Clinical pharmacist interventions in managing Key Monitoring Drugs in China

Jing Yang
Shandong Provincial Third Hospital
Lei Zheng
Shandong Provincial Third Hospital https://orcid.org/0000-0002-7820-6776
Yuyao Guan
Shandong Provincial Third Hospital
Xiaoli Zhang
Shandong Provincial Third Hospital
Chao Song (songchao2021@163.com)
Shandong Provincial Third Hospital https://orcid.org/0000-0002-2897-7927
Yuchao Gu
Ocean University of China

Research article

Keywords: Key Monitoring Drugs, drug cost, evidence-based medicine, rational drug use, Drug-related problems

Posted Date: August 24th, 2020

DOI: https://doi.org/10.21203/rs.3.rs-56430/v1

Abstract

Background Drug-related problems (DRPs) are common in hospitalized patients using Key Monitoring Drugs. Clinical pharmacy services could minimize drug-related harm and improve patient care.

Objective The aim of this study was to standardize the clinical application of Key Monitoring Drugs, reduce the Drug-related problems (DRPs) and drug costs by clinical pharmacist interventions.

Methods Clinical pharmacist formulate management measures for Key Monitoring Drugs using evidence-based medicine and analyze the DRPs of Key Monitoring Drugs over a period of 5 years from 2015 to 2019. The drug cost and DRPs of Key Monitoring Drugs within five years after interventions by clinical pharmacist.

Results In 2019, the total cost of the use of Key Monitoring Drugs decreased by 10.12 million CNY, in comparison to that in 2015. The proportion of revenue from Key Monitoring Drugs decreased by 11.49% from 2015 to 2019. The *per capita* drug cost of Key Monitoring Drugs gradually decreased, this resulted in a saving of 580.07 CNY from 2015 to 2019. The DRPs of Key Monitoring Drugs decreased by 45.50% from 2015 to 2019. Through administrative intervention, prescription review, information management, and pharmaco-economicevaluation, a scientific management system of Key Monitoring Drugs has been established, which can standardize the use of Key Monitoring Drugs and reduce their cost.

Conclusion Clinical pharmacists' interventions assisted in early detection Drug-related problems of Key Monitoring Drugs and prevention of the consequent patient harms.

Background

On July 1, 2019, the first batch of national Key Monitoring Drugs catalogue was released by the medical administration bureau of National Health Commission of the People's Republic of China. Key Monitoring Drugs are defined as"the drugs that help to increase the effect of the main therapeutic drugs or increase their efficacy by influencing the absorption, mechanism of action and metabolism of the main therapeutic drugs, or drugs that help to prevent and treat diseases or functional disorders"[1]. Key Monitoring Drugs included the following drugs: drugs enhancing the tissue metabolism; vitamins; electrolytes; enteral and parenteral nutrition; neurotrophic drugs; free radical scavenging drugs; traditional Chinese medicine for promoting blood circulation and removing stasis; auxiliary treatment drugs for liver disease; auxiliary treatment drugs for tumors; and other drugs as auxiliary treatment drugs.

In recent years, with the development of disease rejuvenation and modern medical treatment, medical expenses have increased year after year, of which drug expenses account for a large proportion. However, the use of Key Monitoring Drugs is growing rapidly owing to their wide indications and commercial promotions, and it leads to a lot of drug-related problems. Through prescription analysis, it can be found that there are lots of drug-related problems (DRPs) in the clinical application of Key Monitoring Drugs,

which imposes a huge economic burden on the patients, and places significant pressure on the medical insurance fund[2].

Global healthcare systems are aiming at improvement of patients' safety and prevention of drug-related problems (DRPs). Therefore, promoting the rational use of Key Monitoring Drugs is the key point in reducing the costs of drugs. In addition, there are many kinds of drugs of the same type and the criteria to use scientific methods to make comprehensive evaluation of the drugs of the same type, so that doctors can select drugs scientifically is also a problem to be addressed[3]. Since 2015, we have been in favor of scientific management of the Key Monitoring Drugs based on evidence-based medicine, and have made some achievements towards this end. The aim of this study was to assess the outcomes of the clinical pharmacist intervention in the irrational use of Key Monitoring Drugs, and to construct a sustainable and improved model of Key Monitoring Drugs management. Several decades ago, clinical pharmacist-led services for improving medication-safety in hospitals and in the community have been shown to improve both patient and costrelated outcomes. Clinical pharmacists participate in the design and implementation of clinical drug treatment programs, assist clinicians in drug selection and rational drug use, so that patients will not suffer or reduce drug-related damage, improve the level of clinical drug treatment, and improve the quality of life of patients.

The aim of this study was to standardize the clinical application of Key Monitoring Drugs, reduce the Drug-related problems (DRPs) and drug costs by clinical pharmacist interventions in a tertiary hospital of China.

Methods

Establishing management organization for Key Monitoring Drugs

The medical department and the pharmaceutical department jointly established a working group for the supervision and management of the rational use of the drugs and formulated measures for the management of their rational use in our hospital; its responsibilities included: the division of responsibilities foreach department, determining the scope of the Key Monitoring Drugs for catalogue, analysis of the dosage, statistics and intervention of DRPs. The key point was to determine the basic principles of the clinical application of the Key Monitoring Drugs and define the use of key drugs according to evidence-based medical practice.

