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RESEARCH ARTICLE

Demonstrating the clinical pharmacist's activity: validation of an intervention oriented classification system

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Abstract *Background* Clinical pharmacists are increasingly involved in detecting and solving drug-related problems. To document their performance, a convenient tool to code pharmaceutical interventions in daily practice is desirable. The Swiss Society of Public Health Administration and Hospital Pharmacists (GSASA) proposed to implement a new classification system for pharmaceutical interventions. *Objectives* To develop and validate a classification system for pharmaceutical interventions and to compare it with the well-established Pharmaceutical Care Network Europe (PCNE) system. *Setting* Rehabilitation clinic, geriatric and orthopaedic wards of a 427-bed teaching hospital. *Methods* Development of the GSASA classification started with expert panel discussions and the validation of the first version (GSASA V1). To assess appropriateness, interpretability, and validity, clinical pharmacists documented during a 6-week period all interventions using GSASA V1 and PCNE version 6.2 (V6.2). Acceptability and feasibility were tested by an 8-item questionnaire with 5-point Likert scale (1 = strongly disagree, 5 = strongly agree), and inter-rater reliability (Fleiss-Kappa coefficients κ) was determined. After revision, the second version (V2) was assessed again for reliability. *Mean outcome measures* User's agreement/satisfaction, comprehensiveness/reliability of the classification system. *Results* The GSASA V1 includes 4 categories and 35 subcategories. Of 115 interventions classified with GSASA V1, 93 (80.9 %) could be completely classified in all categories. This explains that 3 of 6 users could be not satisfied with the comprehensiveness of GSASA V1 (mean user agreement 2.7 ± 0.8). The questionnaire showed that all users could find GSASA V1 (4.0 ± 0.0) easier to use than PCNE V6.2 (3.0 ± 0.9). Users were generally satisfied with the GSASA V1 (3.5 ± 0.8), especially with the adequate time expenditure (4.0 ± 0.7). Inter-rater reliability and acceptability of GSASA V1 were comparable to those of the PCNE V6.2. The agreement among the GSASA V1 users was substantial for the categories 'problem' ($\kappa = 0.66$), 'intervention' ($\kappa = 0.74$), and 'outcome' ($\kappa = 0.63$), while moderate agreement for the category 'cause' was obtained ($\kappa = 0.53$). The final system GSASA V2 includes 5 categories (addition of 'type of problem') and 41 subcategories. Total inter-rater reliability was moderate ($\kappa = 0.52$). *Conclusion* The GSASA classification system appeared to be reliable and promising for documentation of pharmaceutical interventions in daily practice (practical and less time-consuming). The system is validated in terms of appropriateness, interpretability, validity, acceptability, feasibility, and reliability.

Keywords Classification system · Clinical pharmacy · Drug-related problems · Pharmaceutical care · Pharmaceutical interventions · Validation

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Impact of findings on practice statements

- The new classification system GSASA V2 may serve as a helpful tool in daily practice to classify DRPs and clinical interventions undertaken by pharmacists.
- Classification of DRPs together with according interventions enables demonstration of the performance/impact of clinical pharmacy services.
- This classification system could be a helpful instrument to collect and quantify data on pharmaceutical interventions, thus enabling the merging of data for epidemiological studies.

Introduction

Drug-related problems (DRPs) are common in hospitalised patients. As defined by the Pharmaceutical Care Network Europe (PCNE), a DRP is an event or circumstance involving drug therapy that actually, or potentially, interferes with the desired health outcomes [1]. A drug-related problem can be a risk to the patient (potential problem) or cause harm (manifest problem) as an adverse drug event (ADE) or an adverse drug reaction (ADR). Multiple causes for DRPs are known such as medication error, poor documentation, failures in communication, inappropriate processes in the health care setting or the patient's behaviour. A systematic review analysing DRPs in hospitals showed that problems associated with pharmacotherapy lead to a prolonged hospital stay and increased healthcare costs. Medication errors occurred in 5.7 % of all episodes of drug administrations, and 6.1 % of hospitalised patients experienced an ADE or ADR [2].

Increasingly, clinical pharmacists are involved in detecting and solving DRPs on a regular basis. Utilisation of a classification system would aid in the collection of DRPs and the assessment of pharmaceutical interventions; support continuity of care through the promotion of mutual information [3]; and, additionally, such data on pharmacists' activities could be used for epidemiological studies.

