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Evaluation of the Rationality of Antibiotic Use in Diabetic Ulcer Patients Using the Gyssens Method and Its Association with Patients' Clinical Outcomes

Lelly Farida[1], Dini Permata Sari[1], Hendra Farma Johar[1]
[1]Faculty of Pharmacy, 17 Agustus 1945 University Jakarta, Indonesia
Email: zelya.lelly@gmail.com

Abstract. *Diabetic foot ulcer is one of the chronic complications of diabetes mellitus that may lead to severe infection, amputation, prolonged hospitalization, and decreased patient quality of life. Antibiotic therapy is an important component in the management of diabetic foot ulcer infection; however, its use needs to be evaluated to prevent resistance, inappropriate therapy, and failure of clinical outcomes. This study aims to evaluate the rationality of antibiotic use in patients with diabetic foot ulcers using the Gyssens method and to analyze its association with patients' clinical outcomes in a hospital in Jakarta. This study employed a quantitative observational analytic design with a retrospective cross-sectional approach. Data were obtained from the medical records of hospitalized patients with diabetic foot ulcers who received empirical antibiotics during the period of January–December 2025. The independent variable was the rationality of antibiotic use based on the Gyssens categories, while the dependent variable was the patients' clinical outcome. Data were analyzed using univariate and bivariate analyses with the Chi-Square test or Fisher's exact test. This evaluation is expected to serve as a basis for improving the appropriateness of antibiotic therapy, strengthening antimicrobial stewardship, and controlling the risk of diabetic foot ulcer complications.*

Keywords: *Antibiotics, Gyssens, Clinical Outcome, Diabetic Foot Ulcer, Diabetes Mellitus*

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INTRODUCTION

Diabetes mellitus is a chronic metabolic disease characterized by elevated blood glucose levels due to impaired insulin secretion, reduced insulin effectiveness, or a combination of both (Abidin et al., 2025; Rosyidah & Cahyono, 2025; Hartono et al., 2026; Mardiansyah, 2020). This disease has become a public health concern because the number of people affected continues to increase. The International Diabetes Federation estimates that 537 million adults aged 20–79 years were living with diabetes in 2021, and this number is projected to increase to 783 million by 2045 (Magliano & Boyko, 2021). Indonesia ranks fifth among countries with the highest number of people with diabetes in the world, after China, India, Pakistan, and the United States (Askary, 2025; Sun et al., 2022; Dhaif et al., 2025).

Uncontrolled diabetes mellitus can lead to acute and chronic complications. One chronic complication that often causes a severe clinical burden is diabetic foot ulcer. Diabetic foot ulcer occurs as a result of a combination of peripheral neuropathy, vascular disorders, repeated trauma, and infection of foot tissue (Kim, 2023; Raja et al., 2023). It is estimated that 1.9%–4.0% of patients with diabetes develop diabetic foot ulcers each year, while 19%–34% of patients with diabetes are at risk of developing diabetic foot ulcers during their lifetime (Edmonds et al., 2021; McDermott et al., 2023; Lim et al., 2026; Yoon et al., 2026). This condition shows that diabetic foot

ulcer is not merely a local problem of foot wounds, but part of a systemic complication of diabetes that requires comprehensive management.

Infection in diabetic foot ulcers can spread to deep tissues and cause osteomyelitis, gangrene, sepsis, and even amputation. In severe cases, mortality after amputation remains a serious concern in healthcare services (Ferguson et al., 2025). Complications can be prevented through routine foot care, patient education, risk screening, glycemic control, vascular management, and appropriate infection therapy (Miranda et al., 2021; Indonesia, 2021). Antibiotic therapy is an important component in the management of patients with infected diabetic foot ulcers, particularly to suppress the growth of microorganisms causing infection and to prevent the progression of tissue damage. The selection of antibiotics for diabetic foot ulcers should take into accousnt the severity of infection, the possible causative bacteria, history of antibiotic use, risk of resistance, the patient's clinical condition, renal function, and culture results when available (Mizranita et al., 2026; Dewi, 2025). The IWGDF/IDSA guidelines emphasize that antibiotic therapy for diabetic foot infections should be adjusted according to the severity of infection, ranging from mild, moderate, to severe infection (Lipsky et al., 2020; Senneville et al., 2024). Empirical antibiotics are often used at the beginning of treatment because culture results are not yet available. This pattern may increase the risk of inappropriate drug selection, dosage, interval, route, or duration if it is not evaluated systematically (Shrestha & Prajapati, 2019; Sulis et al., 2020; Mira et al., 2015).