Determination of the criteria for the evidence-based evaluation of the Key Monitoring Drugs

For Key Monitoring Drugs, the drug instructions provided by the manufacturer formed the main evaluation standard. For medication beyond the instructions, we referred to the treatment guide of each specialized disease and used a database to search the literature to find any available evidence. Finally, according to the afore-mentioned evidences, we preliminarily defined the indication, dosage, solvent selection, course of treatment, contraindications, and combination of the drugs. We should have also focused on the evaluation and classification of the evidence-based quality, and have established the

evaluation criteria based on theevidence level, and not referred to unqualified documentary evidence. At present, clinical studies that can be retrieved through the database mainly include randomized controlled trials, cohort studies, case-control studies, series of case studies, case reports, traditional reviews, and expert opinions or experiences. The widely accepted evidence classification standards are mainly the evidence classification standards of the evidence-based medicine centeratthe Oxford University, and the GRADE standard formed by combining various classification standards(the standards for evidence-based assessment are detailed in Table 1) [4,5]. The drug use “definition” of each Key Monitoring Drug was entered into the Prescription system, and preliminarily determine whether the Key Monitoring Drugs in the medical order are reasonable according to the above definition[6-8]. The system can remind the doctors immediately, such as “Drug selection”, “Dose selection”, and “Treatment duration” et al.

Table 1 Evaluation criteria

Type of evidence	Evaluation essentials
Guide	Whether the literature has been reviewed comprehensively in the past 12 months, whether the supporting evidence for each recommendation has been marked with the level and the source. When determining the clinical application according to the level of recommendation, if a treatment is recommended as a class, it can be used without contraindications, it can be used as a Class B recommendation, but it is noted that the evidence is not sufficient, and it can be used or not when the reason is sufficient, we should pay attention to the publication of new evidence at any time. If it is a recommendation of Class C or D, it indicates that the evidence is more lacking, with greater uncertainty, and it is clear that the auxiliary treatment drugs are unavailable.
Meta-review	Whether it is a systematic evaluation of randomised controlled trials, whether it has collected and included all relevant studies, whether it has evaluated the quality of a single trial, whether it has homogeneity among trials, whether it is meaningful, that is, how large and accurate the effect is, andthe reliability and application value of its conclusions can be judgedaccording to the evaluation of the authenticity and significance of the results of systematic evaluation.
Randomised controlled trial	High-quality evidence, but if there are limitations, inconsistent results, not providing direct evidence, inaccurate results, and biased reports, the level of evidence will be decreased. The quality level of evidence will be improved if the observational study is designed rigorously, implemented well, found to be of significant efficacy or there is a dose-response relationship.
Expert consensus	To determine whether expert opinions are reliable, this is mainly based on whether their opinions have sufficient evidence basis. If there is no evidence, it can be questioned. In the absence of research evidence, the consensus reached by multiple experts is relatively more reliable than that of individuals. For rare or complex conditions without research evidence, expert opinions have more important reference value.

Types and causes of DRPs of Key Monitoring Drugs and clinical pharmacists’ medication interventions

DRPs were identified and properly managed by the clinical pharmacists who provided their recommendations to the healthcare team for each medication order. The outcome of this study was the number of pharmacists’ interventions provided to manage encountered DRPs. The types and causes of DRPs and the proposed interventions were categorized according to the simplified form of the Pharmaceutical Care Network Europe drug related problem classification (PCNE-DRP), version 9.0. For each event, two clinical pharmacists reach a consensus on the final decision based on the potential or actual clinical harm to the patient [9-11].

Comparative analysis of drug cost

To evaluate the intervention effect of clinical pharmacists, the cost of Key Monitoring Drugs (total cost, *per capita* drug cost, proportion of Key Monitoring Drugs cost in total drug cost) was statistically analyzed from 2015 to 2019, and SPSS 21.0 software was used for single factor analysis [12,13]. Categorical variables were expressed as percentages and continuous variables were expressed as means and standard deviations. Statistical significance was set at p value < 0.05.

Results

Formulation of clinical application principles of Key Monitoring Drugs

The management group shall integrate all expert opinions and discuss with the pharmaceutical management professional committee to determine the principles of clinical application of Key Monitoring Drugs [14]. The general principle is as follows: When the Key Monitoring Drugs are used, the ratio of the drug cost and curative effect should befully considered, the least and the most economical drugs should be used to achieve the expected treatment purpose, and special attention should be paid to the use of Chinese patent medicine injections (see Table 2 for specific clinical application principles).

Table 2 Clinical application principles of Key Monitoring Drugs

Content	Specific requirement
Indication	It is not allowed to approve the indications for drug use beyond the drug specification. The indication medication shall be approved in strict accordance with the drug instructions. The indications for approval of over-specification must be evaluated by evidence-based medicine and recorded in accordance with the relevant provisions of over-specification drug use. The compound preparation of the two components should be carried out when suffering from two main diseases at the same time, otherwise it should not be used as the first drug.
Usage and dosage	Do not overdose. The single dose and daily dose shall not be higher than the recommended dose in the manual. Strictly follow the recommended administration frequency, solvent, and infusion concentration in the instructions. Do not exceed the course of treatment. Do not exceed the minimum number of days of treatment specified in the instructions. If a course of treatment is not prescribed in the instructions or evidence-base, it shall not exceed seven days.
Combined medication	Key Monitoring Drugsof the same type cannot be used in combination. Under non-special circumstances, each patient can only use one type of Key Monitoring Drugs (classified by pharmacological action and indication, no matter whether oral or injection). Special cases only include those where there are professional guidelines or authoritative evidence to recommend joint application.
Contraindication	Do not use contraindications, and do not use Key Monitoring Drugs with drug risks.
Rational use of traditional Chinese medicine injection	Oral administration is not suitable for injection administration. It should be used in strict accordance with the functional indications specified in the drug manual. Traditional Chinese medicine used for promoting blood circulation and removing blood stasis has a wide range of pharmacological effects, but to avoid adverse drug reactions, it is stipulated that: those with bleeding tendency shall not use this kind of medicine; this kind of medicine shall not be used in combination with non-steroidal anti-inflammatory drugs or platelet inhibition drugs. This kind of medicine belongs to the category of traditional Chinese medicine. While mastering its modern pharmacological action, it should be used according to the syndrome differentiation of patients' tongue and pulse signs to play its best role and effect, so as to combine traditional Chinese medicine and Western medicine in an appropriate manner.

