Postgraduate Education in Hospital Pharmacy FPH

Diploma Thesis

Application and Evaluation of an Instrument for the Documentation of Clinical Pharmaceutical Interventions

submitted by

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under the supervision of

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FPH FOEDERATIO PHARMACEUTICA HELVETIAE

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To my little daughter Anne-Sophie

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I am also very grateful to **Monika Gisin, Kristian Schneider** and all their colleagues of **the nursing team** of the two wards where this study was conducted for their friendly support and their great interest in new procedures and developments.

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Table of contents

Abstract

Background: The role of the pharmacist in hospital continues to evolve beyond traditional services. As a clinical pharmacist he can promote the effective, safe and rational use of drugs by the individual patient and by the health care institution. Since clinical pharmacy is not broadly established and accepted in Swiss hospitals, it is important to document and to evaluate pharmacists' clinical activities to obtain additional resources, to justify the cost of such services and to identify systematic problems in the pharmacotherapy process.

Objectives: To document the contributions of a clinical pharmacist (CP) in optimising pharmacotherapy. To evaluate the documentation system in terms of feasibility and suitability in a hospital setting. The documentation should reveal the major topics and thus help to define future activities in the clinical pharmacy service.

Setting: Two medical wards with totally 77 beds in a university hospital.

Methods: Suggestions or contributions of a clinical pharmacist to the optimisation of pharmacotherapy during ward rounds with senior physicians or during review of the case notes with nurses and junior physicians were documented and classified as drug related problems (DRPs) using the PCNE scheme (Pharmaceutical Care Network Europe), version 5.00. This classification system has a hierarchical structure which allows coding for the problem, its cause, the intervention and the outcome.

Results: During 70 observation days 213 problems were documented of which 128 were detected by reviewing the case notes, 33 during ward rounds with senior physicians, 32 by direct reporting to the CP, and 20 on the occasion of non-formulary prescriptions. Problems and causes are shown in table A. Interventions involved 148 suggested changes in pharmacotherapy of which 123 were approved by the responsible physician (change or stop of drug, dose adaptation, more appropriate formulation etc.), 12 ADR reports to the local pharmacovigilance centre and 31 specific information given without further need for action.

Tab. A: Problems and causes classified by the PCNE scheme V5.00

Code	Problems, primary domains	n	Code	Causes, primary domains	n
P1	Adverse reaction	22	C1	Drug/Dose selection	145
P2	Drug choice problem	81	C2	Drug use process	33
P3	Dosing problem	52	C3	Information	11
P4	Drug use problem	7	C4	Patient/psychological	2
P5	Interactions	37	C5	Logistics	11
P6	Other	8	C6	Other	11

An economic evaluation of the DRPs documented showed direct savings of drug costs of € 2058 or € 7349 per year.

Discussion: These data show that DRPs are quite common and that a CP can help in the management of these problems. The majority of suggestions were accepted by the physicians.
Regarding methodology the PCNE system may be considered a rapid and practical tool to document pharmacists' clinical activities. Future work, however, should introduce the possibility to assess the DRP severity and the potential impact of the pharmacist's intervention on patient care.

Glossary

ADR	Adverse drug reaction
ADE	Adverse drug event
DRP	Drug related problems
PCNE	Pharmaceutical Care Network Europe System
€	Euro (1 CHF = 0.6297 € = 0.8372 US$)

1. Introduction

The traditional role of the hospital pharmacist as the specialist of providing pharmaceuticals and related products to the hospital by purchasing and manufacturing has been moving more and more towards a patient-oriented health care provider. Financial constraints and growing awareness of medication errors as well as the increasing complexity of drug treatment regimens may promote the implementation of clinical pharmaceutical services. There is considerable evidence from the international literature that clinical pharmacy services in hospital settings contribute to a better quality of treatment, to the reduction of medication errors and it seems to be cost-effective. Nevertheless, on a local level the impact of clinical pharmacy services must be documented by an appropriate method.

1.1. Definitions of Clinical Pharmacy and Pharmaceutical Care

Clinical Pharmacy is a commonly used term in pharmacy practice and in pharmacy literature, and goes back to the mid 1960s. As defined by the 'European Society of Clinical Pharmacy' (ESCP), it is a health speciality describing the activities and services of the clinical pharmacist to develop and promote the rational and appropriate use of drugs as well as medicinal products and devices by the individual as well as by the society [1]. Clinical pharmacy is concerned with the application of pharmaceutical expertise to help maximise drug efficacy and minimise drug related problems. However, the term 'Clinical Pharmacy' is often incorrectly used and interpreted. 'Clinical' does not necessarily mean an activity implemented in a hospital setting. Clinical pharmacy includes all the services performed by pharmacists practising in hospitals, community pharmacies, nursing homes, home-based care services, clinics and any other setting where medicines are prescribed, dispensed or used. Clinical pharmacy is oriented to the analysis of population and individual needs of medicines, ways of administration, patterns of use and effects of drug therapy. The focus of attention moves from the drug to the single patient or population receiving drugs.

Clinical pharmacy is a relatively new discipline in the field of pharmacy which is based on the traditional 'columns' of the pharmaceutical sciences, i.e., pharmaceutical chemistry, biology, pharmaceutical technology and also pharmacology.

Very closely related to the term of clinical pharmacy is the concept of pharmaceutical care. In 1990, C.D. Hepler and L.M. Strand published the widely used definition of pharmaceutical care from a systems perspective. They state that pharmaceutical care is "the responsible provision of drug therapy for the purpose of achieving definite outcomes which improve a patient's quality of life" [2].

Thus, pharmaceutical care means a style of pharmacy practice provided for an individual patient and with the aim of improving the outcomes of therapy [3].

1.2 Objectives of Clinical Pharmacy and Pharmaceutical Care

The success of pharmacotherapy is not only determined by the right choice of the active ingredient for a specific diagnosis, but by a number of important additional patient- and drug-related factors (see **figure 1**). The way from the prescription of a drug to the desired effect on the patient's health is not straight forward [4].

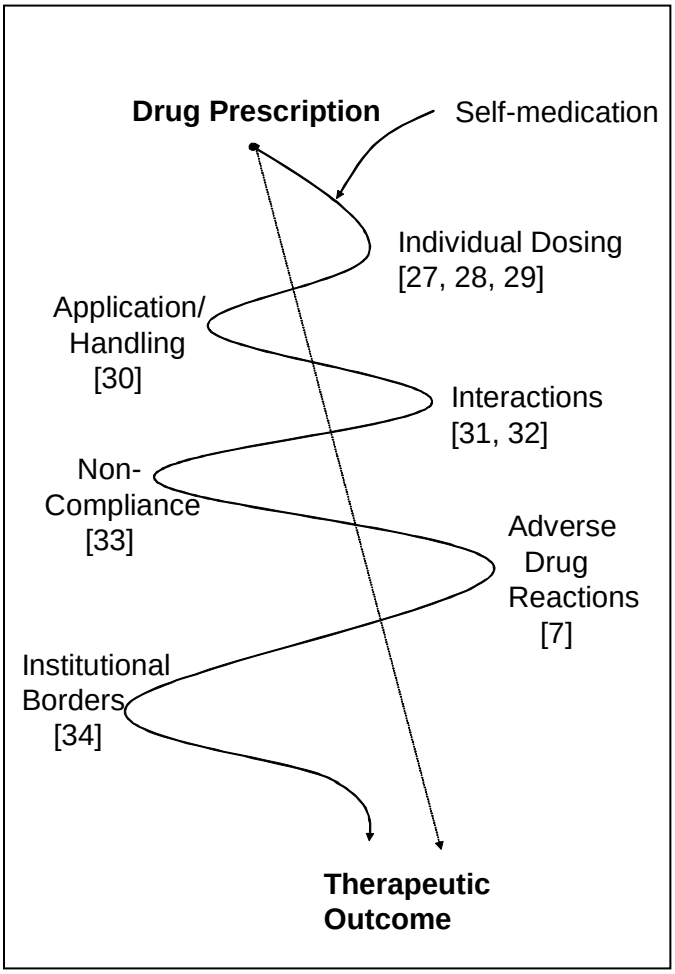

Figure 1: Potential problems on the way to reach the optimal therapeutic outcome (adapted from [4]). Numbers in brackets refer to selected studies from the University Hospital Basel and from the Institute of Clinical Pharmacy, University Basel.

Clinical pharmacy contributes to the rational and correct use of drugs in daily practice and searches evidence for the best ways to do so. Clinical pharmacy focuses on the use of drugs in real life. For research purposes there are – in contrast to the classical pharmaceutical disciplines – only very limited possibilities to standardise environmental factors such as the patients' behaviour or concomitant drug treatment. Studies in this field cannot, therefore, find robust general rules like in the natural sciences, but concentrate on facts and interventions [5]. Relevant facts and factors influencing the therapeutic outcome of a drug therapy regimen are caught by specific and appropriate methods and techniques, and by doing so, these tools are constantly refined. Once these facts are described and assessed in enough detail, interventions are made and re-evaluated, and their impact (economic, clinical and humanistic, e.g., quality of life) is studied. Thus, research in clinical pharmacy and pharmaceutical care has a position between the natural and the social sciences.

A simple example may illustrate the variety of problems which can arise during the drug therapy process: The treatment fails because the patient does not take his medicine. Behind this quite obvious problem, there may be several causes leading to completely different actions:
"The patient does not take the medicine because he/she…

- suffered adverse effects."
- cannot handle the drug, e.g., he/she is unable to swallow the tablet or to open the bottle."
- has not enough information about his/her therapy."
- is not motivated to take it and does not see any benefit from it."
- he/she does not get any reimbursement for this drug from the health insurance company."

Clinical pharmacy in research intends to develop and evaluate tools and procedures for analysing problems and for finding solutions targeted to specified groups of patients or drugs. Pharmaceutical care in daily practice tries to analyse situations and to find an individual solution for a single patient and his drug related problems.

1.3 Evidence of Positive Outcomes by Clinical Pharmacy Activities

Drug related problems and adverse drug events (ADE) are a major safety issue for hospitalized patients. They cause harm to patients and are costly. In a systematic review of the literature from 1991 to 2001, *Kraehenbuehl* [6] found that on average 8% of hospitalised patients experience an ADE, and 5-10% of all drug prescriptions or applications are erroneous. In general internal medicine 14.6% of hospitalized patients and approximately 12% to 17% of patients after discharge experience ADEs [7, 8].

Interventions by clinical pharmacists have been shown to be effective in reducing drug related problems with positive outcomes on the number of ADEs, medication appropriateness or resource use. *Kaboli et al.* [9] give a systematic review of published controlled studies evaluating the effects of interventions by clinical pharmacists on processes and outcomes of care on hospitalized adults. Thirty-six studies met inclusion criteria, including 10 evaluating pharmacists' participation on rounds, 11 medication reconciliation studies, and 15 on drug-specific pharmacist services. Adverse drug events, adverse drug reactions, or medication errors were reduced in 7 of 12 trials that included these outcomes. Medication adherence, knowledge, and appropriateness improved in 7 of 11 studies, while there was shortened hospital length of stay in 9 of 17 trials. No intervention led to worse clinical outcomes and only 1 reported higher health care use. Improvements in both inpatient and outpatient outcome measurements were observed.

