

# Effectiveness of continuous improvement by a clinical pharmacist-led guidance team on the prophylactic antibiotics usage rationality in intervention procedure at a Chinese tertiary teaching hospital

Ping Yang  
Sai-Ping Jiang  
Xiao-Yang Lu

Department of Pharmacy, The First Affiliated Hospital, College of Medicine, Zhejiang University, Hangzhou, China

**Background:** Irrational prophylactic antibiotics usage (PAU) during intervention procedures is common in China. A clinical pharmacist-led guidance team (CPGT) was established and participated in medical teams to advise on the rational usage of antibiotics.

**Objectives:** The objective of this study was to assess the effectiveness of CPGT intervention for the rationality of PAU during intervention procedures.

**Method:** This was a retrospective cross-sectional study with three stages at a Chinese tertiary teaching hospital. Patients who received some specific intervention procedures in the first quarter of 2015 were enrolled as the preintervention group, while those who received the procedures in the second and third quarters of 2015 were enrolled as the postintervention group. CPGT established the criteria for the PAU and conducted the intervention. The pre- and postintervention groups were then compared to evaluate the effectiveness of CPGTs' sustained interventions.

**Results:** A total of 651 patients were enrolled, with 200 patients in the preintervention group, while 233 patients and 218 patients in the first- and second-intervention groups, respectively. With the implementation of CPGTs continuous intervention, the rationality of PAU was significantly improved, including the timing (91.98% vs 97.74%,  $P=0.015$ ), duration (82.72% vs 98.31%,  $P<0.0001$ ), and choice (81.48% vs 93.22%,  $P=0.001$ ) of antibiotics administered during perioperative period. Moreover, the cost of total (US\$34.89±80.96 vs US\$9.81±26.31,  $P=0.025$ ) and inappropriate PAU (US\$28.75±73.27 vs US\$3.57±14.62,  $P<0.0001$ ) per patient was significantly reduced.

**Conclusion:** CPGTs' continuous intervention significantly improved the rationality of PAU during intervention procedures, with a significant reduction in antibiotic cost.

**Keywords:** intervention procedures, prophylactic antibiotics usage, clinical pharmacist-led guidance teams' intervention, prescription evaluation

## Introduction

Prophylactic antibiotics usage (PAU) is applied to prevent surgical site infections (SSIs) following surgery. The American Society of Hospital Pharmacists recommended that prophylactic antibiotics appropriately administered before surgical procedures can reduce the incidence of SSIs.<sup>1</sup> However, inappropriate prescribing and excessive PAU are common in China. Surveys indicated that the rate of PAU in intervention procedures was 82.8%–99.8% in China.<sup>2–5</sup> In addition, irrational PAU during perioperative period

Correspondence: Xiao-Yang Lu  
Department of Pharmacy, The First Affiliated Hospital, College of Medicine, Zhejiang University, 79 Qingchun Road, Hangzhou 310003, China  
Tel/fax +86 571 8723 6533  
Email luxiaoyang666@126.com

was widespread, such as improper timing, duration, and antibiotics prescribed and unnecessary combination of antibiotics. According to Zhang et al,<sup>3</sup> the duration of PAU was 0–14 d, and 45.7% discontinued antibiotic administration within 48 h. Although 4.9% of patients were given antibiotics in 0.5–2 h, 95.1% were given after operation. In addition, 2.4% of patients received combination prophylactic antibiotic therapy during perioperative period. This is a serious public health concern that not only increases the risk of adverse effects and promotes the emergence of resistant organisms but also increases drug costs and wastes health care resources.