Detailed rules for the use of the definition of key drugs

The drugs in the list of Key Monitoring Drugs were defined one-by-one, and have indicated supporting data and classification for the drugs beyond the instructions (see Supplemental Table1 for the catalogue of Key Monitoring Drugs). Table 3 shows an example of drug definition for the Key Monitoring Drugs.

Table 3 Definition of Key Monitoring Drugs

Drug name	Indications and limitations	Contraindication	Single maximum dose Maximum daily dose Maximum administration frequency Course of treatment Compatibility of solvents	Interactions and attention
Tanshinone II: a sodium sulphonate injection	The use for the auxiliary treatment of coronary heart disease, angina pectoris, and myocardial infarction.	Patients with a history of allergy to these drugs	80mg 80mg 1 time only 7 days 5% glucose injection or 0.9% sodium chloride injection 250-500ml	Alprostadil can enhance the efficacy, and the cardiac function should be closely monitored when the two drugs are combined.
Troxerutin Cerebro-protein Hydrolysate Injection	The compound preparation of the two components should be selected when suffering from two main diseases at the same time, otherwise it should not be used as the first drug.	1. Severe renal insufficiency is forbidden. 2. It is forbidden for patients with epileptic persistent state or grand mal.	10ml 10ml 1 time only 20 days 250-500ml 0.9% sodium chloride injection or 5% glucose injection	It should not be used with balanced amino acid injection. Adverse interactions with antidepressants can lead to inappropriate stress. At this time, it is suggested to reduce the dosage of antidepressants[6].
Vinpocetine injection	To improve the symptoms induced by cerebral infarction, cerebral haemorrhage and cerebral arteriosclerosis.	1. In the acute stage of intracranial haemorrhage, those who have not completely stopped bleeding after intracranial haemorrhage are forbidden; 2. Those who have serious ischemic heart disease and serious arrhythmia are forbidden.	30mg 30mg 1 time only 5% glucose or 0.9% sodium chloride injection Use no more than 14 days	When vinpocetine and methyldopa are used together, there is a slight synergistic effect on the latter, so it is suggested to monitor blood pressure when they are used together. Although there is no interaction between vinpocetine and drugs acting on nervous system, or antiarrhythmic and anticoagulant drugs at the same time in clinical research, it is still recommended to pay attention to the observation when using vinpocetine in combination[7].

Drug-related problems

Descriptive statistics were calculated for variables relating to the types of identified DRPs, medications associated with different types of DRPs [15,16]. The percentage error rate was determined by dividing the actual identified DRPs by the total number of reviewed drug prescriptions with potential DRPs. Types and causes of drug-related problems and clinical pharmacists'medication interventions can be seen in Table 4. The DRPs of Key Monitoring Drugs decreased by 45.50% from 2015 to 2019. The main DRPs were "Too many drugs prescribed for indication", "Inappropriate drug according to guidelines/formulary", "Inappropriate combination of drugs". The intervention is mainly the intervention proposed to prescriber, the intervention acceptance rate and the rate of solving problems increased year by year. After intervention proposed or discussed to prescriber, the intervention were accepted and fully or partially implemented by prescriber.

Table 4 Types and causes of DRPs and clinical pharmacists'medication interventions

