International Journal of Medicine and Medical Research

ISSN 2413-6077, e-ISSN 2414-9985
Journal homepage: https://ijmr.com.ua/
Volume 11, No. 2. 2025

UDC 616.379-008.64-06:617.586]-035-085
DOI: 10.63341/ijmmr/2.2025.120

Article's History:
Received: 15.11.2025; Revised: 15.12.2025;
Accepted: 30.12.2025; Published: 06.01.2026

Pharmacoeconomic evaluation of pharmacotherapy of patients with diabetic foot syndrome secondary to type 2 diabetes mellitus

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Abstract. The increasing prevalence of type 2 diabetes mellitus complicated by diabetic foot syndrome and the prescription of high-cost medicines, which are not included in treatment protocols, significantly raise healthcare expenditures and worsen patient outcomes, making the optimisation of pharmacotherapy both a clinical and economic priority. The purpose of this study was to evaluate the rationality of pharmacotherapy for patients with diabetic foot syndrome using an integrated frequency/ABC/VEN analysis. The study applied frequency analysis to assess prescription patterns ATC-classification, ABC-analysis to classify medicines by expenditure levels, and VEN-analysis to determine their therapeutic importance based on national and international treatment guidelines recommendations for type 2 diabetes mellitus. The results demonstrated that etiological and pathogenetic therapies approaches predominated in clinical practice. Antidiabetic agents accounted for the largest share of prescriptions (23%), while antibiotics were essential

Suggest Citation:
Pokotylo O, Volch I, Mykhailyshyn H, Demchuk M, Dub A. Pharmacoeconomic evaluation of pharmacotherapy of patients with diabetic foot syndrome secondary to type 2 diabetes mellitus. Int J Med Med Res. 2025;11(2):120–130. DOI: 10.63341/ijmmr/2.2025.120

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for managing infectious complications. The integrated frequency/ABC/VEN-analyses revealed that "essential" medicines (44.19%) predominated over "vital" (23.26%) and "non-essential" categories (32.56%), indicating the insufficiently rational prescribing practices in accordance with treatment recommendations. However, a high share of healthcare expenditures was concentrated in a group of high-cost medicines (34.89%), suggesting suboptimal allocation of healthcare resources. The results also highlighted the importance of evidence-based antibiotic selection due to the growing risk of antimicrobial resistance. The study provided a foundation for improving the economic efficiency of pharmacotherapy in patients with diabetic foot syndrome by supporting rational prescribing, optimisation of healthcare expenditures, and the promotion of cost-effective Ukrainian medicines alternatives

Keywords: integrated frequency/ABC/VEN analysis; medicinal prescriptions; anti-bacterial agents; antimicrobial resistance; pharmaceutical provision optimisation

Introduction

Type 2 diabetes mellitus (T2DM) is a significant global health challenge due to its increasing prevalence and severe complications, including diabetic foot syndrome (DFS). DFS, characterised by diabetic foot ulcers, infections, and gangrene, substantially exacerbates morbidity, mortality, and healthcare costs in patients with T2DM. Despite advances in pharmacotherapy, the management of DFS remains complex and resource-intensive. Pharmacoeconomic evaluation is essential in optimising pharmacotherapy for patients with DFS secondary to T2DM, given the significant clinical and economic burden of this complication. Careful assessment of treatment costs and outcomes can inform better resource allocation and improve patient outcomes in this complex disease area.

Numerous studies by both foreign and Ukrainian healthcare experts have been devoted to the issue of in-depth investigation about this pathology, its impact on the countries' budget, and the development of ways to optimise expenses for providing high-quality, effective, and safe pharmacotherapy DFS secondary to T2DM. The study by D.G. Armstrong *et al.* [1] provided a comprehensive review of diabetic foot ulcers, emphasising the high morbidity, including risk of amputation and death associated with these ulcers, and the critical role of multidisciplinary care involving surgical debridement, offloading, and infection management. This systemic approach impacts both clinical outcomes and healthcare expenditures profoundly. In turn, M.J. Carter *et al.* [2] highlighted the rising prevalence of chronic wounds among Medicare beneficiaries in the USA, elucidating increasing treatment costs over time and underscoring the urgent need for cost-effective therapeutic options to manage this growing patient population. Additionally, the findings of Y. Zhang *et al.* [3] quantified the global disability burden posed by diabetes-related lower-extremity complications, including diabetic neuropathy and foot ulcers. Moreover, M.A. Del Core *et al.* [4] provided an updated overview of diabetic foot ulcer evaluation and treatment, underscoring the multifactorial etiology involving neuropathy, vasculopathy, and immunopathy, and advocating for comprehensive multidisciplinary management and further randomised clinical trials to refine therapeutic and preventive protocols.