A potential reason for this irrational phenomenon is that the doctor did not pay enough attention to rational PAU, alternatively, showed a lack of relevant knowledge on rational PAU. To standardize clinical rational antibiotic usage in China, the National Health and Family Planning Commission (NHFPC) published “Guiding principles for clinical application of antibiotics” in 2004 and updated in 2015, which clearly established the recommendations for PAU in various operations. Besides, along with the WHO appeal “Against drug resistance: no action today, no drugs available tomorrow” in 2011, the NHFPC of China launched a 3-year period about special rectification activity of clinical application of antibiotics in 2011. The activity aimed at achieving reasonable antibiotic use and allowed pharmacists to participate in medical teams to advise on the rational usage of antibiotics. After the 3-year period of special rectification scheme, the rational PAU in clean incision operations has been improved. Clinical pharmacists have played a larger role in guiding the use of clinical antibiotic therapy. Antibiotic use density, cost of antibiotics, use rate, and duration of antibiotics in urology clean operations decreased through pharmacists participating in antibiotic stewardship programs of the hospital.<sup>6</sup> In addition, a significant increase was observed in the rate of correct choice of antibiotics.<sup>7</sup> In addition, pharmacists can promote the rational PAU in clean incision operations through drug use evaluation.<sup>8</sup>

However, problems about PAU during intervention procedures are still not completely eradicated. Data indicated that the rationality of PAU during cardiovascular intervention procedures could be effectively improved by pharmacists’ intervention in China.<sup>9</sup> Moreover, the related information from abroad are not reported. Therefore, the aim of this study was to improve the rational PAU for eight intervention procedures and assess the value of clinical pharmacist-led guidance teams (CPGTs) during the promotion. For this purpose, we conducted a sustained improvement in PAU by prescription evaluation (PE) and compared the rationality of PAU before and after CPGT’s interventions.

## Methods

### Study design

This study was conducted in a university-affiliated tertiary hospital with 2,500 beds. The hospital is a comprehensive and information-based hospital, where the information of hospitalized patients can be acquired through electronic medical record (EMR). This was a retrospective cross-sectional study conducted from January 2015 to September 2015, with every quarter defined as a stage. It contained a baseline PE followed by PEs with intervention and feedback proceeded every 3 months. In every stage, patients requiring scheduled intervention procedure were extracted by retrieving EMR. Then, the patients who underwent intervention procedure on the tenth of each month were enrolled.

The inclusion criteria were 1) age 18 years or older and 2) undergoing the intervention procedures, including a) coronary arteriography (CA), b) total cerebral angiography by femoral artery catheterization (TCA), c) percutaneous selective venography (PSV), d) percutaneous selective arteriography (PSA), e) percutaneous coronary stent implantation (PCSI), f) cardiac radiofrequency ablation (CRA), g) transcatheter arterial chemoembolization (TACE), and h) endoscopic retrograde cholangiopancreatography (ERCP). The exclusion criteria were patients who had received therapeutic antibiotics to treat bacterial infections prior to the intervention procedure, alternatively, who had symptoms of infection after the intervention procedure.

Ethical approval was acquired from the research review committee of First Affiliated Hospital of ZheJiang University. All patients enrolled in this study provided written informed consent for their information to be used for this study.

### Establishment of CPGTs

We established multidisciplinary CPGTs for the study, which included clinical pharmacists, professional registered doctors in infectious disease department, administrators in the department of medical affairs, hospital infection control, and pharmaceutical management committee.

Clinical pharmacists who had at least 1 year of residency in ward were qualified to be a member of this study. Involved pharmacists took training courses to be familiar with the related guidelines, and then they were allowed to participate in the study as a part of CPGTs.

### Criteria for PAU during intervention procedure

Before initiating the program, we drafted the criteria for PAU of the intervention procedures by an evidence-based method. The reference standards and basis of the criteria

included practice guideline for adult antibiotic prophylaxis during vascular and interventional radiology procedures (2010 version),<sup>10</sup> prophylactic antibiotic guidelines in modern interventional radiology practice,<sup>11</sup> antibiotics in interventional radiology,<sup>12</sup> guiding principles for clinical application of antibiotics (2015 version),<sup>13</sup> clinical practice guidelines for antimicrobial prophylaxis in surgery,<sup>1</sup> national antimicrobial guide,<sup>14</sup> the Sanford guide to antimicrobial therapy (44th edition), and related clinical practice guidelines for evaluation.<sup>15</sup> After the multidisciplinary CPGTs discussed and reached a consensus, the criteria for PAU during intervention procedures in our hospital were finally formulated.

