Original Article

Validating a Drug-Related Problems Classification System in Outpatient Setting in Iran

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ABSTRACT

Objective: Medication Therapy Management service (MTMs) has been introduced to improve cooperation among pharmacists and other healthcare professionals in the management of chronic diseases, drug therapy, and patients on polypharmacy. One part of MTMs is detection and resolution of possible drug-related problems (DRPs). Nowadays, numerous DRPs classification systems are available, but due to some defects none of them are currently accepted and implemented universally. The purpose of this study is to design and validate a comprehensive system for classification and documentation of possible DRPs for the Iranian patients. **Methods:** In this methodological study, four classification systems were studied, and their differences were reviewed, compared. Ultimately, a comprehensive documentation system was developed and tested for validity using experts' opinions. **Findings:** A comprehensive list of 53 DRPs under eight categories was developed and examined for validity. After collecting the data and validity assessment, questions with content validity ratio of <0.4 and content validity index of <70% were excluded and modified. Finally, with the exclusion and modification of eight DRPs, a modified DRPs list was created. **Conclusion:** According to the universality and validity assessment and based on consensus of 20 experts, this DRPs list can be used to regulate the standard operation procedure of outpatient clinics in Iran, and could act toward standardization of this service.

KEYWORDS: *Drug-related problems, medication therapy management, pharmaceutical care, validation*

INTRODUCTION

About 20 years ago, pharmaceutical care was introduced as "the *responsible provision of drug therapy for the purpose of achieving definite outcomes that improve a patient's quality of life.*"[1] Accordingly, the concept of medication therapy management services (MTMs) was introduced for the first time in the Medicare Modernization Act of 2003 to improve cooperation among pharmacists, physicians, and other health-care professionals in the management of chronic diseases, drug therapy, and patients on polypharmacy.[2-5] One of the most important parts of the MTMs is detection and resolution of possible drug-related problems (DRPs).[6] DRPs is *"an event or circumstance involving drug treatment that actually or*

potentially interferes with the patient experiencing an optimum outcome of medical care."[7] Documentation is one of the core elements of the MTMs.[8] According to the Patient Protection and Affordable Care Act, any pharmacist that works in the MTM clinic should document all important and essential information, such as the list of medications as well as the list of DRPs and interventions.[9]

Documentation is key to accurate clinical coding, validating the length of stay, resource utilization, physician profiling, case management and determining

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the severity of illness, assessing the risk of mortality, quality management, risk management, clinical outcomes, regulatory compliance, joint commission accreditation, managed care, and reimbursement.[8] Good documentation minimizes coding errors, reduces claim denials, and optimizes reimbursement, and in the long run, it can improve the service and operation of MTM clinics. Implementing quality improvement strategies that make documentation and coding an organizational priority can positively influence operations, services, and revenue.[8] A classification system appears to be essential to cover and classify all the possible DRPs in this setting method for interprofessional communication, follow-up monitoring, prevention of potential and actual DRPs, development of pharmaceutical care practice, and pharmaceutical care research.[10,11]

Nowadays, more than 20 DRPs classification systems are available. The most important and most implemented DRPs classification systems currently used in Iran are: Cipolle *et al.*,[3] DOCUMENT[11] Westerlund *et al.*,[12] and pharmaceutical care network Europe classification system.[13] Each of these classification systems has some defects, and none of them is absolutely comprehensive and universally valid and accepted.[14] Table 1 provides a comparison of information on these classification systems.[15]

Today in Iran, there are four university-affiliated MTM clinics currently operating with different documentation systems. However, since each DRPs classification system mentioned above has some defects and none of them is absolutely comprehensive, universally valid and accepted,[15] and they differ in the classification of possible DRPs, these centers cannot share data with each other. The purpose of this study is to develop and validate a comprehensive classification system for DRPs documentation for the Iranian patients.

