypertension patients with coexisting diabetes mellitus in a primary care setting

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Introduction: Hypertension of any severity and concomitant diabetes mellitus define the concerned patient as "high-risk" candidate for cardio- and cerebrovascular events. Clinically manifested diabetic nephropathy increases this risk additionally. Effective blood pressure control is important to delay diabetic renal disease progression. Therefore, hypertension societies stress the necessity of intensified antihypertensive drug treatment in diabetics. This in most cases can only be achieved by combination of different substance classes. **Objective:** To evaluate the pattern of antihypertensive drug therapy in diabetics. **Methods:** Use of a prescription database consisting of health insurance files from a random sampling of persons ($n = 7490$) belonging to a large statutory health insurance organization during 1993 – 1994 with complete sampling of the prescribed drug details over one year for each patient. Hypertension and diabetes mellitus patients were identified by ICD-10 codes originating from claim-card diagnoses. **Results:** Out of 1694 hypertension patients on antihypertensive therapy 546 patients suffered from concurrent diabetes mellitus. These patients received significantly more different substance classes than non-diabetics. Antihypertensive monotherapy was given much less in diabetics (31.9%) compared to 49.4% in non-diabetics, therapy with more than 2 different substance classes was much more frequent with 36% vs. 19%. The preferred drug classes were calcium-antagonists (61% vs. 50%) followed by diuretics (40% vs. 24%) and ACE inhibitors (34% vs. 25.7%). β -blockers were prescribed much less to diabetics, however, 51% of their prescription consisted of non-selective substances. **Conclusion:** Intensified drug treatment was provided to hypertensive patients with diabetes mellitus. Calcium antagonists and

ACE inhibitors were drugs of first choice possibly reflecting their beneficial effect on diabetic nephropathy and lack of effects on glucose and lipid metabolism. The high proportion of diuretics may be explained by the intensified treatment in diabetics and favorable synergistic effects in combination with ACE inhibitors.

Drug treatment of hypertension in general practice – is prescribing evidence-based?

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Objectives: To assess general practitioners' adherence to evidence-based treatment recommendations [Guidelines Subcommittee of the World Health Organization-International Society of Hypertension (WHO-ISH) 1999, Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure 1997] concerning the pharmacotherapy of hypertension. **Methods:** We performed a multicentre, retrospective cross-sectional study to analyze prescribing behavior in 14 general practitioners attending the 1999 research workshop of the DEGAM (German Society of General Practice/Family Medicine) in Freiburg/Germany. Doctors' prescription profiles were requested from one of the biggest German health insurance company ("AOK") for all patients who received antihypertensive drug treatment from April – September 1998. GPs indicated patients' comorbidities with regard to pharmacotherapy of hypertension and listed relevant practice data on a standard questionnaire. **Results:** Up to now we analyzed 1983 prescriptions (1203 patients) from 11 GPs. The majority of patients without any comorbidities ($n = 146$) received diuretics (51%), β -blockers (42%), ACE inhibitors (35%) or calcium channel blockers (27%). 242 patients receiving ACE inhibitors (45%) did not have an adequate indication (diabetes, heart fail-

ure, nephropathy or post MI). Subgroup analysis identified 225 patients suffering from depression or asthma (30%), who were prescribed β -blockers without evidence of cardiovascular disease. 17% of elderly patients (> 65 years) with uncomplicated hypertension, received ACE inhibitors, β -blockers or other antihypertensive medication when diuretics (or calcium channel blockers) would have been indicated. **Conclusion:** The results of our study suggest that there is still room for implementing evidence-based recommendations for antihypertensive drug treatment. A after completion of data collection, interviews with all general practitioners will be held to understand discrepancies between doctors' action and evidence-based treatment guidelines.

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HMG CoA reductase inhibitors and cancer: a meta-analysis

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Background: Cardiovascular disease is the leading cause of death and morbidity in the industrialized world. Long-term treatment with statins (HMG CoA reductase inhibitors) has been shown to significantly reduce the incidence of death and non-fatal events from cardiovascular disease. Although the short-term safety and tolerability of statins is well established, their long-term potential for carcinogenicity is still debated. This study was conducted to determine if treatment with statins is safe with respect to the incidence of fatal and