Irrational antibiotic use can increase the risk of resistance, adverse effects, drug interactions, higher treatment costs, and failure of clinical improvement (Patel et al., 2023; Baig et al., 2025; Kilari & Oroszi, 2024; Sharif et al., 2021; Yang et al., 2020; Nagarjuna et al., 2026). Previous studies have shown that antibiotic use in patients with diabetes mellitus complicated by ulcers remains varied, both in monotherapy and combination therapy. An evaluation at Sultan Syarif Mohamad Alkadrie Regional Hospital in Pontianak showed 100% appropriateness of indication, 85% appropriateness of drug selection, 79.06% appropriateness of dosage, and 88.37% appropriateness of administration interval (Pontian et al., 2021). These findings indicate that antibiotic appropriateness still needs to be monitored, especially in cases of diabetic foot ulcers that carry a risk of polymicrobial infection. The Gyssens method is one qualitative evaluation approach for antibiotic use that assesses the appropriateness of indication, drug effectiveness, toxicity, spectrum, cost, dosage, interval, route, duration, and completeness of data. This method is relevant for evaluating antibiotic therapy because it can classify antibiotic use from rational to irrational categories based on specific clinical reasons (Gyssens, 2005). In the context of diabetic foot ulcers, Gyssens evaluation can help hospitals assess whether the empirical antibiotics administered are appropriate to patient needs and treatment guidelines.

Based on preliminary data in the research manuscript, one hospital in Jakarta treats many patients with diabetes mellitus complicated by diabetic foot ulcers. In 2024, the number of hospitalized patients with diabetes mellitus was recorded at 970 patients. This study is directed at evaluating the rationality of empirical antibiotic use in patients with diabetic foot ulcers using the Gyssens method and analyzing its relationship with patients' clinical outcomes. This objective is in line with the research problems stated in the manuscript, namely assessing antibiotic rationality, describing clinical outcomes, and analyzing the relationship between the two.

LITERATURE REVIEW

Diabetes Mellitus

Diabetes mellitus is a group of metabolic disorders characterized by chronic hyperglycemia caused by abnormalities in insulin secretion, insulin action, or both (Elsayed et al., 2023). Insulin plays an important role in regulating glucose uptake into cells as an energy source. Impaired insulin production or insulin resistance causes glucose to remain in the bloodstream and triggers various metabolic disturbances (Rahman et al., 2021; Szablewski, 2024; James et al., 2021). Chronic hyperglycemia may damage organs through microvascular and macrovascular complications, including neuropathy, nephropathy, retinopathy, and an increased risk of

cardiovascular disease (Zakir et al., 2023; Babel & Dandekar, 2021; Mohammed et al., 2025; Mauricio et al., 2023; Vlacho et al., 2024).

Table 1. Classification of Diabetes Mellitus

Classification	Definition
Type 1 diabetes mellitus	Diabetes caused by autoimmune destruction of pancreatic beta cells, which generally leads to absolute insulin deficiency.
Type 2 diabetes mellitus	Diabetes caused by progressive loss of pancreatic beta-cell insulin secretion, often accompanied by insulin resistance.
Gestational diabetes mellitus	Diabetes diagnosed in the second or third trimester of pregnancy, with no clear evidence of diabetes before pregnancy.
Other specific types of diabetes	Diabetes caused by specific conditions, such as monogenic diabetes, exocrine pancreatic disease, glucocorticoid use, HIV/AIDS therapy, or post-organ transplantation therapy.

Source: Aamodt & Powers (2025).