The following two studies illustrate possible benefits as examples: *Leape et al.* demonstrated that clinical pharmacist taking part in clinical rounds on an intensive care unit (ICU) could reduce the rate of preventable drug ordering ADEs by 66% from 10.4 per 1000 patient days to 3.5 [10]. *Kucukarslan et al.* showed in a single-blind, standard care-controlled study that clinical pharmacists reduce preventable ADEs by 78% from 26.5 per 1000 hospital days to 5.7 [11].

Also from the economic point of view clinical pharmacy services seem to be favourable. In a summary of the relevant literature from 1996 to 2000, *Schumock et al.* [12] found from 16 studies reporting a benefit-cost ratio ranging from 1.7 : 1 to 17 : 1 with a median of 4.68 : 1.

1.4 Documentation of Pharmaceutical Interventions

In many of these studies, however, definitions of detected or prevented problems such as adverse drug reactions (ADRs), ADEs, medication errors or drug related problems (DRPs) are confusing and not consistent. This may cause difficulties in documentation and classification of pharmaceutical interventions not only in research studies but also in daily practice. *Ferner & Aronson* [13] give a quite comprehensive overview of used definitions and propose systems for the classification of errors.

Figure 2 shows a possible classification. The different types of problems – medication errors, adverse events and adverse reactions – may be summarized by the term of drug related problems irrespective of their preventability, causes and effects on patients.

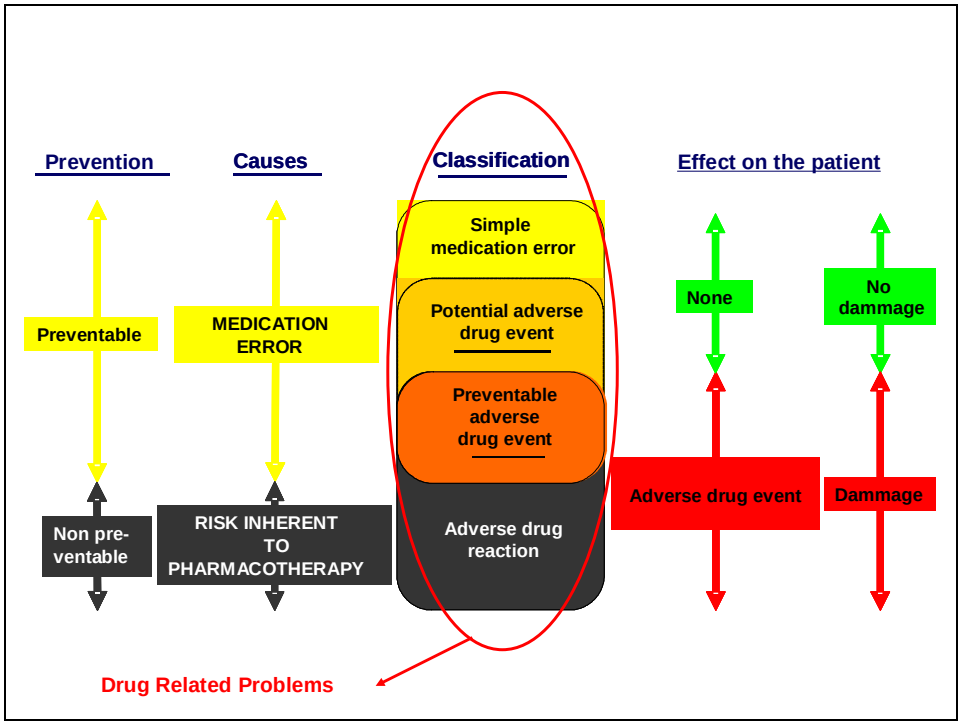

Figure 2: Terms describing drug related problems, adapted from [14].

In spite of these methodological problems documenting the pharmacist's clinical activities is important especially for the promotion and implementation of new clinical services at a local level. Documentation should provide information for staff justification, on the impact of clinical service provided, for identification of staff needs and the planning of future clinical directions and services [15]. Such systems, however, are often laborious and time-consuming in daily routine.

Looking at clinical pharmacy activities in daily practice, they intend to promote the effective, safe and rational use of drugs (according to the ESCP definition). Ineffective, unsafe and irrational drug use may be the consequence of medication errors or inappropriate prescribing [16], they may cause harm and additional costs as an ADE or an ADR or they are risk factors that may lead to ADEs. Whatever the cause or the clinical impact of such ineffective, unsafe or irrational drug use is, it fulfils the definition of a *drug related problem* (**figure 3**). Therefore, the concept of DRPs seems to be a key to the documentation and classification of the clinical pharmacist's interventions. Several classification systems are proposed in the literature [17], some of them being validated [18, 19].

A Drug-Related Problem is an event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes.

Figure 3: Definition of DRP by the Pharmaceutical Care Network Europe (PCNE).

1.5 Clinical Pharmacy Activities at the University Hospital Basel

First steps to assess and implement clinical pharmacists' activities at the University Hospital Basel in collaboration with the Department of Pharmacy were made in the late 1980s. At that time a local drug information centre run by pharmacists and clinical pharmacologists was set up at the Division of Clinical Pharmacology. Initially, the service was offered only to in-house medical and nursing staff [20]; later on, it was expanded to provide drug information to physicians and pharmacists outside the hospital [21, 22].

Another important aspect of clinical pharmacy activities is the therapeutic drug monitoring (TDM), which has been introduced in the University Hospital Basel twenty-five years ago. TDM combines the measurement of drug concentrations in body fluids (especially in plasma, serum, whole blood, saliva) with pharmacokinetic and pharmacodynamic interpretations, taking the patient's individual situation into account. Hence, TDM can be a valuable and useful tool for some

specific drugs to optimise and individualise pharmacotherapy. Furthermore, TDM may contribute to minimise the risk of concentration-dependent adverse drug reactions and therefore, may be an essential part of clinical management [23, 24, 25, 26].

Many factors must play together to obtain a valid interpretation of a drug concentration measurement of which clinical consequences may be derived, i.e., a specific, accurate and precise analytical method must be available, timing of blood samples must be correct (e.g., drug distribution phase completed, sample for peak or trough level), steady state concentrations must be reached, and individual parameters of the patient have to be considered (e.g., renal function, plasma albumin concentration, etc.)

Several studies, however, demonstrate a high proportion of inappropriate drug level determinations [27, 28], leading to unnecessary costs and potentially inadequate decisions based upon these drug levels. In this field, clinical pharmacy should help to develop interventions to bring pharmacokinetic and pharmacodynamic expertise directly to the patient's bed.

On the whole way from drug prescription to the therapeutic outcome, potential problems may arise (see **figure 1**). Data on the prevalence and suggestions for problem solutions were elaborated in our hospital in the last few years. So many different areas of clinical pharmacy could be investigated, such as dose adaptation in renal insufficiency [29], incompatibilities in i.v.-fluids [30], drug-drug-interactions especially at hospital discharge [31, 32], the problem of non-compliance [33], the impact of a clinical pharmacist on the detection and reporting of ADRs [7], and the continuity of care [34].

The most recent development in clinical pharmacy at the University Hospital Basel led to the implementation of a clinical pharmacist at ward level. The aim of this position is to contribute to the optimisation of pharmacotherapy by direct interaction with the medical team (physicians and nurses) and the patient. Pharmaceutical expertise is thus available at the point of pharmacotherapeutic decision making.

These clinical pharmaceutical activities are within the scope of a comprehensive program which aims a better management of medicines in our hospital in terms of safety and economy. The program consists of several projects targeting different steps of the medication process. The first project which has been already realised is the individualisation of drug dispensaries according to the needs of the ward (so-called "ward individualised formulary WIF") [35]. Thus, the leaner drug dispensaries offer good basic conditions for introducing new IT-based systems for the supply chain management as well as for computerised physician order entering (CPOE), two other aspects of the program.

Clinical pharmacy as an element of this medicines management program should serve two different aspects: it should support the maintenance of the WIF by managing non-formulary drug orders (e.g., drug substitution) and it should contribute to the better monitoring of drug therapies in cooperation with the medical team and the division of clinical pharmacology (see **figure 4**).

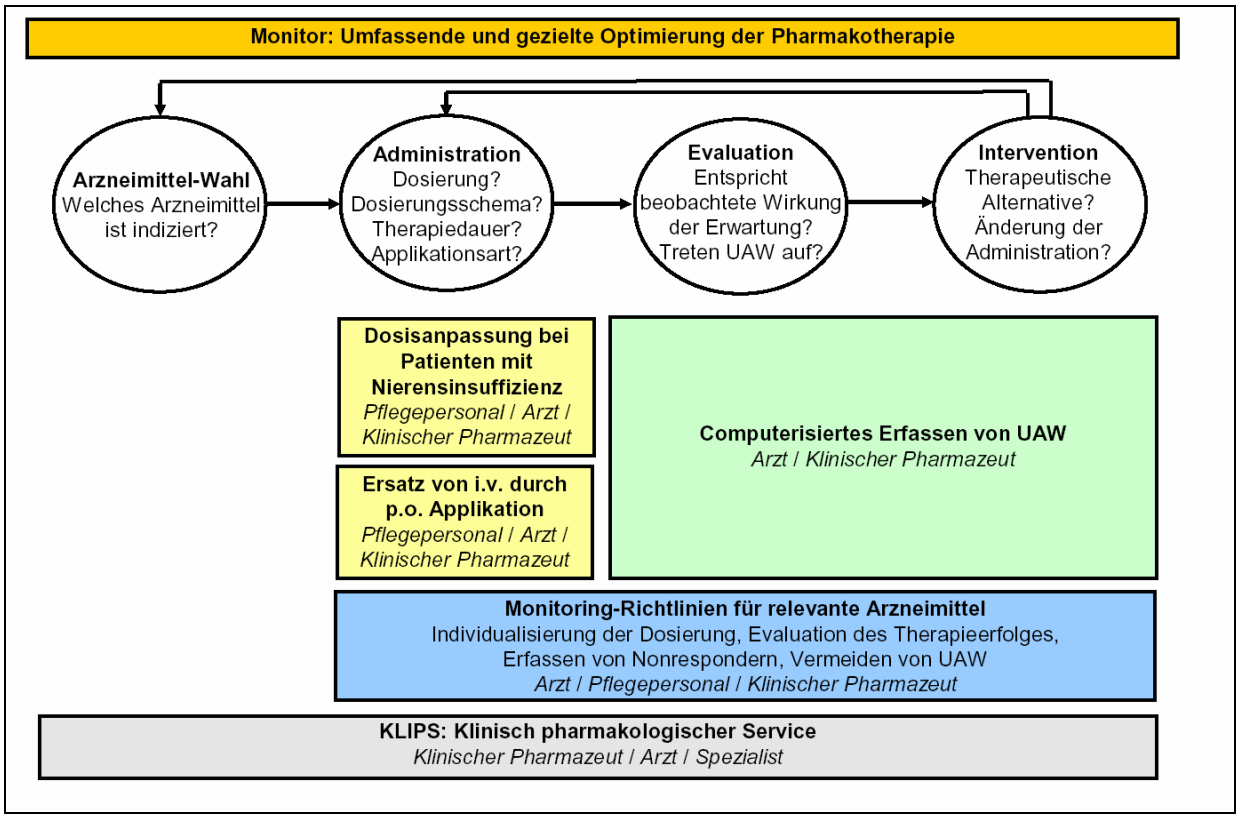

Figure 4: The concept of clinical pharmacy within the hospital's medicines management program.