According to the established criteria, the diagnostic angiography of CA, TCA, PSA, and PSV was regarded as clean procedure and has no PAU indication. For the procedures that have PAU indication, the first preoperative dose should be administered within 0.5–1 h before operation (antibiotics with short infusion times such as cephalosporins) or within 1–2 h (antibiotics with long infusion times such as vancomycin). The evaluation standard about indication, choice, and duration of antibiotics prophylaxis usage is shown in Table 1. Dosage and frequency of antibiotics were referenced to the medicine instruction and relevant guideline.<sup>1</sup>

## CPGTs' intervention

In each stage, CPGTs' intervention was performed as follows: 1) data on the characteristics of the surgical patients were collected from EMR, and the rationality of the PAU during perioperative period was evaluated according to the established criteria. 2) Data about irrational PAU were collected by pharmacist. Two senior clinical pharmacists evaluated, any dispute was resolved through discussion or with the assistance of another clinical pharmacist. 3) Senior clinical pharmacists communicated with the doctors responsible for order entry by e-mail or telephone for some unreasonable cases. 4) After the feedback by doctors, pharmacists should consider the doctors' appeal and advice and check the rationality of the prescription again, revising the criteria if necessary. 5) The results of the final statistical analysis were submitted to the department of medical affairs and published on the hospital administration website. 6) Two senior clinical pharmacists would deliver lectures about PAU to some key departments. The workflow of CPGTs' intervention is illustrated in Figure 1.

## Data collection and statistical analysis

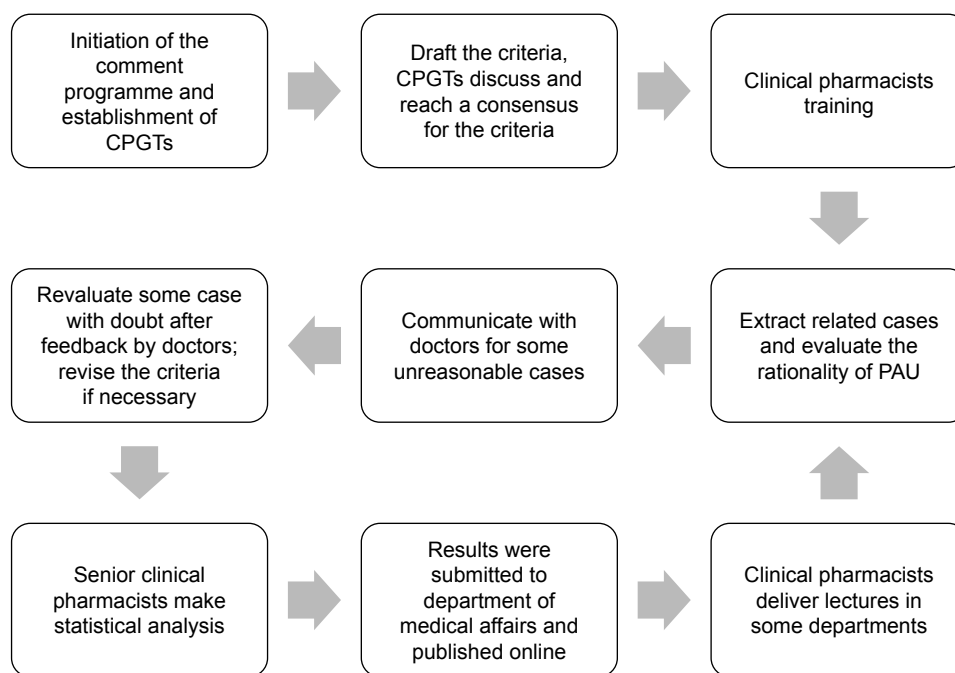
A particular Microsoft Excel table (version 2010; Microsoft Corporation, Redmond, WA, USA) was prepared to register

