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RESEARCH ARTICLE

Drug-related problems: evaluation of a classification system in the daily practice of a Swiss University Hospital

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Abstract *Aim* To evaluate the Pharmaceutical Care Network Europe (PCNE) classification system as a tool for documenting the impact of a hospital clinical pharmacology service. *Setting* Two medical wards comprising totally 85 beds in a university hospital. *Main outcome measure* Number of events classified with the PCNE-system, their acceptance by the medical staff and cost implications. *Methods* Clinical pharmacy review of pharmacotherapy on ward rounds and from case notes were documented, and identified drug-related problems (DRPs) were classified using the PCNE system version 5.00. *Results* During 70 observation days 216 interventions were registered of which 213 (98.6%) could be classified: 128 (60.1%) were detected by reviewing the case notes, 33 (15.5%) on ward rounds, 32 (15.0%) by direct reporting to the clinical pharmacist (CP), and 20 (9.4%) on non-formulary prescriptions. Of 148 suggested interventions by the CP 123 (83.0%) were approved by the responsible physician, 12 ADR reports (8.1%) were submitted to the local pharmacovigilance centre and 31 (20.9%) specific information given without further need for action. An evaluation of the DRPs showed that direct drug costs of €2,058 within the study period or €10,731 per year could be avoided. *Conclusion* We consider the PCNE system to be a practical tool in the hospital setting, which demonstrates the values of a clinical pharmacy service in terms of identifying and reducing DRPs and also has the potential to reduce prescribing costs.

Keywords Adverse drug events · Adverse drug reactions · Classification systems · Clinical pharmacist · Cost · Drug-related problems · Hospital care · PCNE DRP classification · Pharmaceutical interventions · Switzerland

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Impact of findings on practice

- The PCNE-classification system is suitable for daily hospital practice and a useful tool for documenting clinical pharmacy activities.
- Structured documentation with the PCNE-classification allows performance measurement of clinical pharmacy services.

Introduction

Drug-related problems are a major safety issue for hospitalized patients. A review of the literature from 1990 to 2005 found that on average 8% of hospitalised patients experience an adverse drug event (ADE), and 5–10% of all drug prescriptions or drug applications are erroneous [1]. In general internal medicine 14.6% of hospitalized patients and approximately 12% to 17% of patients after discharge experience ADEs [2, 3]. Interventions by clinical pharmacists have been shown to be effective in reducing DRPs with positive outcomes on the number of ADEs, medication

appropriateness and resource use. A systematic literature review of controlled studies evaluating the effects of interventions by clinical pharmacists on hospitalized adults found that ADEs, adverse drug reactions (ADR) and MEs were reduced in 7 of 12 trials that included these outcomes [4]. Medication adherence, knowledge, and appropriateness of drug use improved in 7 of 11 studies and the length of hospital stay was shortened in 9 of 17 trials.

From an economic point of view clinical pharmacy services are also favourable. A summary of literature from 1996 to 2000 found 16 studies reporting a cost-benefit ratio ranging from 1.7:1 to 17:1 with a median of 4.68:1 [5].

In many of these studies, however, definitions of detected or prevented problems such as ADRs, ADEs, medication errors or prescribing errors are not consistent. This may cause difficulties in documentation and classification of pharmaceutical interventions and may impair the comparability of the studies. A comprehensive overview of used definitions has been published recently [6].

Due to the inconsistency of definition we have used the more general term of DRPs in this publication. A drug-related problem (DRP) can be defined as an event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes [7]. It represents ineffective and unsafe drug use, which may cause or constitute risk factors for MEs, ADEs, ADRs [8].

After having introduced a clinical pharmacy service on two wards we documented the effect of a clinical pharmacist's interventions on DRPs. The main objective was to evaluate the practicality of use of the classification system under daily conditions and to explore its usefulness to derive performance indicators of the clinical pharmacy service.

