## Original Research

## ROLE OF ANTIBIOTIC STEWARDSHIP PROGRAM IN IMPROVING RATIONAL THIRD-LINE ANTIBIOTIC USE IN TYPE-2 DM INPATIENTS AT FATMAWATI HOSPITAL

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#### **Abstrak**

Diabetes melitus tipe-2 (T2DM) merupakan gangguan metabolik yang paling umum, disebabkan oleh kombinasi dua faktor: kerusakan sekresi insulin oleh sel β pankreas dan ketidakmampuan jaringan yang sensitif terhadap insulin untuk merespons insulin secara tepat. Data epidemiologi menunjukkan angka yang mengkhawatirkan dan memprediksi masa depan yang memprihatinkan untuk T2DM. Menurut International Diabetes Federation (IDF), pada tahun 2019, diabetes menyebabkan 4,2 juta kematian, dan sebanyak 463 juta orang dewasa berusia 20-79 tahun hidup dengan diabetes, angka yang diperkirakan akan meningkat menjadi 700 juta pada tahun 2045. Berdasarkan data RISKESDAS tahun 2018, prevalensi DM di Indonesia meningkat dari 6,9% pada tahun 2013 menjadi 8,5% pada tahun 2018. Tim Program Pengendalian Resistensi Antimikroba (PPRA) memiliki peran penting dalam penyusunan dan pelaksanaan pedoman serta kebijakan berbasis bukti. Tujuan dari penelitian ini adalah untuk mengetahui profil pasien yang menerima terapi antibiotik dan penggunaan antibiotik lini ketiga pada pasien T2DM di RS Fatmawati selama periode Juli-Desember 2021. Penelitian ini menggunakan desain deskriptif retrospektif dengan pendekatan non-eksperimental. Jumlah sampel terdiri dari 52 rekam medis yang memenuhi kriteria inklusi. Hasil penelitian menunjukkan bahwa pasien yang paling banyak menerima pengobatan antibiotik berusia 55-64 tahun (38,5%), berjenis kelamin perempuan (52%), dan mengalami komplikasi ulkus kaki diabetik (51,8%). Antibiotik tunggal dan kombinasi yang paling banyak digunakan adalah ampisilin-sulbaktam (34,7%) dan ampisilin-sulbaktam + metronidazol (29,2%). Sebanyak 28,8% pasien direkomendasikan untuk menerima antibiotik lini ketiga dan mendapatkan pertimbangan dari tim PPRA, di mana 73,33% dari rekomendasi tersebut disetujui.

Kata kunci: diabetes mellitus tipe-2, DM tipe-2; rasionalitas; antibiotik; PPRA

## **Abstract**

Type-2 diabetes mellitus (T2DM) is the most common metabolic disorders, caused by a combination of two factors: damaged insulin secretion by pancreatic  $\beta$ -cell and the inability of insulin-sensitive tissues to respond appropriately to insulin. Epidemiological data reveal alarming values that predict a concerning future for T2DM. According to the



International Diabetes Federation (IDF), in 2019, diabetes caused 4.2 million deaths, and 463 million adults aged between 20-79 years old were living with diabetes, a number that is projected to increase up to 700 million by 2045. Based on data from RISKESDAS in 2018, the prevalence of DM in Indonesia has increased from 6.9% in 2013 to 8.5% in 2018. The Antimicrobial Resistance Control Program (PPRA) team is essential in the development and implementation of evidence-based guidelines and policies. The purpose of this study was to determine the profile of patients receiving antibiotic therapy and the use of third-line antibiotics in T2DM patients at Fatmawati Hospital during the July-December 2021 period. This research used a retrospective descriptive design with a non-experimental approach. The sample size consisted of 52 medical records that met the inclusion criteria. The results showed that patients receiving the most antibiotic treatment were between the ages of 55-64 years (38.5%), women (52%), and those with diabetic foot complications (51.8%). The single and most used combination antibiotics were ampicillin-sulbactam (34.7%) and ampicillin-sulbactam+metronidazole (29.2%). 28.8% of the patients were recommended to receive third-line antibiotics and received considerations from the PPRA team, of which 73.33% obtained approval.

Keywords: type-2 diabetes mellitus; T2DM; rationality; antibiotics; PPRA

## INTRODUCTION

According to the World Health Organization, diabetes mellitus refers to a cluster of metabolic conditions that exhibit hyperglycemia in the absence of appropriate treatment. The underlying causes of this condition are diverse and can involve impairment in insulin secretion, insulin action, or a combination of both (1). Diabetes Mellitus (DM) is one of the main health problems in the community that has long and short-term complications. There are two types of DM, namely DM type-1 and DM type-2 (2).