non-fatal cancer, compared to treatment with placebo. **Methods:** We performed a systematic search in the MEDLINE database (no language restrictions) between 1966 and March 1999 and selected all randomized controlled trials of monotherapy with a statin compared to a placebo with a minimum treatment duration of 4 years and a total number of at least 1000 patients (treatment + placebo). Information was extracted concerning fatal and non-fatal cancers, subdivided by type of cancer whenever possible, and all-cause mortality. **Results:** Five studies were found which fulfilled all inclusion criteria for a total of 30,817 patients. Because the studies reported cancer outcomes differently, 7 meta-analyses had to be performed according to the outcomes reported. The meta-analyses performed and their estimates of absolute risk difference between treatment and placebo (95% confidence interval in brackets) were as follows (negative risks mean that treatment is better than placebo): Non-fatal cancer: excluding non-melanoma skin cancer: 0.2% (-0.3%, 0.8%); including all cancers: 0.0% (-0.8%, 0.8%). Fatal cancer: excluding non-melanoma skin cancer: -0.1% (-0.6%, 0.3%), including all cancers: -0.1% (-0.7%, 0.4%). Fatal and non-fatal cancer combined: excluding non-melanoma skin cancer: 0.0% (-0.6%, 0.6%), including all cancers: -0.1% (-1.1%, 0.8%). A meta-analysis of overall mortality produced a combined estimate of risk difference between treatment and placebo of -1.5% (-2.8%, -0.2%). **Conclusion:** Our meta-analyses of large randomized trials provide evidence that there is no association between the use of statins over a period of five to six years and an increased risk of cancer incidence or death. They confirm previous findings of a significant reduction in all-cause mortality with statin treatment. Fears concerning the carcinogenic potential of statins used over a 5-year period seem to be unfounded.

New drugs – the two-fold dilemma for doctors

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Since 1995 quite a number of new – and therefore expensive – drugs have been developed for diseases that are often treated by General Practitioners. When new agents come into the market only little is known about the therapeutic benefit compared to existing therapies. This situation produces a two-fold dilemma for the doctors: on the one hand they lack independent information to decide if any and which of their patients may benefit from the prescribing of the new drug. On the other hand their caution to take up newly developed drugs may be interpreted as being mainly driven by financial considerations. The aim of the presentation is to show how this topic was dealt with in pharmacotherapeutic circles using prescription analysis (PTC). **Database:** Prescriptions (II. quarter 1998) of 8 PTCs of the KV Hessen (1 circle with 13 moderators trained in pharmacology; 7 circles with 100 GPs with high drug costs). New drugs are defined as drugs brought into the market between 1993 – 1997 (i.e. 161 substances). **Results:** Doctors vary in their attitude towards the prescribing of new drugs: one third of GPs initiated 55% of the prescriptions with new drugs (1/3 25%, and 1/3 20%). On an average, moderators prescribed 12.4 packages of new drugs per 100 drug recipients and participants 15.9. Moderators and participants differ as well in their attitude towards the prescribing of SSRI for patients older than 60 years where the therapeutic benefit is discussed comparatively (moderators: 6%, participants: 15%). Non-peptide angiotensin II receptor antagonists (C09CA/DA) are classified as drug of "reserve". The moderator issued 7.2% of the renin angiotensin system drugs (C09) for new and 11.5% for all non-peptide angiotensin II receptor antagonist compared to 11.2% (respectively 14.5%) of the participants. **Conclusion:** Moderators are more cautious in prescribing new drugs when they turn up on the market. The prescribing of new drugs represents a relevant topic for PTCs in order to exchange information, to develop deci-

sion strategies and to reduce the imbalanced situation of information.

Can prescribing in general practice be changed by quality circles?

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Aims and objectives: In Germany more than 70,000 medications are on the market and prescribing in general practice results in relative high costs. The aim of this study was to demonstrate how prescribing patterns of general practitioners (GPs) could be changed in terms of cost and quality by participation in a quality circle. **Methods:** 90 GPs from 97 urban and rural practices of the Magdeburg area volunteered to participate in 11 quality circle sessions of 2 1/2 hours each. The discussions were based on a detailed analysis of all prescriptions issued by each practice during a three-month period for the patients insured by a major health insurance company (AOK), and background information about the topics discussed. A group of 87 randomly selected practices from the same region was used as a control without intervention showing the same mean value of patients per practice and nearly the same amount of females. However, in the control group the average age of patients with medications was 2.5 years under the age of the intervention group. **Results:** After the intervention costs of medication per patient decreased by 0.8% from the second quarter of 1996 (DM 206,57) compared with the second quarter of 1998 (DM 204,87). In the control group costs increased from DM 174,60 (II/96) to DM 183,30 (II/98) by 5.0%. The increase in the control group was comparable to the national figures about costs for medication over the two-year period observed. The number of medications prescribed per patient decreased by 13.5% in the intervention group and by 9.3% in the control group. An analysis of the drugs prescribed showed that on the one hand there was a general tendency to prescribe modern drug combinations for example in the treatment of peptic

ulcer. On the other hand there was a substantial decrease of prescriptions issued for drugs which have questionable effects. Results from a second trial with 258 practices are currently under analysis. **Conclusions:** Quality circles based on an analysis of prescriptions are effective in terms of cost and quality.