Methods

Classification system

Several classification systems have been proposed in the literature, with only some of them being validated [9–11]. We chose the PCNE classification system for drug-related problems (version 5.00) [7], since it contains most of the required aspects described in a late review of classification systems [12]. To our knowledge the system has been used in primary care but not in hospital settings. To support continuity of care one single system for the documentation of clinical pharmacy activities is desirable. The PCNE system attributes four items to each observation—(1) coding for the problem itself, (2) the actual or suspected cause of the problem, (3) the intervention required to resolve the DRP, and (4) its outcome. An example to illustrate this code is given in Fig. 1.

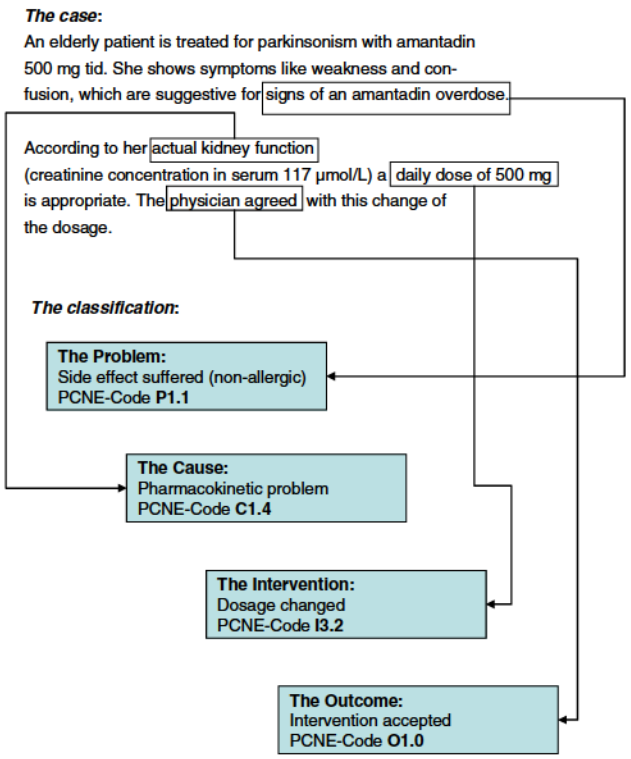

Fig. 1 Example of a pharmaceutical intervention classified as a drug related problem according to PCNE Classification System V5.00

Study design and setting

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

During the period between May to December 2005 (32 weeks) one senior clinical pharmacist (ML) conducted 70 observation days taking part in clinical ward rounds and reviewing daily all the non-formulary prescriptions and the case notes of one of five nursing subunits of the ward (representing 10–15 patients). All clinical pharmaceutical interventions were classified as DRPs according to the PCNE System V5.00 and then entered into an Excel spread sheet (Microsoft Corp., Redmond, Oregon) including the drugs involved.

Acceptance of pharmacists' interventions

In the PCNE classification the items 11.3–11.5 were all considered suitable for a modification in therapy. Interventions at prescriber level proposing an approved change in drug therapy, were classified at drug level in order to get more detailed information.

The acceptance rate was calculated as the sum of interventions with PCNE codes 11.3 and 13.x divided by the sum of all interventions proposing modifications (PCNE codes 11.3, 11.4, 11.5, and 13.x).

Cost avoidance

The cost avoidance of interventions directly linked to a reduction in medication usage was calculated. 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 (P3.2 [Drug dose too high] in combination with 13.2 [Dosage changed]) and stopping unnecessary medications (13.5 [Drug stopped]). For the calculation we presumed that inappropriate drug therapies would have continued for three days without being detected. As an assumption, we counted reduction of dosage as half price. Drug costs were calculated on the basis of defined daily doses and official prices given in the Swiss Drug Formulary [13]. In order to get a yearly estimate, all the directly cost-linked interventions during the 70 observation days were added up to a year of 365 working days.

Results

Classification of drug-related problems

In the observation period, 1, 444 patients were discharged from the two wards representing 17,476 patient days. There were 0.15 interventions per patient counting up to 1.22 interventions per 100 patient days.

A total of 213 pharmaceutical interventions were recorded, whereof 33 (15.5%) were initiated on ward rounds, 128 (60.1%) on case note review, 32 (15.0%) as a consequence of specific requests and 20 (9.4%) interventions by non-formulary drug orders. To each intervention a cause and a problem code could be attributed except six cases (2.8%) without a suitable problem category. The non-classified problems are listed in Table 1.