METHODS

A preliminary study was conducted between December 2016 and May 2017 in Ahvaz Jundishapur University of Medical Sciences (AJUMS). In this study,

a group of experts was formed in MTMS including clinical pharmacy specialists who were practicing in MTM clinics (faculty members of the clinical pharmacy department at AJUMS and MTM consultants in 13-Aban pharmacotherapy clinic in Tehran). This group evaluated different DRPs classification systems from several aspects such as the adaptation of their process to the Iranian pharmacy practice, ability to implement them in MTM clinics, collection of these classification systems to include all potential DRPs based on various coding systems and the legal aspects of the health system. Ultimately, a comprehensive list of all possible DRPs consisting of 8 groups and 53 subgroups was created [Table 2], underwent validity test using experts' evaluation.

For the content validity test, we used the content validity ratio (CVR) and the content validity index (CVI). CVR is a linear transformation of a symmetrical level of concurrence on how many "experts" within a penal rate an item as essential, this formula yields values ranging from +1 to −1; positive values demonstrate that at least half of the experts rated the item as essential. The mean CVR across items may be used as an indicator of overall test content validity.[16] CVI is the most widely used method of quantifying content validity for multi-item scales which is based on expert ratings of relevance.[17] Accordingly, a questionnaire containing a list of the proposed 53 DRPs was presented to 20 clinical pharmacy specialists and residents of clinical pharmacy who had experience in MTMs setting. Each DRP was evaluated as necessary, useful but unnecessary and unnecessary. The collected data were then tested for validity using CVR and CVI. The minimum number of experts required to approve a DRP as essential was calculated as 14 by CRITBINOM function.[18] This test is usually used for measuring content validity.

After data collection and validity assessment, questions with CVR of <0.4 and CVI of <70% were excluded from the study.

For assessment of construct validity of the DRPs classification systems, three methods including convergence (the correlation coefficient of these two classification systems [our system and DOCUMENT] with the patient data), the comparison method between our classification system and DOCUMENT system, and factorial validity were used.[19]

To evaluate the criterion validity, we used Receiver Operating Characteristic (ROC) curve. For this purpose, the area under the ROC curve should be considered, where the values closer to 1 possess a greater criterion validity.[20]

For the face validity, we could use quantitative and qualitative parameters, because the quantitative face

Table 1: Drug-related problems classification systems

DRP classification system	Health care setting	Number of category
Cipolle[3]	Multiple	7 categories
DOCUMENT[11]	Community Pharmacy	8 categories and 30 subcategories
PCNE[13]	Multiple	4 categories and 11 subcategories
Westerlund[12]	Community Pharmacy	11 categories

PCNE=Pharmaceutical Care Network Europe

validity is only for questionnaires and needs participant's comments. Furthermore, regarding the specialty of items and their unfamiliarity to patients, we used qualitative face validity. For this purpose, experts' comments were asked about each of DRPs, and they were used to find the level of difficulty, the degree of mismatch, and ambiguity of phrases.[21]

RESULTS

The proposed DRPs classification system and the results of the panel rating of DRPs are presented in Table 2.

For face validity, the expert's comments were utilized to modify and optimize the DRPs classification system.

The correlation coefficient of our DRPs classification system and DOCUMENT was 0.621 and 0.897, respectively [Table 3].

The statistical significance of our system's score was less than that of the DOCUMENT system in construct validity. Our system with one factor had 87% variance. DOCUMENT system with four factors, factors one and two accounted for 58% and 69% variance, respectively. In the construct validity analysis of our system and DOCUMENT system, one factor was obtained. According to the results in Table 4, the construct validity of the system was confirmed.

For criterion validity, the area under the ROC curve for our system and DOCUMENT was 0.78 and 0.96, respectively. The obtained levels of the curves for our system were acceptable and well evaluated.