According to the Riskesdas 2018 survey, the prevalence of diabetes mellitus in Indonesia is 6.9%. This means that around 16.7 million people in Indonesia have diabetes. The prevalence of diabetes mellitus in Indonesia has been increasing in recent years, and it is becoming a major public health concern. Diabetes can lead to serious health complications, including cardiovascular disease, kidney disease, nerve damage, and blindness. The Riskesdas 2018 survey also found that diabetes is more common among older age groups, with the highest prevalence among those aged 65 years and above (21.8%) (3). Antibiotics are typically required for inpatients with type 2 diabetes when they have an infection that necessitates antibiotic treatment. Diabetic patients are at a higher risk for infections, and if left untreated, infections can lead to serious complications, such as sepsis or gangrene (4).

In a study conducted by Eflia and Anita in 2022 on type-2 diabetes mellitus (DM) patients who were admitted to the Grandmed Lubuk Pakam Hospital, data from medical records of 57 patients were analyzed. The study found that the antibiotics used in the treatment of these patients included Ceftriaxone (65.8%), Meropenem (18.4%), Levofloxacine (7.9%), and Metronidazole (7.9%). Additionally, combination antibiotics such as Ceftriaxone + Metronidazole (78.9%), Meropenem + Metronidazole (10.5%), and Levofloxacine + Metronidazole (10.5%) were used in the treatment. The accuracy of the antibiotics used was evaluated, and the results showed that the indication for the antibiotic use was 100% correct, the correct drug was administered in 89.5% of cases, the correct dose was administered in 86.0% of cases, and the right duration of administration was 82.5% (5).

Antibiotics may be needed in the treatment of type-2 diabetes mellitus (DM) when a bacterial infection occurs, which can be common in patients with poorly controlled diabetes. According to the American Diabetes Association (ADA), bacterial infections can occur in various parts of the body, including the skin, respiratory tract, urinary tract, and gums, among others.

These infections can be serious and may require antibiotic treatment. One common infection in patients with diabetes is diabetic foot infections, which can lead to amputation if not treated properly. Antibiotic therapy is recommended for diabetic foot infections and should be chosen based on the severity of the infection, the presence of necrotic tissue, and the causative organism(s) (2). High blood sugar due to DM can affect the immune system, interfere with the ability of white blood cells to come to the site of infection, stay in infected areas and kill microorganisms. Due to plaque buildup in blood vessels associated with DM, areas of infection may receive poor blood supply, which further decreases the body's ability to fight infection and heal wounds (6). Respiratory tract infections, skin and soft tissue infections, gastrointestinal infections and urinary tract infections seem to be more common in those with DM. Not only is it more frequent, but this infection seems to have a worse response and progress faster into a severe form of infection in DM patients (7).

The Antimicrobial Resistance Control Program (PPRA) plays a crucial role in promoting responsible and effective antibiotic use for diabetic patients and preventing the development and spread of antimicrobial resistance. By developing and implementing evidence-based guidelines and policies and monitoring and evaluating antibiotic use in diabetic patients, the PPRA can help ensure that third-line antibiotics are used only when necessary and that the risks and benefits are carefully considered for each individual patient (8).

Research on the evaluation of antibiotic use in type-2 DM patient needs to be conducted to determine the profile of patients receiving antibiotic therapy and to evaluate the use of third-line antibiotics adjusted to the Guidelines for Antibiotic Use (PPAB) Fatmawati Hospital. Evaluation of the use of third-line antibiotics is a variable that distinguishes this study from previous studies because the use of third-line antibiotics must be in line with the recommendations of the Antimicrobial Resistance Control Program (PPRA) team and is closely related to the rationality of antibiotic use. This research is expected to improve the quality of antibiotic management services in type-2 DM patients and reduce mortality and morbidity rates in type-2 DM patients due to infectious complications.

## **METHODS**

This study involves several stages, starting with literature search, determination of patient criteria both inclusion and exclusion, evaluation of antibiotic use, antibiotic use. Literature search includes literature review on improving the quality of hospital services, rationality for drug use, evaluation of drug use and criteria for using Diabetes Mellitus drugs.