**Table 1** Protocol for antibiotics prophylaxis usage in intervention procedure

Procedure	Indication for routine antibiotics prophylaxis	First-choice antibiotic	Duration
Diagnostic angiography	No	None	None
PCSI	1. Repeat intervention within 7 d 2. Arterial sheath is left in overnight 3. Undergoing multiple endovascular intervention	Cefazolin	Preoperative administration of a single dose
CRA	Routine antibiotics prophylaxis was recommended	Cefazolin	Preoperative administration of a single dose
TACE	1. Prior biliary surgery 2. Diabetes 3. Portal vein thrombosis 4. Biliary obstruction 5. Gallstones	1. Ampicillin/sulbactam 2. Cefazolin + metronidazole 3. Ampicillin + gentamicin 4. Ceftriaxone 5. Tazobactam/piperacillin <sup>a</sup> 6. First/second generation of cephalosporin ± metronidazole <sup>b</sup>	Within 24 h
ERCP	1. Occurred biliary tract infection/sepsis 2. Hilar tumors 3. Organ transplants/immune-suppressed patients 4. The procedure of pancreatic pseudocyst 5. Primary sclerosing cholangitis 6. Cardiac patients with moderate-to-high risk	1. Tazobactam/piperacillin 2. Ceftriaxone 3. Ampicillin/sulbactam 4. Ciprofloxacin 5. Second generation of cephalosporin 6. Ceftazidime	Within 48 h or even can be used until the drainage unobstructed

**Notes:** <sup>a</sup>For patients without intact sphincter of Oddi. <sup>b</sup>The first and second generations of cephalosporin were regarded as cefazolin and cefuroxime by evidence-based medicine.

**Abbreviations:** PCSI, percutaneous coronary stent implantation; CRA, cardiac radiofrequency ablation; TACE, Transcatheter arterial chemoembolization; ERCP, endoscopic retrograde cholangiopancreatography; d, days; h, hours.



**Figure 1** Workflow of CPGTs' intervention in this study.

**Abbreviations:** CPGT, clinical pharmacist-led guidance team; PAU, prophylactic antibiotics usage.

the patients' demographics (gender and age), intervention procedures (procedure name and operative time), antibiotic usage (generic names, dosing schedules, and timing duration), cost (total and inappropriate cost of PAU), and antibiotics consumption quantity (total and inappropriate consumption of PAU). All costs were exchanged to US dollars (6.63 yuan = US \$1) and, finally, reported in US dollars.

The cost of total and inappropriate PAU per patient was defined as the ratio of the total and inappropriate expenses of PAU to the total number of patients during every stage, respectively. Inappropriate PAU expenses included the cost from unreasonable antibiotics prescribed and unnecessary prolonged duration of PAU. At the same time, the defined daily dose system (DDDS) of total and inappropriate PAU per patient was defined as the ratio of the total and inappropriate antibiotics consumption to defined daily dose (DDD) value of every antibiotic, respectively. DDDS per patient means the ratio of the total DDDS to the total number of patients during every stage. Inappropriate antibiotics consumption included the antibiotics consumption from unreasonable antibiotics prescribed and unnecessary prolonged duration of PAU.

Data were collected from the hospital information system and were put into the prepared EXCEL table, then subsequently analyzed by SPSS software (version 17.0; SPSS, Inc., Chicago, IL, USA). Comparisons between the pre- and postintervention stages were performed such as patient characteristics, rational rate of PAU (indication, timing, duration,

and choice of antibiotics) and medical cost per patient. Comparisons between the pre- and postintervention stages with regard to the age of the patients were conducted by Student's *t*-test for continuous variables. Categorical variables were expressed as frequencies and percentages, which were then analyzed by the chi-squared test. The variables not continuously distributed were analyzed with the nonparametric Mann–Whitney *U* test. All reported *P*-values are two sided, and  $P < 0.05$  was considered as statistically significant.