In the literature several classification systems have been proposed. Most instruments, such as APS-Doc [4], DOCUMENT [5], and PI-Doc [6], were considered too time-consuming in practice. Another such system, the PCNE [12] classification system, was originally developed for a research and community pharmacy setting and has a strong focus on patient behaviour, therefore making it less appropriate for the hospital setting. Typical hospital medication errors such as application errors, incompatibilities, and incorrect transcription cannot be classified [3]. The large number of subcategories (n = 71) renders the tool very comprehensive, but hinders its application in a daily routine setting. Allenet et al. validated an instrument for the documentation of clinical pharmacists' interventions (SFPC system), which proved to be suitable for daily practice [7]. However, this simple system lacks subcategories to document detailed information, and the cause of the DRPs is not assessed. Hence, validated, structured, and standardised classification systems for pharmaceutical interventions, which fulfil both requirements of comprehensive classification and simple use in daily clinical practice, are rare.

Validation confirms, through the provision of objective evidence, that the requirements for a specific use or application are fulfilled [8]. Validation of a classification system is necessary, not only to ensure that one code reflects a unique DRP, but to guarantee that this coding is understandable to user. The literature describes the following criteria for validating DRP classification systems: (1) appropriateness (is the classification content appropriate to the questions the application seeks to address?) (2) acceptability (is the classification acceptable to the users?) (3) feasibility (is the application easy to use?) (4) interpretability (how well can the classification codes be interpreted?) (5) reliability (does the classification generate results that are reproducible and internally consistent?) (6) validity (does the classification measure what it claims to measure?) (7) responsiveness (does the classification offer options to follow up interventions and monitor outcomes of interventions?) [9].

Up to now, there was no national consensus in Switzerland on how to demonstrate the clinical pharmacist activities to obtain data allowing epidemiological studies for research and political purposes. The working group on clinical pharmacy of the Swiss Society of Public Health Administration and Hospital Pharmacists (GSASA), comprising eight French- and German-speaking clinical pharmacists, recognised the need for the development of a new standardised and practical tool. To ease the recording of interventions in inpatients during daily practice, a tool was developed, which seeks to combine the advantages of existing systems such as SFPC (validated, practical, and based on hospital setting) and PCNE (validated, logical basic structure with the categories cause and intervention) systems. The classification system focused on interventions to enable a more objective assessment, and increased quality and reliability of data recording. We used the PCNE system, which is validated, well-established and internationally used, as a benchmark for our new intervention oriented classification system [3, 10]

Aim of the study

The aim of the study was to develop a classification system for drug-related problems and pharmaceutical interventions, and to validate this system using inpatients and against the PCNE classification system V6.2.

Ethical approval

According to the requirements of the Swiss federal law on human research this study is exempt from ethical approval.

Methods

Overview of development process

Figure 1 illustrates the process involved in developing the new GSASA classification system, which comprised four main steps. The topics were based on those of the PCNE classification system, while the structure followed that of the French classification system [7]. The first version (GSASA V1) of the classification system was developed by an expert panel of eight clinical pharmacists (GSASA working group on clinical pharmacy). After validation, a second version was developed (GSASA V2) which was revalidated.

We defined a "pharmaceutical intervention" as a recommendation initiated by a pharmacist in response to a DRP occurring in an individual patient in any phase of the medication process. The intervention aims at optimising pharmacotherapy, in terms of efficacy, safety, economic, and humanistic aspects [11].