The cause	Frequency (%)				
	2015	2016	2017	2018	2019
C1 Drug selection					
C1.1 Inappropriate drug according to guidelines/formulary	25(12.5)	22(11.64)	21(12.21)	21(12.88)	16(14.68)
C1.2 Inappropriate drug (within guidelines but otherwise contra-indicated)	14(7)	10(5.29)	9(5.23)	9(5.52)	2(1.83)
C1.3 No indication for drug	12(6)	13(6.88)	13(7.56)	11(6.75)	12(11.01)
C1.4 Inappropriate combination of drugs, or drugs and herbal medications, or drugs and dietary supplements	25(12.5)	23(12.17)	24(13.95)	23(14.11)	13(11.93)
C1.7 Too many drugs prescribed for indication	35(17.5)	27(14.29)	22(12.79)	23(14.11)	12(11.01)
C3 Dose selection					
C3.1 Drug dose too low	4(2)	5(2.65)	7(4.07)	5(3.07)	5(4.59)
C3.2 Drug dose too high	22(11)	17(8.99)	19(11.05)	16(9.82)	9(8.26)
C3.3 Dosage regimen not frequent enough	3(1.5)	5(2.65)	3(1.74)	2(1.23)	2(1.83)
C3.4 Dosage regimen too frequent	20(10)	21(11.11)	17(9.88)	15(9.2)	9(8.26)
C4 Treatment duration					
C4.1 Duration of treatment too short	10(5)	13(6.88)	7(4.07)	6(3.68)	6(5.5)
C4.2 Duration of treatment too long	17(8.5)	20(10.58)	16(9.3)	20(12.27)	11(10.09)
C9 Other					
C9.1 No or inappropriate outcome monitoring (incl. TDM)	13(6.5)	13(6.88)	14(8.14)	12(7.36)	12(11.01)
Total	200	189	172	163	109
Interventions					
I1 At prescriber level					
I1.1 Prescriber informed only	37(18.5)	26(13.76)	23(13.37)	20(12.27)	15(13.76)
I1.2 Prescriber asked for information	37(18.5)	30(15.87)	22(12.79)	19(11.66)	12(11.01)
I1.3 Intervention proposed to prescriber	72(36)	85(44.97)	89(51.74)	95(58.28)	64(58.72)
I1.4 Intervention discussed with prescriber	54(27)	48(25.4)	38(22.09)	29(17.79)	18(16.51)
I3 At drug level					
I3.1 Drug changed to ...	60(30)	59(31.22)	44(25.58)	40(24.54)	27(24.77)
I3.2 Dosage changed to ...	50(25)	48(25.4)	45(26.16)	40(24.54)	24(22.02)
I3.3 Formulation changed to ...	25(12.5)	19(10.05)	20(11.63)	22(13.5)	18(16.51)
I3.4 Instructions for use changed to ...	8(4)	9(4.76)	10(5.81)	9(5.52)	8(7.34)
I3.5 Drug paused or stopped	27(13.5)	29(15.34)	28(16.28)	28(17.18)	17(15.6)
I3.6 Drug started	30(15)	24(12.7)	25(14.53)	24(14.72)	15(13.76)
Intervention Acceptance					
A1 Intervention accepted	147(73.5)	151(80.32)	143(83.14)	138(84.66)	97(88.99)
A1.1 Intervention accepted and fully implemented	101(50.5)	109(57.67)	110(63.95)	115(70.55)	92(84.4)
A1.2 Intervention accepted, partially implemented	28(14)	30(15.87)	20(11.63)	13(7.98)	2(1.83)
A1.3Intervention accepted but not implemented	18(9)	12(6.35)	13(7.56)	10(6.13)	3(2.75)
A2 Intervention not accepted	53(26.5)	37(19.68)	29(16.86)	25(15.34)	12(11.01)
A2.1 Intervention not accepted: not feasible	23(11.5)	24(12.7)	23(13.37)	21(12.88)	8(7.34)
A2.2 Intervention not accepted: no agreement	30(15)	13(6.88)	6(3.49)	4(2.45)	4(3.67)
Status of the DRP					
O1 Problem solved	108(54)	120(63.49)	115(66.86)	111(68.1)	82(75.23)
O2 Problem partially solved	21(10.5)	19(10.05)	15(8.72)	17(10.43)	12(11.01)
O3 Problem not solved	71(35.5)	49(25.93)	42(24.42)	35(21.47)	15(13.76)

Effect evaluation: statistics of drug consumption under key monitoring

To evaluate the overall effect, the consumption of Key Monitoring Drugs was assessed from multiple perspectives, including the total amount used, the proportion of income of Key Monitoring Drugs, and the cost of Key Monitoring Drugs *per capita*.In 2019, the total cost of the use of Key Monitoring Drugs decreased by 10.12 million CNY (Figure 1), in comparison to that in 2015.

In 2019, compared with 2015, the proportion of revenue from Key Monitoring Drugs (revenue from Key Monitoring Drugs / total drug use) decreased by 11.49% (Figure 2).

From 2015 to 2019, the *per capita* drug cost of Key Monitoring Drugs of inpatients gradually decreased, and in 2019, this resulted in a saving of 580.07 CNY compared with that in 2015, the *per capita* drug cost of Key Monitoring Drugs of outpatients gradually decreased, and in 2019, this resulted in a saving of 74.61 CNY compared with that in 2015 (Figure 3).

SPSS 21.0 software was used for one-way ANOVA to assess the *per capita* Key Monitoring Drugs cost of in-patients. The data include the *per capita* Key Monitoring Drugs cost of in-patients in five years (2015-2019) and 60 months, which is expressed in the form of mean ± standard deviation ($x \pm s$). From the results in Figure 3, the *per capita* cost of Key Monitoring Drugs for in-patients has a downward trend in 2015-2019. Based on the results of one-way ANOVA, the *P*-value is less than the significance level of 0.01, which is statistically significant, indicating that the *per capita* cost of Key Monitoring Drugs for in-patients has decreased significantly in five years (Supplemental Table 2).

Discussion

To the best of our knowledge, this is the first prospective study describing the prevalence of drug-related problems in patients admitted to Key Monitoring Drugs in mainland China. DRPs are common in this patient population. This highlights the needs for clinical pharmacy service in the use of Key Monitoring Drugs. The causes of the DRPs identified were mainly at the drug selection, dose selection, treatment duration, this demonstrates the necessity of medication reconciliation by pharmacists. The interventions of the DRPs identified were mainly at the prescriber level, including prescriber informed only, prescriber asked for information, intervention proposed to prescriber, intervention discussed with prescriber. At drug level, most DRPs were drug changed to..., Dosage changed to …, Drug paused or stopped, Drug started. The intervention acceptance rate was increased from 73.5% to 88.99%, the rate of solved problem was increased from 54% to 75.23%.

We should make full use of evidence-based medicine to scientifically manage all the drugs that meet the definition of Key Monitoring Drugs to improve the safety of drug use, to put an end to the use of contraindications, and to reduce the phenomenon of unreasonable drug use, such as over-indications. The exploration and formation of an Key Monitoring Drugs information management platform to improve the work efficiency and coverage, and the formation of a new management modehave been realized. Meanwhile, we compared the pharmaco-therapeutics and pharmaco-economics of the same kind of Key

Monitoring Drugs with large dosage, so as to provide more scientific references for clinical drug selection [17].