## Results

### Patients characteristic

The study carried out three stages of PE, with 651 patients who received intervention procedures between January 2015 and September 2015. A total of 200 patients were in the pre-intervention group (phase I), while 233 patients and 218 patients were in the first- and second-intervention groups (phase II and phase III), respectively. General data for the three groups of patients are shown in Table 2. A total of 72.78% patients were male, while 27.22% patients were female. There were no significant differences between the three groups of patients regarding demographic characteristics, such as age, gender, and type of intervention procedures ( $P > 0.05$ ).

### Evaluation on indication of PAU

According to the established criteria, there is no indication of PAU for diagnostic angiography. As shown in Table 3,

**Table 2** General data of included patients

Characteristics	Preintervention	Postintervention		P-value
	Phase I (n=200)	Phase II (n=233)	Phase III (n=218)	
Gender				
Male, n (%)	152 (76.0)	163 (69.96)	160 (73.39)	NS*
Age, mean $\pm$ SD	60.79 $\pm$ 12.74	58.51 $\pm$ 14.46	59.23 $\pm$ 13.01	NS
Type of intervention procedure, n (%)				
Diagnostic angiography	38	46	41	NS
PCSI	60	73	65	NS
CRA	21	24	28	NS
TACE	64	70	66	NS
ERCP	17	20	18	NS

**Note:** \* $P > 0.05$ .

**Abbreviations:** NS, not significant; PCSI, percutaneous coronary stent implantation; CRA, cardiac radiofrequency ablation; TACE, transcatheter arterial chemoembolization; ERCP, endoscopic retrograde cholangiopancreatography; SD, standard deviation.

three (1.5%) cases in phase I and one (0.43%) case in phase II received PAU during the diagnostic angiography. We noted that, there was no PAU in diagnostic angiography after the second intervention. However, there was no significant difference in the rationality of PAU indication between phase I and phase II (98.5% vs 99.57%,  $P=0.246$ ) and phase I and phase III (98.5% vs 100%,  $P=0.07$ ).

### Evaluation on timing of PAU

For the procedure that has PAU indication, the appropriateness of timing and duration of PAU before and after the intervention is documented in Table 4.

The correct administration timing in the pre- and postintervention groups was compared. As shown in Table 4, 13 (8.02%) cases in phase I, 16 (8.56%) cases in phase II, and 4 (2.26%) cases in phase III did not comply with the criteria about correct administration timing. There was a significant improvement in the rationality of adherence to the correct administration time after the second intervention, from 91.98% to 97.74% ( $P=0.015$ ). However, the improvement was not observed after the first intervention.

**Table 3** Appropriateness of indications on prophylactic antibiotics usage before and after the intervention

Intervention procedure	Phase I (n=200)	Phase II (n=233)	Phase III (n=218)
Diagnostic angiography	35	45	41
PCSI	60	73	65
CRA	21	24	28
TACE	64	70	66
ERCP	17	20	18
Total	197 (98.5%)	232 (99.57%)	218 (100%)

**Note:** The  $P$ -value of phase II vs phase I was  $P=0.246$ , while phase III vs phase I was  $P=0.070$ .

**Abbreviations:** PCSI, percutaneous coronary stent implantation; CRA, cardiac radiofrequency ablation; TACE, transcatheter arterial chemoembolization; ERCP, endoscopic retrograde cholangiopancreatography.