Diabetic Foot Ulcer

Diabetic foot ulcer is a wound on the foot of a patient with diabetes that may involve the epidermis, dermis, subcutaneous tissue, muscles, tendons, joints, and bones. This condition is associated with peripheral neuropathy, peripheral vascular disease, repeated pressure on the foot, unnoticed minor trauma, and bacterial infection (McDermott et al., 2023; Raja et al., 2023). Patients with sensory neuropathy often do not feel pain when a wound occurs. Small wounds may develop into infections due to delayed detection and impaired healing caused by hyperglycemia (Kim, 2023). Classification of diabetic foot ulcers is needed to assess wound severity and determine appropriate therapy. One commonly used classification system is the Meggitt-Wagner classification. This classification divides ulcers into grades 0 to 5 based on wound depth, the presence of abscess, osteomyelitis, localized gangrene, or extensive gangrene (Liao et al., 2022).

Table 2. Classification of Diabetic Foot Ulcers According to Meggitt-Wagner

Grade	Lesion	General Management
0	No ulceration, but there is a risk of ulcer development	Prevention, education, and control of risk factors
1	Superficial ulcer involving the skin or subcutaneous tissue	Glycemic control, wound care, and antibiotics if infection is present
2	Deeper ulcer with cellulitis, without abscess or bone involvement	Debridement, antibiotics, and glycemic control
3	Deep ulcer with extensive abscess, deep infection, or osteomyelitis	Debridement, intensive antibiotic therapy, and evaluation for surgical intervention
4	Localized gangrene of the toe or heel	Debridement and limited amputation if required
5	Gangrene involving the entire foot	Major amputation, infection control, and patient stabilization

Source: Indonesia (2021).

Diabetic Foot Ulcer Infection

Diabetic foot ulcer infection may be classified as mild, moderate, or severe. Determining the severity of infection is important because it is directly related to antibiotic selection, route of administration, duration of therapy, need for hospitalization, and risk of surgical intervention. The IDSA/PEDIS classification assesses infection based on local signs, such as erythema, edema, pain, warmth, purulent discharge, spread of infection to deeper tissues, and systemic signs, including fever, tachycardia, tachypnea, and changes in leukocyte count (Lipsky et al., 2020).

Table 3. Classification of Diabetic Foot Ulcer Infection Severity According to IDSA/PEDIS

Classification	Clinical Manifestations	Infection Severity
Uninfected	No local signs or symptoms of infection	Uninfected
Mild infection	At least two local signs are present, such as edema or induration, erythema of 0.5–2 cm around the ulcer, local pain, warmth, or purulent discharge	Mild
Moderate infection	Local infection with erythema >2 cm or infection involving deeper structures such as tendons, muscles, joints, or bones, without systemic signs	Moderate
Severe infection	Local infection accompanied by at least two systemic signs, such as temperature >38°C or <36°C, heart rate >90 beats/minute, respiratory rate >20 breaths/minute or $PaCO_2$ <32 mmHg, leukocyte count <4 × 10^9/L or >12 × 10^9/L	Severe

Source: Lipsky et al. (2020).

Antibiotic Therapy in Diabetic Foot Ulcers

Antibiotic therapy in diabetic foot ulcers is given when signs of infection are present. Antibiotics are not intended to directly accelerate wound closure, but to control bacterial infection so that the healing process can proceed more effectively (Hutagalung et al., 2019; Pitocco et al., 2019). Mild infections are generally dominated by gram-positive bacteria, whereas moderate to severe infections may involve gram-negative bacteria, anaerobes, and resistant pathogens such as MRSA. Empirical antibiotic selection should consider infection severity, previous antibiotic exposure, local resistance patterns, comorbidities, and the risk of toxicity (Lipsky et al., 2020; Senneville et al., 2024). Antibiotics commonly used for diabetic foot ulcer infections include cephalosporins, beta-lactam/beta-lactamase inhibitor combinations, fluoroquinolones, metronidazole, clindamycin, carbapenems, or certain combinations according to the patient's clinical condition (Utama & Mutmainah, 2025). Empirical antibiotic use should be evaluated after culture results, sensitivity testing, and clinical progress are available. This evaluation is important because diabetic foot ulcer infections may involve bacteria such as *Staphylococcus aureus*, *Escherichia coli*, and other microorganisms with different resistance patterns (Fauzan & Mahfudz, 2023).