This study focussed on how to evaluate the drug use scientifically and reasonably in the management of Key Monitoring Drugs. On one hand,through the use of evidence-based medicine to evaluate the rationality of drug use, it can provide cutting-edge safe and rational drug use services for clinical use and resolve the issues facing the multiple drug delivery schemes at present, which can not be evaluated in terms of efficacy and economics. On the other hand, it can strengthen the medical practice around the use of Key Monitoring Drugs and improve the comprehensive level and effect ontheir management[18,19]. Finally, through the collection of drug efficacy cases for the purposes of economic comparison, if a scientific and orderly evaluation standard for the same types of drugs can be formed, the selection of clinical drugs can provide more suitable suggestions for clinical needs and gradually achieve the ultimate goal of individualized drug use and refined drug treatment.

In April 2019, China's Health Commission issued the notice on drug use monitoring and clinical comprehensive evaluation, which requires comprehensive evaluation of drug use and applies the evaluation results to the improvement of local medical support system,clinical diagnosis, and treatment service quality. Key Monitoring Drugs are the agents that aid or increase the action of the principal drug (drugsynergism) or that affect the absorption, mechanism of action, metabolism, or excretion of the primary drug (pharmaco-kinetics) in such a way as to enhance its effects. It is commonly used in the prevention or treatment of cancer, and liver, cardiovascular, and cerebrovascular diseases. If the proper use of Key Monitoring Drugs is beneficial forthe recovery of patients fromthe disease, it can not only shorten the time of hospitalization, but can also reduce the cost of hospitalization so that the country's medical resources can be more effectively allocated. Conversely, it canincrease the risk of having adverse drug reactions due to increased use of combination of drugs or the unnecessary use of drugs. It canincrease the risk of having new adverse effects, prevent the rehabilitation of the original diseases, prolong the length of stay, and increase the economic burden on patients and the healthcare system.

How to strengthen the management of rational drug use and reduce the economic burden of patients has become a problem of public concern. The management of adjvant drugs has become an important part of the management of rational drug use. The current excessive use of Key Monitoring Drugs not only can easily lead to an increased incidence of adverse drug reactions and bodily damage, butcan alsoincrease the economic burden on patients, resulting in wastage of medical resources. In 2017, the Chinese State Council issued a number of opinions on further reforming and improving the policy ondrug production and circulation. The document requires monitoring the use of antibiotics, Key Monitoring Drugs, and nutritional drugs, publicizing the limits on irrational prescriptions, and establishing an interview system.

This is the first study to document clinical pharmacist-led interventions in identifying and solving DRPs in the Key Monitoring Drugs. The impact of the clinical pharmacists' long-term interventions on reducing the number of hospital readmission or financial saving was also evaluated compared with past studies [20-24]. However, this study is only conducted in one hospital, and the sample size is not large enough.

Conclusions

The clinical use of Key Monitoring Drugs has been standardized by the scientific management system of Key Monitoring Drugs established based on the prescription review, administrative intervention, information management, and pharmaco-economic evaluation. The use of Key Monitoring Drugs in our hospital has become increasingly standardized, the level of drug treatment has been improved, the proportion of Key Monitoring Drugs has decreased, and the unnecessary drug expenses for patients have been saved. This study has practical and effective reference value for the scientific management of Key Monitoring Drugs in other hospitals. Clinical pharmacists' recommendations assisted in prevention and alleviation of many DRPs and their further complications and were generally well-accepted by physicians.

Impacts on practice: The establishment of scientific management methods can promote the rational use of Key Monitoring Drugs and reduce the cost thereof. The clinical use of Key Monitoring Drugs has been standardized by the scientific management system, which was established based on prescription review, administrative intervention, information management, and pharmaco-economic evaluation. Clinical pharmacists' interventions assisted in early detection of drug problems and prevention of the consequent patient harms. The impact of the clinical pharmacists' interventions on reducing the number of hospital readmission or financial saving was evaluated also.

Declarations

Acknowledgments

We acknowledge the editors and the anonymous reviewers for insightful suggestions on this work. We would also like to acknowledge our outstanding colleagues working on the front lines of our hospital.

Authors' contributions

All authors have read and approved the manuscript. Jing Yang was the project leader, designing methodology, collecting data, analysing data and writing the manuscript. Lei Zheng was involved in review of the literature for this manuscript, data analysis and writing the manuscript. Yuyao Guan was involved in designing methodology, collecting data, analysing and interpreting data and writing the manuscript. Xiaoli Zhang was involved in interpretation of the data and preparation of the manuscript. Chao Song and Yuchao Gu were involved in the management of the project and data collection in China and contributed to the conceptualisation of the study and manuscript.

Funding

Shandong Province 2019 TCM science and technology development plan project: Construction of TCM evaluation system based on real world evidence, decision tree and Markoff model (2019-0329); Key projects of China Pharmaceutical Association for promoting the dissemination of precision medicine science and technology (grant no. CMEI2019KPYJ(JZYY)00204).

Availability of data and materials

The datasets used and/or analysed during the current study are available on reasonable request and with permission of the corresponding author.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests and no conflicts of interest related to the publication of this manuscript.