### Evaluation on duration of PAU

As for the PAU duration, 28 (17.28%) cases in phase I, 24 (12.83%) cases in phase II, and 3 (1.69%) cases in phase III were considered as unnecessary prolonged duration of prophylaxis. Compared with the preintervention, significant increase in the rationality of PAU duration was observed in phase III (82.72% vs 98.31%,  $P < 0.0001$ ) but not observed in phase II (82.72% vs 87.17%,  $P=0.244$ ). As shown, 25 (15.43%) cases in phase I, 24 (12.83%) cases in phase II, and 15 (8.47%) cases in phase III received PAU until discharged. There was significant decrease in phase III ( $P=0.047$ ) but not in phase II ( $P=0.486$ ). Moreover, mean PAU duration was 0.90 d, 0.79 d, and 0.53 d in phase I, phase II, and phase III, respectively, a significant reduction was found after the second intervention (0.90 $\pm$ 1.99 vs 0.79 $\pm$ 1.79,  $P=0.012$ ), whereas not found after the first intervention (0.90 $\pm$ 1.99 vs 0.53 $\pm$ 1.04,  $P=0.084$ ).

### Evaluation on choice of antibiotics

For the procedures that required PAU, Table 4 depicted the comparative results of the rate of correct antibiotics prescribed in the pre- and postintervention groups. A total of 30 (18.52%) cases in phase I, 18 (9.63%) cases in phase II, and 12 (6.78%) cases in phase III were inappropriately prescribed. Compared with the preintervention, the rationality of antibiotic agent choice was significantly increased after the first intervention (81.48% vs 90.37%,  $P=0.016$ ) and second intervention (81.48% vs 93.22%,  $P=0.001$ ).

We noted that latamoxef sodium ( $n=16$ , 2.46%), sulbenicillin sodium ( $n=12$ , 1.84%), and moxifloxacin ( $n=7$ , 1.08%) were the top three inappropriate antibiotics prescribed in the whole study. In the preintervention group, a high rate of sulbenicillin sodium ( $n=11$ , 5.5%) was observed, followed by latamoxef sodium ( $n=6$ , 2.58%) and moxifloxacin

**Table 4** Appropriateness of timing and duration of prophylactic antibiotics usage before and after the intervention

Intervention procedure	Phase I (n=162)	Phase II (n=187)	Phase III (n=177)	P-value	
Correct timing of antibiotics administered				$P_1^a=0.858$	$P_2^b=0.015$
PCSI	56	69	65		
CRA	20	23	28		
TACE	58	63	62		
ERCP	15	16	18		
Total	149 (91.98%)	171 (91.44%)	173 (97.74%)		
Appropriate prolonged duration of prophylaxis				$P_1=0.244$	$P_2<0.0001$
PCSI	45	63	65		
CRA	20	23	28		
TACE	57	59	63		
ERCP	12	18	18		
Total	134 (82.72%)	163 (87.17%)	174 (98.31%)		
Rational choice of antibiotic agent				$P_1=0.016$	$P_2=0.001$
PCSI	47	71	65		
CRA	20	23	26		
TACE	52	59	59		
ERCP	13	16	15		
Total	132 (81.48%)	169 (90.37%)	165 (93.22%)		
PAU until discharge, n (%)	25 (15.43)	24 (12.83)	15 (8.47)	$P_1=0.486$	$P_2=0.047$
Duration of PAU, d, mean (SD)	0.90 (1.99)	0.79 (1.79)	0.53 (1.04)	$P_1=0.084$	$P_2=0.012$

**Notes:** <sup>a</sup> $P_1$  means the P-value of phase II compared with phase I. <sup>b</sup> $P_2$  means the P-value of phase III compared with phase I.

**Abbreviations:** PCSI, percutaneous coronary stent implantation; CRA, cardiac radiofrequency ablation; TACE, Transcatheter arterial chemoembolization; ERCP, endoscopic retrograde cholangiopancreatography; SD, standard deviation; d, days.

(n=4, 1.83%). After twice CPGTs' intervention, the usage rate of these three antibiotics decreased. However, the significant decrease was not observed in latamoxef sodium and moxifloxacin ( $P>0.05$ ). The implementation of CPGTs' intervention had significant impacts on the rational use of sulbenicillin sodium after the first (94.5% vs 99.57%,  $P=0.001$ ) and second interventions (94.5% vs 100%,  $P=0.0004$ ).