Gyssens Method and Clinical Outcomes

The Gyssens method is used to qualitatively evaluate the rationality of antibiotic use. The assessment includes data completeness, the presence or absence of antibiotic indication, appropriateness of drug selection, availability of more effective alternatives, toxicity, spectrum, cost, dose, interval, route, and duration of therapy (Gyssens, 2005). Category 0 indicates rational antibiotic use, while other categories indicate problems in antibiotic use. Clinical outcomes in patients with diabetic foot ulcers can be assessed based on wound improvement, reduction of inflammatory signs, decreased or normalized leukocyte count, normal body temperature, reduced purulent discharge, and physicians' notes indicating clinical improvement. In this study, clinical outcomes were classified into improved and not improved. Improved outcomes were indicated by at least three indicators, such as normal blood glucose levels, normal body temperature, decreased or normal leukocyte count, reduced erythema or edema, and physician documentation of clinical improvement. Not improved outcomes included worsening wounds, gangrene, amputation, increased leukocyte count, fever, complications, or death.

METHODS

This study used an analytical observational quantitative design with a retrospective cross-sectional approach. Data were obtained from the medical records of hospitalized diabetic ulcer patients who received empirical antibiotic therapy at a hospital in Jakarta during the period of January–December 2025. The study was conducted at the Medical Records and Pharmacy

Departments from January to March 2026. The study population consisted of all hospitalized diabetic ulcer patients who received antibiotics, with a total population of 330 patients in 2025. The sample was selected using a purposive sampling technique based on inclusion and exclusion criteria. The inclusion criteria included patients aged ⩾18 years, diagnosed with diabetic ulcers with mild to severe infection, receiving single or combination empirical antibiotic therapy, having complete medical records, and undergoing treatment until clinical outcomes could be evaluated. The exclusion criteria included incomplete medical records, patients who died within <48 hours of hospitalization, patients with severe immunocompromised conditions, non-diabetic ulcers, patients who were referred or discharged against medical advice before evaluation, and patients who did not receive empirical antibiotics. The independent variable of the study was the rationality of antibiotic use based on the Gyssens method, including the appropriateness of indication, drug selection, dosage, interval, route, duration, and completeness of evaluative data. The dependent variable was the clinical outcome of diabetic ulcer patients, categorized as improved and not improved based on changes in wound condition, inflammatory parameters, laboratory results, and the assessment of the physician in charge of the patient. Data were collected using a medical record extraction form and a Gyssens evaluation sheet. Data analysis was performed using univariate analysis to describe patient characteristics, antibiotic use patterns, treatment rationality, and clinical outcomes, as well as bivariate analysis using the Chi-square test or Fisher's exact test to assess the relationship between antibiotic rationality and clinical outcomes, with a significance value of $p < 0.05$.

RESULT AND DISCUSSION

Participant Selection and Analytic Dataset

The hospital register contained 330 inpatient records of patients with diabetic foot ulcers during the 2025 study period. After application of the eligibility criteria, 62 records were retained for the descriptive analysis and 268 records were excluded. The source manuscript did not provide a category-specific breakdown of the exclusions; therefore, the final manuscript should add the numbers excluded because of incomplete records, non-diabetic ulcers, early death, referral or discharge against medical advice, severe immunocompromise, and absence of evaluable empirical-antibiotic exposure.

Among the 62 included records, 55 patients (88.7%) were recorded as receiving a systemic antibiotic and seven patients (11.3%) were coded as receiving no systemic antibiotic. This coding conflicts with the eligibility criterion requiring empirical antibiotic therapy. The available dataset does not clarify whether the seven patients had completed systemic therapy before the medication review, received antibiotics before hospitalization, received topical therapy only, or received no antibiotic. Consequently, the full cohort of 62 patients is retained below for demographic, wound, and surgical descriptions, whereas the eligibility and antibiotic-exposure status of these seven records must be verified against the original medical records before the Gyssens and outcome-association analyses are finalized.