References

1. S. National Library of Medicine. Adjuvants,pharmaceu- tic[EB/OL]. [2016-06-27]. http://www.ncbi.nlm.gov/ mesh/68000277.
2. Herxheimer A. Educating doctors to use drugs well [editorial]. Br J of Clin Pharmacol1976; 3:111-112.
3. Han S, Zhong M T, Li J, Zhen Jiancun. The application status of Key Monitoring Drugs in our country and the management countermeasures study.Chin JPhar2016; 51:96-
4. Steurer J, Roner S, Gnannt R, Hodler J. Quantitative radiologic criteria for the diagnosis of lumbar spinal stenosis: A systematic literature review. Bmc Musculoskelet Disord2011; 12:175.
5. Zhào Hóngyi, Liu Yu, Zeng Jing,Huang Y. Troxerutin cerebroprotein hydrolysate injection ameliorates neurovascular injury induced by traumatic brain injury – via endothelial nitric oxide synthase pathway regulation. Int J of Neurosci 2018; 128:1118-1127.
6. Yu-Xing Y I, Zhang P, Wang R. Observation on the effect of Vinpocetine injection in treatment of the elder cerebral infarction.Chine JModern Drug Appl 2013; 83:327-331.
7. Moradi M, Mojtahedzadeh M, Mandegari A, et al. The role of glutathione-S-transferase polymorphisms on clinical outcome of ALI/ARDS patient treated with N-acetylcysteine. RespirMed 2009;103:0-441.
8. Neuroimmunology group of neuroimmunology branch of Chinese society of immunology, neuroimmunology group of Neurology branch of Chinese Medical Association, neuroimmunology group of Neurology Professional Committee of science and Technology Committee of Chinese people's Liberation Army. Diagnosis and treatment guide of central nervous system tumor like demyelinating disease. Chin JNeuroimmunolNeuro2017; 5:23-90

9. Jin H, Wang S, Hou L, et al. Clinical treatment of traumatic brain injury complicated by cranial nerve injury. Injury2010;41:918-923.
10. Wu S, Sena E, Egan K, Macleod M, Mead G. Edaravone improves functional and structural outcomes in animal models of focal cerebral ischemia: A systematic review. Int JStroke 2014; 9:101-106.
11. Xiaochen W, Liqin Z, Chunge W, Qi D,Xin L. Systematic review of the efficacy and safety of gangliosides in preventing chemotherapy-induced peripheral neurotoxicity. Chin J Clin Pharmacol2015;24:2462-2464.
12. Min L I, Tang Z Y, Shen X P. Efficacy and safety of low molecular weight heparin combined with edaravone in the treatment of progressive cerebral infarction:A systematic review. J EvidBased Med2013; 13:218-224.
13. Neural Injury and Repair Branch of Chinese Academy of Neuroscience. Expert Consensus on Neurological Damage and Repair of Brain Injury. Chin J Neurotrauma Surg (Electronic Edition)2016; 2:100-104.
14. Department of Neurological Injury, Traumatology Branch of Chinese Medical Association. Monosialic acid tetrahexose ganglioside sodium salt injection——Expert consensus on treating patients with brain and spinal cord injury. Chin J Trauma2010; 1: 6-8.
15. Gang SC, XueZY. Edaravone: Good outcome as supplementary treatment for patients presenting with crescendo transient ischemic attack. J Chin Clin Med2009; 4:444-447.
16. Jin W, Lisheng Z, Li Y, et al. Therapeutic effect of monosialic acid tetrahexose ganglioside sodium combined with edaravone on acute cerebral infarction. Evaluation and Analysis of Drug-Use in Hospitals of China 2018;169: 61-62.
17. LiaoX, Zhang Y, XieYM, et al. Analysis of Diemailing Kudiezi injection use in real world in 7 189 patients with cerebral infarction. China J Chinese Materia Medica2016; 41:4442-4450.
18. Yang J Zheng L Chen L, Song C. Establishment of clinical use management mode of adjuvant therapy drugs in our hospital. China Phar2017; 28:3545-3548.
19. Yang J, Zheng L, Guan Y, Song C. Analysis of the impact of antimicrobial management and rational use of antibiotics. Eur J Hosp Pharm. Published Online First: 19 January 2019. doi: 10.1136/ejhpharm-2018-001609.
20. Qu, C., Meng, L., Wang, N. et al. Identify and categorize drug-related problems in hospitalized surgical patients in China. Int J Clin Pharm 2019;41:13–17.
21. Zhu, Y., Liu, C., Zhang, Y. et al. Identification and resolution of drug-related problems in a tertiary hospital respiratory unit in China. Int J Clin Pharm 2019;41:1570–1577.
22. Ali, M.A.S., Khedr, E.M.H., Ahmed, F.A.H. et al. Clinical pharmacist interventions in managing drug-related problems in hospitalized patients with neurological diseases. Int J Clin Pharm 2018;40: 1257–1264.
23. Zheng, Y., Li, D., Zeng, N. et al. Trends of antihypertensive agents in patients with hypertension and coronary artery disease in a tertiary hospital of China. Int J Clin Pharm 2020;42: 482–488.

24. Chen, Q., Jin, Z., Zhang, P. et al. Characteristics of drug-related problems among hospitalized ischemic stroke patients in China. Int J Clin Pharm (2020). https://doi.org/10.1007/s11096-020-01081-6