2. Objectives

To develop and implement future strategies in the treatment process, it is important to collect data on existing drug-related problems in the daily routine of a hospital setting. Clinical pharmacy at the point of decision, i.e., very close to the prescribing process, may detect such problems in a very early stage when they have had no negative impact yet. Detailed analyses of these data on drug-related problems can lead to the development of targeted interventions and to sustainable ameliorations in the drug use process.

After having introduced a clinical pharmacist on two internal medical wards we aimed to document the drug-related problems detected by the clinical pharmacist by the means of a selected DRP classification system. The main objective was to evaluate the practicability of this classification system under daily conditions and to explore its usefulness in the qualitative and economic evaluation of the pharmaceutical interventions.

3. Methods

3.1 Classification system

Although classification of drug related problems (DRP) is still being discussed and optimal solutions remain to be found, we chose the PCNE classification system for drug related problems Version 5.00 [36] (see Appendix I), because it comes closest to the required aspects described by *Schäfer* [37] (see textbox) as *van Mil et al.* [17] stated in their review of classification systems. To our knowledge the system has been used in primary care but not yet in a hospital setting. In respect of the continuity of care between primary and hospital sector using one single system for the documentation of pharmaceutical care/clinical pharmacy activities would be desirable.

The PCNE system allows attributing four items to each observation coding for the problem itself, the actual or suspected cause of the problem, the intervention and the outcome of the intervention.

1. The coding system should be suitable not only for – sometimes very specific – scientific studies but for the broader implementation of Pharmaceutical Care in the pharmacy.
2. A suitable coding system must be easy to use in daily routine and consist of three parts: the classification of the drug-related problem, the intervention taken to solve the problem and the degree to which the problem could be solved.
3. The coding system is preferably structured like a decision tree (main groups and sub-groups) supporting later computer-aided use.
4. The coding system has to have an open structure to include new problems, preferably on sub-group levels. Additional coding levels can be introduced without changing the basic structure and still allowing international comparison on the more aggregated levels of the main groups.
5. Problems defined should be clear and – if possible – leading to only one choice of coding. Users should not be encouraged to over report (i.e. to name several problems for one). This will probably also require clear definitions of the categories.
6. The coding should focus on the problem itself not on its cause or consequence. This, however, may depend on the purpose of the study.
7. The coding system should also be suitable for the documentation necessary for the remuneration of cognitive services.

Textbox showing the criteria for a suitable DRP classification system according to *Schäfer* [38].

3.2 Study design and setting

We conducted a prospective, observational study of clinical pharmaceutical interventions in a tertiary 700-bed university hospital setting by a single clinical pharmacist. The two observed wards (42 and 43 beds) included patients in general internal medicine, gastroenterology, oncology, nephrology and haematology.

In the period between May 9th 2005 to December 22nd 2005 (32 weeks) one senior clinical pharmacist (i.e., the author) conducted 70 observation days taking part in clinical ward rounds and reviewing daily 10 to 15 case notes. All detected DRPs and interventions were classified according to the PCNE System V5.00 and then filled in an Excel sheet (Microsoft Corp., Redmond, Oregon). Drugs involved in the DRP were documented separately (see appendix II).

3.3 Economic evaluation

The economic outcome of interventions directly linked to a reduction in medication costs was evaluated. These interventions were: switching from i.v. to p.o. of the same drug (represented by PCNE code P2.2 [Inappropriate drug form] in combination with C1.3 [More cost-effective drug available]), dose reductions (PCNE code P3.2 [Drug dose too high] in combination with I3.2 [Dosage changed]) and stopping unnecessary medications (PCNE code I3.5 [Drug stopped]). For the calculation we presumed that inappropriate drug therapies would have continued three days without being detected by the clinical pharmacist. Drug costs were calculated on the basis of defined daily doses and official prices as given in the Swiss Drug Formulary [38]. In order to get a yearly estimate, all the directly cost-linked interventions during the 70 observation days were counted up to a year of 250 working days.

4. Results

4.1 Classification of drug related problems

A total of 213 pharmaceutical interventions were recorded, whereof 33 were initiated on ward rounds, 128 on case note review, 32 as a consequence of specific requests and 20 interventions by nonformulary drug orders (see **figure 5**). In the observation period, 1'444 patients were discharged from the two wards; they represent 17'476 patient days. Per patient 0.15 interventions took place or 1.22/100 patient days.

To all of these interventions a cause could have been attributed, but in six cases no suitable problem category existed, so that only 207 problems were classified. The non-classified problems are listed in **table 1**.

Table 1: Problems which could not be classified by the PCNE-System

#	Cause	Intervention	Drug	Description of problems
1	C2.1	I3.4	Pradif	Drug should be taken before the meals
2	C2.1	I3.4	Rifater	Dito
3	C2.1	I3.4	Creon	Dito
4	C2.1	I3.4	Tazobac	Drug should not be administered parallel to a certain other drug (incompatibility problem)
5	C3.1	I2.2	Efudix	Topical cytostatic drug, special instructions for use must be followed
6	C5.2	I3.1	Aprovel	Obvious prescribing error (no more details available)

4.1.1. The problems

The problems found and classified by the clinical pharmacist are shown in **figure 6**. Most commonly, drug choice problems (P2) arose in 38% (n=81) of all observations. Second with 24% (n=52) were questions around drug dosing (P3) followed by manifest or potential drug-drug or drug-food interactions (P5) in 17% (n=37)). Adverse reactions to drugs (P1) accounted for 10% (n=22) of the problems detected by the pharmacist.

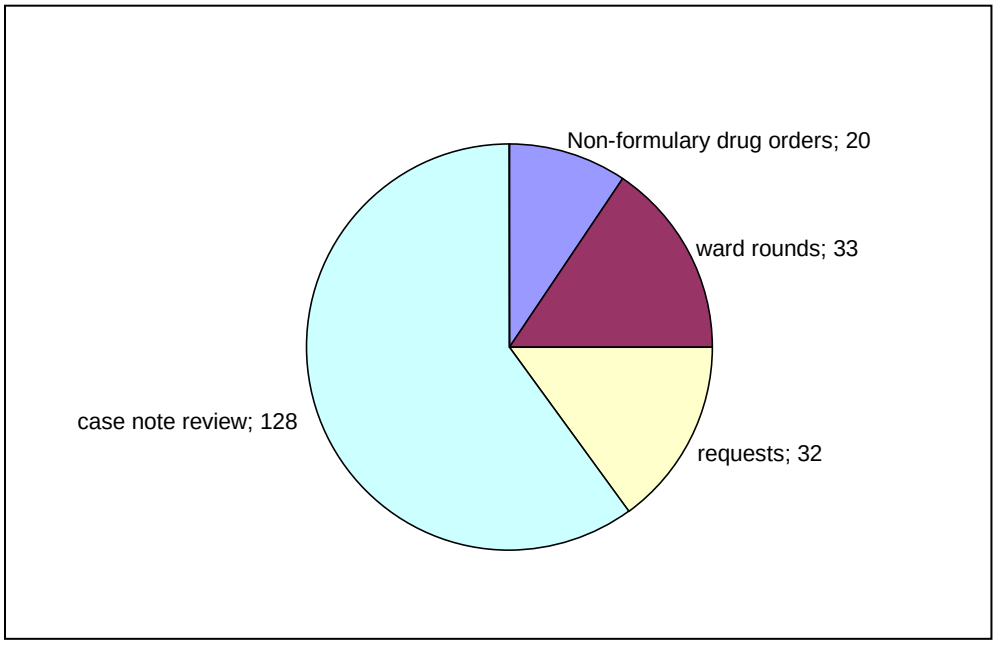

Figure 5: Sources of problem detection (n=213)

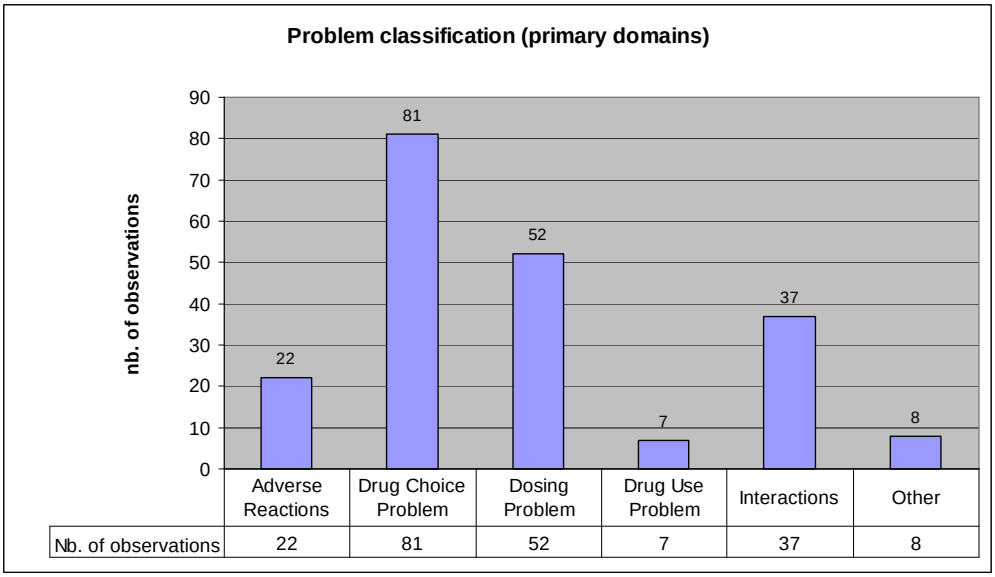

Figure 6: Primary domains of PCNE DRP-classification and number of problems.

An analysis of the detailed problems according to PCNE is shown in **table 2**. The most commonly addressed problems were potential interactions (n=34; P5.1), followed by "drug dose too high or dosage regime too frequent" (n=30; P3.2) and "inappropriate drug form (not most appropriate for indication)" with 26 observations (P2.2). These three leading groups of problems detected by the pharmacist were followed by 20 problems because of "drug dose too low or dosage regime not frequent enough" (P3.1), 15 observations with "no clear indication for drug use" (P2.5) and 14 times "side effect suffered (non-allergic; P1.1).

