

Analysis on the Impact of Antibiotic Abuse on Public Health and Its Pharmaceutical Intervention Measures

Yanzhe Wang

College of Pharmacy, Zhejiang University of Technology, Hangzhou, 315500, China

Abstract. This paper examines the severity and multi-dimensional impact of antibiotic abuse in global public health problems and analyzes effective pharmaceutical interventions for it. The discovery of antibiotics has greatly enhanced human ability to treat bacterial infections, but due to improper use, the number of drug-resistant strains has risen sharply, posing a serious health threat to people. Research shows that antibiotic abuse is mainly caused by improper prescriptions, patients' unauthorized use of drugs, excessive use in agriculture and animal husbandry, and inadequate supervision by medical institutions. This abuse has not only led to the rapid development of drug resistance, but also caused a series of problems such as adverse drug reactions, microecological imbalance, rising medical costs and environmental pollution. This paper presents multi-level pharmaceutical intervention strategies for these challenges: Build a complete antibiotic management system and implement a "graded management, professional review" model, enhance the consultation, guidance and supervision role of pharmacists in rational drug use and promote the participation of clinical pharmacists in consultation, establish an electronic monitoring system for antibiotic use and strengthen education for medical staff and the public, improve the norms for agricultural and livestock drug use and promote the research and development of new antibiotics. Through literature analysis and case studies, this paper demonstrates that systematic pharmaceutical intervention is of great significance for controlling antibiotic abuse, reducing the level of drug resistance development, and safeguarding public health, thereby providing theoretical basis and practical experience for establishing a long-term mechanism for the rational use of antibiotics.

Keywords: Antibiotic abuse; Bacterial resistance; Public health; Pharmaceutical intervention; Rational drug use.

1. Introduction

Antibiotics are the key weapon against bacterial infections. Since the widespread use of penicillin in the 1940s, they have played an irreplaceable role in saving many lives and transforming medical practice. However, as the scope of antibiotic use has expanded and the frequency has increased, abuse has become a major challenge in the field of global public health. According to data from the World Health Organization (WHO), about 129 countries reported severe antibiotic resistance problems in 2020, and more than 70 percent were directly related to the irrational use of antibiotics.

The situation of antibiotic abuse in China's medical and health sector is also not optimistic. The "Measures for the Clinical Use of Antibiotics" issued by the National Health Commission shows that the intensity of antibiotic use in China's medical institutions decreased from 2019 to 2023 but was still about 25% higher than the international average, and in primary medical institutions and the agricultural and pastoral sectors, There are obvious loopholes in the supervision of antibiotic use, and the problem of insufficient rationality of prescriptions is particularly prominent.

Antibiotic abuse has evolved from a mere medical use issue to a complex social public health problem, with consequences that not only increase individual health risks but also lead to rapid development of bacterial resistance, an increased burden on the medical system and changes in the environmental microbiota, a series of chain reactions, According to conservative estimates, if no effective intervention measures are taken, 10 million people may die each year from drug-resistant bacterial infections worldwide by 2050, with related economic losses amounting to 100 trillion US dollars.

In this context, pharmaceutical intervention is one of the key strategies to control antibiotic abuse, and its importance is increasingly prominent. Pharmacists, as gatekeepers of medication safety, have

irreplaceable professional strengths and responsibilities in promoting the rational use of antibiotics and reducing the development of drug resistance. This article intends to analyze the current situation and causes of antibiotic abuse from a systematic perspective. It also delves into its multi-dimensional impact on public health and provides corresponding interventions from a pharmaceutical perspective, hoping to provide references for building a long-term mechanism for the rational use of antibiotics.