The excluded and the modified DRPs are as follows: precaution apparent (CVI = 55%),

Table 2: The proposed drug-related problems classification system and the results of the panel rating of drug-related problems

Category	DRPs	Necessary	Useful but unnecessary	Unnecessary	CVI (%)	CVR
Drug Selection	Duplication	18	1	1	90	0.8
	Drug interaction	19	1	0	95	0.9
	Wrong drug	18	1	1	90	0.8
	Incorrect strength	15	2	3	75	0.5
	Inappropriate dosage form	18	1	1	90	0.8
	Precaution apparent	11	5	4	55	0.1
	Contraindication	15	4	1	75	0.5
	No indication apparent	14	5	1	70	0.4
	Using expired drugs	14	4	2	70	0.4
	Lack of efficacy	15	2	3	75	0.5
	More effective drugs	13	5	2	65	0.3
	Lack of proper medication storage	19	1	0	95	0.9
	Inappropriate medical treatment period	18	0	2	90	0.8
	Other drug selection problem	14	4	2	70	0.4
Over or Under use	Prescribed dose too high	19	0	1	95	0.9
	Prescribed dose too low	18	0	2	90	0.8
	Unclear dose instruction	19	1	0	95	0.9
	Dose adjustment	18	1	1	90	0.8
	Wrong time medication administration	16	3	1	80	0.6
	Other dose problem	13	1	6	65	0.3
Compliance	Under use by consumer	15	4	1	75	0.5
	Over use by consumer	17	3	0	85	0.7
	Erratic use of medication	16	4	0	80	0.6
	Drug misuse	14	4	2	70	0.4
	Difficulty using dosage form	15	3	2	75	0.5
	Noncompliance due to not believing in medication efficacy	12	5	3	60	0.2
	Noncompliance due to ADR and toxicity concern	14	3	3	70	0.4
	Failure to learn drug Administration	16	0	4	80	0.6
	Forgetting to take medication	14	3	3	70	0.4
	Other compliance problem	12	4	4	60	0.2

Contd...

Table 2: Contd...

Category	DRPs	Necessary	Useful but unnecessary	Unnecessary	CVI (%)	CVR
Undertreated	Condition undertreated	15	3	2	75	0.5
	Condition untreated	14	4	2	70	0.4
	Preventive therapy required	18	1	1	90	0.8
	Other untreated indication problem	13	6	1	65	0.3
Monitoring	Laboratory monitoring	20	0	0	100	1
	Nonlaboratory monitoring	17	3	0	85	0.7
	Other monitoring problem	12	4	4	60	0.2
Education or Information	Consumer requests drug information	16	4	0	80	0.6
	Consumer requests disease management advice	16	3	1	80	0.6
	Lack of patient knowledge about disease and medication	16	2	2	80	0.6
	Medical devices training and education	17	2	1	85	0.7
	Other education or information problem	15	4	1	75	0.5
	Drug shortage	15	3	2	75	0.5
	The high cost of medicine ratio patient outcome	15	3	2	75	0.5
Not Classifiable	Not classifiable under another category	12	4	4	60	0.2
Toxicity	Toxicity due to dose	19	0	1	95	0.9
	Toxicity due to interaction	18	1	1	90	0.8
	ADR	18	0	2	90	0.8
	Side effect of start or sudden increase of the dose	17	3	0	85	0.7
	Inadequate drug safety for patient	15	3	2	75	0.5
	Risk of toxicity due to long term use of medication	14	5	1	70	0.4
	Drug allergy	14	4	3	70	0.4
	Other toxicity problems	14	5	1	70	0.4

DRPs=Drug-related problems, CVI=Content validity index, CVR=Content validity ratio, ADR=Adverse drug reaction

Table 3: Correlation coefficient of drug-related problems classification system

Classification systems	DRPs	Item-scale correlations
Our classification system	1	0.5
DOCUMENT	1	0.95
	2	0.94
	3	0.84
	4	0.75

DRPs=Drug-related problems

Table 4: Factor loading of drug-related problems classification system

Classification systems	DRPs	First factor	Second factor
Our classification system	1	0.89	0.91
DOCUMENT	1	0.59	0.45
	2	0.76	0.69
	3	0.49	0.73

DRPs=Drug-related problems

more effective drugs (CVI = 65%), other dose problems (CVI = 65%), noncompliance due to not believing in medication efficacy (CVI = 60%), other compliance problems (CVI = 60%), other untreated indication problems (CVI = 65%), other monitoring problems (CVI = 60%), and not classifiable under another category (CVI = 60%). Finally, with the exclusion and modification of eight DRPs, a new DRPs list with 7 categories and 45 subcategories was created [Table 5]. Given that the deleted items were mostly miscellaneous and the CVI average was more than 70% (S-CVI/Ave = 78.2%), the validity of the system was confirmed.