## Economic benefit and antibiotic consumption analysis between pre- and postintervention

As depicted in Table 5, compared with the preintervention group, mean cost of total PAU was significantly reduced after the second intervention (\$34.89 vs \$9.81,  $P=0.025$ ) but not after the first intervention (\$34.89 vs \$17.95,  $P=0.096$ ). Moreover, cost of inappropriate PAU per patient was significantly reduced after the second intervention (\$28.75 vs \$3.57,  $P<0.0001$ ), but not observed after the first intervention (\$28.75 vs \$13.47,  $P=0.081$ ).

The DDDS of total PAU usage per patient was not significantly reduced after twice intervention. However, the DDDS of inappropriate PAU per patient was significantly reduced after the second intervention ( $0.53\pm 1.25$  vs  $0.13\pm 0.62$ ,  $P<0.0001$ ) but not observed after the first intervention ( $0.53\pm 1.25$  vs  $0.46\pm 1.51$ ,  $P=0.17$ ).

## Discussion

The use of prophylactic antibiotics in perioperative period has received growing attention; however, few data are available on PAU in intervention procedures, especially studies comparing the improvement by pharmacists' intervention. To our knowledge, this was the first study to investigate PAU during intervention procedures at a Chinese tertiary teaching hospital. We reported a pre-to-postintervention study to confirm the efficacy of CPGTs' continuous improvement on PAU in intervention procedure.

In this study, we established multidisciplinary CPGTs at a Chinese tertiary teaching hospital to promote the rationality

**Table 5** Cost and consumption of antibiotics before and after the intervention

Cost and DDDS	Phase I (n=200)	Phase II (n=233)	Phase III (n=218)	P-value	
Cost of PAU per patient, USD, mean (SD)	34.89 (80.96)	17.95 (51.69)	9.81 (26.31)	$P_1^a=0.096$	$P_2^b=0.025$
Cost of inappropriate PAU per patient, USD, mean (SD)	28.75 (73.27)	13.47 (45.06)	3.57 (14.62)	$P_1=0.081$	$P_2<0.0001$
DDDS of PAU per patient, mean (SD)	0.66 (1.43)	0.61 (1.72)	0.36 (0.98)	$P_1=0.210$	$P_2=0.061$
DDDS of inappropriate PAU per patient, mean (SD)	0.53 (1.25)	0.46 (1.51)	0.13 (0.62)	$P_1=0.170$	$P_2<0.0001$

**Notes:** <sup>a</sup>The P-value with phase II vs phase I. <sup>b</sup>Phase III vs phase I.

**Abbreviations:** DDDS, defined daily dose system; PAU, prophylactic antibiotics usage; USD, United States Dollar; SD, standard deviation.

of perioperative PAU. First, CPGTs established the criteria for PAU during intervention procedure through evidence-based method. Then, we standardized prophylactic antibiotics administration through regular monitoring, PE, and communication with doctors. In addition, administrative measure was also used.

By CPGTs' sustained intervention, the rationality of perioperative antibiotics prophylaxis was significantly increased ( $P < 0.0001$ ). To be precise, more correct timing of antibiotics administered, more appropriate duration of prophylaxis after procedure, and better choice of antibiotics during perioperative period were implemented. Moreover, costs of total and inappropriate PAU per patient as well as DDDS of inappropriate PAU per patient were significantly reduced.