2. The current situation and causes of antibiotic abuse

2.1 Analysis of the current situation of antibiotic abuse

The problem of antibiotic abuse in China is characterized by both prevalence and severity. According to monitoring data from the China Antimicrobial Management Network, in 2022, the proportion of antibiotic prescriptions in outpatient clinics in China reached 30.2%, significantly higher than the 20% standard recommended by the WHO. The antibiotic usage rate among inpatients was as high as 49.7%. This figure also exceeded the upper limit recommended by the world. It is particularly notable that the intensity of antibiotic use in primary care institutions and township health centers is typically 15 to 20 percentage points higher than that in tertiary hospitals, reflecting urban-rural disparities in the regulation of antibiotic use.

In China, third-generation cephalosporins and quinolones account for as much as 42.3 percent of total antibiotic use. These broad-spectrum antibiotics, which are supposed to be reserved drugs, are being used extensively in primary care, resulting in a significant increase in the risk of resistance. Meanwhile, according to the 2023 drug Market monitoring report, the sale of over-the-counter antibiotics in China has been explicitly banned, but the illegal acquisition of antibiotics through various channels still exists, such as self-medication without completing the course of treatment and improper dosage, which is widespread among the community population. This has become a key factor in exacerbating the abuse of antibiotics.

2.2 The main causes of antibiotic abuse

The causes of antibiotic abuse are complex and diverse, mainly involving multiple aspects including the patient management system of medical providers. From the perspective of medical providers, some medical staff do not have a sufficient grasp of the relevant knowledge of the rational use of antibacterial drugs. When making clinical decisions, they often rely too much on experience for medication rather than on evidence from evidence-based medicine. A survey of 24 provinces in China showed that about 27.4% of doctors would use antibiotics[2] preventively in the absence of clear evidence of bacterial infection. In a context of tense doctor-patient relationships, defensive medical practices have led to the overuse of antibiotics, thus avoiding potential medical disputes.

From the perspective of patients, there are significant biases in public perception of antibiotics. About 35.6 percent of the respondents believe that "antibiotics can treat colds and viral infections," while 41.2 percent are accustomed to purchasing and storing antibiotics on their own, and due to the imbalance in medical accessibility and differences in health service capabilities, In some areas, patients tend to make their own judgments about medication use, and the imperfect medical security system has also stimulated some medical institutions to increase the use of antibiotics in order to improve their economic benefits to a certain extent. The use of antibiotics for growth promotion and preventive purposes in agriculture and animal husbandry is also a major source of abuse. The contradiction between insufficient regulation and the pursuit of economic benefits has exacerbated this problem.