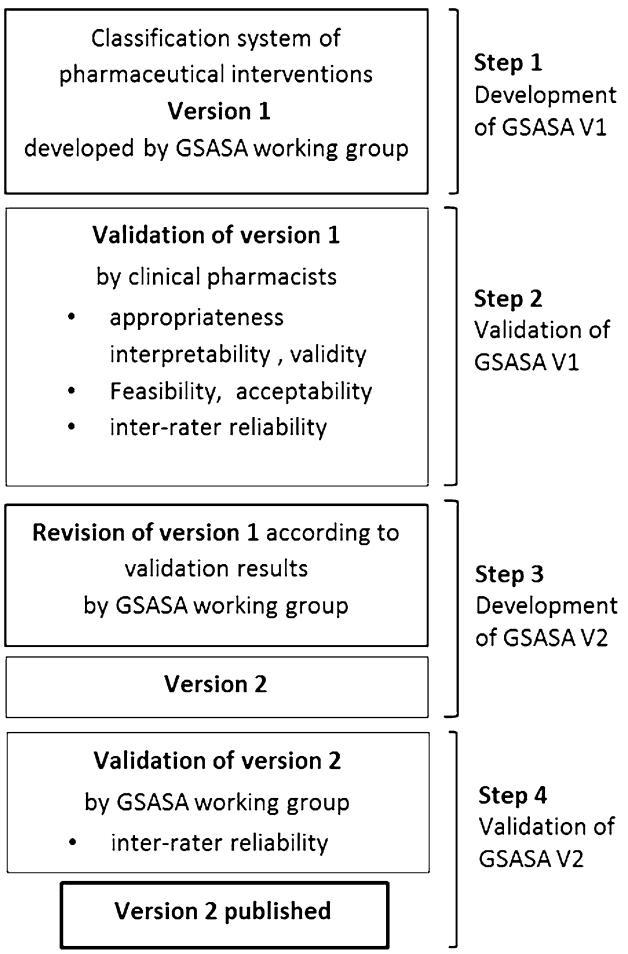

Fig. 1 Process of developing the classification system

Step 1: Development of classification system GSASA V1

The GSASA working group (=expert panel) comprised four French and four German speaking clinical pharmacists (n = 8) from 8 different hospitals, whose professional experience in clinical pharmacy ranged from 3 to 14 years. Seven of them had previously used a DRP classification system. The first version, developed by the aforementioned GSASA working group, was based on the PCNE classification system for DRPs [12] and the instrument for documentation of clinical pharmacists' interventions of the French Society of Clinical Pharmacy [7]. Any discrepancies were resolved by discussion.

Step 2: Validation of classification system GSASA V1

Version 1 was validated assessing appropriateness, interpretability, validity, feasibility, acceptability, and inter-rater reliability.

Appropriateness, interpretability, and validity

We measured appropriateness, interpretability, and validity of the classification systems by assessing the proportion of completely classified interventions. Classification was considered complete when all categories were filled out. At a 427-bed teaching hospital, six experienced clinical pharmacists used the GSASA V1 during a 6-week period to classify the interventions they performed themselves from their routine ward rounds (in geriatric ward, rehabilitation clinic, and orthopaedic ward). Additionally, they classified the same data with PCNE V6.2, and entered the classification codes into a Microsoft Excel sheet. For each DRP, only one choice per category was possible. Special attention was paid to the cases that could not be completely classified.

The pharmacists received training prior to data collection. Training mainly comprised classification of model cases according to standardised documentation forms of PCNE and GSASA, followed by plenum discussions. Validated model cases in a German translation were used [13]. The collected data were analysed by descriptive statistics.

Acceptability and feasibility

To evaluate acceptability and feasibility of both classification systems, an 8-item questionnaire, which has been used in an earlier study, was completed by the six pharmacists [13, 14].

The extent of their agreement or disagreement was assessed by a 5-point Likert scale (1 = strongly disagree, 2 = disagree, 3 = neutral, 4 = agree, 5 = strongly agree). Time spent for classification and the free text comments was then evaluated. A Mann–Whitney U test was used for statistical evaluation. The significance level was accepted at $p < 0.05$.

Inter-rater reliability

Three of the six senior clinical pharmacists assessed the reliability of the classification systems. Each had more than 5 years of professional experience in clinical pharmacy, and had worked with DRP classification systems before. They classified 10 model cases using GSASA V1 and PCNE V6.2. The model cases consisted of five validated model cases taken from the literature [15], and five model cases developed for the validation of PCNE V5.0 taken from the German translation. Drug names were only modified to suit the Swiss market. We randomised the order of model cases and classification systems, and each rater received the same instructions. For both classification systems, only one choice per category was possible to classify each detected problem.

