A retrospective cohort study on a pharmaceutical consultation mode of multidisciplinary individualized medication recommendations

Xiucong Fan[1], Danxia Chen[2], Siwei Bao[2], Rong Bai[2], Fang Fang[2], Xiaohui Dong[2], Yuyi Zhang[2], Xiaogang Zhang[2], Yabin Ma[2], and Xiaobo Zhai[2]

[1]Tongji University Affilliated East Hospital
[2]Affiliation not available

May 11, 2021

Abstract

Aims: To develop a pharmaceutical consultation mode of multidisciplinary individualized medication recommendations, to improve the quantity and quality of clinical pharmacists' consultations Methods: A retrospective study of 542 clinical pharmacists-led consultations was conducted. In the pre-intervention group, medication advice was given based on the purpose of the consultation. In the post-intervention group, a consultation mode of multidisciplinary individualized medication recommendation was implemented, in which clinical pharmacists with specialties of anticoagulation, gastroenterology and nutrition were asked to give individualized medication recommendations and a set of evaluation criteria for rational drug use was formulated. Outcomes, including the patterns and number of consultations, individualized medication recommendations, acceptance rate and effectiveness rate, were compared between the two periods. Results: A total of 651 cases were reviewed, and 542 cases of which meeting the predesigned inclusion and exclusion criteria were included, with 94 and 448 patients in the pre-intervention and post-intervention groups, respectively. The total number of consultations increased year by year, so did the number of general consultations, multidisciplinary difficult consultations, departments applying for general consultations, departments applying for multidisciplinary difficult consultations, anti-infection consultations and non-anti-infection consultations in details. The effectiveness rate of consultations in the post-intervention group was 81.7% vs 70.2% in the pre-intervention group ($P < 0.05$). No difference was shown between two groups in acceptance rate (96.9% vs 95.7%, p=0.578).

A retrospective cohort study on a pharmaceutical consultation mode of multidisciplinary individualized medication recommendations

Xiucong Fan, Danxia Chen, Siwei Bao, Rong Bai, Fang Fang, Xiaohui Dong, Yuyi Zhang, Xiaogang Zhang, Yabin Ma, Xiaobo Zhai

Department of Pharmacy, Shanghai East Hospital, Tongji University School of Medicine, Shanghai, China

Correspondence: Xiaobo Zhai and Yabin Ma, Department of Pharmacy, Shanghai East Hospital, Tongji University School of Medicine, Shanghai, China. Email: xiaobo_zhai@163.com and 15021877977@163.com

Funding information: Key Specialties Foundation of Clinical Pharmacy of Shanghai Municipal Health Commission in China, Grant/Award Number: SWLCYXZX-2018-001; Research on the Epidemiology of Severe Drug-induced Diseases of the Chinese Society of Toxicology, Grant/Award Number: CST2019CT304

Conflict of interest: The authors have no conflicts of interest to declare.

Ethics statement: The Ethics Board of the Shanghai East Hospital, Tongji University School of Medicine, China, reviewed and approved the study protocol.

Xiucong Fan and Danxia Chen are joint first authors.

PI statement: The authors confirm that the Principal Investigators for this paper are Xiaobo Zhai, and Xiaobo Zhai had direct clinical responsibility for patients.

Patient consent statement: Not required.

Data Availability Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Key words: clinical pharmacy, clinical pharmacists' consultations, multidisciplinary individualized medication recommendations, rational drug use

Word count: 4443, table count: 3, figure count: 3

What is already known about this subject:

- Chinese clinical pharmacists treat consultation as a vital role in demonstrating their professionalism and participation.
- So far, consultation work is mainly for the purpose of anti-infection treatment and the recommendations are limited in this.
- Few studies have proposed new mode to improve the current consultation status.

What this study adds:

- The multidisciplinary individualized medication consultation mode may increase the types, quantity and quality of consultations, and expand clinical pharmacists' influence.
- Consultation recommendations on anticoagulant, PPIs and nutritional support can reflect individualized rational medication.
- Clinical pharmacists should focus on all the medication of patients' other than consultation itself.

Abstract: Aims: To develop a pharmaceutical consultation mode of multidisciplinary individualized medication recommendations, to improve the quantity and quality of clinical pharmacists' consultations

Methods: A retrospective study of 542 clinical pharmacists-led consultations was conducted. In the pre-intervention group, medication advice was given based on the purpose of the consultation. In the post-intervention group, a consultation mode of multidisciplinary individualized medication recommendation was implemented, in which clinical pharmacists with specialties of anticoagulation, gastroenterology and nutrition were asked to give individualized medication recommendations and a set of evaluation criteria for rational drug use was formulated. Outcomes, including the patterns and number of consultations, individualized medication recommendations, acceptance rate and effectiveness rate, were compared between the two periods.

Results: A total of 651 cases were reviewed, and 542 cases of which meeting the predesigned inclusion and exclusion criteria were included, with 94 and 448 patients in the pre-intervention and post-intervention groups, respectively. The total number of consultations increased year by year, so did the number of general consultations, multidisciplinary difficult consultations, departments applying for general consultations, departments applying for multidisciplinary difficult consultations, anti-infection consultations and non-anti-infection consultations in details. The effectiveness rate of consultations in the post-intervention group was 81.7% vs 70.2% in the pre-intervention group ($P < 0.05$). No difference was shown between two groups in acceptance rate (96.9% vs 95.7%, p=0.578).

Conclusions: Our study preliminarily suggests that the development of the new consultation mode can improve the quantity and quality of pharmaceutical consultations, which is worthy of further promotion and large-scale research.