Problems

The major DRPs identified were related to incorrect drug choice (PCNE-Code P2) in 38% ($n = 81$); 24% ($n = 52$) were drug dosage problems (P3), followed by drug-drug or drug-food interactions (P5) in 17% ($n = 37$). ADRs (P1) accounted for 10% ($n = 22$) of the problems. The detailed analysis of the 207 DRPs are shown in Table 2: potential drug interactions (16.4%, $n = 34$; P5.1) are most frequent, followed by overdose (14.5%, $n = 30$; P3.2) and inappropriate choice of drug form (12.6%, $n = 26$, P2.2), 20 (9.7%) problems regarding too low a dose (P3.1), 15 (7.2%) observations with no clear indication for drug use (P2.5) and 14 (6.8%) non-allergic ADRs (P1.1).

Causes

The overview of the causes ($n = 213$) shows a majority (68%, $n = 145$) that was related to the selection of the drug and/or dosage schedule (C1). The second most common cause with 15% ($n = 33$) involved the drug use process (C2), i.e., administration and timing of drugs. Patient factors (C4) seemed to play a minor role (1%, $n = 2$). Aspects concerning information about the treatment (C3), logistics (C5), e.g., availability of drugs, and other causes (C6) were noted each in 11 cases (5%).

The detailed analysis of the causes (Table 3) shows that pharmacokinetics due to organ dysfunction and interactions (C1.4) played a major role (19%) followed by inappropriate timing of administration and dosing intervals (C2.1; 11%, $n = 24$) and inappropriate drug selection (C1.1; 10%, $n = 22$).

Inverventions

All of the causes led to an intervention ($n = 213$). Most of them took place at the drug level (13; 54%, $n = 116$), followed by interventions at the prescriber level e.g. explaining a drug-drug interaction (11; 32%, $n = 69$). The rest of interventions were at the patient/carer level (12) or "other activity" (14), each resulting in 7% ($n = 14$) of interventions (Table 4).

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

No.	Cause	Intervention	Drug	Description of problems
1	C2.1	13.4	Tamsulosin	Drug should be taken before the meals
2	C2.1	13.4	Isoniazid/Pyrazinamid/Rifampin	Drug should be taken before the meals
3	C2.1	13.4	Lipase/Amylase/Protease	Drug should be taken before the meals
4	C2.1	13.4	Piperacillin/Tazobactam	Drug should not be administered parallel to a certain other drug (incompatibility problem)
5	C3.1	12.2	Fluorouracil	Topical cytostatic drug, special instructions for use must be followed
6	C5.2	13.1	Irbesartan	Obvious prescribing error (no more details available)

Table 2 Detected drug-related problems ($n = 207$), classified according to PCNE-Classification V5.0 [11]

Primary domain	Code	Detailed classification	*n*	%
1. Adverse reactions	P1	Total	22	10
Patient suffers from an adverse drug event	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	P2	Total	81	38
Patient gets or is going to get a wrong (or no drug) drug for his/her disease and/or condition	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	P3	Total	52	24
Patient gets more or less than the amount of drug he/she requires	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	P4	Total	7	3.4
Wrong or no drug taken/administered	P4.1	Drug not taken/administered at all	6	2.9
	P4.2	Wrong drug taken/administered	1	0.5
5. Interactions	P5	Total	37	17
There is a manifest or potential drug-drug or drug-food interaction	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

Acceptance indicator

In the PCNE classification the items 11.3 to 11.5 and all the interventions at drug level (13.x) can be considered as propositions for a modification in therapy (changes in drug prescription or other non-pharmacological measures such as the monitoring of drug levels or other laboratory parameters) subjected to physician's approval. In our sample 148 interventions of 213 concerned therapy modifications (69%). 83% were adopted by physicians (PCNE Codes 11.3/13.x, 6% were rejected (11.4), and in 16 cases (11%) the outcome remained unknown (11.5) (Fig. 2).