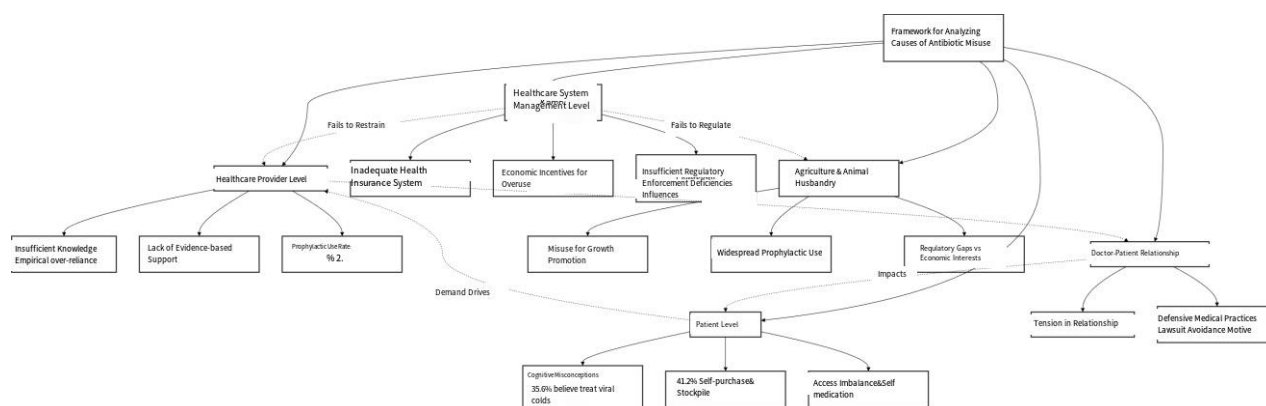


Figure 1. Framework for analyzing the main causes of antibiotic abuse

2.3 Characteristics of antibiotic abuse behavior among different groups

There are significant differences in antibiotic use behavior among different groups. At the medical institution level, primary medical institutions tend to use antibiotics through empirical treatment. Survey data from 2021 to 2023 indicated that the rate of microbiological testing before antibiotic use in medical institutions below the county level was 18.3%, much lower than 62.7% in tertiary hospitals. The antibiotic usage rates in the respiratory and pediatric departments of general hospitals are as high as 68.3% and 57.6% respectively, and they have become the "hotspots"[3] of antibiotic use. In terms of prescription types, cephalosporins are the main component in oral antibiotics, while β -lactam / β -lactamase inhibitor compound preparations are the most widely used in injectable antibiotics.

Among the general public, people of different ages and educational backgrounds have different medication habits. The highly educated group has a strong sense of self-medication but is more likely to complete the entire course of treatment, while the less educated group often stops taking medication as soon as symptoms are relieved, making the problem of insufficient course of treatment prominent. Studies show that people over 65 years old and children under 14 years old are at high risk of antibiotic overuse, and the elderly are prone to multiple medications due to multisystem diseases, while children are treated aggressively due to parents' excessive concern about infectious diseases in children. And rural residents, who have difficulty accessing medical resources, are more inclined to keep and share antibiotics, creating a specific "family medicine box" phenomenon that further exacerbates the problem of improper use of antibiotics.

3. The impact of antibiotic abuse on public health

3.1 The emergence and spread of drug-resistant strains

The most direct and serious consequence of antibiotic abuse is the accelerated development of bacterial resistance, according to the latest data from the National Bacterial Resistance Surveillance Network (CARSS), the resistance rate of major pathogenic bacteria in China has shown a continuous upward trend. In 2022, the resistance rate of *Escherichia coli* isolated clinically against third-generation cephalosporins reached 56.3%. The methicillin-resistant rate of *Staphylococcus aureus* is 38.7%, and the carbapenem antibiotic resistance rate of *Klebsiella pneumoniae* has climbed to 25.4%. These figures reflect the dire situation of bacterial resistance in our country, with some "superbugs" developing resistance[4] to most of the existing antibiotics.

The emergence of drug-resistant bacteria involves a multitude of complex biological processes. Antibiotic selection pressure forces bacteria to acquire resistance in the form of gene mutations and gene transfers, and the irrational use of antibiotics greatly accelerates this process. It is particularly worth noting that the transmission routes of drug-resistant genes are diversified and are no longer confined to the hospital environment. Studies have shown that drug-resistant bacteria and their genes can spread through food chains, water resources, animal contact and many other pathways among humans, animals and the environment, thereby creating an "integrated health" problem. During

monitoring of sewage treatment systems in major Chinese cities from 2020 to 2023, it was found that bacteria carrying important drug-resistant genes such as NDM-1 and KPC-2 were widely present in urban drainage systems, thus forming an environmental reservoir of drug-resistant genes.