1.Introduction

In China, the pilot work of Chinese clinical pharmacist system began in 2008. Then the regulations on "Administration of Pharmaceutical Affairs in Medical Institutions" [1] promulgated and implemented in 2011

further promoted the transformation of pharmacists' role and refined their responsibilities in clinical work. In the same year, the pharmacist-led management method was introduced into Antimicrobial Stewardship Program,which strengthened the status of clinical pharmacists in the treatment of infectious diseases. According to the guidance of documents and preliminary practices, Chinese clinical pharmaceutical work mainly includes pharmaceutical ward round, medical order review, prescription review, consultation, therapeutic drug monitoring, adverse drug reaction monitoring and reporting[2]. Among them, consultation plays a vital role in demonstrating their professionalism and participation,the importance of which is pointed out in "Notice on Strengthening Pharmacy Administration and Changing the Pattern of Pharmaceutical Care" issued in July 2017 [3]. As a result, Chinese clinical pharmacists take improving the quantity and quality of consultations as an important task during the construction of clinical pharmacy specialty.

In order to improve the clinical recognition and irreplaceability, vast majorities of clinical pharmacists in different specialties choose anti-infection treatment as their main entry point to participate in clinical drug medication, and the effect is remarkable. This is clearly reflected in the purpose and acceptance rate of clinical pharmacists' consultations [4-7]: more than 80% of the consultation purposes are the rational use of antibiotics. The acceptance rate of consultations is more than 90% and the effectiveness rate is close to 90%.

The clinical pharmacy specialty of Tongji University Affiliated East Hospital is the key specialty of clinical pharmacy in Shanghai, China. During the construction of it, improving the quantity and quality of clinical pharmacists' consultations is the key work. We integrated multidisciplinary individualized medication recommendations into the anti-infection consultations, so as to achieve the goal. In this study, we retrospectively analyzed the consultations and improvement measures in last three years (2018-2020), in order to provide a reference for developing better approaches for consultations and improving the expertise of clinical pharmacists.

2. Methods

2.1Patients and Setting

A single-center retrospective pre- and post-intervention study was conducted in Tongji University Affiliated East Hospital, which is a tertiary teaching hospital with 2000 beds. Clinical pharmacists' consultations applied by clinical departments in 2018 and 2019-2020 were enrolled in the pre-intervention and post-intervention group, respectively. Consultations received by clinical pharmacists were eligible. The exclusion criteria were as follows: incomplete consultation records, consultation cases about permissions to drug use and consultation patients died within 72 hours after consultation or stopped treatment for other reasons.

2.2Intervention

In the pre-intervention period, upon receiving the consultation application from clinical department, any qualified clinical pharmacist evaluated the current situation of the patient and proposed consultation recommendations according to the purpose of the consultation.

In the post-intervention period, the following interventions were taken on the basis above: After comprehensively evaluating the patient's situation, clinical pharmacists with specialties of anticoagulation, gastroenterology and nutrition were asked to give individualized medication recommendations. In addition to the anti-infection treatment, consultation recommendations were recorded in terms of the consultation purpose, anticoagulation treatment, the usage of proton-pump inhibitors (PPIs) and nutrition support. After consultation, follow-up monitoring measures were taken. A set of evaluation criteria for rational use of anticoagulant, PPIs, anti-infection and nutrition support were formulated according to the latest guidelines, experts' recommendations and previous pharmaceutical practices. Furthermore, clinical pharmacists regularly discussed difficult consultation cases for re-examination and internal business learning. At last, the acceptance of consultation recommendations and patients' outcomes were assessed.

2.3 Evaluation criteria and the consultation mode of multidisciplinary individualized medication

2.3.1 Anti-infection treatment consultation recommendations

The current anti-infection treatment or prevention effect was evaluated based on the current infection of the patient. The main consultation mode was that under the guidance of anti-infection pharmacists, the consultation pharmacists on duty give treatment recommendations, including drug name, dosage, frequency and route of administration, and the course of treatment. The precautions and adverse events to be monitored were also put forward.

2.3.2 Anticoagulant consultation recommendations

Padua [8] score and Caprini[9,10] score were used to evaluate the embolism risk of internal medicine inpatients and surgical patients, respectively, whose hemorrhage risk was evaluated according to Crusade score [11-12].The hemorrhage risk assessment criteria for Atrial Fibrillation (AF) patients and patients taking oral anticoagulant was HAS-BLED score [13].The stroke risk of AF patients was evaluated by CHA2DS2-VASc score[13]. According to the scoring criteria above, patients were given individualized scores and consultation recommendations. If the risk of embolism was significantly higher than that of hemorrhage, anticoagulant medication shall be given. If equivalent, physical prevention advice or consultation with Department of Rehabilitation shall be given. For patients with hemorrhage or consultations aimed at the application of anticoagulant drugs, suggestions shall be given by pharmacists of anticoagulant specialty.

2.3.3 PPIs use recommendations

The evaluation criteria for the rational use of PPIs are mainly divided into two parts: one was the necessity of preventive medication, while the other was the rationality of therapeutic medication. The evaluation criteria referred to Stress ulcer prophylaxis in the postoperative period[14], Stress-related mucosal disease in the critically ill patient:risk factors and strategies to prevent stress-related bleeding in the intensive care unit[15], Stress ulcer prophylaxis in hospitalized patients not in intensive care units[16], Expert recommendations for stress ulcer prophylaxis (2018)[17] and Expert consensus on optimal application of proton pump inhibitors [18]. Stressors should be recorded. If the preventive measure was needed, recommended PPIs and dosage shall be given. If the current utilization was inappropriate, suggestions for improvement shall be put forward. In terms of consultations for the purpose of PPIs application, pharmacists of gastroenterology specialty shall give suggestions.

2.3.4 Nutrition support recommendations

Nutritional risk assessment was performed for patients who were highly suspected to need nutritional support. The assessment standard was Nutritional Risk Screening 2002 (NRS 2002). According to patients' risk assessment scores, current dietary status, relevant guidelines and recommendations [19-21], corresponding enteral/parenteral nutritional suggestions were given. The key principle was that enteral nutrition supplement was given priority for patients who were unable to eat on their own [22]. Supplementary parenteral nutrition could be given only when enteral nutrition was absolutely contraindicated or cannot meet the target requirement. The supply standard is described as follows: the energy supply is 25-30kcal/ (kg/d), the protein is 1.2-2g/ (kg/d), and the ratio of sugar to lipid and non-protein calorie: nitrogen is 5:5 and (100-200): 1, respectively. For the consultations aimed at the application of nutrition support, pharmacists of nutrition specialty will give recommendations. If necessary, the nutrition department should be invited to assist in the consultation.