Demographic Characteristics of Patients

The study population was predominantly female, with 39 patients (62.9%), whereas 23 patients (37.1%) were male. Most patients were aged 40-59 years (37 patients; 59.7%), followed by those aged 60-74 years (20 patients; 32.3%) and 20-39 years (5 patients; 8.1%). The mean age was 52.1 years, with a range of 24-73 years. This distribution indicates that diabetic foot ulcers were concentrated in middle-aged and pre-elderly adults, in whom longer diabetes duration, neuropathy, vascular impairment, and delayed wound recognition may increase the risk of ulceration and infection.

Table 4. Distribution of Patient Characteristics (n=62)

Characteristic	Category	Number (n)	Percentage (%)
Age	20–39 years	5	8,1
	40–59 years	37	59,7

	60-74 years	20	32,3
	≥75 years	0	0,0
Gender	Male	23	37,1
	Female	39	62,9

Ulcer Severity and Wound Status after Intervention

Before intervention, Wagner Grade 2 was the most frequent category (23 patients; 37.1%), followed by Grade 1 (19; 30.6%), Grade 4 (14; 22.6%), and Grade 3 (6; 9.7%). Thus, 20 patients (32.3%) presented with Grade 3-4 ulcers, indicating deep infection, extensive tissue involvement, or gangrene. After intervention, Grade 1 accounted for 31 patients (50.0%), Grade 2 for 19 (30.6%), Grade 3 for 7 (11.3%), and Grade 4 for 5 (8.1%). The decline in the aggregate proportion of Grade 4 ulcers from 22.6% to 8.1% suggests an overall shift toward less severe wound status. However, because the manuscript provides only marginal distributions rather than patient-level paired transitions, the exact number of individual patients whose Wagner grade improved, remained unchanged, or worsened cannot be determined from these totals alone.

Table 5. Wagner-Meggitt Grade before and after Intervention (n = 62)

Wagner Grade	Before n (%)	After n (%)	Aggregate change
Grade 1	19 (30.6)	31 (50.0)	+12
Grade 2	23 (37.1)	19 (30.6)	-4
Grade 3	6 (9.7)	7 (11.3)	+1
Grade 4	14 (22.6)	5 (8.1)	-9
Total	62 (100.0)	62 (100.0)	

Surgical Management

Surgical reporting was revised to separate the number of patients from the number of procedures. Of the 62 patients, 34 (54.8%) received conservative management and 28 (45.2%) underwent at least one surgical procedure. The 28 surgically managed patients underwent 31 procedures because three additional procedures occurred in patients who received more than one intervention. Therefore, patient-level percentages use 62 as the denominator, whereas procedure-level percentages use 31 as the denominator.

Table 6. Patient-Level Distribution of Surgical Management (n = 62)

Surgical-management status	Patients (n)	% of patients
No surgical procedure	34	54.8
At least one surgical procedure	28	45.2
Total	62	100.0

Table 7. Distribution of Surgical Procedures (31 Procedures Among 28 Patients)

Procedure	Procedures (n)	% of procedures
Debridement	20	64.5
Debridement + fasciotomy/necrotomy	4	12.9
Debridement + rotation/advancement flap	3	9.7
Amputation + debridement	2	6.5
Debridement + roserplasty/excision	2	6.5
Total procedures	31	100.0

Debridement represented nearly two-thirds of all procedures and was consistent with the need to remove necrotic tissue, reduce bacterial burden, and support wound healing. Surgical treatment is an important co-intervention and must be considered when interpreting clinical outcomes; wound improvement cannot be attributed to antibiotic therapy alone.