The criteria for patients included in the study were patients with cases of Type 2 Diabetes Mellitus obtained from medical record data of type 2 DM inpatients at Fatmawati Hospital for the July-December 2021 period. Patient criteria were then determined, including inclusion criteria such as patients with type-2 diabetes mellitus who experience infectious complications and receive antibiotic therapy, patients aged over 18 years, and complete medical record data. Exclusion criteria include patients referred to other hospitals, forcibly discharged patients, pregnant and lactating patients, patients undergoing hemodialysis, and TB patients with OAT.

Evaluate the drug use profile is determined by the antibiotic class and type used, dosage, route of administration, as well as the timing and duration of drug administration. In addition, the evaluation is also seen from the appropriate aspect of using line 3 antibiotics. The analysis of data is conducted through a descriptive approach, which involves describing the data gathered from medical records to identify the patterns of infectious diseases and antibiotic usage. The

completeness of the data is verified, and any potential errors in data entry are rectified. The data is then classified based on various factors, including age group, gender, disease complications, and the profiles of antibiotic usage and the use of 3rd-line antibiotics.

## RESULT AND DISCUSSION

The results of this study were obtained from medical record data of type-2 DM patients for the July-December 2021 period. Of the total 90 medical record samples, there were three medical record statuses that could not be found, so that the remaining 87 medical records were used. It was found that 35 patients were excluded, consisting of two patients under the age of inclusion criteria, namely 17 years old and 5 years old. Eleven patients received hemodialysis therapy, eleven patients who did not receive antibiotics, six TB patients with OAT, and five patients were forcibly discharged. So that 52 samples were obtained that met the inclusion criteria as research subjects.

# 3.1. Characteristics of Type 2 DM Patients Who Get Antibiotics

## 3.1.1. By Age

The distribution of type-2 DM inpatients by age group is presented in the form of the following diagram.

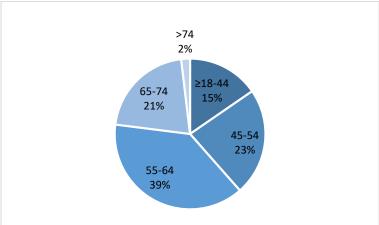


Figure 1. Distribution Diagram by Age

The results obtained in the picture above show that type-2 DM patients who received the most antibiotic therapy at the age of 55-64 years, which was 38.5% (20 patients). According to a study conducted by Mustafa et al. (2016), type-2 DM commonly affects individuals under the age of 60, with the most prevalent complication being diabetic ulcers. The incidence of type-2 DM in individuals under 60 years of age can be attributed to age-related processes that lead to a decline in insulin production and increased insulin resistance, resulting in suboptimal blood glucose control (9). Similar research suggests that the risk of developing DM and glucose intolerance increases with age due to degenerative factors, particularly impaired glucose metabolism occurring in individuals aged 45 or above (10). After the age of 40, there is a significant decline in physiological functions, and diabetes tends to manifest in individuals over 45 years of age who are overweight and exhibit reduced insulin sensitivity. Moreover, glucose intolerance, particularly the ability of  $\beta$  cells to metabolize glucose and produce insulin, is compromised (11).

3.1.2. By Gender

The distribution of type-2 DM inpatients receiving antibiotic therapy by sex is presented in the following diagram.

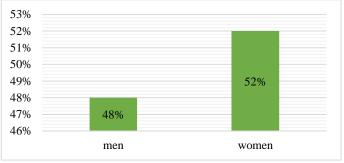


Figure 2. Distribution by Sex

The findings revealed that the highest proportion of antibiotic treatment among type-2 DM patients at Fatmawati Hospital was observed in women, accounting for 52% (27 patients). These results align with a study conducted by Fitria et al. (2017), which also reported a higher prevalence of type-2 DM among women. This can be attributed to the decline in estrogen production and increased insulin resistance experienced by women. Women who undergo early menopause have a higher risk of developing diabetes mellitus (12). According to Suba (2013), postmenopausal women may experience hormonal imbalances, including disruptions in steroid hormones and estrogen, along with an increased risk of metabolic syndrome (13). Estrogen, a hormone produced in adipose tissue, plays a crucial role in regulating glucose homeostasis in the bloodstream. A decrease in estrogen levels can lead to reduced insulin sensitivity (12).

## 3.1.3. Based On the Complication of Diseases

The distribution of type-2 DM inpatients receiving antibiotic therapy based on disease complications is presented in the following diagram.