For the four categories of both classification systems (detected problem, cause, intervention, outcome of intervention) Fleiss kappa was calculated using a Microsoft Excel template [16]. Resulting values were interpreted according to Landis and Koch [17] as 'almost perfect' (Fleiss' κ 0.81–1.00), 'substantial' (0.61–0.80), 'moderate' (0.41–0.60), 'fair' (0.21–0.40), 'slight' (0.00–0.20), and 'poor' (<0.00). A kappa higher than 0.4 indicates that the system is reliable.

Step 3: Development of classification system GSASA V2

Revision of version 1

The GSASA working group reviewed the results of the validation of GSASA V1. Conclusions were drawn and discussed until consensus was reached.

Translation

The GSASA working group translated the German GSASA V2 into French during an open discussion. For the purpose of this paper, we additionally translated version 2 into English.

Step 4: Reliability of classification system GSASA V2

Inter-rater reliability

The GSASA working group assessed the inter-rater reliability of the German and French versions of GSASA V2 as described in step 2. They classified the same 10 model cases using the GSASA V2.

Results

Step 1: Development of classification system GSASA V1

The first version included 4 main categories and a total of 35 subcategories, i.e., detected problem (3 subcategories), cause of intervention (17 subcategories), intervention (10 subcategories), and outcome of intervention (5 subcategories).

Step 2: Validation of classification system GSASA V1

Appropriateness, interpretability, and validity

DRPs were collected from daily work on the wards during a 6-week period. We classified 115 DRPs with PCNE V6.2 and GSASA V1. The proportion of the classified cases and the categories involved are shown in Table 1. In both classification systems, the majority of the cases could be completely classified (PCNE 81.7 %, GSASA 80.9 %).

Acceptability and feasibility

The six pharmacists completed an 8-item questionnaire on the usability of PCNE V6.2 and GSASA V1 using a 5-point Likert scale. Data was compared using Mann–Whitney *U* Test. The results of the questionnaire were not statistically significant. Table 2 shows the differences of the results for acceptability and feasibility of the two classification systems (questions 1–7).

Question 8 allowed the pharmacists to record their comments and suggestions. The subcategories 'untreated

Table 1 Proportion of classified cases per system and per category

	PCNE V6.2		GSASA V1	
	n	%	n	%
All cases	115	100	115	100
Completely* classified cases	94	81.7	93	80.9
Per category				
Problem	106	92.2	99	86.1
Cause	108	93.9	110	95.6
Intervention	110	95.6	114	99.1
Outcome	115	100	115	100

* Classification was considered complete when all categories were filled out

indications' and 'documentation errors' were missing in the category 'problem', 'duplication' and 'insufficient effect of drug treatment/inappropriate drug' in the category 'cause' and 'recommendations of laboratory test' in the category 'intervention'.

Inter-rater reliability

Figure 2 illustrates the inter-rater reliability of the four classification categories, i.e., problem (GSASA V1 $\kappa = 0.66$, PCNE V6.2 $\kappa = 0.32$), cause (GSASA $\kappa = 0.53$, PCNE $\kappa = 0.44$), intervention (GSASA $\kappa = 0.74$, PCNE $\kappa = 0.40$), and outcome (GSASA $\kappa = 0.63$, PCNE $\kappa = 0.52$). The three pharmacists showed a fair agreement for the category 'problem' and a moderate agreement for the other categories of the PCNE classification system. In comparison, GSASA V1 reached a moderate agreement for the category 'cause' and a substantial agreement for the other categories.

Step 3: Development of classification system GSASA V2

The results of the validation of GSASA V1 and the suggestions from the six users were discussed in the expert group, and resulted in the addition of one new category 'type of problem' and seven new subcategories, and in the modification of three subcategories. The subcategory 'untreated indication' was moved from the category 'cause' to 'problem'. The major change concerned the category 'detected problem'. To precisely describe the DRPs, we included two additional subcategories to this category, and introduced the new category 'type of problem' to differentiate potential and manifest DRPs. Table 2 describes the English version 2 and the modifications with respect to version 1. The resulting