Table 2: Detected drug-related problems (n=207), classified according to PCNE-Classification V5.0 [36]

Primary domain	Code	Detailed classification	n	in %
1. Adverse reactions Patient suffers from an adverse drug event	**P1**	**Total**	**22**	**10%**
	P1.1	Side effect suffered (non-allergic)	14	6.8%
	P1.2	Side effect suffered (allergic)	5	2.4%
	P1.3	Toxic effects suffered	3	1.4%
2. Drug choice problem Patient gets or is going to get a wrong (or no drug) drug for his/her disease and/or condition	**P2**	**Total**	**81**	**38%**
	P2.1	Inappropriate drug (not most	11	5.3%
	P2.2	Inappropriate drug form (not most appropriate for indication)	26	12.6%
	P2.3	Inappropriate duplication of therapeutic group or active ingredient	7	3.4%
	P2.4	Contra-indication for drug (incl. Pregnancy/breast feeding)	12	5.8%
	P2.5	No clear indication for drug use	15	7.2%
	P2.6	No drug prescribed but clear indication	10	4.8%
3. Dosing problem Patient gets more or less than the amount of drug he/she requires	**P3**	**Total**	**52**	**24%**
	P3.1	Drug dose too low or dosage	20	9.7%
	P3.2	Drug dose too high or dosage regime too frequent	30	14.5%
	P3.3	Duration of treatment too short	0	0.0%
	P3.4	Duration of treatment too long	2	1.0%
4. Drug use problem Wrong or no drug taken/administered	**P4**	**Total**	**7**	**3.4%**
	P4.1	Drug not taken/administered at all	6	2.9%
	P4.2	Wrong drug taken/administered	1	0.5%
5. Interactions There is a manifest or potential drug-drug or drug-food interaction	**P5**	**Total**	**37**	**17%**
	P5.1	Potential interaction	34	16.4%
	P5.2	Manifest interaction	3	1.4%
6. Others	**P6**	**Total**	**8**	**3.9%**
	P6.1	Patient dissatisfied with therapy despite taking drug(s) correctly	4	1.9%
	P6.2	Insufficient awareness of health and diseases (possibly leading to future problems)	2	1.0%
	P6.3	Unclear complaints. Further clarification necessary	1	0.5%
	P6.4	Therapy failure (reason unknown)	1	0.5%

4.1.2. The causes

Looking at the overview of the causes (n=213; see **figure 7**) for the drug related problems the overwhelming majority of 68% (n=145) was related to the selection of the drug and/or dosage schedule (C1). The second most common cause with 15% (n=33) regarded the drug use process (C2), i.e., administration and timing of drugs. Patient factors (C4) seem to play a minor role (1%, n=2), but had not been in the focus in this setting. Aspects concerning information about the treatment (C3), logistic (C5), e.g., availability of drugs and other causes (C6) were each noted in 11 cases (5%).

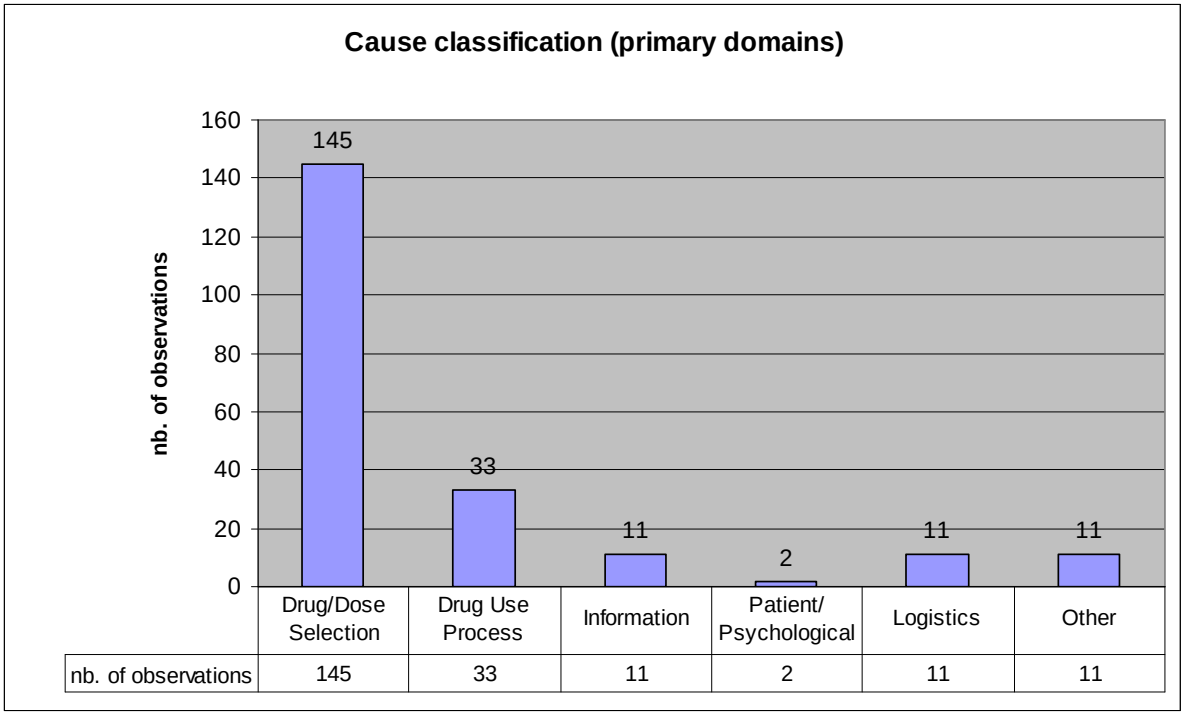

Figure 7: Primary domains of PCNE DRP-classification and number of causes.

The detailed causes (**table 3**) show that pharmacokinetics inclusively organ dysfunction and interactions (C1.4) played the major role (19% of all causes, n=41), followed by inappropriate timing of administration and dosing intervals (C2.1; 11%, n=24) and inappropriate drug selection (C1.1; 10%, n=22).

Table 3: Causes for drug-related problems (n=213), classified according to PCNE-Classification V05 [36]

Primary domain	Code	Detailed classifcation	N	in %
1. Drug/Dose selection The cause of the DRP is related to the selection of the drug and/or dosage schedule	**C1**	**Total**	**145**	**68%**
	C1.1	Inappropriate drug selection	22	10.3%
	C1.2	Inappropriate dosage selection	15	7.0%
	C1.3	More cost-effective drug available	18	8.5%
	C1.4	Pharmacokinetic problems, incl. ageing/ deterioration in organ function and interactions	41	19.2%
	C1.5	Synergistic/preventive drug required and not given	6	2.8%
	C1.6	Deterioration/improvement of disease state	17	8.0%
	C1.7	New symptom or indication revealed/presented	12	5.6%
	C1.8	Manifest side effect, no other cause	14	6.6%
2. Drug use process The cause of the DRP can be related to the way the patient uses the drug, in spite of proper dosage instructions (on the label)	**C2**	**Total**	**33**	**15%**
	C2.1	Inappropriate timing of administration and/or dosing intervals	24	11.3%
	C2.2	Drug underused/under-administered	2	0.9%
	C2.3	Drug overused/over-administered	1	0.5%
	C2.4	Therapeutic drug monitoring required	1	0.5%
	C2.5	Drug abused (unregulated overuse)	1	0.5%
	C2.6	Patient unable to use drug/form as directed	4	1.9%
3. Information The cause of the DRP can be related to a lack or misinter-pretation of information	**C3**	**Total**	**11**	**5.2%**
	C3.1	Instructions for use/taking not known	6	2.8%
	C3.2	Patient unaware of reason for drug treatment	0	0.0%
	C3.3	Patient has difficulties reading/understanding patient information form/leaflet	1	0.5%
	C3.4	Patient unable to understand local language	0	0.0%
	C3.5	Lack of communication between healthcare professionals	4	1.9%
4. Patient/Psychological The cause of the DRP can be related to the personality or behaviour of the patient.	**C4**	**Total**	**2**	**1%**
	C4.1	Patient forgets to use/take drug	0	0.0%
	C4.2	Patient has concerns with drugs	0	0.0%
	C4.3	Patent suspects side-effect	0	0.0%
	C4.4	Patient unwilling to carry financial costs	0	0.0%
	C4.5	Patient unwilling to bother physician	0	0.0%
	C4.6	Patient unwilling to change drugs	0	0.0%
	C4.7	Patient unwilling to adapt life-style	0	0.0%
	C4.8	Burden of therapy	1	0.5%
	C4.9	Treatment not in line with health beliefs	0	0.0%

	C4.10	Patient takes food that interacts with drugs	1	0.5%
5. Logistics The cause of the DRP can be related to the logistics of the prescribing or dispensing mechanism	**C5**	**Total**	**11**	**5.2%**
	C5.1	Prescribed drug not available	6	2.8%
	C5.2	Prescribing error (only in case of slip of the pen)	4	1.9%
	C5.3	Dispensing error (wrong drug or dose dispensed)	1	0.5%
6. Others	**C6**	**Total**	**11**	**5.2%**
	C6.1	Other cause; specify	1	0.5%
	C6.2	No obvious cause	10	4.7%

4.1.3. The interventions

All of the causes led to an intervention (n=213). Analysis of the interventions showed in the overview (**figure 8**) that most of the interventions took place at drug level (I3; 54%, n=116), followed by interventions at prescriber level (I1; 32%, n=69). The rest of interventions were at patient/carer level (I2) or "other activity" (I4), each resulting in 7% (n=14) of interventions.