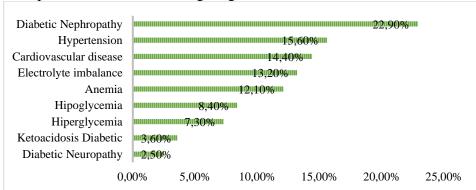


Figure 3. Distribution Based on Complications of Non-Infective Diseases

It is important to note that one patient may be counted multiple times if they have one or more complications related to the disease. According to Figure 3, the highest non-infectious disease complication among hospitalized patients with type-2 DM is diabetic nephropathy, accounting for 22.90% (19 patients). This finding is consistent with a study conducted by Amalia (2010), which reported that diabetic nephropathy is the most common complication observed in type-2 DM patients at Dr. Soetomo Hospital Surabaya's inpatient department, affecting 58.4% (129 out of 228 patients) (6). Diabetic nephropathy (DN) is a leading cause of kidney failure and

carries the highest mortality rate among all DM-related complications. The United Kingdom Prospective Diabetes Study (UKPDS) identified cardiovascular disease, peripheral vascular disease, retinopathy, and diabetic nephropathy as the most significant chronic complications in DM. Consequently, mortality in diabetes is often attributed to these complications rather than hyperglycemia itself. Compared to individuals without diabetes, DM patients have a 5-fold increased risk of developing gangrene, a 17-fold increased risk of kidney disorders, and a 25-fold increased risk of blindness (14). Cardiovascular disease ranks third in terms of the distribution of non-infectious disease complications, affecting 14.40% (12 patients). Macrovascular complications of the cardiovascular system are the main causes of pain and mortality in DM patients. These complications manifest as early atherosclerosis and can impact vital organs such as the heart and brain. The risk of cardiovascular disease is heightened in individuals with DM (15). The Framingham Heart Study indicates an elevated risk of peripheral artery disease (PAD), congestive heart failure (CHF), coronary heart disease (CHD), myocardial infarction (MI), and sudden death (with a risk increase ranging from 1 to 5 times) in people with DM (16).

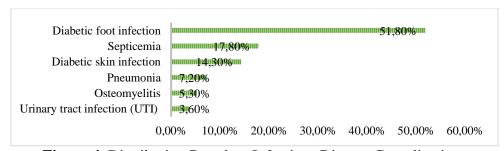


Figure 4. Distribution Based on Infectious Disease Complications

According to figure 4, diabetic foot infection is the most prevalent infectious disease complication among hospitalized patients with type-2 diabetes, accounting for 51.80% (29 patients). A study conducted by Corina (2018) also found that diabetic foot infection is the most common complication experienced by type-2 diabetes patients at Dr. Soetomo Surabaya Hospital's endocrine poly, with a prevalence of 29.9% (17). Diabetic foot complications refer to infections, ulcers, and/or deep tissue damage associated with neuropathy and peripheral vascular disease in the lower limbs. Uncontrolled diabetic foot conditions can lead to disability and even death. These lower limb abnormalities are caused by blood vessel disorders (angiopathy), nerve disorders (neuropathy), and infections.

In figure 4, sepsis is the second most common infectious disease complication, accounting for 17.80% (10 patients). The Centers for Disease Control and Prevention (CDC) in the United States reported that in 2005, nearly 21 million people, or 7% of the population, had diabetes-associated sepsis (18). Sepsis is a systemic inflammatory response to infection, where pathogens or toxins are released into the bloodstream, triggering an inflammatory process. Diabetes mellitus induces immune deficiency through various mechanisms, including the impairment of phagocyte function in chemotaxis and the migration of inflammatory cells to the site of inflammation due to elevated blood sugar levels (19).

## 3.2. Antibiotics Used

The use of antibiotics in patients with type-2 diabetes can be categorized into two types: single antibiotics and combination antibiotics. The table below illustrates the usage of single antibiotics in the treatment of type-2 diabetes inpatients at Fatmawati Hospital.

**Table 1.** Use of Single Antibiotics in Type-2 DM Inpatients at Fatmawati Hospital

Group	Antibiotic type	Quantity	Percentage
Penicillin	Ampicillin-sulbactam	17	34.7%
Cephalosporin	Ceftriaxone	12	24.5%
Carbapenem	Meropenem	7	14.3%
Quinolone	Levofloxacin	4	8.2%
Penicillin	Co-Amoxiclav	2	4.1%
Cephalosporin	Cefazolin	2	4.1%
Anaerobic antibiotic	Metronidazol	2	4.1%
Quinolone	Ciprofloxacin	1	2.0%
Aminoglicoside	Amikacin	1	2.0%
Cephalosporin	Cefiksime	1	2.0%
Total		49	100%