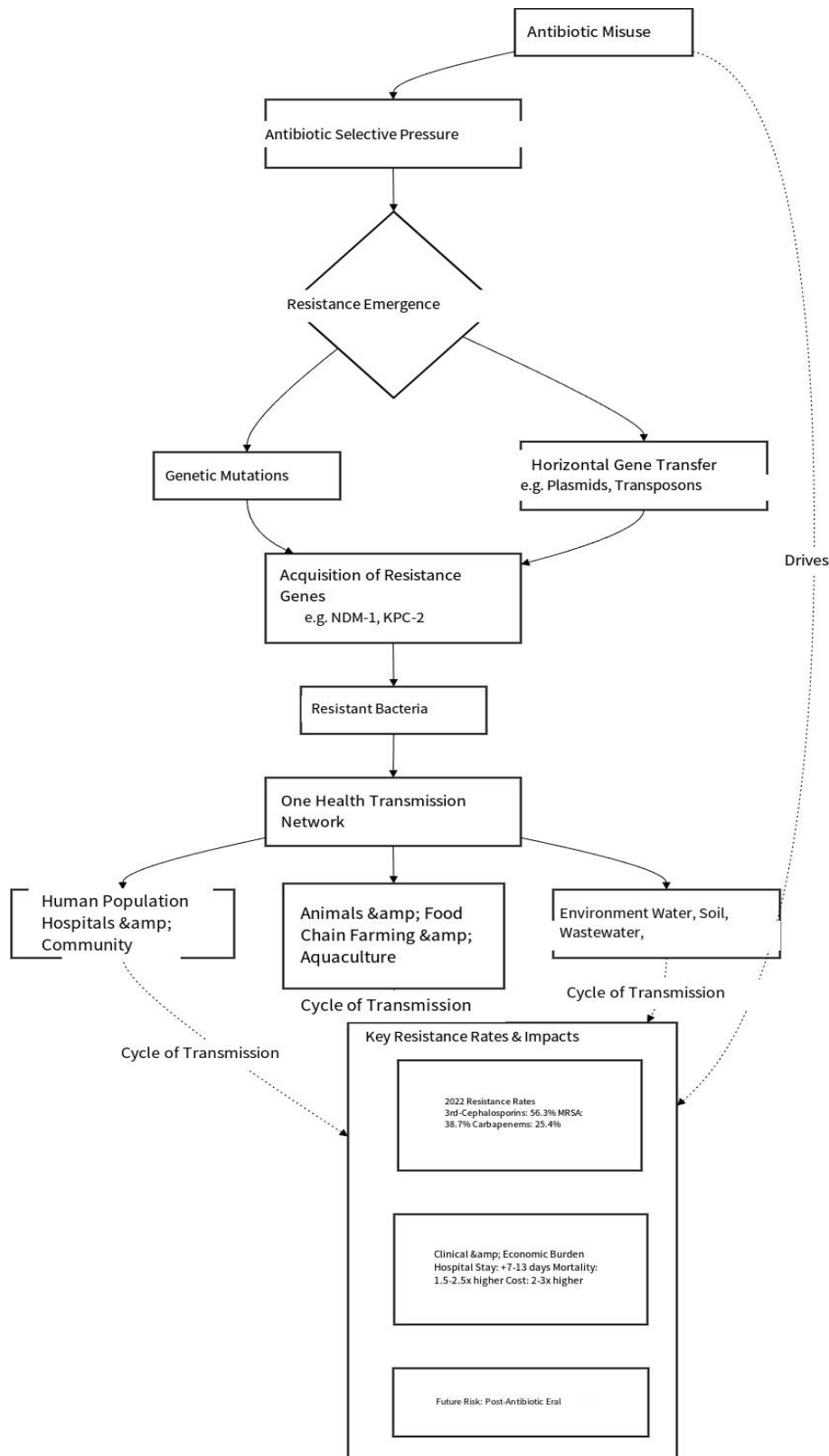


Figure 2. Mechanism of antibiotic abuse leading to the emergence and spread of drug-resistant bacteria

The spread of drug-resistant bacteria in clinical treatment poses an extremely serious challenge. Data show that patients' hospital stays are extended by an average of 7 to 13 days due to drug-resistant

infections, mortality is increased by 1.5 to 2.5 times, and treatment costs are increased by 2 to 3 times. What is even more worrying is the rising resistance rate of "last line of defense" antibiotics such as polymyxin tigecycline, the number of treatment options available to clinicians is decreasing, and humanity may once again fall into the "pre-antibiotic era", when many common infections are difficult to treat effectively and the progress made in medicine faces a serious risk of regression.