Figures

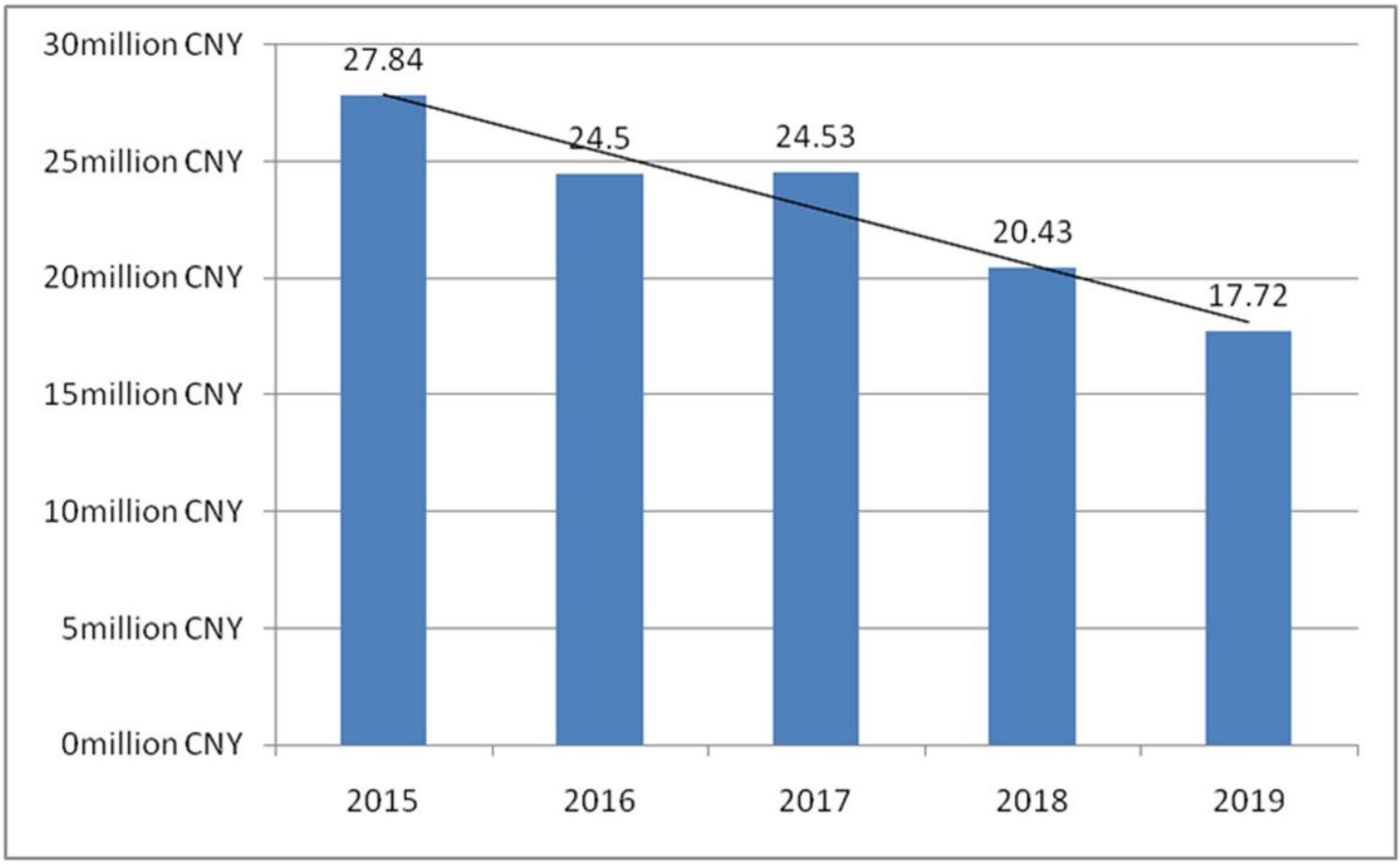

Figure 1

Changes in the total cost of Key Monitoring Drugs （CNY）

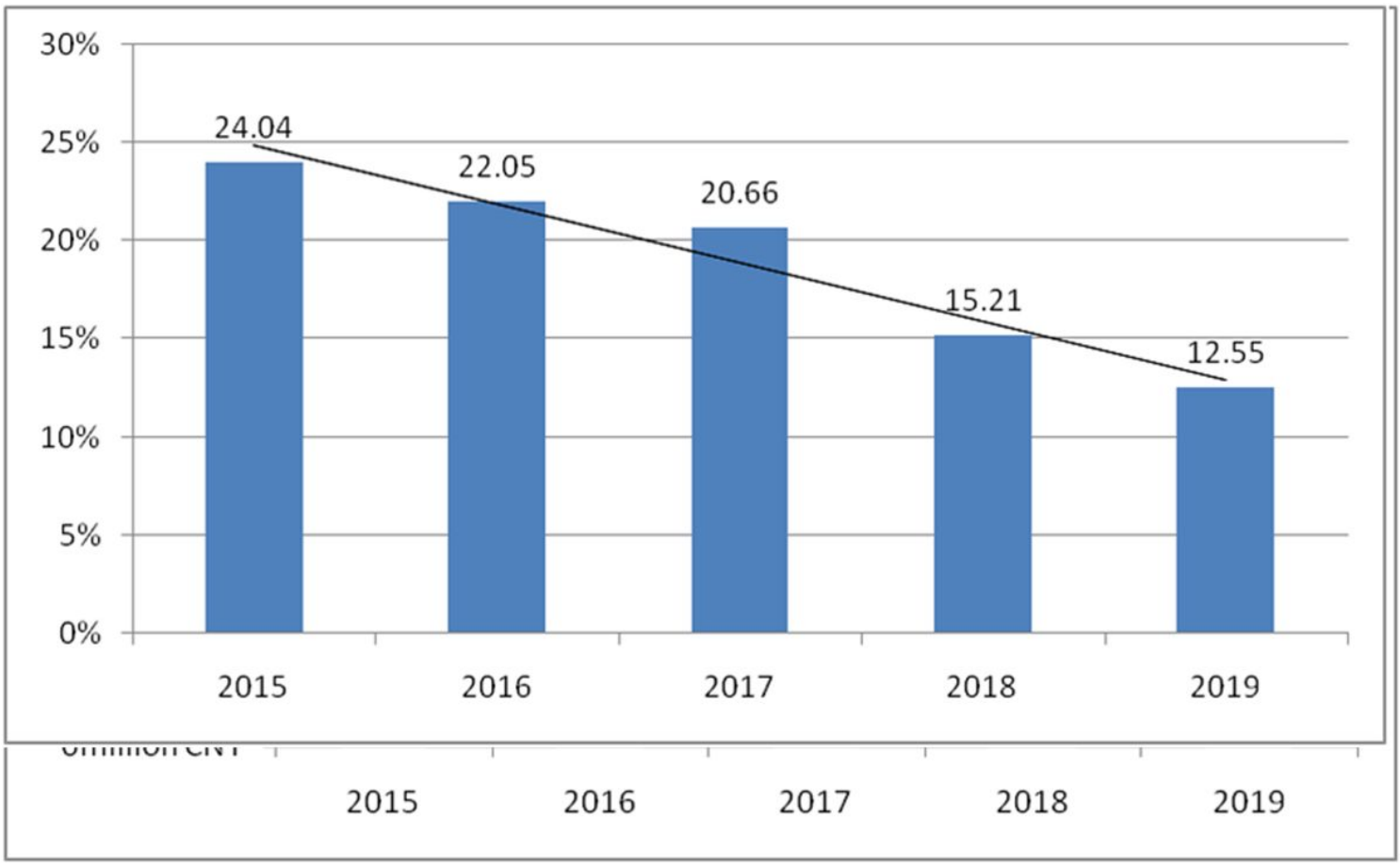

Figure 2

Changes in the proportion of Key Monitoring Drugs costs (%)