**Table 2.** Use of Combination Antibiotics in type-2 DM Patients at Fatmawati Hospital

Group & Antibiotic type	Quantity	Percentage
Penicillin+ Anaerobic antibiotic		
Ampicillin-sulbactam+Metronidazole	5	29.2%
Fluoroquinolone+Carbapenem		
Levofloxacin+Meropenem	2	11.8%
Carbapenem+Antifungal		
Meropenem+Fluconazole	2	11.8%
Penicillin+Flouroquinolone		
Ampicillin-sulbactam+Levofloxacin	2	11.8%
Cephalosporin+ Anaerobic antibiotic		
Ceftriaxone+Metronidazole	2	11.8%
Fluoroquinolone+ Anaerobic antibiotic		
Levofloxacin+Metronidazole	1	5.9%
Penicillin+Antibiotik anaerob		
Co-amoxiclav+Metronidazole	1	5.9%
Carbapenem+Antibiotik anaerob		
Meropenem+Metronidazole	1	5.9%
Cephalosporin+Flouroquinolone		
Ceftriaxone+Levofloxacin	1	5.9%
Total	17	100%

In patients with type-2 diabetes, two types of antibiotics are commonly used: single antibiotics and combination antibiotics. Among the single antibiotics, ampicillin-sulbactam is the most widely used, accounting for 34.3% of cases. This is primarily due to the high incidence of complications related to diabetic foot infections in type-2 DM patients. Research conducted at RSUP Friendship by Yusi et al (2015) supports the frequent use of ampicillin-sulbactam in diabetic foot infection patients, as it has shown improved clinical outcomes (20).

The second most used single antibiotic is ceftriaxone, representing 24.5% of cases. This contrasts with the findings of research conducted by Efilia & Anita (2022), which identified ceftriaxone as the most used antibiotic in type-2 DM inpatients. Ceftriaxone, a third-generation cephalosporin, exhibits strong activity against Enterobacteriaceae and its long half-life enhances patient compliance (21). Pseudomonas aeruginosa is recognized as the predominant pathogen in diabetic foot infections (22). It is an aerobic gram-negative bacterium (23). Ceftriaxone is effective in targeting gram-negative bacteria by disrupting their cell walls, leading to bacterial elimination. The Infectious Diseases Society of America (IDSA) recommends ceftriaxone as the empirical antibiotic of choice for moderate to severe diabetic foot infections. The infectious bacteria commonly encountered include Methicillin-Resistant Staphylococcus Aureus (MRSA), Streptococcus species, Enterobacteriaceae, and anaerobes (24).

Meropenem, a single antibiotic, was used in 21.2% (7 patients) of type-2 DM hospitalized cases. Meropenem is known for its broad-spectrum activity against the causative bacteria. Its effectiveness stems from the ability of carbapenems to inhibit and disrupt bacterial cell walls, resulting in osmotic lysis (8).

Carbapenems, including meropenem, are commonly prescribed for infections caused by organisms that are resistant to Pseudomonas aeruginosa. These antibiotics are considered the preferred choice for treating infections caused by gram-negative bacteria with broad-spectrum beta-lactamase. Meropenem specifically exhibits strong activity against gram-negative aerobes (23).

Other research studies have also shown that meropenem has a larger inhibitory zone compared to ciprofloxacin, cefotaxime, ampicillin, and ceftazidime. The inhibitory zone diameter for meropenem is measured at 29mm. The chemical structure of meropenem includes a beta-lactam ring, which plays a crucial role in inhibiting bacterial synthesis. Meropenem is a relatively new antibiotic derived from Streptomyces cattleya (25).

# **3.3.** Use of 3rd-line Antibiotics and The Role of Antibiotic Stewardship Program (PPRA) Team in Providing Policies

The increasing prevalence of pathogenic microorganisms that are resistant to specific antibiotics, known as antimicrobial resistance or multiple drug resistance, poses significant challenges in the treatment process. The ineffectiveness of first-line antibiotics necessitates the use of second-line or third-line alternatives. However, this poses a dilemma as these higher-line antibiotics are often more expensive. Furthermore, there is also a concern that microorganisms may develop resistance to second- and third-line antibiotics (26).

At Fatmawati General Hospital, the use of antibiotics adheres to the hospital's Antibiotic Stewardship Program (PPAB), which involves stratifying antibiotics based on patterns of microbial resistance. The use of antibiotics followed the hospital's PPAB by stratifying antibiotics based on the results of germ pattern mapping, showing germs only sensitive to 3rd-line antibiotics, the lack of clinical improvement or worsening of the patient's condition after 1st- or 2nd-line antibiotic therapy for 3 days, patients treated as referrals from other hospitals with sensitive germ culture results for 3rd-line antibiotics, and other criteria based on the patient's condition, and the approval of the attending physician and the PPRA team.