DISCUSSION

DRPs is one of the major health problems which can cause mortality, morbidity, and cost.[22] According to other studies, the incidence of DRPs in outpatient setting is high and comparable with that of inpatient setting.[23] Documentation and classification of DRPs are one of the most important parts of MTMs and pharmaceutical care processes.[24] Since the existing documentation system is neither universal nor comprehensive, developing a comprehensive system of classification to cover all possible DRPs across Iranian patients seems necessary. In this study, a number of the most widely used DRPs classification systems have been studied, and differences were compared and reviewed by a group of experts in MTMs independently. Ultimately, a comprehensive system was designed for classification and documentation of possible DRPs in Iranian patients,

Table 5: Categories of drug-related problems classification system

Category	Sub-category
Drug selection	Duplication (D1)
	Drug interaction (D2)
	Wrong drug (D3)
	Incorrect strength (D4)
	Inappropriate dosage form (D5)
	Precaution apparent and contraindication (D6)
	No indication apparent (D7)
	Using expired drugs (D8)
	Lack of efficacy or more effective drugs (D9)
	Inappropriate medical treatment period (D10)
Over or under use	Prescribed dose too high (O1)
	Prescribed dose too low (O2)
	Unclear dose instruction (O3)
	Dose adjustment (O4)
	Lack of proper medication storage (O5)
Compliance	Under use by consumer (C1)
	Over use by consumer (C2)
	Erratic use of medication (C3)
	Drug misuse (C4)
	Difficulty using dosage form (C5)
	Noncompliance due to safety or efficacy concern (C6)
	Failure to learn drug administration (C7)
	Forgetting to take medication (C8)
	Drug shortage (C9)
	The high cost of medicine ratio patient outcome (C10)
Undertreated	Condition undertreated (U1)
	Condition untreated (U2)
	Preventive therapy required (U3)
Monitoring	Laboratory monitoring (M1)
	Nonlaboratory monitoring (M2)
Education or information	Consumer requests drug information (E1)
	Consumer requests disease management advice (E2)
	Lack of patient knowledge about disease and medication (E3)
	Medical devises training and education problem (E4)
	Other education or information problem (E0)
Toxicity	Toxicity due to dose (T1)
	Toxicity due to interaction (T2)
	ADR (T3)
	Side effect of start or sudden increase of the dose (T4)
	Inadequate drug safety for patient (T5)
	Risk of toxicity due to long term use of medication (T6)
	Wrong time medication administration (T7)
	Drug allergy (T8)
	Other toxicity problems (T0)

ADR=Adverse drug reaction

and the validity of this DRPs classification was evaluated through questionnaires.

Compared to others DRPs classification systems such as Westerlund *et al.* system,[12] Cipolle *et al.* classification system,[3] and Hepler–Strand classification system,[1] our system had a greater emphasis on laboratory and nonlaboratory monitoring. Meanwhile, Cipolle *et al.* system does not classify drug interactions. Our list covers more DRPs than the other classification systems. For example, our classification system has separated patient compliance issues from education and information, which is not observed in any other classification system. As shown in Table 5, in addition by including medical device training (CVI = 85%), most of these DRPs were related to toxicity and side effects, which are less addressed in other systems. Our classification system was similar to that of the DOCUMENT system, except that our system covered more problems. Given the fact that many patients have difficulty in educational and information issues, and these problems increase the likelihood of occurrence of DRPs, it is necessary to pay attention to this issue, which has been adequately discussed in our system.

According to the universality and validity assessment, and based on consensus of 20 experts, this DRPs list can be used to regulate the standard operation procedure of outpatient pharmacotherapy clinics in Iran, and could act toward standardization of this service. Defnitely, the reliability of this system should also be examined in another study.

AUTHORS' CONTRIBUTION

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Conflicts of interest

There are no conflicts of interest.

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