2.4 Evaluation of consultation effectiveness and acceptance

Effectiveness rate of consultations: 72 hours after consultation, two off-duty pharmacists evaluated the effectiveness, which was defined as one or more of relevant symptoms and signs have significantly improved or laboratory tests have decreased by more than 30%. The main reference standard was based on the outcome evaluation of the consultation purpose. If the medication suggestion was given for the purpose of prevention, patients' positive signs should be examined.

Effectiveness rate of consultations (ERC) = Effective consultations/ (Effective consultations + Ineffective

consultations) ×100%.

Acceptance rate of consultations: (1) Not accepted: the physician rejected the consultation suggestions; (2) Partially accepted: the physician partially accepted the consultation suggestions; (3) Completely accepted: the physician completely accepted the consultation suggestions. Accepted consultations=completely accepted consultations+ partially accepted consultations.

Acceptance rate of consultation (ARC) = Accepted consultations / Total consultations ×100%.

2.5 Data collection and statistical analysis

The data were gathered and recorded from Electronic Medical Record System, which were crosschecked by two independent pharmacists using Microsoft Office Excel 2017.Software IBM SPSS 25.0 was applied to perform statistical analyses. Categorical variables were presented as numbers with percentages. Chi-square tests were used for group comparisons. $P<0.05$ was considered statistically significant.

3. Results

From 2018 to 2020, 651 consultation cases were included in the study, of which 542 cases met the inclusion criteria. Among the 542 consultation cases, 94 cases of 2018 were in the pre-intervention group, and 448 cases (2019 / 2020,197 / 251) were in the post-intervention group. Figure 1 describes the procedure of case selection.

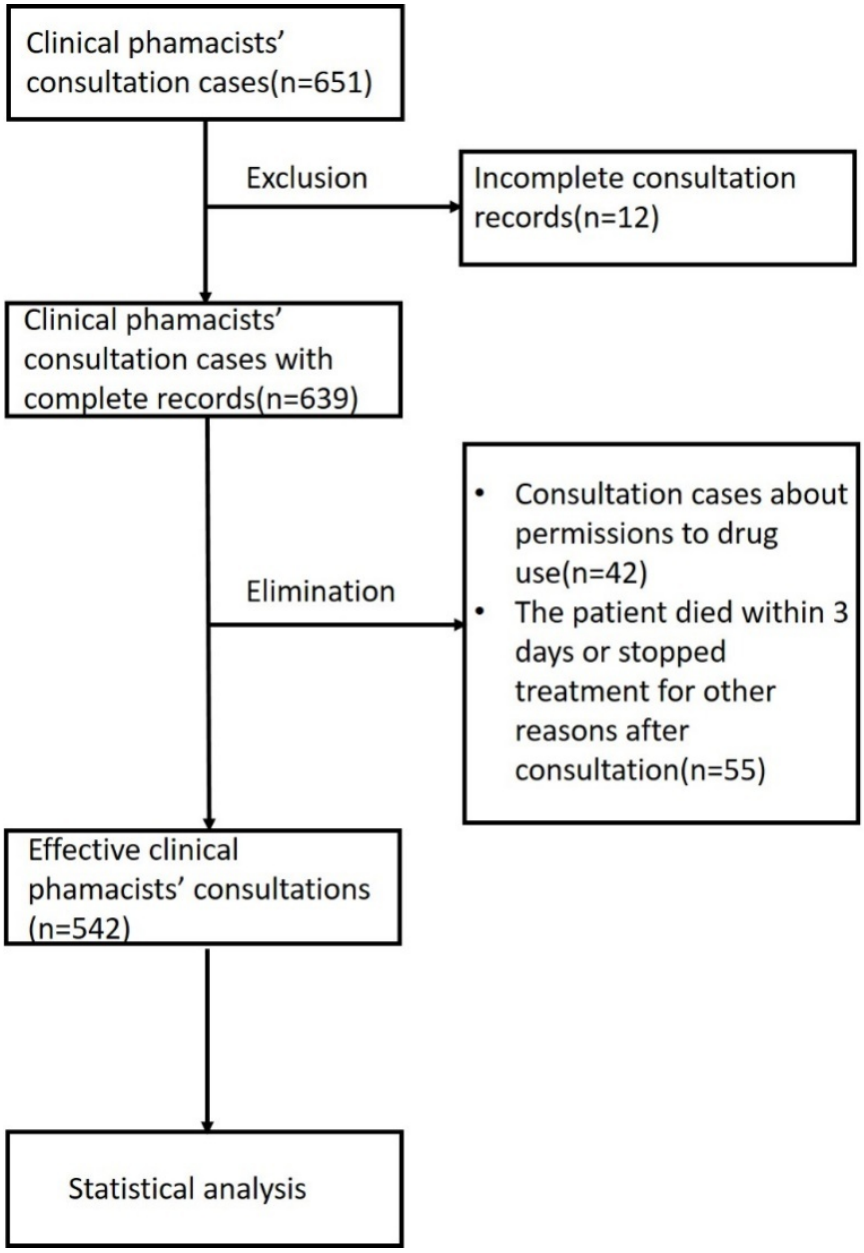

Figure1 Flow chart of the study

3.1 Consultation patient characteristics

Characteristics of the patients included in the analysis is shown in Table 1. In the post-intervention group, the proportion of patients > 66 years old was the highest (52.0%), while in the pre-intervention group, the proportion of patients aged 18-65 years old was the highest (59.6%). In the post-intervention group and the pre-intervention group, the number of patients with abnormal liver function, abnormal renal function and basic diseases were 105(23.4%) and 17 (18.1%), 149(33.2%) and 29 (30.8%), 367 (81.9%) and 72 (76.6%), respectively. In the post-intervention group, patients of 222 cases (47.3%), 113 cases (25.2%), 161 cases (35.9%) and 58 cases (12.9%) were at high risk of embolism, bleeding, stress ulcer and abnormal nutritional status, respectively.