3.2 Individual health hazards

The impact of antibiotic abuse on individual health is far greater than the problem of bacterial resistance. The first factor that leads to an increase in the incidence of adverse drug reactions is the improper use of antibiotics. According to statistics from the National Center for Adverse Drug Reaction Monitoring, antibiotic-related adverse reaction reports accounted for 28.7% in 2021. Among them, serious adverse reactions accounted for 13.5%. Common adverse reactions included rashes, anaphylactic shock, liver and kidney function impairment, etc. Some patients had to extend their hospital stays or even lose their lives[5] because of this. The probability of allergic reactions to penicillin drugs is between 3% and 10%, and the risk of tendinitis and tendon rupture caused by fluoroquinolone antibiotics is particularly significant in the elderly population.

Antibiotic use has a very significant impact on the balance of the human microbiome. Studies have shown that short periods of broad-spectrum antibiotic treatment can reduce the diversity of the gut microbiota by 30 to 50 percent, with some beneficial microbiota taking months or even longer to recover. Microbiome imbalance is associated with an increased risk of multiple diseases. Such as *Clostridium difficile* infection, inflammatory bowel disease, allergic disease, etc., the latest research also found that frequent use of antibiotics in childhood is associated with an increased risk of metabolic syndrome autoimmune disease in adulthood, suggesting that antibiotic abuse may have long-term health effects.

When antibiotics are used normally, abuse can affect the normal treatment effect. Clinical data show that inappropriate prophylactic antibiotic use not only fails to prevent the target infection, but may also mask infection symptoms, delay diagnosis and increase the difficulty of subsequent treatment, and patients diagnosed with infection may use drugs improperly, such as insufficient dosage or incomplete course of treatment, It will reduce the cure rate, prolong the course of the disease, leave conditions for drug-resistant bacteria to choose, and create a vicious cycle that ultimately harms the health rights of patients.

3.3 Burden on the Medical System and Socio-economic Impact

The problem of antibiotic resistance caused by antibiotic abuse has already imposed an extremely heavy burden on the medical system and the social economy. According to the China Society for Medical Security Research, in 2022, the direct increase in medical expenditure due to bacterial resistance in China exceeded 35 billion yuan, accounting for as much as 18.4% of the medical insurance expenditure related to anti-infection during the same period. Drug-resistant infections typically require the use of more expensive antibiotics, longer hospital stays, increased frequency of auxiliary examinations, and treatment costs for some critically ill drug-resistant infections can be three to five times[6] that of ordinary infections. The pressure on the medical insurance fund is on the rise, and in some regions, the rationality of antibiotic use has already been included in the assessment indicators for medical insurance cost control.

From the perspective of medical resource allocation, a large amount of advanced medical resources are occupied by drug-resistant infection management, the bed turnover rate of infectious disease departments in tertiary hospitals has decreased, and the occupancy time of ICU beds has increased, resulting in an unbalanced distribution of medical resources. Statistics show that there are approximately 87,000 cases of multi-drug resistant bacteria infections across the country that require isolation treatment in 2023. This has consumed the time and protective supplies of many medical staff, thereby indirectly affecting the treatment efficiency of other patients.

From a macroeconomic perspective, the impact of antibiotic abuse goes far beyond the medical field, with drug-resistant infections causing labor damage, reduced productivity and rising care costs. According to the World Bank's estimates, if antibiotic abuse is not effectively controlled by 2030, China's GDP loss due to drug resistance could reach 1 trillion yuan. In addition, food safety problems caused by the use of antibiotics in agriculture and animal husbandry, barriers in international trade, and the cost of ecological restoration due to environmental pollution are also not to be underestimated. Studies have shown that antibiotic abuse has become the third leading source of disease economic burden after cardiovascular diseases and tumors, and its long-term socio-economic effects will last for [7] decades, combined with direct and indirect economic losses.