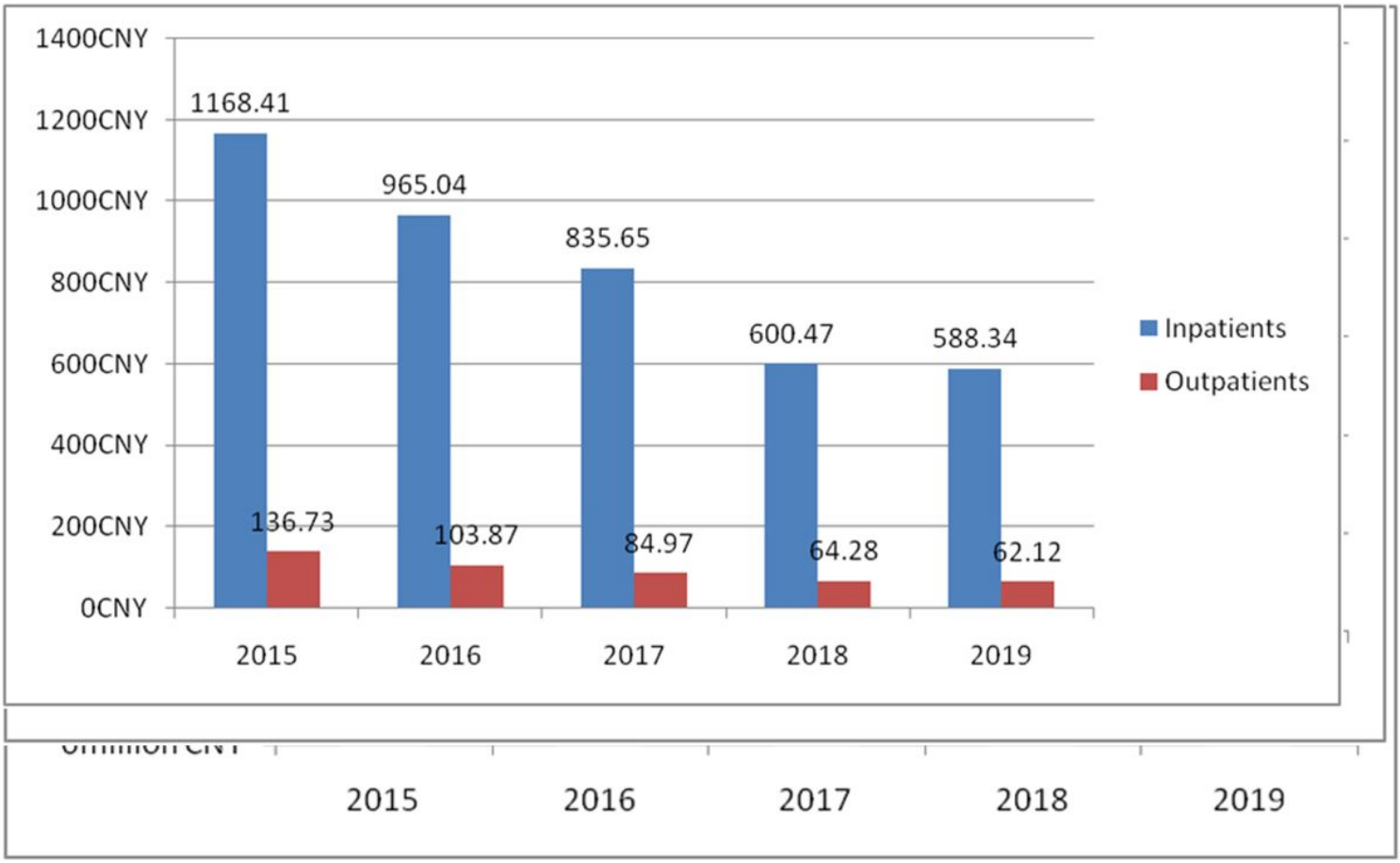

Figure 3

Changes in per capita cost of Key Monitoring Drugs (CNY)

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- SupplementalTable1.doc
- SupplementalTable2.docx