Characteristics	Characteristics	Pre-intervention group (n=94, %)	Post-Intervention group (n=448,%)
Male	Male	45(47.9)	276(61.6)
Age	0-17	1(1.1)	3(0.7)
	18-65	56(59.6)	211(47.1)
	>66	37(39.4)	233(52.0)
Abnormal liver function	Abnormal liver function	17(18.1)	105(23.4)
Abnormal kidney function	Abnormal kidney function	29(30.8)	149(33.2)
Abnormal infection index	Abnormal infection index	81(86.2)	388(86.6)
With underlying disease	With underlying disease	72(76.6)	367(81.9)
With embolism risk	Embolism patients	1(1.1)	21(4.7)
	Patients with high risk factors of embolism(Padua score)	15(16.0)	120(26.8)
	Patients with high risk factors of embolism(Caprini score)	11(11.7)	70(15.6)
	Patients with high risk factors of embolism(CHA2DS2-VASC score)	7(7.4)	21(4.7)
	Patients with high risk factors of embolism(WELLs score)	0(0)	1(0.2)
	Total number of high risk factors of embolism groups	33(35.1)	222(47.3)
With bleeding risk	With bleeding risk	17(18.1)	113(25.2)
Gastrointestinal risk	with gastrointestinal bleeding	1(1.1)	19(4.2)
	With high risk factors of stress ulcer	29(30.8)	161(35.9)
Abnormal nutritional status	Abnormal nutritional status	5(5.3)	58(12.9)

Table1 Characteristics of the patients included in the analysis (n=542)

3.2 Information on clinical pharmacists' consultations

The detail information of 542 consultation cases are shown in Figure 2. From 2018 to 2020, the number of consultation cases were 94, 197 and 251 respectively. The number of general consultations, multidisciplinary difficult consultations, anti-infection consultations, non-anti-infection consultations, departments applying for general consultations and departments applying for multidisciplinary difficult consultations increased year by year. The number of departments applying for general consultations in the post-intervention group

increased significantly compared with the pre-intervention group (53.6% vs 33.9%, P =0.036).

Among non-anti-infection consultation cases, consultations of individualized medication regimens and adverse reactions accounted for the highest proportion, both of which were 29.5% (18 cases). 14.8% (9 cases) were for the purpose of anticoagulation consultation, while 13.1% (8 cases) were for nutrition consultation, as were shown in Figure 3.

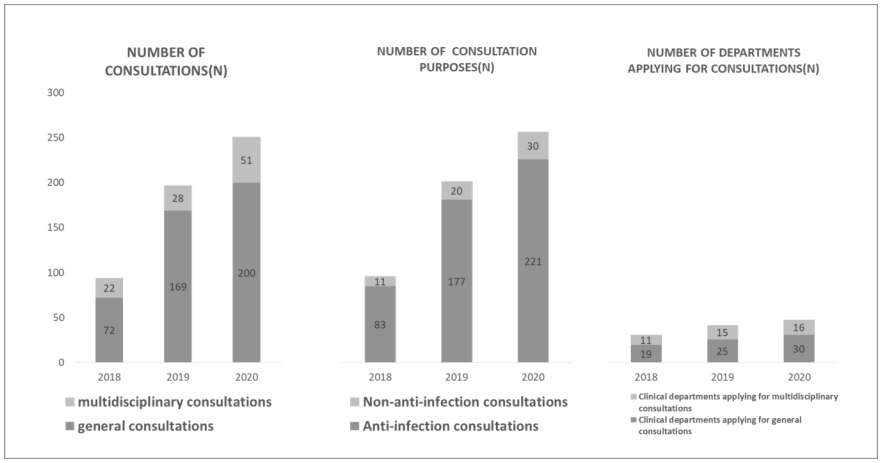

Figure2 Clinical pharmacists' consultation types and application departments

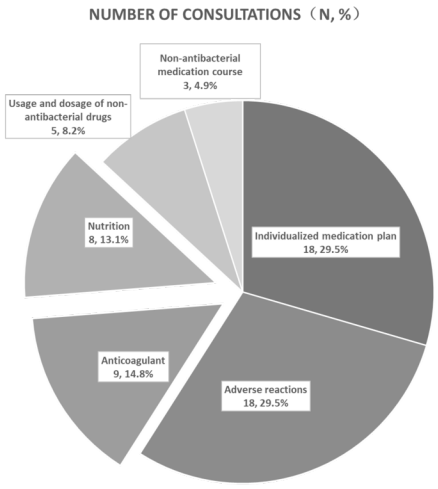

Figure3 Purposes of non-anti-infection consultations

3.3 Information on the consultation mode of multidisciplinary individualized medication recommendations

After intervention, 627 individualized medication recommendations were proposed in 2019, and 906 were in 2020, showing an increasing trend compared with 2018(290 cases).The number of recommendations for anticoagulation, nutrition support and follow-up monitoring rose significantly. In 2018, 2019 and 2020, the proportion of physical method in anticoagulation recommendations was the highest, which were 43.2% (60 cases), 47.5% (126 cases) and 46.6% (153 cases) respectively. Preventive use ratio in PPIs application was the highest, with 33.3% (4 cases), 24.1% (7 cases) and 30.8% (16 cases) in 2018, 2019 and 2020, respectively. It

was demonstrated that nutrition support recommendations were mainly enteral nutrition recommendations. Infection indicators and liver and kidney function accounted for the highest proportions in treatment follow-up monitoring. Pharmacists' multidisciplinary individualized medication recommendations are shown in Table 2.