4. Pharmaceutical Interventions for Antibiotic abuse

4.1 Intervention strategies at the institutional level

Medical institutions are the main battlefield for the use of antibiotics. The intervention strategies therein are of vital significance in controlling the abuse of antibiotics. According to data from the National Health Commission, the antibiotic usage rate in China's tertiary hospitals has dropped from about 60% in 2015 to below 40% since 2020. This is attributed to the effective intervention measures implemented by medical institutions. At present, large medical institutions in China have widely established "antibiotic management task forces", which are composed of experts from various departments such as the hospital director, the pharmacy department, the infectious disease department, and the microbiology laboratory, working together to formulate and supervise the implementation of rational drug use systems. These task forces have effectively controlled the irrational use of antibiotics by conducting regular antibiotic use assessments, formulating guidelines and implementing prescription reviews. Research shows that the rational use rate of antibiotics has increased by 15% to 25% in hospitals that have implemented the antibiotic grading management system.

Another effective strategy is to build a computer-assisted decision support system (CDSS). A 2022 survey showed that more than 65% of tertiary hospitals in the country have deployed intelligent prescription review systems to achieve real-time monitoring and intervention of antibiotic prescriptions, which can be based on the actual situation of patients. Based on the results of bacterial culture and drug sensitivity tests, individualized dosing suggestions are provided and warnings are given for unreasonable prescriptions. The data indicated that the proportion of irrational antibiotic prescriptions in hospitals decreased by an average of 23.7% after the application of CDSS, and the use of broad-spectrum antibiotics decreased by 18.5%. Additionally, a regular network of nosocomial infection monitoring and antibiotic resistance monitoring was established to provide medical institutions with the trend of changes in the bacterial resistance spectrum in the region. It has also become a key basis for guiding rational drug use in clinical practice [8].

4.2 The Role of Pharmacists in the Rational Use of Antibiotics

Pharmacists, as drug experts, play an indispensable role in the rational use of antibiotics. With the gradual deepening of China's medical system reform, the functions of pharmacists have shifted from traditional drug dispensing to clinical pharmacy services, in accordance with the relevant provisions of the "Pharmacist Law" (implemented in 2023), Pharmacists have the right to question unreasonable prescriptions and to refuse dispensing, which provides legal protection for pharmacists' participation in antibiotic management. The number of clinical pharmacists in China has grown from about 50,000 in 2018 to more than 80,000 in 2023 over the past five years, and the importance of pharmaceutical intervention in antibiotic management has become increasingly prominent.

In hospital pharmacy administration, antibiotic use management mainly relies on the participation of pharmacists in the following ways: First, conducting prescription review work and intervening in antibiotic prescriptions that do not conform to the medication guidelines. Data from 2022 shows that the acceptance rate of pharmacist prescription intervention reached 83.5%. 2. Participate in clinical consultations to develop individualized medication plans for complex infection cases, especially in

special departments such as ICU, oncology, and hematology. Data show that the success rate of antibiotic treatment increased by 12% to 18% [9] in cases where clinical pharmacists participated in consultations. Third, build a drug therapy management (MTM) service to manage long-term medication use in patients with chronic diseases, thereby reducing unnecessary antibiotic use. Fourth, conduct drug concentration monitoring (TDM) to provide evidence for the precise use of antibiotics such as aminoglycosides and vancomycin, with data showing that the incidence of adverse reactions in patients decreased by more than 40 percent after implementing TDM.

Pharmacists also play a key role at the community and retail pharmacy levels. According to statistics, the proportion of over-the-counter antibiotic sales in domestic retail pharmacies dropped by 35% in 2021. This phenomenon is closely linked to pharmacists' strengthened management of OTC antibiotic sales and the provision of patient medication consultation services. Pharmacists have become a key force in controlling antibiotic abuse in the community by correcting public misconceptions about antibiotics through various means such as face-to-face consultation and online Q&A platforms and leading rational drug use practices.