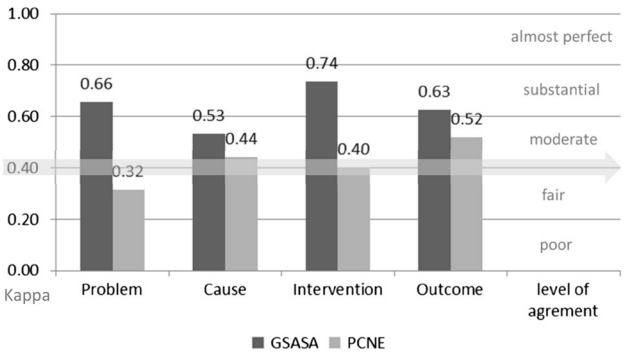

Fig. 2 κ-Coefficients of PCNE V6.2 and GSASA V1 classification systems for the four categories, based on standard cases (n = 10) classified by raters (n = 3)

classification system GSASA V2 includes 5 categories with a total of 41 subcategories as follows: detected problem (5 subcategories), type of problem (potential/manifest) (2 subcategories), cause of intervention (18 subcategories), intervention (11 subcategories), and outcome of intervention (5 subcategories) (see Table 3).

Only one choice per category is possible. Therefore, if a detected problem involved multiple interventions, each intervention required the use of a new form or line in the Excel sheet. An example to illustrate this classification is given in Fig. 3.

Step 4: Reliability of classification system GSASA V2

Inter-rater reliability

The working group assessed the level of agreement of the version V2 in German and French (Table 4). They classified the same 10 cases used in step 2. Inter-rater reliability was moderate ($\kappa = 0.52$) for all categories.

Table 2 Users' agreement on the classification systems adapted from AbuRuz et al. [14]

	GSASA V1		PCNE V6.2	
	Mean ± SD	Median	Mean ± SD	Median
(1) The classification system was comprehensive and included all drug-related problems I identified (n = 6)	2.7 ± 0.8	2.5	3.8 ± 1.0	4
(2) I did not have problems finding out the proper classification of drug-related problem I identified (n = 6)	3.2 ± 0.8	3	3.0 ± 0.9	3
(3) The classification system was easy to use and practical (n = 6)	4.0 ± 0.0	4	3.0 ± 0.9	3
(4) I will use the classification in my practice in the future (n = 6)	3.8 ± 0.8	4	4.0 ± 0.6	4
(5) In general, I am satisfied with the classification system (n = 6)	3.5 ± 0.5	3.5	4.0 ± 0.6	4
(6) The expenditure of time to classify the problems was adequate (n = 6)	3.5 ± 0.8	4	2.7 ± 0.8	2.5
(7) The classification would be a good tool to document the activities of hospital pharmacy/clinical pharmacy (n = 5)	4.0 ± 0.7	4	3.6 ± 0.5	4

Table 3 Description manual of the classification system GSASA V2 and illustrations with examples (bolded text category or subcategory added for version 2, italicized text subcategory modified)

Code	Category	Code	Subcategory	Subcategory description	Example
1	Detected problem	1.1	Treatment effectiveness	Any problem or circumstance which may modify the effectiveness of a medication (type of problem: potential), or any signs or symptoms (type of problem: manifest) suggesting lacking or unsatisfactory effectiveness	No effect of the quinolone therapy due to formation of non-absorbable complexes with multivalent cations
		1.2	**Untreated indication**	Preventive, therapeutic, or concomitant medication not prescribed for a valid indication	No laxative prescribed together with opioid therapy
		1.3	Safety of treatment	Any problem or circumstance which may expose the patient to an increased risk for an adverse drug event (type of problem: potential) or any signs or symptoms (type of problem: manifest) suggesting a lacking or unsatisfactory medication safety	Risk of torsades de pointes due to combination of amiodarone and clarithromycine
		1.4	Treatment costs	Any issue associated with the cost of a drug treatment (e.g., high price, reimbursement, cost-effectiveness, patient's economic situation, generic substitution)	Switch original product to generic (generic substitution) because of lower treatment costs; i.v antibiotics administration longer than necessary
		1.5	**Patient dissatisfaction**	Any complaint or concern regarding drug therapy expressed by the patient or the caregivers/relatives	Patient complains about high number of prescribed drugs, about swallowing difficulties, lack of information, etc
2	**Type of problem**	**2.1**	**Manifest**	Patient shows signs or symptoms of an adverse drug event, therapy failure or non-treatment. Problem is present → Reactive, corrective intervention	Electrocardiogram shows QT interval prolongation induced by clarithromycine in combination with amiodarone
		2.2	**Potential**	Patient is at risk for an adverse event but does not present signs or symptoms of adverse clinical outcomes Problem is in the future → Preventive intervention	Loss of cardio protective effect of acetylsalicylic acid (ASS) in combination with ibuprofen causes an increased risk for myocardial infarction
3	Cause of intervention	Therapy choice			
		3.1a	No concordance with guidelines or contraindication	Drug selection does not comply with treatment guidelines	ASS is not prescribed in a patient after myocardial infarction
				Patient shows a contraindication to the therapy due to his medical conditions	Metformin contraindicated in patient with renal failure
		3.1b	*Drug not indicated or duplication*	Drug use without an indication or inappropriate use of two drugs from the same therapeutic class	Potassium supplementation in spite of normal blood level Combination of ACE inhibitor and angiotensin receptor blocker
		3.1c	Interaction	Combination of a drug with another drug or with food representing a potential or manifest negative outcome	Calcium in combination with levothyroxine
		3.1d	Adverse effect	Response to a drug that is noxious and unintended and occurs at doses normally used in man for the prophylaxis, diagnosis or therapy of disease, or for modification of physiological function	Tremor as sign for lithium toxicity
		3.1e	**Incomplete patient documentation**	Lack of patient information in case notes/ laboratory results	Allergies not reported in patient cases
		Drug choice			
		3.2	Inappropriate dosage form	Wrong drug administration route or method, or wrong form, or incompatibility	Sustained release tablets crushed for the administration through feeding tube