Consultation recommendations	**Consultation recommendations**	**2018**	**2019**
Number of anti-infection recommendations n (%)	Empirical application	25(18.0)	50(18.9)
	Drug use adjustment	60(43.2)	126(47.5
	Whether to apply antibacterial drugs	6(4.3)	11(4.2)
	Whether to deactivate antibacterial drugs	3(2.2)	18(6.8)
	Preventive use	1(0.7)	1(0.4)
	Dosage adjustment	19(13.7)	18(6.8)
	Treatment course	7(5.0)	7(2.6)
	Other recommendations	18(12.9)	34(12.8)
	Total	139(100)	265(100)
Number of anticoagulant recommendations n (%)	Empirical application	2(16.7)	3(7.7)
	Drug use adjustment	1(8.3)	1(2.6)
	Dosage selection	2(16.7)	6(15.4)
	Treatment course	1(8.3)	1(2.6)
	Whether to apply anticoagulant drug	1(8.3)	8(20.5)
	Whether to deactivate antibacterial drug	3(25.0)	6(15.4)
	Physical method	1(8.3)	12(30.8)
	Other recommendations	1(8.3)	2(5.1)
	Total	12(100)	39(100)
Number of PPIs application recommendations n (%)	Whether to apply PPIs	1(8.3)	5(17.2)
	Choice of drugs	3(25.0)	8(27.6)
	Preventive use	4(33.3)	7(24.1)
	Dose adjustment	2(16.7)	7(24.1)
	Treatment course	1(8.3)	1(3.4)
	Other recommendations	1(8.3)	1(3.4)
	Total	12(100)	29(100)
Number of nutritional support recommendations n (%)	enteral	2(66.7)	17(81.0)
	parenteral	1(33.3)	4(19.0)
	Total	3(100)	21(100)
Number of follow-up monitoring recommendations n (%)	Liver and kidney function	32(25.8)	58(21.2)
	Coagulation index	6(4.8)	28(10.3)
	Infection index/signs	73(58.9)	136(49.8
	Bleeding	2(1.6)	10(3.7)
	Nutrition improvement	3(2.4)	15(5.5)
	Adverse reactions	8(6.5)	26(9.5)
	Total	124(100)	273(100)
Total(n)		290	627

Table2 2018-2020 multidisciplinary individualized medication recommendations

3.4 Acceptance rate and effectiveness rate of consultations

The acceptance rate and effectiveness rate of consultations are presented in Table 3. In the pre-intervention group, 95.7% (90 cases) were accepted and 96.9% (434 cases) were accepted in the post-intervention group. No differences were shown between two groups in acceptance rate. The effectiveness rate of consultations in the post-intervention group was 81.7% vs 70.2% in the pre-intervention group ($P < 0.05$).

group	Acceptance rate n (%) Accepted	Acceptance rate n (%) Rejected	Acceptance rate n (%) Total	Effectiveness rate n (% Effective
pre-intervention group	90(95.7)	4(4.3)	94(100)	66(70.2)
post-intervention group	434(96.9)	14(3.1)	448(100)	366(81.7)
χ^2	0.309			6.334
p	0.578			0.012

Table3 Acceptance rate and effectiveness rate of the consultations

4 Discussion

4.1 Improvement of anti-infection consultation quality

From 2018 to 2020, the number of consultations increased significantly, and anti-infection consultations were still dominant. On the one hand, health administrative authorities in China attached great importance to the rational use of antibacterial drugs, which was included in hospital management and performance evaluation indicators. On the other hand, Chinese clinical pharmacists vigorously invested in anti-infection consultation work, which dramatically improved the consultation effect and expanded their influence in the management of antibacterial drugs[22-24]. The main purpose of anti-infection consultations in our hospital was to adjust the anti-infection scheme, and the main working mode was to adjust the scheme when the bacterial culture result was not available or negative, or screen the scheme if it was available. As a result, how to improve the ability of anti-infection treatment is a crucial problem that clinical pharmacists should always pay attention to.

The top three clinical departments applying for pharmaceutical consultations were Department of Spinal Surgery (99 cases, 18.3%), Department of Urology (68 cases, 12.5%) and Central Intensive Care Unit (CICUs) (55 cases, 10.1%). In our hospital, the amount of spinal surgery is large, so is the number of patients with fever after operation. Surgeons lack experience in using antibiotics, especially the choice of drugs for anti-tuberculosis treatment, which should attract clinical pharmacists' attention. In terms of Department of Urology, the patients' characters are more distinct. They tend to be elder with liver and kidney dysfunction and multiple chronic disease, so more needs are for adjusting dosage and identifying drug interactions. Consultations in Intensive Care Units (ICUs) mainly focus on multidisciplinary difficult cases. Our main concern is the individualized medication of patients with multi-drug resistant bacteria or rare pathogenic bacteria infection. In order to provide better pharmacy services for ICUs patients, senior clinical pharmacists regularly hold consultation case discussions and literature reading reports in 4 ICUs. The topics mainly include high-quality anti-infection literature, the rational use of special grade antibiotics such as ceftazidime、avermectin and polymyxin B, and individualized medication experience analysis, which provide a learning and communication platform for physicians.

It is worth noting that with the rapid increase in the incidence of fungal infections [25], there is a corresponding increase in need for the rational use of anti-fungal drugs. Such consultations are often difficult to give recommendations due to the long course of broad-spectrum antibiotics treatment for patients. On the premise of evaluating risk factors with WVUH deep fungal infection score, clinical pharmacists strictly controlled the abuse of antifungal drugs and achieved good therapeutic effects.

4.2 Discussion on the consultation mode of multidisciplinary individualized medication

Pharmacists should take initiative to pay attention to all the medication of patients. Only in this way can we broaden the breadth and depth of clinical pharmacists' consultations. To create multidisciplinary pharmaceutical consultation is the purpose of developing the mode of multidisciplinary individualized medication consultation in our hospital. According to the data above, there are 11 non-anti-infection consultation cases in 2018, 20 cases in 2019 and 30 cases in 2020, demonstrating an increasing trend year by year. The total number of non-anti-infection consultations in three years accounts for 11.3%, which is equivalent to the

average proportion of tertiary hospitals in other regions of China [7]. Among them, anticoagulation consultations accounted for 9 cases (14.8%), and nutrition consultations accounted for 8 cases (13.1%). There is still a certain gap between the breadth of drug selection and the difficulty of consultations, by comparison to national clinical pharmacy specialty hospitals [26-27].