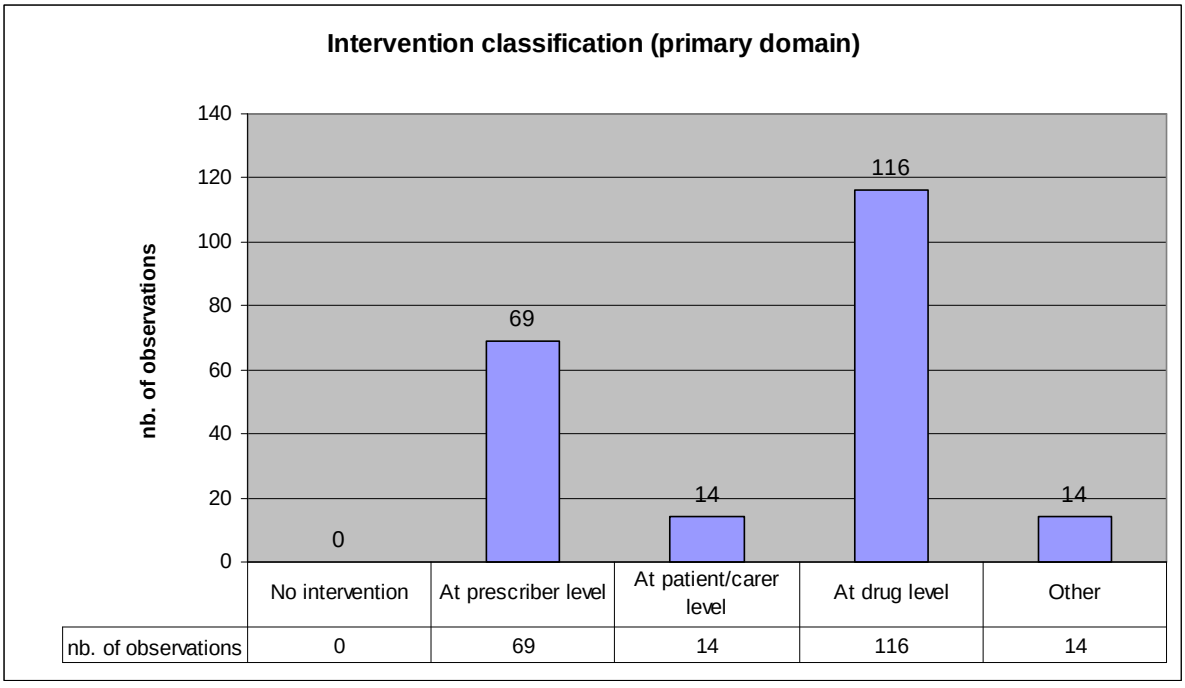

Figure 8: Primary domains of PCNE DRP-classification and number of interventions.

The interventions can be grouped in those proposing a modification in drug therapy and in others. In the PCNE classification the items I1.3 to I1.5 and all the interventions at drug level

(I3.x) can be considered as propositions for a modification in therapy. In our sample 148 interventions of 213 concerned therapy modifications (69%). In the remaining 65 interventions almost half of them (31) were information given to the prescriber. Typically, information about potential drug-drug interactions requiring closer patient monitoring are found in this category. Another twelve interventions were the reporting of adverse drug reaction to authorities.

Regarding acceptance of the propositions by physicians of the 148 interventions 123 (83%) were accepted (PCNE Codes I1.3/I3.x[1]), 9 (6%) were rejected (I1.4), and in 16 cases (11%) the outcome remained unknown (I1.5).

Table 4: Pharmacist's interventions for drug-related problems (n=213), classified according to PCNE-Classification V05 [36]

Primary Domain	Code	Intervention	n	in %
No intervention	I0.0	No Intervention	0	0.0%
1. At prescriber level	**I1**	**Total**	**69**	**32%**
	I1.1	Prescriber informed only	31	14.6%
	I1.2	Prescriber asked for information	6	2.8%
	I1.3	Intervention proposed, approved by	7	3.3%
	I1.4	Intervention proposed, not approved by	9	4.2%
	I1.5	Intervention proposed, outcome unknown	16	7.5%
2. At patient/carer level	**I2**	**Total**	**14**	**6.6%**
	I2.1	Patient (medication) counselling	4	1.9%
	I2.2	Written information provided only	10	4.7%
	I2.3	Patient referred to prescriber	0	0.0%
	I2.4	Spoken to family member/caregiver	0	0.0%
3. At drug level	**I3**	**Total**	**116**	**54%**
	I3.1	Drug changed	22	10.3%
	I3.2	Dosage changed	28	13.1%
	I3.3	Formulation changed	10	4.7%
	I3.4	Instructions for use changed	27	12.7%
	I3.5	Drug stopped	22	10.3%
	I3.6	New drug started	7	3.3%
4. Other intervention or activity	**I4**	**Total**	**14**	**6.5%**
	I4.1	Other intervention (specify)	2	0.9%
	I4.2	Side effect reported to authorities	12	5.6%

[1]Whenever a proposed therapy modification was accepted by the physician, it was classified – if possible - at drug level (not in I1.3) in order to get more detailed information about the modification.

4.2 Pharmacoeconomic evaluation

Most of the interventions were aimed at improving quality and/or safety of care (n=158, 75%). The remaining 53 interventions (25%) were identified as directly cost-relevant according to our definition (see chapt. 3.3) while equally improving quality of care.

Of these 53 cost-relevant interventions 22 (42%) accounted for stopping of no longer needed medications, 18 (34%) for switching from i.v. to p.o. medications and 13 (25%) for dosage adjustments.

The interventions stopping unnecessary drugs showed a mean value of € 10.11 resulting in € 795 for the period of one year (250 working days; see **table 5**).

Tabelle 5: Cost reduction by stopping unnecessary drugs, n=22

DCI/Drug name**	Dosage[§]	Route	Price(€)***	Price (3 days treatment, €)[‡]
Pantoprazol/Pantozol®	20mg qd	po	1.88	5.64
Alendronat/Fosamax®	70mg/wk	po	11.29	11.29
Glutamin/Dipeptiven®	100ml qd	iv	36.59	109.78
ASA/Aspégic®	300mg qd	po	0.16	0.48
Esomeprazol/Nexium®*	40mg qd	po	2.90	8.72 x 2= 17.44
Ibuprofen/Brufen®*	400mg tid	po	0.86	3.50 x 2= 7.00
Clopidogrel/Plavix®	75 mg qd	po	2.25	6.77
Loperamid/Imodium	2mg tid	po	1.40	4.20
Paracetamol/Dafalgan®**	1g qid	po	0.94	2.83 x 4= 11.32
Potassium chloride/KCl ret.®*	10 mmol tid	po	0.45	1.36 x 2= 2.72
Saccharomyces b./Perenterol®	250mg tid	po	4.07	12.23
Magnesium/Mg-Sulfat	2g	iv	1.88	7.52
Amiodaron/Coradarone®	200mg qd	po	0.80	2.41
Clotrimazol/Imazol Cream®*	30 g (1 package)	dermal	11.24	11.24 x 2 = 22.48
Metoclopramid/Paspertin®	10mg tid	po	0.34	1.03
Total (22 interventions in 70 days)				**222.31 = 10.11/intervention**
Total 1 year (250 days)				**795 €**

* Occurred twice
** Occurred four times
*** Official price of original product, smallest package divided by units contained. Source: Swiss Drug Formulary [38]
[§] Regular dosage assuming normal renal and hepatic function according to Swiss Drug Formulary
[‡] Assuming continued application of this drug for another 3 days
qd = daily
qid = four times daily
tid = three times daily
wk = week

As can be seen in **table 6**, 13 interventions within 70 observation days led to switching an i.v. drug application to p.o. application resulting in a mean cost reduction of € 14.83 per intervention, i.e., € 331 counted up to a year of 250 working days.

Tabelle 6: Cost reduction by switching i.v. drugs to p.o., n=13

DCI/Drug name	Daily iv dosage[§]	Price (€) *	Daily po dose[§§]	Price (€)	Price difference(€)/switch**
3 x Paracetamol/Perfalgan®	4x1 g	21.63	4x1 g	1.48	60.45 (x 3) = 181.35
3 x Amoxicillin-clavulanic acid/Augmentin®	3x1.2 g	10.95	3x625 mg	7.61	9.72 (x 3) = 29.16
Multivitamins/Cernevit®	1x1 Amp.	5.13	1 tabl. (Supradyn)	0.42	14.13
3 x Levofloxacin/Tavanic®	2x500 mg	113.14	2x500 mg	12.95	300.57 (x 3) = 901.71
Rifampicin/Rimactan®	2x300 mg	5.29	2x300 mg	2.82	7.41
Acetylic salicylic acid/ Aspégic®	1x500 mg	1.85	1x300 mg	0.16	5.07
Vitamin B-complex/Beco-5®	2 ml	0.75	1 tbl.	0.17	1.74
Thiamine/Benerva®	300 mg	2.82	300 mg	0.36	7.38
Doxicyclin/Vibravenös®	2x100 mg	11.98	2x100 mg	3.71	24.81
Clarithromycin/Klacid®	2x500 mg	111.31	2x500 mg	4.63	320.04
Total (13 observations in 70 days)					**1492.80 = 114.83 /switch**
Total 1 year (250 days)					**5331 €**

* Official price of original product, smallest package divided by units contained. Source: Swiss Drug Formulary [38]
** assuming 3 days i.v. therapy continuing
§ Regular dosage assuming normal renal and hepatic function
§§ Po drugs used on the local medication list

Assuming that dose reductions equal half price of the daily regular dose of a drug for three treatment days, cost reduction by dose adjustments for the 13 interventions led to a cost reduction of € 342.66 for all and € 26.35 per single dose adjustment (see **table 7**). Counting up the cost reduction for a working year of 250 days, the dose adjustment savings sum up to € 1223.

Table 7: Cost reduction by dose adjustment, n=13

DCI/Drug name	Dosage[§]	Route	Price(€) **	Cost reduction* (€)
3x Amoxicillin-Clavulanic acid/ Augmentin®	3x1.2 g	iv	10.95	16.42 x 3 = 49.27
Ethambutol/Myambutol®	1800 mg	po	2.57	3.86
2x Ciprofloxacin/Ciproxin®	2x500 mg	po	0.57	0.85 x 2 = 1.70
Fentanyl/Durogesic®	25 µg q3d	dermal	3.27 qd	4.91
Tobramycin/Obracin®	3x80 mg	iv	40.71	61.06
2x Vancomycin/Vancocin®	4x500 mg	iv	66.75	100.12 x 2 = 200.24
Pantoprazol/Pantozol®	1x20 mg	po	1.88	2.82
Odansetron/Zofran®	1x8 mg	po	7.80	11.70
Normal Saline/NaCl 0.9% Braun	1x1000 ml	iv	4.73	7.10
Total (13 interventions in 70 days)				**342.66 = 26.35/dose adjustment**
Total 1 year (250 days)				**1223 €**

* 3 days' treatment at 50% price
*** Price for one day, original product, smallest package divided by units contained. Source: Swiss Drug Formulary [38]
[§] Regular dosage assuming normal renal and hepatic function according to Swiss Drug Formulary

Taken together, the cost-effective interventions sum up to € 7349 for one year in mere drug cost savings not counting the impact on length of stay, ADE rate and possible litigation.

5. Discussion

5.1 Discussion of the results

We found in our study using the PCNE system that clinical pharmaceutical activitites have a high impact on clinical decision making regarding detection of DRPs and following pharmaceutical interventions. The latter were taking place three times a day on average.

The majority of DRPs detected concerned potential drug-drug interactions, too high dose selections and inappropriate drug formulations for a specific situation or patient. The latter represents a topic to which the pharmacist's specialized know-how can bring substantially different aspects to solve the problems. We suppose that the selection of the most appropriate dosage form and its correct handling and application may be often neglected. Indeed, errors in drug application are about one third of all medication errors, another third are prescribing errors, the rest mainly transcribing and dispensing errors [39]. In our study, most of the problems can be considered as "prescribing problems". Application errors or problems (in part PCNE C2.x) as well as patient-related factor/psychological aspects (PCNE C4.x), however, are probably underestimated in our setting since ward rounds with physicians and nurses and case note reviews were in the focus.