4.3 Public education and health promotion

The public's lack of awareness of the reasons for antibiotic abuse has led to the abuse of antibiotics, so health education has become an indispensable intervention measure. Data released by the National Health Commission shows that the awareness rate of basic knowledge about antibiotics among the national population reached 65.3% in 2023, an increase of 12 percentage points compared with 2018, but still more than one-third of the population has a lack of awareness. In response to this situation, medical institutions at all levels and health administrative departments have launched various types of educational campaigns, such as the "Rational Drug Use Awareness Week" and "World Antimicrobial Alert Week", using popular science lectures, brochures, short videos and other means to popularize knowledge [10] about antibiotic use among the public.

In terms of school education, since 2020, many places have included the rational use of antibiotics in the health education curriculum of primary and secondary schools to help teenagers form correct medication concepts, and the Internet platform has also become a key channel for antibiotic science popularization. According to statistics in 2022, the total number of readings of antibiotic-related popular science content pushed by major domestic medical and health apps and public accounts exceeded 200 million times, generating a good social impact. Through systematic public education, the proportion of people who know that "antibiotics cannot cure viral infections" has risen from 45% in 2018 to 68% in 2023, and the proportion of people who buy antibiotics on their own has dropped by 21.5%, showing that health education has achieved positive results in changing public behavior.

4.4 Policy, Regulation and regulatory system construction

A sound policy and regulatory system is the institutional guarantee to curb the abuse of antibiotics. Since 2011, China has launched a special campaign to rectify the clinical use of antibiotics and has now established a relatively complete management and regulatory system. The "Measures for the Administration of the Clinical Use of Antibiotics" was revised in 2020 to further clarify the requirements for antibiotic classification management and prescription authority, and to set assessment indicators for the intensity of antibiotic use in medical institutions. Meanwhile, the National Medical Products Administration has strengthened supervision over the production and distribution of antibiotics. In the post-market supervision and administration Measures for drugs implemented in 2021, drug manufacturers are required to conduct regular monitoring of adverse antibiotic reactions and risk management, and a monitoring network for the clinical application of antibiotics has been established at the national level in the field of regulatory technical means. The bacterial resistance monitoring network, which covers more than 2,500 medical institutions across the country, has achieved real-time monitoring and analysis of antibiotic use data, providing a scientific basis [11] for policy formulation. In addition, the adjustment of medical insurance payment policies has become an important lever to guide rational drug use, effectively curbing the excessive

use of antibiotics by adjusting the proportion of antibiotic reimbursement and restricting irrational combinations of drug use.

5. Conclusions

In response to the significant threat to global public health, antibiotic abuse is a major cause of which accelerates the development of bacterial resistance and brings harm such as microecological imbalance, adverse drug reactions, and environmental pollution, this study analyzes the effectiveness and feasibility of multi-level pharmaceutical intervention measures. The study shows that the establishment of antibiotic management task forces in medical institutions, the use of prescription review systems and the implementation of clinical pathways, the active participation of pharmacists in prescription review, clinical consultation and patient education, the conduct of public health campaigns, and the establishment of a sound policy, regulation and supervision system, all these factors together form a comprehensive defense line against antibiotic abuse, These interventions, when combined, have achieved remarkable results in reducing irrational prescriptions, lowering the incidence of drug-resistant strains, and raising public awareness of medication use. Further efforts should be made to strengthen the multi-disciplinary collaboration model, highlight the leading role of pharmacists in antibiotic management, improve information-based regulatory means, and continuously promote public education and health literacy to establish a long-term mechanism for the rational use of antibiotics to ensure public health safety.