Department of Cardiology is characterized by radiofrequency ablation of heart failure, arrhythmia and atrial fibrillation. It has a high reputation in Shanghai, China. In addition, the Department of Respiration is a rapidly developing specialty in recent years, in which anticoagulant outpatient service is badly in need. The anticoagulant pharmacy services our hospital have carried out are embodied in pharmacy rounds and the support of physician-pharmacist joint anticoagulation outpatient clinics. The addition of anticoagulant recommendations in pharmacists' consultations is another attempt of pharmaceutical intervention. First, during the intervention process, we found that the both physicians and nursing staffs have established a relatively standardized evaluation process and medication habits for postoperative anticoagulation management. However,for elderly patients with renal insufficiency,physicians are often confused about the choice of medication and dosage; Secondly, for the non-surgical patients, physicians tend to ignore whether they are at high risk of embolism, which leads to inaccurate application timing of anticoagulant drugs. Besides, during the process of medication, hemorrhage risk is not easy to pay attention to, resulting in increased risk of adverse consequences. Finally, how to balance embolic risk and hemorrhage risk, and how to carry out physical prevention are also weak links. In response to the problems above, clinical pharmacists give interventions in consultations and play a certain effect. After intervention, no consultation patients have experienced embolism or hemorrhage due to the unreasonable use of anticoagulants. At present, the participation of clinical pharmacists in anticoagulant work in China is still in the initial stage. The work mainly focuses on patient follow-up and assisting doctors in patient education management. Besides, current anticoagulant management norms and standardized anticoagulant effect evaluation system are also in the exploratory stage[28]. We need to find our own way out to catch up with other countries. In the future, we intend to continue implementing this mode to improve the quality and quantity of anticoagulation consultations.

PPIs are widely used in clinical practice. In the previous pre-prescription review and key monitoring drugs review, we found that physicians had many irrational PPIs use, including inappropriate timing of medication, unreasonable choice of dosage and dosage form, inappropriate use of drugs, etc. After the implementation of the intervention, we gave individualized suggestions to patients. The recommendations mainly include reasonable therapeutic and preventive dose, choice between oral and intravenous drip dosage form and the incidence of adverse reactions caused by drug interaction, which were generally welcomed and accepted by physicians. In China, due to the increasingly serious problems of PPIs abuse, a series of targeted measures have been implemented and preliminary results have been achieved [29-30]. The addition of PPIs recommendations in clinical pharmacists' consultations is our attempt. With the continuous promotion of this mode, we hope to further rationalize PPIs use and reduce unnecessary drug expenditures.

In China, clinical nutrition support is developed late,so is the work of nutrition pharmacists. Besides, nutrition pharmacists' work content overlaps with that of the Department of Nutrition, resulting in the relatively slow work progress. The nutritional pharmaceutical care in our hospital is still in its infancy, which does not match the needs of its tumor specialty characteristics. In fact, nutrition support is indeed urgently in need. In the face of the needs of a large number of tumor patients and rapid development of new varieties and dosage forms of nutritional drugs in the market, oncologists need nutrition pharmacists' support.

At present, although the total number of nutrition consultations is small, we have basically achieved individualized nutritional score screening for each patient, which is related to the low prevalence of malnutrition [31].That means we have taken the first step of nutritional screening at the pharmaceutical level. But it is far from enough to give recommendations on enteral or parenteral nutrition based on screening scores. The next step is to publicize our nutrition support and promote propaganda and education on problems of nutritional risk screening, early low calorie supply, enteral nutrition priority, etc. We plan to sort out the classification of enteral and parenteral preparations in our hospital, and introduce energy density, sugar fat ratio, preparation characteristics and pharmacoeconomic evaluation to physicians, so as to let them know

our expertise in nutrition support.

When giving consultation recommendations, it is equally important to focus on the effect of medication advice, the monitoring of adverse reactions, and whether they should ask other departments for help. In the future, we should also pay attention to follow-up monitoring and multidisciplinary cooperation.

4.3 Evaluation of consultation effects

The ARC of the post-intervention group was not significantly increased, compared with the pre-intervention group (96.9% vs 95.7%, P = 0.578). But it was higher than what was reported in domestic literature[8-10]. This was probably due to the frequent interactions with physicians and the general recognition of ability. The ERC in the post-intervention group was significantly higher than that in the pre-intervention group (81.7% vs 70.2%, $P < 0.05$), but lower than was reported in the domestic literature. It may attribute to the fact that our hospital is the leading phase I tumor clinical research center in China, which attracts large numbers of patients with advanced malignant tumor. The consultation patients are often infected seriously and combined with multiple organ failure, which lead to poor prognosis and affected the effectiveness of consultations.

4.4 Case in point

A 92-year-old female was admitted to our hospital with the diagnosis of malignant tumor of colon. She had a history of peptic ulcer and heart failure. After admission, the patient had repeated fever and was treated with levofloxacin and moxifloxacin hydrochloride injection successively. At present, she was still in fever with liver dysfunction (total bilirubin 42.4 umol·L^{-1}, direct bilirubin 37.1 umol·L^{-1}, AST 66 U·L^{-1}, r-GT 183 U·L^{-1}) and renal dysfunction (creatinine 233 umol·L^{-1}). The infection index was abnormal (WBC 14.59 × 10^9 L^{-1}, CRP 126.64 mg·L^{-1}) and the mental response was poor.

Purpose of consultation: To adjust the anti-infection scheme.