Table 3 continued

Code	Category	Code	Subcategory	Subcategory description	Example
		Dose choice			
		3.3a	Underdose	Prescribed dose too low	Pantoprazol 20 mg in duodenal ulcer
		3.3b	Overdose	Prescribed dose too high	Prescribed dose of acetaminophen exceeds maximal daily dose
		3.3c	Inappropriate monitoring	Inappropriate process of observing, recording and detecting the effects or safety of a therapy, incl. therapeutic drug monitoring (TDM)	No thyroid hormones control in substituted hypothyroidism Wrong timing of blood collection for determination of drug serum levels
		3.3d	**Dose not adjusted to organ function**	No dose adjustment required due to organ impairment (renal/liver failure, etc.) and pathological changes	High dose allopurinol was prescribed daily in renal impairment
		Therapy duration			
		3.4	Inappropriate therapy duration	Duration of therapy too long or too short	Folic acid substitution in spite of adequate serum levels Too short antibiotic therapy; too long topical application of a cortisone cream
		Drug use			
		3.5a	Treatment not received	Any problem or circumstance which prohibited the patient to get the treatment originally prescribed	The nurse forgot to administer a prescribed dose
		3.5b	*Inappropriate timing or frequency of administration*	Wrong timing of drug intake regarding circadian rhythm or food intake, or no respect of the dosing interval	Bisphosphonate intake with breakfast Nitrate-free interval too short
		Logistics			
		3.6a	Prescribed drug not available	Drug not in stock, drug shortage or any other logistic problems in drug provision	Drug prescribed, but not in stock
		3.6b	Error in medication process	Any error appearing during drug prescription, transcription, distribution or administration	No transfer of the indicated drug from the prescription sheet to the case notes (transcription error)
		Patient			
		3.7	Insufficient compliance	Patient does not take his medication as prescribed	Patient forgot to intake a prescribed drug
		Others			
		3.8a	Insufficient knowledge of caregivers	Caregivers (e.g., nurse, physician) lack information about therapy or disease	Physician does not know about a drug–drug interaction
		3.8b	Insufficient knowledge of the patient	Patient lacks information about their medication or disease	Patient does not know how to use an asthma device
4	Intervention	4.1	Therapy started/ restarted	Introduce a drug to the treatment plan	Restart oral anticoagulants after bridging with heparin
		4.2	Therapy stopped	Withdraw a drug without substitution by another drug	Stop proton pump inhibitor, which was prescribed without indication/ risk factors
		4.3	Substitution	Replace a drug by another for the same indication	Switch from esomeprazole to pantoprazole
		4.4	Dose adjustment	Adjust drug dose or therapy duration regarding medical and personal conditions	Reduce enalapril dose due to renal insufficiency
		4.5	Therapy monitoring	Observe, record, or detect the effects of a drug administered to an individual, by indication of safety or efficacy, incl. TDM	Suggest medical analysis of uric acid in suspicion of gout Suggest TDM in a patient treated with vancomycin