An interesting result, yet surprising, was that in the study period of 70 days 12 reports about ADRs were generated and submitted to the pharmacovigilance authorities. But this confirms the findings of *Schlienger* [7] demonstrating that the presence of a clinical pharmacist on the ward improves ADR reporting.

The acceptance of the pharmacist's interventions was 83%. This is well in accordance with other studies. *Klopfer & Einarson* [40] in a total of 23 published studies an average acceptance rate of 85.5%. In single studies, however, acceptance rates up 99% have been found [10], but in this study also the provision of drug information as an intervention was a matter of acceptance, whereas in our calculation this item (PCNE I1.1: Prescriber informed only) was not included.

We showed - as other authors have done before - that clinical pharmacy service can avoid or reduce drug costs. Twenty-five percent of the interventions had direct influence on drug costs, a similar rate to the study of *McMullin* [41] with 26%. A recent study from Denmark [42] assessed the effects, especially the cost effects of a clinical pharmacist in a controlled prospective study. The authors focused their interventions on ten target areas. Cost reductions resulted in 43% of the interventions with total savings of direct drug costs of 3442 € within the study duration of 12 months. The difference to our findings of cost savings up to more than 7000 €/y can be explained by methodological differences. Our result is an estimation based on some presumptions for calculation. Minor changes in the presumptions would lead to different results. Secondly, we base

on an extrapolation from our study period of 70 observation days in a period of 8 months to a whole year (250 working days). In such a design random effects may occur (one single case with extraordinary high costs or cost savings) which is then also extrapolated to one year. And - last but not least – the objective of our study was not the economic outcomes.

But in spite of these restrictions, our findings do not seem unrealistic in comparison to other studies. *Ganso* [43] found cost reductions ranging from 17 to 27 €/intervention on average in four different wards (3 surgery wards, 1 endocrinology ward). We calculate 34 €/intervention. Especially the cost savings of switching from i.v. to p.o. application is well within the range of former results. *Rüttimann* [44] gives costs savings of about 93 € per switch looking at antibiotics versus 115 € in our study.

Though it was not the primary aim of this work to show the benefit of clinical pharmacy, the results - in qualitative aspects as well as in economical – are encouraging to continue this way within the scope of the medicines management program.

5.2 Discussion of the documentation method

The major objective of this study was first to evaluate the practicability of the PCNE classification system for drug related problems in a hospital setting and in daily routine and secondly to explore the usefulness of the data collected in the qualitative and economical evaluation of pharmacist-initiated interventions.

As discussed above our findings essentially confirm the results of former studies, though we used a very different methodological approach. The documentation of DRPs with the PCNE system in everyday practice seems to provide realistic and comparable data about the impact of clinical pharmacy service on drug treatment. The classification of each DRP on four different levels (problem-cause-intervention-outcome) gives enough details allowing qualitative and economic analyses. A prerequisite for such analyses is that besides the classification itself the drugs involved are documented.

As the PCNE system has been created for the documentation of DRPs mainly in the public pharmacy setting, certain items are lacking for the hospital setting. Incompatibilities, application errors or wrong transcriptions as typical DRPs in the hospital setting cannot be coded in a satisfactory way. The primary domain of the problems' section "drug use problem" is too restricted and should be adapted for the use in the hospital setting. *Allenet et al.* [18] suggest a documentation system which is well adapted to the hospital setting. In the intervention section it contains items often used like "administration mode optimisation" or "change of administration

route", in the problems section "improper administration". A disadvantage, to our opinion, of their system is that no description of the cause of a problem is given and there are no options for the documentation of interventions at the patient's level (e.g., medication counselling). Combining the PCNE system with some of the elements mentioned above would create a well adapted tool. Future work should additionally introduce the possibility to assess the DRP severity and the potential impact of the pharmacist's intervention on patient care. Proposals for assessing the severity of errors, the value of service or the cost relevance are given in literature [45, 46, 47]

From the perspective of practicability in daily routine the PCNE system proved itself to be easy to use and not very time-consuming. The daily documentation, i.e., the classification of the DRP and entering the PCNE codes and the drugs involved into the database (Excel spreadsheet) took only a few minutes. *Ganso* [43] using the PI-Doc system and an electronic database (Microsoft Access) measured the time for the documentation of pharmaceutical interventions. He found on average 1.9 min for the classification and 6.5 min for the electronic documentation per intervention. To accept a documentation system as a routine tool time is often a key aspect. In our approach we tried to document as few items as possible but as many as necessary to evaluate the clinical pharmacist's performance and to get an overview of the most common DRPs. We resigned from collecting patient data like sex, age or diagnosis.

5.3 Limitations

Our study has several limitations. As already discussed the objective of the study was not demonstrating the outcome clinical pharmaceutical interventions. The results are liable to bias since only one person identified, resolved and classified the DRPs. The number and type of DRPs highly depend on the clinical pharmacist's qualification and personal interests. The results do not necessarily reflect the real distribution of DRPs.

The economic evaluation is based on some presumptions. We assumed that an inappropriate treatment would continue three days if the clinical pharmacist would not have identified it. This may be criticised and seems to be speculative, but it is transparent and everyone may recalculate our findings using other presumptions.

5.4 Conclusions

In conclusion, we consider the PCNE system a very useful and easy tool for the documentation of clinical pharmacy service not only for research purposes but also in daily practice. In order to

implement this tool in the clinical routine, some adaptations to the hospital setting would be necessary.

Such documentation helps to demonstrate the clinical activities of the pharmacist what is more and more important for staff justification. The information about a DRP given by the four levels of classification is detailed enough to allow further analyses. The number and type of DRPs identified and resolved and the number and type of interventions made and accepted are indicators for the clinical effectiveness of this service [15]. The combination of the PCNE code with the drug involved gives the possibility of realistic estimations of economic outcomes.

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6. Outlook

6.1 Future Challenges for Clinical Pharmacy in Research and Practice

The pharmacists' scope of practice is changing and political moves have taken place to integrate them more into the clinical setting. Collaborative care with medical doctors acknowledging the values of pharmacists' involvement in daily hospital care is a major political issue in the US [48]. We can see this trend towards more patient oriented activities provided by hospital pharmacists also in Switzerland. Patient safety and risk management are important topics not only at a local but also at a national level [49, 50]. Linking different episodes of care and different health care providers is one element of this safety strategy. New opportunities like the personal electronic health card will be a challenge also for clinical pharmacy.

6.2 Continuity of Care

Drug treatment is becoming increasingly complex regarding the whole regimen of a patient and also regarding single drugs (e.g., proteins as drug substances which require specific knowledge about their handling and application). On the other hand, the length of hospital stay has decreased significantly over the past years. These two tendencies demand more intense care in the hospital and posthospital phase and require a high degree of self-management abilities from the patient. To assure these prerequisites for the optimal therapeutic outcome after a hospital stay, all the relevant information must be transferred between the different levels of care (see **figure 9**). This continuity of care can be defined as:

"The degree to which the service system links episodes of treatment into a seamless, uninterrupted whole, in **conformity with the needs of the patient**. Continuity of care is a multidimensional concept including integration and co-ordination of services, communication among the various service providers and the stability of patient caregiver relationship over time." [51]

Whereas on the levels of daily activities and medical care continuity is more or less given, there is a gap on the level of pharmaceutical care. Until today, only in very few hospitals in Switzerland pharmacists are involved in bed-side patient care. At hospital discharge, the information from hospital to the community pharmacy is restricted to the discharge prescription. Only few knowledge about the pharmaceutical care issues of discharge patients and about their specific drug related problems is available. It is well documented that discrepancies between drug treatment at hospital admission and at discharge are a common problem [52]. Recently, we initiated a study in collaboration with the Institute of Clinical Pharmacy, University of Basel, to document the drug related problems related to discharge prescriptions.

To support complex drug treatments after a hospital stay in order to contribute to an optimal compliance and to detect and prevent drug related problems, the information given by the discharge prescription is not enough. An important issue for the future development of clinical pharmacy will therefore be, to find ways to bridge this gap in pharmaceutical care across institutional borders.

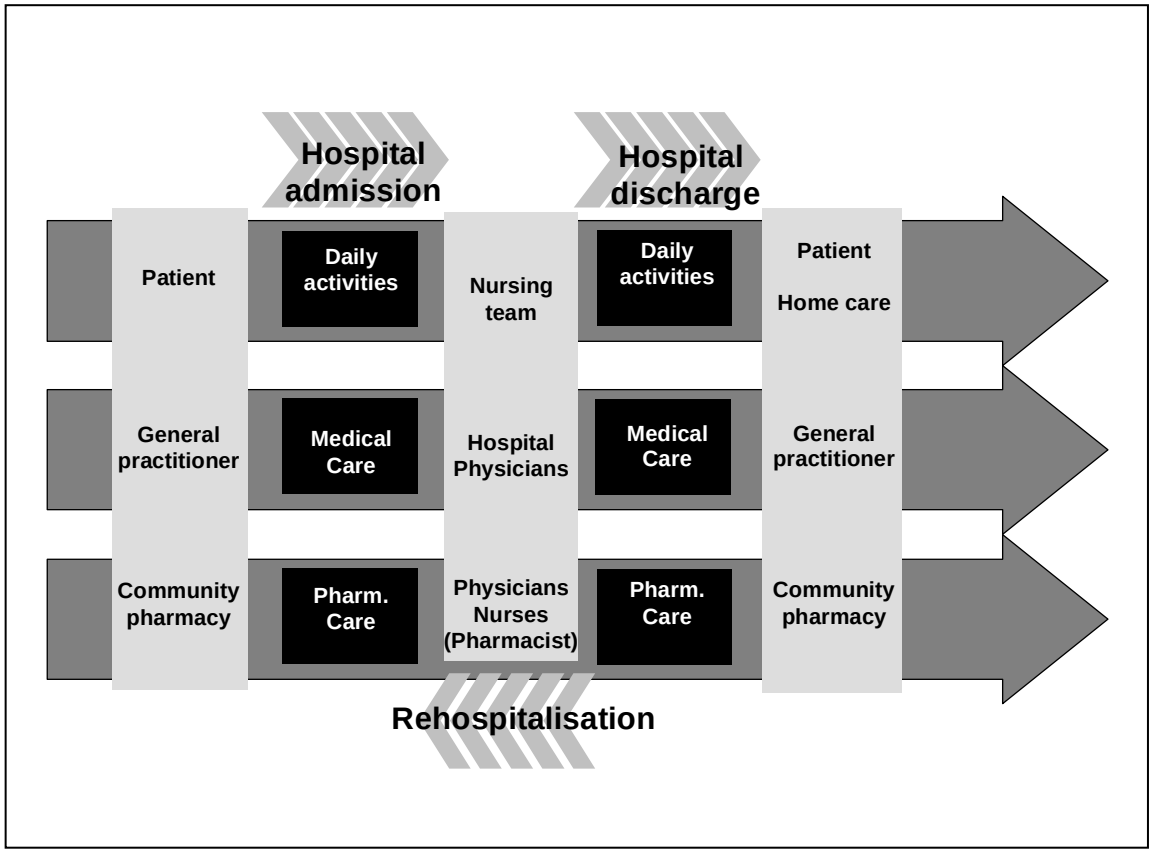

Figure 9: Multidimensions of perihospital patient care (adapted from [16]).