Clinical pharmacists suggest that: (1) The patient's current inflammatory indicators are progressively elevated with frequent urination symptoms. Midstream urine culture repeatedly shows multidrug-resistant Klebsiella pneumoniae (+), which needs to be treated with another antibiotic. Considering that the patient is at the advanced age of 92 with abnormal liver and kidney function, polymyxin is not suitable because of its nephrotoxicity and neurotoxicity, neither is compound sulfamethoxazole because of its hepatotoxicity and nephrotoxicity. In addition, the concentration of tigecycline in urinary tract is low, which should not be the primary choice in treating urinary tract infections. Considering the conditions above, we recommend to use ceftazidime avibatam sodium for injection 1.25g q12h ivgtt (creatinine clearance rate of 32ml·min^{-1}). Blood routine, CRP and PCT should be reexamined after 3 days of medication. (2) The patient's Padua score is 6 points (stay in bed for at least 3 days 3'+advanced age 1'+heart failure 1'+infection 1'), indicating a high risk of embolism. So it is recommended to use low molecular weight heparin 4000 IU qd. (3) The patient has a history of peptic ulcer, uncontrolled infection and liver dysfunction, which are risk factors of stress ulcer. So pantoprazole 40 mg bid ivgtt is recommended. (4) According to NRS2002 nutritional screening score, the patient gets 3 points (malignant tumor1'+ recent weight loss1'+decreased food intake1'), which suggests severe malnutrition. So we suggest to use ENSURE on demand. (5) The patient is currently using compound amino acid injection (18AA). In view of the abnormal liver function, we suggest to select branched chain amino acids preparations. As a result, we suggest to use compound amino acid injection (20AA) instead.

Follow-up: Physicians accepted the consultation recommendations above. After 3 days of treatment, the patient's temperature decreased and the infection index gradually returned to normal. No thrombosis or upper gastrointestinal bleeding occurred. The nutritional status improved.

4.5 Conclusion

During the specialty construction of Shanghai clinical pharmacy, we strengthened the training of clinical pharmacists, and further improved the pharmaceutical services. In terms of the pharmaceutical consultation work, we created a multidisciplinary individualized medication consultation mode. During the implementa-

tion of this mode, we added anticoagulation, PPIs use, nutrition and individualized follow-up monitoring to the consultation recommendations, which increased the total number of consultations year by year. In details, the number of general consultations, multidisciplinary difficult consultations, departments applying for general consultations, departments applying for multidisciplinary difficult consultations, anti-infection consultations and non-anti-infection consultations increased correspondingly. The ARC continued to be higher than the average level in China and the ERC was significantly higher than that in the pre-intervention stage, which reflected clinical pharmacists' value in rational drug use.

4.6 Limitations

The limitations of this study are listed as follows: 1.This study is a retrospective study, so the baseline is difficult to be flattened when the subjects are included in the study. In addition, some of the consultation subjects are in critical situation and require multidisciplinary diagnosis and treatment. Their outcomes cannot be completely attributed to the acceptance or rejection of clinical pharmacists' consultations, and the evaluation of effectiveness needs to be viewed objectively. 2. As the study is a single center study, the vast majority of patients are only limited in Pudong New Area of Shanghai, China. In order to further evaluate the impact of the new consultation mode on the consultation effects, multi-center, large sample studies should be carried out.

Acknowledgments

This study was supported by Key Specialties Foundation of Clinical Pharmacy of Shanghai Municipal Health Commission in China (SWLCYXZX-2018-001) and Research on the Epidemiology of Severe Drug-induced Diseases of the Chinese Society of Toxicology (CST2019CT304).

References

[1]Ministry of Health of China. Regulations on Pharmaceutical Administration of medical institutions. Available at: http://www.satcm.gov.cn/fajiansi/gongzuodongtai/2018-03-24/2269.html. Accessed April 7, 2011.

[2]Cui M, Liu XY, Pang XY, Gu ZC. Analysis of the entry point of clinical pharmacists in implementing pharmaceutical care. *Pharm Care Res* .2015; 15(4):318-320.

[3]National Health Commission of the People's Republic of China, State Administration of Traditional Chinese Medicine. Notice on strengthening pharmaceutical management and transforming the mode of pharmaceutical care. Available at: http://www.nhc.gov.cn/yzygj/s7659/201707/b44339ebef924f038003e1b7dca492f2.shtml.Accessed July 12, 2017.

[4]Zhang WY, Liu F, Lu RZ, Li YR. Analysis of summary of 3847 cases of consultation of clinical pharmacists and typical cases. *Chinese Journal of Drug Application and Monitoring* .2020; 17(2):120-123.

[5]Zhang J, Qian X , Zhang L , et al. Evaluation of the Effectiveness of Clinical Pharmacists' Consultation in the Treatment of Infectious Diseases: A Single-Arm, Prospective Cohort Study. *Front Pharmacol* .2019; 10:187.

[6]Zhang J, Li X, Xie J, Zheng W. Evaluation of a clinical pharmacist consultation service for patients with infectious diseases in China: a systematic review and meta-analysis. *Eur J Hosp Pharm* . 2020 May; 27(3): 131–136.

[7]Peng GL, Xing XF, Jia LL, Wang YH, Jin GL, Han Y. Current status of pharmacy consultation in a tertiary general hospitals based on literature analysis. *Chinese Journal of Clinical Pharmacy* .2019; 28(3):223-226.

[8]Barbar S,Noventa F,Rossetto V,el a1.A risk assessment model for the identification of hospitalized medical patients at risk for venous thomboembolism:the Padua Prediction Score.*J Thomb Haemost* .2010;8(11):2450-2457.

[9] Surgery branch of Chinese Medical Association. Guidelines for the prevention and management of perioperative thrombosis in general surgery in China. *Chinese Journal of Practical Surgery* . 2016; 36(5):469-474.

[10] Caprini JA. Thrombosis risk assessment as a guide to quality patient care. *Dis Mon* ,2005,51(2-3):70-78.

[11] Kahn SR,Lim W,Dunn AS,et a1.Prevention of VTE innonsurgical patients: Antithmmbotic Thempy and Prevention of Thrombosis,9thed:American College of Chest Physicians' Evidence-Based Clinical Practice Guidelines.*Chest* .2012;141(2 Suppl):e195S-e226S.

[12] Gould MK,Garcia DA,Wren SM,et a1.Prevention of VTE in nonorthopedic surgical patients: Antithrombotic Therapy and Prevention of Thombosis,9th ed:American College of Chest Physician Evidence-Based Clinical Practice Guidelines. *Chest* .2012;141(2 Suppl):e227S-e277S.