Table 3 continued

Code	Category	Code	Subcategory	Subcategory description	Example
		4.6	Change of administration route	Find an appropriate drug administration route	Switch intravenuous antibiotic therapy to oral therapy
		4.7	Optimisation of administration	Change the treatment plan to suit patient or to optimise drug response, regarding e.g., meal interval, posture, fasting intake, swallowing difficulties	Recommend bisphosphonate intake on empty stomach and in upright position
		4.8	Counselling of patient, training	Advice and educate patient about his medicines	Instruct the use of an asthma device
		4.9	Information to caregivers	Inform caregivers about any problem or circumstance	Explain a potential drug–drug interaction
		4.10	Clarification in the case notes	Complete or correct patient notes	Clarify a prescribed drug without indication in the case notes
		4.11	**Report to pharmacovigilance centre**	Report ADR of medicines to a reporting centre/health authorities	Report a case of agranulocytosis observed under metamizol therapy
5	Outcome of intervention	5.1	Accepted	Recommendation of intervention approved by physician and implemented	Drug without indication is stopped
		5.2	*Partially accepted without implementation*	Recommendation of intervention partially approved by physician but not implemented or not possible to implement	Drug without indication is evaluated (search for diagnosis or clarify with the patient), or physician accepted the recommendation but not the patient
		5.3	Not accepted	Physician does not agree with recommendation	Drug without indication is continued without clarification
		5.4	Not known	Outcome of intervention not known	No feedback after written recommendation
		5.5	Not applicable	Intervention needing no approval or implementation	Information given to the caregiver

Discussion

Our study showed that most (80.9 %) of the 115 pharmaceutical interventions could be documented with the first GSASA classification system V1 and a similar ratio of 81.7 % with the PCNE classification V6.2, our benchmark. Moreover, we found comparable inter-rater reliability and acceptability for the GSASA and PCNE systems. On the other hand, the comparative evaluation of the two systems revealed differences with respect to usability. Indeed, the category 'intervention' of the GSASA system allowed a more complete classification of the cases than the PCNE. This reveals that our system respected his original approach, which was focusing on recording the interventions.

The structure of the two systems could also explain these differences. The four main categories of GSASA V1 corresponded with the ones of PCNE V6.2. However, PCNE V6.2 contained a twofold larger choice of subcategories (n = 71) than GSASA V1 (n = 35) enabling the precise classification of most DRPs. Consequently, users could find the PCNE instrument to be more comprehensive

The case

An immunosuppressed patient is treated for gout with allopurinol 100 mg. According to his chronic renal failure (creatinine concentration in serum 200 µmol/L, GFR 25 mL/min), a daily dose of <100 mg is appropriate. The physician agreed with the recommendation of monitoring the uric acid levels and adapting the dose according to the laboratory data.

The classification GSASA V2

1) detected problem: Safety of treatment (code 1.3)
2) type of problem: Potential (code 2.2)
3) cause of intervention: Dose not adjusted to organ function (code 3.3d)
4) intervention: Therapy monitoring (code 4.5)
5) outcome of intervention: Accepted (code 5.1)

Fig. 3 Example of a pharmaceutical intervention classified as a drug-related problem according to classification system GSASA V2

Table 4 Level of agreement of the GSASA V2 among experts (n = 8), 10 standard cases

	Kappa coefficient (agreement)		
	French-speaking experts (n = 4)	German-speaking experts (n = 4)	All experts (n = 8)
Detected problem	0.58 (moderate)	0.26 (fair)	0.43 (moderate)
Type of problem	0.48 (moderate)	0.66 (substantial)	0.57 (moderate)
Cause of intervention	0.53 (moderate)	0.56 (moderate)	0.55 (moderate)
Intervention	0.77 (substantial)	0.40 (moderate)	0.58 (moderate)
Outcome of intervention	0.44 (moderate)	0.51 (moderate)	0.48 (moderate)
Average agreement	0.56 (moderate)	0.48 (moderate)	0.52 (moderate)