The remaining 65 interventions are not subject to physician approval. Almost half of these (47.7%, $n = 31$) involved giving more information to the prescriber, typically about potential drug-drug interactions requiring closer clinical patient monitoring. Another twelve interventions were ADRs reported to the pharmacovigilance centre.

Cost avoidance

A total of 51 interventions (24%) were considered to be directly related to a cost saving without affecting quality of care (Table 5).

Of these 51 cost-relevant interventions 22 (43.1%) accounted for stopping of medication, which was no longer required, 16 (31.4%) for switching from i.v. to p.o. medications and 13 (25.5%) for dosage adjustments.

The interventions stopping unnecessary drugs showed a mean saving of €10.11 resulting in €1,158 for the period of one year (365 working days). Interventions which switched

Table 3 Causes for drug-related problems ($n = 213$), classified according to PCNE-Classification V05 [11]

Primary domain	Code	Detailed classifcation	*N*	%
1. Drug/dose selection	C1	Total	145	68
The cause of the DRP is related to the selection of the drug and/or dosage schedule	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	C2	Total	33	15
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)	C2.1	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	C3	Total	11	5.2
The cause of the DRP can be related to a lack or misinter pretation of information	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	C4	Total	2	1
The cause of the DRP can be related to the personality or behaviour of the patient	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	C5	Total	11	5.2
The cause of the DRP can be related to the logistics of the prescribing or dispensing mechanism	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

an i.v. drug to p.o. ($n = 13$) resulted in a mean cost saving of €93.30 per intervention, i.e., €7,785 annually. Assuming that dose reductions equate to half the price of the daily regular dose of a drug for three treatment days, dose adjustments for the 13 interventions led to a cost reduction of €343 for all and €26.35 per single dose adjustment. Over

Table 4 Pharmacist's interventions for drug-related problems ($n = 213$), classified according to PCNE-Classification V05 [11]

Primary domain	Code	Intervention	*n*	%
No intervention	I0.0	No intervention	0	0.0
1. At prescriber level	11	Total	69	32
	11.1	Prescriber informed only	31	14.6
	11.2	Prescriber asked for information	6	2.8
	11.3	Intervention proposed, approved by Prescriber	7	3.3
	11.4	Intervention proposed, not approved by Prescriber	9	4.2
	11.5	Intervention proposed, outcome unknown	16	7.5
2. At patient/carer level	12	Total	14	6.6
	12.1	Patient (medication) counselling	4	1.9
	12.2	Written information provided only	10	4.7
	12.3	Patient referred to prescriber	0	0.0
	12.4	Spoken to family member/caregiver	0	0.0
3. At drug level	13	Total	116	54
	13.1	Drug changed	22	10.3
	13.2	Dosage changed	28	13.1
	13.3	Formulation changed	10	4.7
	13.4	Instructions for use changed	27	12.7
	13.5	Drug stopped	22	10.3
	13.6	New drug started	7	3.3
4. Other intervention or activity	14	Total	14	6.5
	14.1	Other intervention (specify)	2	0.9
	14.2	Side effect reported to authorities	12	5.6

the course of one year, the dose adjustment savings equal €1,788.

Together, the cost-relevant interventions equal €10,731 for one year as mere cost avoidance not counting the effect on length of stay, ADE rate and possible litigation costs.

Discussion

Our study shows that of 213 interventions by the clinical pharmacist (CP) almost all (97.8%) could be documented and rated with the PCNE 5.00 system. By far the most DRPs were found in the realm of drug prescription. The classification of each DRP on four different levels (problem-cause-intervention-outcome) gives enough details allowing qualitative and economic analyses. As the PCNE system has been created for the documentation of DRPs in the public pharmacy setting, certain items are lacking for in-patients. Typical DRPs in the hospital setting like incompatibilities, application errors or faulty transcriptions cannot be coded in a satisfactory way; this should be taken into consideration when developing further versions of PCNE. The primary domain of the problems' section "drug use problem" is too restrictive and should be adapted for the in-hospital setting. Allenet et al. suggest such a documentation system. In their proposed intervention section it contains items often used like "administration mode optimisation" or "change of administration route", and in the problems section "improper administration" [10]. A major draw-back of their system is that neither a description of the cause nor options for the documentation of interventions at the patient level are provided. Combining the PCNE system with these elements would create a well-adapted tool. Future work should additionally address the assessment of DRP severity and the clinical impact of the pharmacist's intervention as proposed in literature [14–16].