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Systemic Antibiotic Use and Reconciliation of Numerical Inconsistencies

The verified descriptive table in the source manuscript records ceftriaxone in 35 patients (56.5%), cefixime in 19 (30.6%), clindamycin in one (1.6%), and no systemic antibiotic in seven (11.3%). These figures sum to 62 and are retained as the primary antibiotic-distribution results. The previous cross-tabulation by Wagner grade reported totals of 21 cefixime users, two clindamycin users, and four patients without systemic antibiotics. Because those row totals conflict with the primary distribution, the cross-tabulation and its reported chi-square result (chi-square = 24.315; p = 0.004) have been removed from the revised section. The association between antibiotic type and ulcer severity should be recalculated only after the original records have been reconciled.

Table 8. Distribution of Recorded Systemic Antibiotic Use (n = 62)

Recorded antibiotic status	n	%	Route
Ceftriaxone	35	56.5	Intravenous
Cefixime	19	30.6	Oral
Clindamycin	1	1.6	Oral/IV
No systemic antibiotic recorded	7	11.3	-
Total	62	100.0	

Ceftriaxone was the predominant recorded agent, reflecting the frequent use of parenteral broad-spectrum therapy in hospitalized patients. Cefixime was the second most common agent and was administered orally. Interpretation of appropriateness requires more than the drug name: infection severity, suspected pathogens, culture results, renal and hepatic function, dose, interval, route, duration, prior antibiotic exposure, and surgical source control must be assessed together (Gyssens, 2005; Lipsky et al., 2020; Senneville et al., 2024).

Rationality of Antibiotic Use Based on the Gyssens Method

The source manuscript reported a Gyssens classification for all 62 records. Category 0, indicating antibiotic use judged appropriate on the assessed components, was assigned to 28 records (45.2%). The remaining 34 records (54.8%) were classified as non-rational in at least one assessed aspect. The most frequent classification was Category IVA, interpreted in the source manuscript as an inappropriate route, in 21 records (33.9%). Twelve records (19.4%) were classified as Category IIA/IIB because of inadequate spectrum or effectiveness, and one record (1.6%) had combined spectrum, effectiveness, interval, and dose problems. The category labels below reproduce the coding used in the source manuscript; they should be checked for consistency with the Gyssens flowchart and category definitions stated in the Methods section.

Table 9. Distribution of Gyssens Categories Reported in the Source Dataset (n = 62)

Gyssens Classification Used in Source Manuscript	n	%
Category 0 - appropriate use	28	45.2
Category IVA - inappropriate route	21	33.9
Category IIA/IIB - inappropriate spectrum/effectiveness	12	19.4
Category IIA/IIB/IVB/IVC - spectrum, effectiveness, interval, and dose problems	1	1.6
Total	62	100.0

The main reasons for non-rational use were related to route and antimicrobial coverage. Oral cefixime used in hospitalized patients with moderate-to-severe wounds was judged problematic when parenteral therapy was clinically required and when coverage of gram-positive or anaerobic organisms was inadequate. Metronidazole monotherapy was judged insufficient because it covers anaerobic organisms but does not provide adequate activity against the aerobic gram-positive and gram-negative organisms commonly involved in diabetic foot infection. One metronidazole regimen administered twice daily was additionally classified as having inappropriate interval and total daily dose. Oral clindamycin or oral metronidazole in

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patients requiring inpatient parenteral treatment contributed to the route-related category. These findings identify specific targets for antimicrobial-stewardship review: confirmation of infection severity, early culture acquisition, selection of adequate aerobic and anaerobic coverage when indicated, timely intravenous-to-oral transition based on clinical stability, and dose adjustment based on organ function.

Clinical-Outcome Frequencies

The original Methods defined clinical improvement using a composite of at least three clinical or laboratory indicators. The available Results tables do not provide patient-level counts for that prespecified composite. To make the available wound outcome explicit without overstating the evidence, the final Wagner status was summarized as a descriptive proxy: Grades 1-2 were grouped as a favorable final wound status and Grades 3-4 as an unfavorable final wound status. On this basis, 50 patients (80.6%) had a favorable final wound status and 12 (19.4%) had an unfavorable final wound status. This proxy must not be presented as identical to the prespecified composite outcome unless the original medical records confirm the required clinical and laboratory indicators for each patient.