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Appendix

I. PCNE Classification of Drug Related Problems, V5.00

II. Raw data of DRP classification

Datum	Quelle	Problem	Ursache	Intervention	Ergebnis	Arzneimittel
09.05.2005	OA-Visite	P1.1	C1.8	I4.2	O3.4	Truxal
18.05.2005	OA-Visite	P2.2	C1.7	I3.3	O1.0	diverse
22.05.2005	Mappexvisite	P5.1	C2.1	I3.4	O1.0	Noroxin
22.05.2005	Mappexvisite		C2.1	I3.4	O1.0	Pradif
23.05.2005	Mappexvisite	P3.2	C2.1	I3.4	O1.0	Nitroderm
30.05.2005	Mappexvisite	P3.1	C2.1	I3.4	O2.0	Beloc ZOK
30.05.2005	Mappexvisite	P3.2	C1.2	I3.2	O1.0	Augmentin iv
10.06.2005	OA-Visite	P2.5	C6.2	I3.5	O1.0	Pantozol
10.06.2005	Mappexvisite	P3.2	C1.4	I3.2	O1.0	Ethambutol
10.06.2005	Mappexvisite	P5.1	C1.2	I3.1	O1.0	Seropram
10.06.2005	OA-Visite	P6.1	C1.1	I1.3	O1.0	Madopar
13.06.2005	OA-Visite	P5.1	C1.4	I1.1	O3.4	Rapamune
13.06.2005	Mappexvisite		C2.1	I3.4	O1.0	Rifater
15.06.2005	Mappexvisite	P2.2	C1.7	I3.3	O1.0	diverse
16.06.2005	Mappexvisite	P2.4	C1.4	I3.5	O1.0	Fosamax
17.06.2005	Mappexvisite	P1.1	C1.8	I4.2	O3.4	Sortis
18.06.2005	Mappexvisite	P1.1	C1.8	I4.2	O3.4	Sortis
18.06.2005	Anfrage	P3.2	C3.1	I3.1	O1.0	Refludan
20.06.2005	Mappexvisite	P1.1	C1.8	I4.2	O3.4	Xefo
20.06.2005	Mappexvisite	P1.1	C1.8	I4.2	O3.4	Aredia
20.06.2005	Mappexvisite	P1.1	C1.8	I4.2	O2.0	Sortis
20.06.2005	Mappexvisite	P2.6	C1.6	I3.5	O1.0	Nexium
20.06.2005	Mappexvisite	P3.2	C1.4	I3.2	O1.0	Augmentin iv
20.06.2005	Mappexvisite	P3.2	C1.4	I3.2	O3.4	Ciproxin
20.06.2005	Mappexvisite	P5.2	C2.1	I3.4	O1.0	Rifater
20.06.2005	Mappexvisite	P5.2	C2.1	I3.4	O1.0	Rifater
22.06.2005	Mappexvisite	P2.1	C1.4	I3.1	O1.0	Pethidin
27.06.2005	OA-Visite	P3.2	C2.1	I3.4	O1.0	Aprovel
27.06.2005	OA-Visite	P5.1	C1.4	I1.1	O1.0	Rifater
29.06.2005	Mappexvisite	P1.1	C1.1	I3.1	O2.0	Heparin
01.07.2005	OA-Visite	P2.6	C1.5	I3.6	O2.0	Resource
08.07.2005	OA-Visite	P2.6	C1.7	I3.6	O2.0	Nutriflex
12.07.2005	Mappexvisite	P3.2	C6.2	I1.4	O3.2	Imovane
12.07.2005	Anfrage	P4.1	C5.1	I4.1	O1.0	Colchicin
13.07.2005	Mappexvisite	P3.1	C1.4	I1.5	O2.0	Zyloric
13.07.2005	OA-Visite	P5.1	C2.1	I3.4	O1.0	Resonium
15.07.2005	OA-Visite	P2.6	C1.5	I3.6	O2.0	Resource
15.07.2005	Mappexvisite	P3.2	C1.4	I1.3	O1.0	Augmentin iv
18.07.2005	Sonderbestellung	P4.1	C5.1	I3.1	O2.0	Depakine
19.07.2005	Mappexvisite	P1.1	C1.8	I2.2	O3.4	Methotrexat
19.07.2005	Mappexvisite	P1.3	C1.8	I1.1	O3.4	Neomercazol
19.07.2005	Mappexvisite	P3.1	C1.2	I1.1	O2.0	Myfortic
19.07.2005	Mappexvisite	P3.1	C2.2	I1.3	O1.0	Morphin

19.07.2005	Mappexvisite	P3.2	C1.2	I3.2	O1.0	Durogesic
19.07.2005	Sonderbestellung	P4.1	C5.1	I3.1	O1.0	Cotrim
20.07.2005	Mappexvisite	P2.1	C1.3	I3.1	O1.0	Perfalgan
20.07.2005	Mappexvisite	P2.2	C1.3	I1.4	O3.2	Augmentin iv
20.07.2005	Mappexvisite	P3.2	C2.1	I3.4	O1.0	Nicotinell TTS
25.07.2005	OA-Visite	P2.2	C1.7	I3.3	O1.0	diverse
25.07.2005	OA-Visite	P2.2	C1.7	I3.3	O1.0	diverse
25.07.2005	OA-Visite	P2.2	C2.6	I3.4	O3.3	Foradil
25.07.2005	Sonderbestellung	P2.2	C5.1	I3.1	O1.0	Antemin
25.07.2005	OA-Visite	P2.5	C6.2	I3.5	O1.0	Nexium
25.07.2005	OA-Visite	P2.6	C1.1	I1.3	O2.0	Serevent
25.07.2005	OA-Visite	P3.1	C1.2	I1.5	O2.0	Orfiril
28.07.2005	Mappexvisite	P1.2	C1.8	I1.1	O3.4	Augmentin iv
28.07.2005	Mappexvisite	P2.3	C1.1	I3.5	O1.0	Brufen
28.07.2005	OA-Visite	P2.3	C1.1	I3.5	O1.0	Brufen
28.07.2005	Mappexvisite	P3.2	C1.4	I1.1	O3.4	Inderal
28.07.2005	Mappexvisite	P5.1	C2.1	I3.4	O1.0	Ciproxin
29.07.2005	OA-Visite	P2.4	C1.6	I3.5	O1.0	Plavix
02.08.2005	Mappexvisite	P3.2	C1.4	I3.2	O1.0	Ciproxin
02.08.2005	Mappexvisite	P5.1	C2.1	I3.4	O1.0	Ciproxin
10.08.2005	Sonderbestellung	P3.1	C1.1	I3.1	O1.0	Uralyt
11.08.2005	Mappexvisite	P4.1	C3.5	I1.1	O1.0	Zometa
11.08.2005	Anfrage	P5.1	C4.10	I2.2	O3.4	Rifampicin
12.08.2005	Sonderbestellung	P2.2	C1.3	I3.2	O1.0	Cernevit
12.08.2005	Anfrage	P6.1	C2.2	I3.2	O1.0	Paspertin
15.08.2005	OA-Visite	P2.1	C1.1	I1.3	O1.0	Esidrex
15.08.2005	OA-Visite	P2.3	C1.6	I1.1	O1.0	KCl
15.08.2005	OA-Visite	P2.5	C6.1	I3.5	O1.0	Aspegic
19.08.2005	Anfrage	P1.2	C1.1	I3.5	O2.0	Imodium
19.08.2005	Anfrage	P1.2	C1.7	I2.2	O3.4	Salofalk
19.08.2005	Mappexvisite	P1.2	C1.8	I4.2	O2.0	Novalgin
19.08.2005	Anfrage	P2.1	C3.1	I3.4	O1.0	Sandimun
06.09.2005	Anfrage	P1.1	C1.7	I4.2	O3.4	Salofalk
06.09.2005	Mappexvisite	P1.1	C1.8	I4.2	O3.4	Velbe
06.09.2005	Mappexvisite	P2.4	C1.1	I3.5	O1.0	Dafalgan
06.09.2005	Mappexvisite	P2.5	C1.6	I3.5	O1.0	Kalium
06.09.2005	Mappexvisite	P2.6	C1.5	I3.6	O1.0	Nexium
06.09.2005	Mappexvisite	P6.2	C2.6	I2.2		Seretide
19.09.2005	Sonderbestellung	P2.1	C1.1	I1.5		Halcion
19.09.2005	OA-Visite	P2.1	C1.4	I3.1	O1.0	Lescol
19.09.2005	OA-Visite	P3.1	C1.2	I3.1	O1.0	Co-Aprovel
20.09.2005	Anfrage	P2.2	C1.3	I3.3	O1.0	Tavanic
20.09.2005	Anfrage	P2.2	C1.3	I3.3	O2.0	Rimactan
21.09.2005	Mappexvisite	P2.2	C1.3	I1.1	O3.4	Tavanic
21.09.2005	Mappexvisite	P2.2	C1.3	I3.1	O1.0	Perfalgan
21.09.2005	Anfrage	P2.2	C2.6	I3.1	O1.0	Rifater