Time is a key aspect for the acceptance of a documentation system. Practicability of the PCNE system in daily routine proved to be easy to use and barely time-consuming. The daily documentation classifying the DRP and entering the PCNE codes and the drugs into the database (Excel spreadsheet) took only a few minutes. *Ganso* using the PI-Doc system on a Microsoft Access database measured on average 1.9 min for the classification and 6.5 min for the electronic documentation/intervention [17].

The documentation of DRPs with the PCNE system in everyday practice seems to provide realistic and comparable data about the impact of clinical pharmacy services on drug treatment. The acceptance of the pharmacist's interventions was 83%, a figure well in accordance with

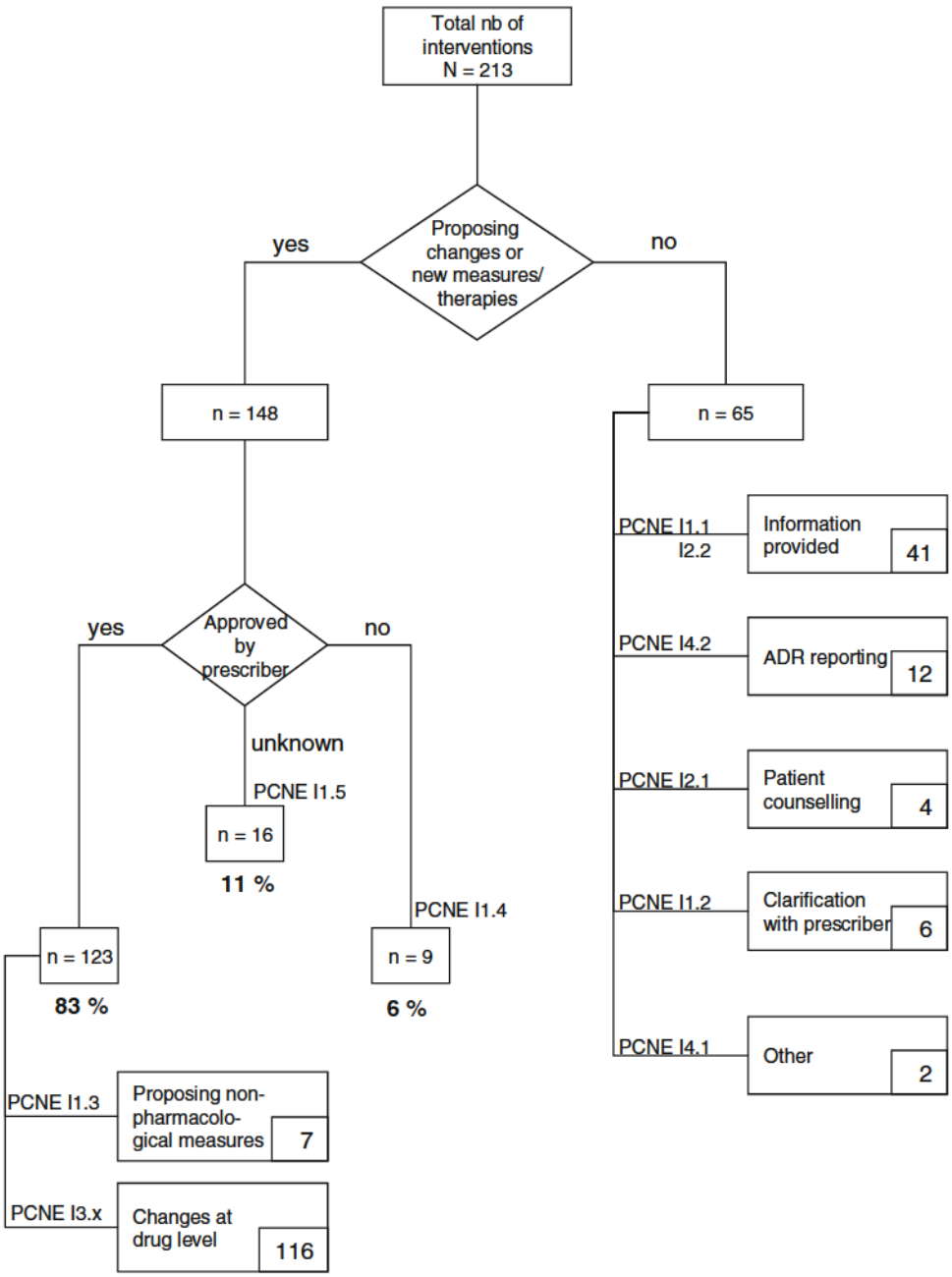

Fig. 2 Types of pharmaceutical interventions and their acceptance by the prescribers

Table 5 Cost avoidance by clinical pharmaceutical interventions

	PCNE Code	No. of observations	Avoided costs (€)	One year estimate (365 days;€)
Stopping unnecessary drugs	13.5	22 (43.1%)	222[a]	1,158
Switching from i.v. to p.o.	[P2.2+C1.3]	16 (31.4%)	1,493[b]	7,785
Dose adjustments	[P3.2+13.2]	13 (25.5%)	343[c]	1,788
Total		51 (100%)	2058	10,731

[a] Assuming continued application of this drug for another 3 days

[b] Assuming continuation of 3 days i.v. therapy

[c] 3 days' treatment at 50% price

other studies. A review of 23 studies found an average acceptance rate of 85.5% [18]. Some studies, however, may show acceptance rates of up to 99%, but the provision of drug information was also counted as an intervention, whereas in our calculation this item (PCNE 11.1: Prescriber informed only) was not included [19].

Clinical pharmacy service can reduce drug costs. Our study of a single CP's activity showed a cost avoidance of over 10,000 €/year. Twenty-five percent of interventions had direct influence on drug costs, a similar rate to the study of McMullin with 26% [20]. A recent study from Denmark assessed the cost effects of a clinical pharmacist in a controlled prospective study [21]. Cost reductions resulted in 43% of the interventions with total savings of direct drug costs of 3442 € within one year. The difference to our findings showing cost savings up to more than 10,000 €/year