References

- [1] Silah Basir, Muhammad Shaheer Khan, Sumra Sohail, Sardar Umer Irshad, Ahmad Mohammad Saifan, Irfan Ullah. Drivers of antibiotic misuse and resistance in Pakistan: a public health challenge. [J]. *Annals of medicine and surgery* (2012),2025,87(12):
- [2] Bahar Madran, Francisco Almeida, Elena Carrara, Diamantis Kofteridis, Nuno Rocha Pereira, Giulio Pieve, Nikolaos Tziolos, İlker Kayi, Şiran Keske, Onder Ergonul, Sibel Sakarya. Youdaoplaceholder1 of antibiotics misuse and overuse in high-risk countries in the European region: a multidisciplinary Delphi study[J]. *European Journal of Clinical Microbiology & Infectious Diseases*,2025,(prepublish):
- [3] Wahyu Pudji Nugraheni, Bunga Astria Paramashanti, Dea Anita Ariani Kurniasih, Asep Kusnali, Syarifah Nuraini, Debri Rizki Faisal. Poor and non-poor gaps in antibiotic misuse in Indonesia: A Blinder-Oaxaca decomposition analysis[J]. *Clinical Epidemiology and Global Health*,2025,36
- [4] Jeevan Nammi, Roshini Pasala, Nikhil Andhe, Ramakanth Vasam, Ausrit Datta Poruri, Ravishankar Raj Sherikar. Antibiotic Misuse: An In-Depth Examination of Its Global Consequences and Public Health Challenges[J]. *Cureus*,2025,17(6):
- [5] Zainab Attia Abdallah, Tanazor Hemdan Abdel Hamid, Sameh S. Zaghlool, Abdelaziz Hendy, Khalid Al Mugheed, Sally Mohammed Farghaly Abdelaliem, Amany Anwar Saeed Alabdullah, Salwa Sayed, Ahmed Hendy, Ayiat Allah Wagdy Farag. Awareness program for controlling the misuse of antibiotics and related resistance among mothers of children under 5 years[J]. *Journal of Health, Population and Nutrition*,2025,44(1):
- [6] Arifa Saif, Tahir Mehmood Khan, Allah Bukhsh, Muhammad Osama Yaseen, Alia Saif. Cross-sectional survey to explore knowledge, attitude, practices and impact of an intervention programme related to antibiotic misuse and self-medication among general population of Pakistan. [J]. *BMJ public health*, 24,2(1):
- [7] Hafez Sameer Hamdy, Tamam Sabry M., Mohamed Noha Ahmed, Sagiron Elwaleed Idris, Abdalla Yahya Hussein Ahmed, Ahmed Mohammed Ateeg Abdelrahman, Shuib Sharfeldin Mohammed, Hamed Elsadig Eltaher, Saied Harfoush Mohamed, Alshahrani Mohammed Abdulrahman, Alshehri Ahmad A., Ali Ahmed Salah, Loutfy Ahmed, Abdalla Abdalla Mohamed Ahmed Osman, Alwesabi Sadeq Abdo Mohammed, Ibrahim Ateya Megahed. Nursing-based intervention to optimize the self-prescribed and the misuse of antibiotics among mothers of children less than 5 years[J]. *International Journal of Africa Nursing Sciences*, 24,20

- [8] Nair Mohit, Engel Nora, Zeegers Maurice P, Burza Sakib. Perceptions of effective policy interventions and strategies to address antibiotic misuse within primary healthcare in India: A qualitative study. [J]. *Journal of infection prevention*,2023,24(3):
- [9] Misau Y A, Mogere D, Mbaruk S, Usman U S,Bello S, Oduwole O, Moriam C. Educational Interventions for Antibiotics Misuse and Self-Medication in Africa: A Systematic Review and Meta-Analysis [Protocol]. [J].*West African journal of medicine*,2023,40(1):
- [10] Goggin Kathy, Hurley Emily A, Lee Brian R, BradleyEwing Andrea, Bickford Carey, Pina Kimberly, Donis de Miranda Evelyn, Yu David, Weltmer Kirsten, Linnemayr Sebastian, Butler Christopher C, Newland Jason G, Myers Angela L. Let's Talk About Youdaoplaceholder0: a randomised trial of two interventions to reduce antibiotic misuse. [J]. *BMJ open*, 2022, 12(11):
- [11] Li Xingxing; Tao Liang; Clostridium difficile infection - a global public health threat caused by antibiotic abuse [J]. *Science*,2021(03):4+44-46+53.