than the GSASA system, knowing that, due to the small number of raters, the comparison of both tools showed no statistically significant results. In contrast, the GSASA system could be easier to use and more practical than the PCNE system. Time is an essential element for the acceptance of a classification system. In routine settings, application of the GSASA system in clinical practice demonstrated this tool to be less time-consuming than the PCNE system. This important factor should increase the chances of a successful and systematic use of the GSASA system. By addition or modification of several subcategories, the number of non-classifiable cases should decrease. In this way, the usefulness/comprehensiveness of the GSASA system could be enhanced without affecting its well-established practical use. In summary, the validation of the two existing systems showed an acceptable performance in enabling documentation and a better acceptability and feasibility of the GSASA system. The comments of the users provided helpful input for further improvement and the development of the classification system GSASA V2.

The goal of this development process was to create a classification system that permits the classification of DRPs detected and the recording of any pharmaceutical intervention. Van Mil et al. describe essential characteristics of classification systems [10]. Accurate classification of a detected problem should lead to only one choice per category. Therefore, the comprehensiveness of our instrument allows its systematic use and the consistency in the documentation of the interventions. Its detailed description manual, illustrated with practical examples, should enable homogenous data collection. In this way, the classification system would allow to collect and pool data from different sites, and by this generating a representative overview of clinical pharmacy activities within a given region. As a disadvantage, our instrument allows limited entry of details on individual cases. However, its open structure enables to enter additional and important information about the coded interventions.

The classification GSASA V1 reached good inter-rater reliability. Indeed, the four classification categories of GSASA V1 ($\kappa = 0.64$, which indicated a substantial agreement) was more reliable than the four categories of PCNE V6.2 ($\kappa = 0.42$, moderate agreement). Inter-rater reliability of GSASA V2 ($\kappa = 0.52$) was acceptable, although the κ-coefficients were lower than those calculated for the initial version. This decrease of the inter-rater agreement can be explained by the extension of the classification system from 4 to 5 categories. Additionally, the raters for the second version were more heterogeneous in terms of language, professional experience, and clinical background. Due to minor changes in GSASA V1 only inter-rater reliability was repeated when revalidating GSASA V2.

Average inter-rater agreement for GSASA V2 was moderate ($\kappa = 0.52$). This Kappa value was similar to that of the DOCUMENT [5] instrument ($\kappa = 0.53$), a recent validated system for classifying DRPs and clinical interventions in community pharmacy. Similarly, the APS-Doc system obtained a substantial agreement for the categories and a moderate agreement for the subcategories [4]. Considering that (a) the pharmacists involved in our study had only little experience with the GSASA system, (b) they had never used a description manual to aid in DRPs classification, and (c) that Kappa value higher than 0.4 indicates the internally acceptability and the good comprehensiveness of the classification system, these results fulfil the minimum requirement for an acceptable classification system. In the future, the use of the descriptive manual to assist with the classification should improve the Kappa score.

This study involved several limitations. As in most classification systems, subcategories are not mutually exclusive. The GSASA system shows similarities with the PCNE and SFPC systems, which it stemmed from. The validation and reliability of GSASA V1 were based on a small number of pharmacists (n = 6 and 3, respectively), so we cannot exclude a selection bias. Many raters were involved in the different stages in the development process. Therefore, we cannot ensure the generalisability of the system. We limited the validation of GSASA V2 on reliability as only minor changes were required in the first version. We considered most results of GSASA V1 validation as transferable to GSASA V2. To enable its implementation we tested the classification system in a limited number of

users (n = 8). All were qualified clinical pharmacists, each classifying 10 cases. On-going projects aim to evaluate the implementation and the user's satisfaction of GSASA V2 in daily practice and to analyse the pooled data retrieved from Swiss hospitals. In addition, we are currently adapting the system to also suit the community pharmacy setting and to support seamless documentation and transition from secondary to primary care.

Conclusion

The intervention oriented classification system GSASA V2 appeared to be valid and easy to use in daily clinical practice. The system is validated in terms of appropriateness, interpretability, validity, acceptability, feasibility, and reliability. The description manual assists in categorisation and hereby will increase the quality of data due to an appropriate use of the standardised classification system. Systematic use of the procedure will provide information on the performance of clinical pharmacy services on the whole. On-going epidemiological research aims to merge all interventions classified with the classification system GSASA V2 in Switzerland and to evaluate its implementation.

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