can be explained by methodological differences. Our results base on assumptions for calculation. Minor changes in the assumptions would lead to different results. Second, we extrapolate from our study period of 70 observation days in a period of 8 months to a whole year of 365 working days. In such a design random effects may occur (one single case with extraordinary high costs or cost savings) which are then extrapolated to one year.

But in spite of these restrictions, our findings do not seem unrealistic in comparison to other studies. *Ganso* found cost reductions ranging from 17 to 27 €/intervention on average in four different wards (3 surgery wards, 1 endocrinology ward) [17] whereas we calculated 34 €/intervention. In particular the cost savings of switching from i.v. to p.o. application is well within the range of former results. Our study confirms *Ruettimann's* cost savings of 93 € per switch of antibiotics [22]. Our estimations still are conservative taken into account we assumed work during daytime only.

Our study has several limitations. A major limitation is the possible bias in the detection and classification of DRPs since all the pharmaceutical interventions derive from a single site, a single medical floor and only one person identified, resolved and classified the DRPs. Using a crossover design with two pharmacists and kappa statistics would substantially reduce this bias. Local staffing restrictions unfortunately did not allow us to follow such a design. Furthermore, results from wards of other medical specialties should be compared to the medical wards in our study. Third, we show cost avoidance by the CP's interventions. The use of billing data, outcome measures and adjustment for age, gender and casemix, would enable real costs to be computed.

Conclusion

In conclusion, we consider the PCNE system with the four levels of classification a very useful and easy-to-use tool for the documentation of clinical pharmacy services not only for research purposes but also in daily hospital practice. Data generated by such a documentation system are increasingly important to provide information on the impact of the clinical pharmaceutical services supplied and identification of staff needs [23].

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