21.09.2005	Mappexvisite	P2.2	C6.2	I1.5		Seretide
21.09.2005	Mappexvisite	P2.4	C1.4	I1.1	O3.4	Dafalgan
22.09.2005	Mappexvisite	P4.1	C5.1	I4.1	O1.0	Isozid
22.09.2005	Mappexvisite	P5.1	C2.1	I3.4	O1.0	Ciproxin
23.09.2005	Mappexvisite	P1.1	C1.8	I4.2	O3.4	Temodal
23.09.2005	Mappexvisite	P1.2	C1.8	I1.1		Cordarone
23.09.2005	Mappexvisite	P3.2	C1.4	I1.4	O3.4	Augmentin iv
23.09.2005	Mappexvisite	P6.1	C1.1	I1.5		Heparin
27.09.2005	Mappexvisite	P2.2	C1.3	I1.4	O3.2	Perfalgan
27.09.2005	Mappexvisite	P2.5	C1.6	I3.5	O1.0	Perenterol
27.09.2005	Mappexvisite	P4.1	C3.5	I1.2	O1.0	Fosamax
27.09.2005	Mappexvisite	P5.1	C1.4	I1.1	O1.0	Digoxin
27.09.2005	Mappexvisite		C2.1	I3.4	O1.0	Creon
29.09.2005	Mappexvisite	P2.1	C1.1	I1.5		Dafalgan
29.09.2005	Mappexvisite	P2.1	C1.1	I1.5		Dafalgan
29.09.2005	Mappexvisite	P2.1	C1.2	I1.5		Dafalgan
29.09.2005	Mappexvisite	P5.1	C2.1	I3.4	O1.0	Ciproxin
29.09.2005	Mappexvisite	P5.1	C2.1	I3.4	O1.0	Resonium
03.10.2005	OA-Visite	P2.5	C2.3	I3.2	O1.0	Nexium
03.10.2005	OA-Visite	P3.1	C1.2	I3.2	O1.0	Nexium
03.10.2005	Anfrage	P5.1	C6.2	I2.1	O1.0	Neotigason
04.10.2005	Mappexvisite	P3.1	C1.6	I3.2	O1.0	Pantozol
04.10.2005	Mappexvisite	P6.4	C1.5	I3.6	O1.0	KCl
05.10.2005	Anfrage	P1.3	C1.2	I2.2	O2.0	Tegretol
05.10.2005	Mappexvisite	P2.3	C6.2	I1.2	O1.0	Klacid
05.10.2005	Mappexvisite	P2.3	C6.2	I1.2	O2.0	Plavix
05.10.2005	Mappexvisite	P5.1	C1.4	I1.1	O2.0	Rifater
05.10.2005	Mappexvisite	P5.1	C1.4	I1.1	O2.0	Rifater
07.10.2005	OA-Visite	P2.4	C1.1	I1.4	O2.0	Brufen
07.10.2005	OA-Visite	P3.2	C1.2	I3.2	O1.0	Augmentin iv
07.10.2005	OA-Visite	P5.1	C1.4	I1.1	O1.0	Methadon
23.10.2005	Sonderbestellung	P2.5	C1.3	I3.5	O1.0	Dipeptiven
23.10.2005	Anfrage	P3.2	C1.4	I3.2	O1.0	Obracin
25.10.2005	Mappexvisite	P2.2	C1.3	I1.4	O1.0	Augmentin iv
25.10.2005	Mappexvisite	P2.5	C6.2	I1.1	O2.0	Pantozol
25.10.2005	Mappexvisite	P2.6	C1.7	I1.1	O2.0	
25.10.2005	Mappexvisite	P3.2	C1.4	I1.5	O2.0	Augmentin po
25.10.2005	Mappexvisite	P3.2	C1.4	I3.2	O1.0	Vancocin
25.10.2005	Sonderbestellung	P3.2	C2.5	I2.1	O2.0	Chloraldurat
02.11.2005	Anfrage	P2.5	C1.1	I3.5	O1.0	Magnesium iv
02.11.2005	Anfrage	P2.6	C1.5	I3.6	O1.0	Cernevit
02.11.2005	Mappexvisite		C2.1	I3.4	O1.0	Tazobac
03.11.2005	Mappexvisite	P2.2	C1.3	I1.4	O1.0	Augmentin
03.11.2005	Sonderbestellung	P2.2	C1.3	I3.2	O1.0	Aspegic iv
03.11.2005	Mappexvisite	P2.4	C1.4	I3.5	O1.0	Dafalgan
08.11.2005	Mappexvisite	P2.4	C1.1	I3.1	O1.0	Dafalgan

08.11.2005	Mappexvisite	P5.1	C2.1	I3.4	O1.0	Ciproxin
11.11.2005	OA-Visite	P3.2	C1.2	I3.2	O1.0	NaCl
11.11.2005	OA-Visite	P6.1	C1.5	I1.1	O2.0	Miacalcic
14.11.2005	Anfrage	P2.6	C1.7	I1.1	O1.0	
14.11.2005	Anfrage	P5.1	C3.1	I2.2	O1.0	various i.v.
14.11.2005	Sonderbestellung		C3.1	I2.2	O1.0	Efudix
15.11.2005	Mappexvisite	P3.2	C1.4	I1.5		Ciproxin
15.11.2005	Mappexvisite	P5.1	C1.4	I1.5		Saroten
15.11.2005	Mappexvisite	P5.1	C1.4	I3.5	O1.0	Cordarone
15.11.2005	Mappexvisite	P5.1	C2.1	I3.4	O1.0	Ciproxin
16.11.2005	Mappexvisite	P2.6	C1.7	I3.6	O1.0	Sortis
16.11.2005	Mappexvisite	P3.1	C3.5	I1.2	O2.0	Phenhydan
16.11.2005	Mappexvisite	P3.2	C1.1	I3.5	O1.0	Dafalgan
17.11.2005	Mappexvisite	P2.3	C6.2	I1.2	O1.0	Plavix
17.11.2005	Mappexvisite	P3.2	C2.4	I1.3	O1.0	Phenhydan
18.11.2005	Anfrage	P1.1	C1.7	I2.2	O1.0	Trileptal
22.11.2005	Mappexvisite	P2.3	C1.1	I3.5	O2.0	Dafalgan
22.11.2005	Sonderbestellung	P3.1	C1.4	I1.1	O1.0	Dafalgan
22.11.2005	Mappexvisite	P5.1	C1.4	I1.5	O2.0	Cordarone
22.11.2005	Sonderbestellung		C5.2	I3.1	O1.0	Aprovel
28.11.2005	Anfrage	P1.3	C1.4	I1.1	O2.0	Orfiril
28.11.2005	Sonderbestellung	P2.2	C1.3	I3.1	O1.0	Serevent
28.11.2005	Sonderbestellung	P2.4	C1.6	I1.5	O2.0	Ezetrol
28.11.2005	Sonderbestellung	P3.1	C6.2	I1.2	O2.0	Bactrim
28.11.2005	Sonderbestellung	P6.3	C5.1	I1.5	O2.0	Medrol
29.11.2005	Mappexvisite	P2.4	C1.1	I1.5	O2.0	Pethidin
29.11.2005	Mappexvisite	P2.4	C1.4	I3.1	O1.0	Resyl Plus
29.11.2005	Mappexvisite	P3.1	C1.4	I1.1	O1.0	Orfiril
29.11.2005	Mappexvisite	P5.1	C1.4	I1.1	O1.0	Cordarone
30.11.2005	Mappexvisite	P2.5	C1.6	I3.2	O1.0	KCl
30.11.2005	Mappexvisite	P2.5	C1.6	I3.2	O1.0	Pantozol
30.11.2005	Mappexvisite	P2.5	C1.6	I3.2	O1.0	Nexium
30.11.2005	Mappexvisite	P3.4	C1.6	I3.5	O1.0	Imazol Creme
30.11.2005	Anfrage	P5.1	C1.4	I2.2	O1.0	Rimactan
01.12.2005	Mappexvisite	P2.2	C1.3	I3.3	O1.0	Tavanic iv
01.12.2005	Anfrage	P2.5	C1.6	I1.1	O2.0	KCl
01.12.2005	Anfrage	P3.2	C2.1	I1.1	O2.0	Triatec
01.12.2005	Anfrage	P5.1	C1.4	I1.1	O2.0	Cordarone
01.12.2005	Anfrage	P5.1	C1.7	I1.1	O1.0	Cymevene
01.12.2005	Mappexvisite	P5.1	C2.1	I3.4	O1.0	Tavanic po
02.12.2005	Mappexvisite	P3.4	C1.6	I3.5	O1.0	Imazol Creme
05.12.2005	OA-Visite	P1.1	C1.4	I4.2	O1.0	Marcoumar
07.12.2005	Mappexvisite	P2.5	C1.6	I3.2	O1.0	Nexium
07.12.2005	Mappexvisite	P3.1	C1.2	I3.2	O1.0	Vancocin
07.12.2005	Mappexvisite	P3.1	C3.1	I3.4	O1.0	Vancocin
07.12.2005	Sonderbestellung	P3.1	C3.5	I3.1	O1.0	Diflucan

07.12.2005	Mappexvisite	P3.2	C1.6	I3.5	O1.0	Paspertin
07.12.2005	Mappexvisite	P5.1	C1.4	I1.1	O2.0	Rifinah
07.12.2005	Mappexvisite	P5.1	C2.1	I3.4	O1.0	Ferrosanol
07.12.2005	Anfrage	P5.2	C1.1	I2.1	O1.0	Marcoumar
08.12.2005	Anfrage	P2.2	C3.1	I3.4	O1.0	Streptase
08.12.2005	Mappexvisite	P3.1	C5.2	I3.2	O1.0	Litalir
08.12.2005	Anfrage	P5.1	C1.4	I1.1	O1.0	Methotrexat
08.12.2005	Mappexvisite	P5.1	C1.4	I3.1	O1.0	Sortis
08.12.2005	Mappexvisite	P5.1	C2.1	I3.4	O1.0	Tavanic
09.12.2005	Mappexvisite	P1.1	C1.4	I4.2	O1.0	Marcoumar
09.12.2005	Anfrage	P2.4	C1.8	I2.2	O1.0	Heparin
13.12.2005	Mappexvisite	P2.1	C1.1	I1.5		Dafalgan
13.12.2005	Mappexvisite	P2.2	C1.3	I3.1	O1.0	Beco 5
13.12.2005	Mappexvisite	P2.2	C1.3	I3.3	O1.0	Benerva
13.12.2005	Sonderbestellung	P2.2	C1.3	I3.3	O1.0	Vibravenös
13.12.2005	Mappexvisite	P2.2	C4.8	I3.1	O1.0	Triatec
13.12.2005	Sonderbestellung	P2.4	C1.1	I1.4	O3.1	Celebrex
13.12.2005	Mappexvisite	P3.1	C5.2	I3.2	O1.0	Serevent
13.12.2005	Mappexvisite	P3.1	C5.3	I3.2	O1.0	MST
13.12.2005	Mappexvisite	P5.1	C1.4	I1.1	O1.0	Diflucan
13.12.2005	Sonderbestellung	P5.1	C2.1	I3.4	O1.0	Ciproxin
19.12.2005	OA-Visite	P3.2	C1.6	I3.2	O1.0	Pantozol
20.12.2005	Anfrage	P2.1	C2.6	I3.1	O1.0	Pantozol
20.12.2005	Mappexvisite	P2.2	C1.3	I3.3	O1.0	Klacid
20.12.2005	Anfrage	P2.5	C1.6	I3.5	O1.0	Kalium
20.12.2005	Mappexvisite	P3.2	C1.4	I3.2	O1.0	Vancocin
21.12.2005	Mappexvisite	P3.1	C1.2	I3.2	O1.0	Seretide
21.12.2005	Mappexvisite	P3.2	C1.2	I1.4	O2.0	Cordarone
21.12.2005	Mappexvisite	P3.2	C1.2	I3.2	O1.0	Zofran
21.12.2005	Mappexvisite	P3.2	C1.4	I1.1	O1.0	Digoxin
21.12.2005	Mappexvisite	P4.2	C5.2	I1.3	O1.0	Resyl Plus
22.12.2005	Anfrage	P6.2	C3.3	I2.1	O2.0	