The study revealed that the most common irrational choices of antibiotic agent in the study period were latamoxef sodium, sulbenicillin sodium, and moxifloxacin. Latamoxef sodium and sulbenicillin sodium were broad-spectrum antibiotics, which have weaker activity against *Staphylococcus* infections compared to first- or second-generation cephalosporins. Moreover, according to the guiding principles for clinical application of antibiotics (2015 version), prophylactic use of fluoroquinolones during perioperative period should be severely restricted because of high drug resistance rate to *Escherichia coli*. According to the practice guideline,<sup>10</sup> for the procedure of stent implantation and CRA, the potential organisms were *Staphylococcus aureus* and coagulase-negative staphylococcus, while for liver and biliary intervention, the possible organisms were *Enterococcus* spp., *Streptococcus* spp., aerobic Gram-negative organisms, *Clostridium* spp., and so on. As a result, these three antibiotics were not rational choice in perioperative antibiotics prophylaxis. The usage rate of sulbenicillin sodium was significantly declined; however, the decline was not observed in latamoxef sodium and moxifloxacin even though with the CPGTs' continuous communications and intervention. The possible reasons were the surgeons' prescribing habits and poor understanding of antibacterial spectrum. Therefore, it is suggested that the intervention should be intensified and multifaceted. The emphasis of further step will be the education to the physician about the reasonable choice of antibiotics prophylaxis during the operation period.

The timing of the first-dose administration is an important parameter for rational usage of perioperative antibiotic prophylaxis. It is demonstrated that postoperative administration increased the rate of infection, even resulted in no difference in infection rate compared with the control group.<sup>16</sup> Preoperative administration of antibiotics within

2 h before operation decreased the risk of SSI compared with too early administration ( $>2$  h before operation) or postadministration.<sup>17</sup> Therefore, the current guidelines suggest that antibiotic prophylaxis (with short infusion times) be administered 30–60 min before incision. In our study, 8.02% patients were administered their first dose with an inappropriate time before the CPGTs' intervention, the remarkable outcome of twice interventions showed that the physicians were aware of the optimal timing of administration and its role in SSI prevention.

With respect to duration of administration, several studies have evaluated that a single appropriately timed dose is as effective as a multiple-dose protocol. Moreover, in some biliary drainage procedures, the risk of postprocedural bacteremia caused by intravasation of organisms into the bloodstream remains present until the organ is adequately drained. Therefore, antibiotics administration should be continued until satisfactory drainage is achieved. In our study, 17.28% of the patients in the preintervention group received unnecessary prolong duration of prophylaxis, while 15.43% cases received prophylactic antibiotics until discharged. Some cases even continued to oral antibiotics after discharge. All the above caused unnecessary resources and economic waste. With the CPGTs' sustained communications, most of the physicians gradually recognized the conception such as "a longer duration of prophylaxis results in a lower rate of postprocedure infection" is wrong. As a result, the duration of PAU in days, the case of unnecessary PAU duration, and the case of PAU until discharge were significantly reduced.

The study implied that the supervision of CPGTs can improve economic outcomes. Cost of total and inappropriate PAU per patient was significantly reduced; furthermore, DDDS of inappropriate PAU per patient also effectively decreased. Although many agreeable clinical and economic outcomes were achieved in the postintervention group, it is worth noting that the index such as DDDS of total PAU per patient was not significantly reduced. A possible explanation for this could be that some misunderstandings are perpetuated among in Chinese physicians, for example, more antibiotics usage can minimize the possibility of infection. So, clinical pharmacists should prolong working time to increase communication with physicians, which can help to correct physician's misunderstanding.

There are some limitations in this study. First, this was a retrospective cross-sectional cohort study with only a single center and no control group. Second, although the patients with symptoms of infection were excluded, some confounding factors such as the other complications in patients were not assessed. Finally, the present study investigated only

the short-term effects of CPGTs' intervention. For all these reasons, a larger sample size and more rigorous design are required in future studies.

## Conclusion

Implementation of CPGTs' intervention significantly improved the PAU rationality in a relatively short period, including indication, timing, duration, and choice of prophylactic antibiotics. However, the inappropriateness phenomenon still cannot be completely avoided, and multi-faceted measures should be applied, such as the integration of a decision support system about automatic hints and warnings into a computerized physician order entry system. Moreover, long-term and continuous CPGTs' intervention should be conducted.

## Acknowledgment

The authors wish to thank all the clinical pharmacists who implemented the CPGTs' intervention during the study period.

## Disclosure

The authors report no conflicts of interest in this work.

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