[13] Camm AJ, Lip GY, de Caterina R, et al. 2012 focused update of the ESC Guidelines for the management of atrial fibrillation an update of the 2010 ESC Guidelines for the management of atrial fibrillation Developed with the special contribution of the European Heart Rhythm Association. *Eur Heart J* . 2012; 33(21):2719-2747.

[14]Allen ME, Kopp BJ and Erstad BL. Stressulcer prophylaxis in the postoperative period. *Am J Health Syst Pharm* .2004; 61(6):588-596.

[15]Steinberg KP.Stress-related mucosal disease in the critically ill patient:Risk factors and strategies to prevent stress-related bleeding in the intensive care unit. *Crit Care Med* .2002;30(6Suppl):362-364.

[16]Grube RR and May DB. Stress ulcer prophylaxisin hospitalized patients not in intensive care units. *Am J Health Syst Pharm* .2007; 64(13): 1396-1400.

[17] Writing Group of Expert Consensus on the Preventive Application of Proton Pump Inhibitors. Expert consensus on the preventive application of proton pump inhibitors. *Journal of Chinese Physician* .2018; 12(20):1775-1781.

[18]Zhang Y, Zhao J, Tong RS, et al. Expert consensus on optimal application of proton pump inhibitors. *Chin J Hosp Pharm* . 2020; 1-24.

[19]Society of Parenter and Enteral Nutrition of Chinese Medical Association. Expert consensus on oral nutrition supplement for adults. *Chin J Gastrointest Surg* . 2017; 20(4):361-365.

[20] Geriatric Nutrition Support Group. Guidelines for the application of parenteral and enteral nutritionin elderly Chinese patients. Chin J Geriatr.2020; 39(2):119-132.

[21]Society of Parenter and Enteral Nutrition of Chinese Medical Association. Expert consensus on supplemental parenteral nutrition. *Chin J Gastrointest Sur* g. 2017; 20(1):9-13.

[22]Singer P, Blaser AR, Berger MM, et al. ESPEN guideline on clinical nutrition in the intensive care unit. *Clin Nutr* . 2019; 38(1):48-79.

[23]Zhang J, Li X, Xie J, Zheng W. Evaluation of a clinical pharmacist consultation service for patients with infectious diseases in China: a systematic review. *Eur J Hosp Pharm* .2020; 27(3):131-136.

[24] Li Z, Cheng B, Zhang K, Xie G, Wang Y, Hou J, et al. (2017).Pharmacist-driven antimicrobial stewardship in intensive care units in East China: a multicenter prospective cohort study. *Am J Infect Control* .2017; 45(9):983-989.

[25]Horn CB, Wesp BM, Fiore NB, et al. Fungal Infections Increase the Mortality Rate Three-Fold in Necrotizing Soft-Tissue Infections.*Surg Infect* .2017; 18(7):793-798.

[26]Yang X, Zhang S, Guo H, Zhang G. Nutrition specified clinical pharmacists participating in clinical nutrition support. *Central South Pharmacy* .2018; 16(5):692-694.

[27] Li P, Bu S, Yao H, Liu X, Zhou J, Yang Y. Summary of clinical pharmacists involvement in 43 cases of anti-thrombotic consultation and analysis of difficult points. *Pharm Care Res* .2020; 20(3):169-173.

[28]Li S, Hui X, Jin Y, Wang J, Zhang H, Wang B, Xu H. Evaluation of Anticoagulant Effects of Clinical Pharmacist Management in Anticoagulation Clinic.*China Pharmacy*.2020; 31(18):2289-2293.

[29]Hong Y, Ye Z, Gao Z, Rao Y. Continuous improvement on the rationality of prophylactic injectable PPIs usage by a clinical pharmacist-led guidance team at a Chinese tertiary teaching hospital.*J Int Med Res* , 2020, 48(10):1-15.

[30]Zhang Y, Yang H, Kong J, Liu L, Li R, Zhang X,Yun J,Gu Q. Impact of interventions targeting the inappropriate use of proton-pump inhibitors by clinical pharmacists in a hepatobiliary surgery department[J]. *J Clin Pharm Ther* . 2021; 46(1):149-157.

[31] Meijers JM,Tan F,Schols JM,Halfens RJ. Nutritional care; do process and structure indicators influence malnutrition prevalence over time?. *Clin Nutr* . 2014;33(3):459-465.

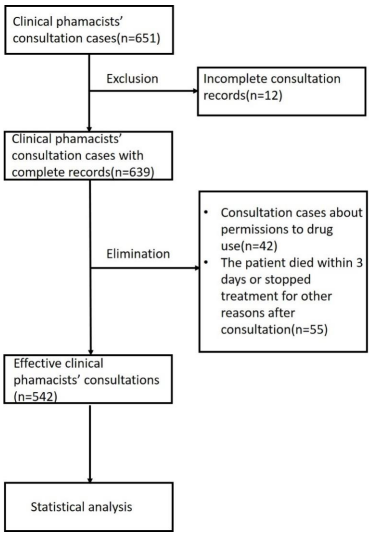

Figure1 Flow chart of the study

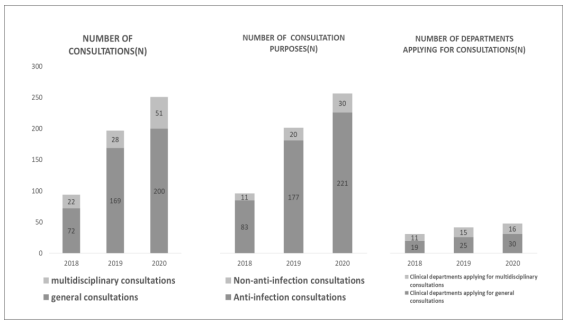

Figure2 Clinical pharmacists' consultation types and application departments

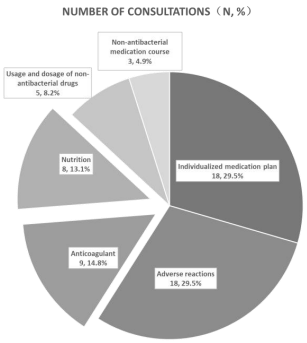

Figure3 Purposes of non-anti-infection consultations