Table 3	Annroval	and Hee	of 3rd-line	Antibiotics
Table 5.	Abbiovai	and Use	or sta-time	Antibiotics

Third-line		PPRA approval	Without PPRA approval	
Antibiotic	Diagnose		Continued	Not used
			use	Not used
	Covid 19-cellulitis-back abscess	1		
Meropenem	Sepsis, diabetic foot ulcer	2	1	2
	Sepsis, post-operative	5	1	
	debridement/amputation			
	Diabetic foot ulcer, necrotic finger	1		
	Diabetic foot ulcer	2		
Total		11 (73,33%)	2 (13,33%)	2 (13,33%)

Table 3 shows that out of the type-2 DM inpatients, out of a total of 52 patients, 15 patients were planned by the doctor to receive third-line antibiotic treatment with meropenem. Seventy-three percent of the patients obtained approval from the PPRA team to use meropenem as a third-line antibiotic after reviewing clinical examinations, laboratory results, and bacterial cultures. However, four of these 15 patients did not receive approval from the PPRA team. The rejections were based on two patients having negative culture results, one patient being found to be resistant to meropenem based on the culture, and one patient who unfortunately passed away before being consulted by the PPRA team.

Among the 12 patients who received approval from the PPRA team to use meropenem as a third-line antibiotic, seven were diagnosed with sepsis. Sepsis is a serious condition that requires immediate attention, particularly in patients with DM, who are at a higher risk of infection and related complications. The doctor conducted clinical evaluations of the patients, including their medical history, symptoms experienced, and physical examinations. Laboratory tests were also conducted to aid in the diagnosis of sepsis. These tests included a complete blood count (CBC) to check for an increased number of white blood cells, which can be an indicator of infection, as well as to monitor platelet levels. Blood tests may also include organ function analysis, such as monitoring blood glucose levels to control diabetes and evaluating kidney and liver function. Examinations of signs and symptoms of sepsis included detecting an elevated body temperature, rapid heart rate (tachycardia), increased respiratory rate (tachypnea), low blood pressure (hypotension), and signs of mental impairment or confusion. All patients diagnosed with sepsis showed increased leukocyte counts, D-dimer levels, and blood urea. Additionally, all patients experienced hypoalbuminemia. These sepsis patients also presented with decreased consciousness, shortness of breath, fever, and confusion.

One patient diagnosed with necrotic diabetic foot ulcer and necrotic finger received meropenem treatment after a culture revealed *Acinetobacter baumannii* as the causative bacteria, which was found to be sensitive to ampicillin-sulbactam. Based on these results, the PPRA team recommended a switch from meropenem (1g every 8 hours) to ampicillin-sulbactam (1.5g every 6 hours). In this case, antibiotic de-escalation was implemented, which is an approach in infection treatment where the initially administered antibiotic type or spectrum is reduced or changed to a narrower or more targeted antibiotic after the results of culture and sensitivity are known or when the patient's clinical condition improves.

The de-escalation antibiotic approach offers several benefits, including reducing the risk of antibiotic resistance by avoiding unnecessary or excessive antibiotic use, which can contribute to the development of bacterial resistance. Additionally, it helps ensure that the patient's treatment aligns with the actual cause of the infection, thereby increasing treatment effectiveness (27).

## **CONCLUSION**

The results showed that patients receiving the most antibiotic treatment were between the ages of 55-64 years (38.5%), women (52%), and those with diabetic foot complications (51.8%). The single and most used combination antibiotics were ampicillin-sulbactam (34.7%) and ampicillin-sulbactam+metronidazole (29.2%). Twenty-eight-point eight percent (28.8%) of the patients were recommended to receive third-line antibiotics and received considerations from the PPRA team, of which 73.33% obtained approval from the PPRA team. The chosen third-line antibiotic was Meropenem. The PPRA team at Fatmawati Hospital has fulfilled its role in reducing the risk of antibiotic resistance by avoiding unnecessary or excessive antibiotic use, which can contribute to the development of bacterial resistance. This approach helps ensure that patients receive treatment that aligns with the actual cause of infection, thereby enhancing treatment effectiveness.

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## **CONFLICT OF INTEREST**

All authors declared that there was no conflict of interest.

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