Table 10. Descriptive Final Wound-Status Outcome (n = 62)

Final wound-status category	n	%
Favorable final wound status (Wagner Grade 1-2)	50	80.6
Unfavorable final wound status (Wagner Grade 3-4)	12	19.4
Total	62	100.0

Association between Antibiotic Rationality and Clinical Outcomes

A valid chi-square or Fisher exact test requires a patient-level 2 x 2 cross-tabulation linking each patient's Gyssens classification (Category 0 versus non-Category 0) to that patient's clinical outcome (improved versus not improved). The available manuscript provides only the separate marginal totals of 28 rational and 34 non-rational records and the descriptive final wound-status totals of 50 favorable and 12 unfavorable outcomes. These marginal totals are insufficient to reconstruct the four joint cell counts. Therefore, a p-value, effect estimate, or conclusion regarding the relationship between antibiotic rationality and clinical outcome cannot be calculated validly from the available aggregate information and is not fabricated in this revision.

Table 11. Required Patient-Level Cross-Tabulation for the Primary Association Analysis

Antibiotic rationality	Improved n	Not improved n	Total n
Rational (Gyssens Category 0)	To be verified	To be verified	28
Non-rational (other categories)	To be verified	To be verified	34
Total	To be verified	To be verified	62

Before submission, the authors should return to the 62 individual records, apply the prespecified outcome definition after 48-72 hours, and enter the four cell counts in Table 11. The chi-square test may be used when expected counts meet its assumptions; otherwise, Fisher's exact test should be reported. The manuscript should present the exact p-value and an effect estimate such as an odds ratio with a 95% confidence interval. Until this re-tabulation is completed, the study can describe Gyssens rationality and wound status but cannot claim that antibiotic rationality is or is not associated with clinical outcome.

Integrated Interpretation and Limitations

The central verified finding is that 54.8% of records were classified as having at least one antibiotic-use problem, particularly inappropriate route and inadequate antimicrobial spectrum or effectiveness. At the same time, the aggregate wound distribution shifted toward lower Wagner grades after treatment. This improvement occurred in the context of combined care, including glycemic management, wound care, debridement, reconstructive procedures, and

amputation when necessary. Antibiotic rationality is therefore only one determinant of outcome, and confounding by baseline wound severity, vascular status, neuropathy, surgical source control, glycemic control, renal function, and comorbidities must be considered.

The retrospective design and incomplete linkage between antibiotic evaluation and patient-level outcomes limit causal interpretation. The unresolved coding of seven patients without recorded systemic antibiotics, inconsistency between antibiotic-distribution tables, absence of category-specific exclusion counts, reliance on aggregate pre/post Wagner distributions, and lack of a linked Gyssens-outcome cross-tabulation are material data-quality limitations. These issues should be resolved through re-audit of the original medical records and the analytic dataset before the manuscript makes a definitive conclusion about the primary association.

CONCLUSION

Among 62 patients with diabetic foot ulcers, the source dataset classified 28 records (45.2%) as rational antibiotic use and 34 (54.8%) as non-rational use. The principal problems were inappropriate route in 21 records (33.9%), inadequate spectrum or effectiveness in 12 (19.4%), and combined spectrum, effectiveness, interval, and dose problems in one (1.6%). The aggregate final wound distribution comprised 50 patients (80.6%) with Wagner Grade 1-2 and 12 (19.4%) with Grade 3-4. However, the patient-level cross-tabulation linking Gyssens category to the prespecified composite clinical outcome was not available, so the primary association and its p-value cannot be determined validly from the current aggregate tables. The seven records coded as receiving no systemic antibiotic and the inconsistent antibiotic totals must be verified against the original medical records. A final re-analysis should then report the 2 x 2 table, exact statistical test, effect estimate, and 95% confidence interval before conclusions are drawn regarding the relationship between antibiotic rationality and clinical outcomes.

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