Drug utilization research on the basis of a longitudinal patient database

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For an effective subject- and object-orientated drug utilization research IMS HEALTH owns two medical databases, MediPlus and DTI, which provide the opportunity to investigate long-term continuous patient care and total practice treatment behavior. MediPlus is a database with an anonymous access to a representative panel of doctors and patients within the Federal Republic of Germany. In total, more than 900 medical practices including more than 5 million patients and over 75 million prescriptions can be analyzed in a cross and/or longitudinal section. The longest time period per patient is more than 10 years (7/89 – 9/99). On principle, nearly all medical consultations of the patients of selected medical practices are available within defined time periods. The diagnosis- and therapy index (DTI) records and documents data of estimated 15 million acutely hospitalized patients per year in hospitals with more than 50 beds. The DTI reflects as completely as possible any events in the hospital from the day of reception until the day of discharge. In this lecture we will point out the following topics and results: effect of hospitals on the prescription behavior of practitioners, observation of dose schedules, evaluation of guidelines, i.e. eradication of *Helicobacter pylori*, and growth potential of medical consumption articles in practices.

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Usage-trends of ASA drugs in Germany 1984 – 1999 – Data of the National Health Surveys of the GCP and the Federal Health-Survey

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Background: It can be observed that during the past years the usage of ASA drugs has been rising continuously in Germany due to drug effects discussed in a general public setting and general conditions within the health care system. At the same time reports concerning ADRs of ASA drugs also have appeared. **Objectives:** Because ASA drugs belong to the group of OTC drugs we tried to get reliable consumption data from pharmacoepidemiological surveys done with representative population samples. **Method:** Within five population-representative surveys done for the inhabitants aged 25 – 69 years ~ 25,000 study participants were medically examined and subject to a standardized interview concerning the drugs used during the last seven days before the examination. Measurement of pharmacologically active substances in serum samples of the study participants like salicylic acid, caffeine, benzodiazepines, cardiac glycosides and others enabled us to verify the information gained from the questionnaire. Clinical chemistry, physiological and sociodemographic data completed the survey. **Results:** The usage of ASA drugs has risen continuously since 1984 especially for the indication of platelet inhibition. While the serum concentration of salicylic acid remained relatively constant with the indication of analgesic use (mean value 0.02 mg salicylic acid/dl) the serum concentration changed from 0.96 mg salicylic acid/dl in 1984/86 to 0.08 mg salicylic acid/dl in 1999 (mean values). **Conclusion:** The steadily rising usage of ASA drugs, especially with the indication platelet inhibition, should alert doctors to have a keen look at the possible adverse drug reactions of ASA drugs. This is a prerequisite to prevent ASA-induced asthma and/or gastrointestinal complications.

The effect of short-term self-medication with NSAIDs on relative risk estimates of NSAID-induced GI bleeding derived from database studies

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Background: It is well known that NSAIDs increase the risk for gastrointestinal complications; however, the magnitude of the reported relative risks varies markedly. An important source of variation in database studies may be missing information on self-medication. **Objectives:** The purpose of the present study was to determine the degree of self-medication and its consequences for the study of GI bleeding due to NSAIDs when data comes from a prescription database. **Methods:** Results from three German national health surveys (1984 – 1991) assessing seven days prescribed as well as self-medication exposure to all NSAIDs including acetyl salicylic acid usage were applied to the results of a database study to calculate the relative risk estimates (RR) that would have been obtained had self-medication been documented in this study. **Results:** Self-medication accounts for 47% of all NSAID exposure in the German survey. ASA consumption is responsible for 69% of all NSAID consumption, and was taken as self-medication by 64.2% of the respondents. Non-differential exposure misclassification led to slight underestimation of the RR which varied from 5.1 to 4.1. Slight differential exposure misclassification, on the other hand, led to important changes in RR estimates. **Conclusion:** In database studies, the rate of NSAID exposure is underestimated by 50%; this important non-differential misclassification, however, has little effect on the estimated OR. However, great attention should always be given to factors that might affect drug use differentially.

Laxative use in Germany

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Introduction: Laxative drugs play an important role in the self-medi-