Furthermore, B.J. Petersen *et al.* [5] documented higher mortality rates and increased healthcare resource utilisation during episodes of care for diabetic foot ulceration, highlighting the profound economic and clinical consequences of this complication. National diabetes statistics report [6] further underscored the continued rise in diabetes prevalence and related complications, reinforcing the public health imperative to optimise pharmacotherapeutic management of DFS. The study by K. McDermott *et al.* [7] analysed disparities in diabetic foot ulcer incidence and outcomes, drawing attention to the socio-economic and racial factors contributing to suboptimal care and increased costs, thus illustrating the complexity of delivering equitable and cost-effective diabetes care.

N.W. Cortes-Penfield *et al.* [8] focused on diabetes-related foot infections, a major DFS complication, highlighting the substantial morbidity and financial costs associated with infection management, including antimicrobial therapy and potential surgery. This study stressed the necessity of multidisciplinary teams and individualised treatment strategies to improve outcomes and reduce costs. In addition, A. Jodheea-Jutton *et al.* [9] reviewed recent health economic trends in diabetic foot ulcer treatment, advocating for accelerated therapeutic approaches and enhanced care models aimed at cost containment and efficacy improvement. Ultimately, the study by E. Sutrisno *et al.* [10], through descriptive and statistical pharmacoeconomic analysis, compared the economic burden of conservative versus amputation treatment modalities for diabetic foot ulcers, emphasising the importance of strategic therapeutic decision-making to optimise healthcare spending without compromising patient outcomes.

In the context of DFS, a serious and costly complication of type 2 diabetes prevalent in Ukraine, rational pharmacotherapy is essential. T.H. Bakaliuk *et al.* [11] showed that rehabilitation methods, when combined with standard protocols, significantly improve ulcer healing rates and patient quality of life in diabetic foot syndrome, implying potential cost savings through enhanced clinical outcomes. Altogether, these studies affirm that complex ABC/VEN analysis is a valuable tool in pharmacoeconomics, enabling healthcare providers in Ukraine to efficiently allocate limited resources, prioritise essential medicines, and optimise treatment outcomes in challenging settings such as DFS. Case in point, the study by I.A. Kostiuk & K.L. Kosiachenko [12] demonstrated the application of integrated

ABC/VEN analysis to evaluate medicinal prescribing in pediatric bronchial asthma pharmacotherapy, highlighting the capacity of this approach to optimise resource allocation and ensure prioritisation of vital and essential medicines.

Therefore, the purpose of this study was to implement methodological approaches of frequency/ABC/VEN analyses for the assessment of the rationality of medicinal prescriptions in the pharmacotherapy of patients with diabetic foot syndrome resulting from T2DM.

Materials and Methods

The integrated frequency/ABC/VEN analyses was conducted using medical prescriptions of 80 inpatients with T2DM complicated by DFS admitted to the Surgical Department of the Municipal Non-Profit Enterprise "Ternopil City Municipal Hospital" during 2023, February-October. The inclusion criteria: adult patients of both sexes (≥18 years) verified diagnosed with T2DM complicated by DFS, who provided informed consent to participate. The exclusion criteria: the presence of chronic diseases in the acute or decompensated phase, ongoing glucocorticosteroid therapy, pregnancy, mental disorders, malignancies or suspected cancer, and refusal to participate. The methodology of pharmacoeconomic research involved the combined analysis of the frequency of medical prescriptions of inpatients, ranking of expenses for pharmacotherapy (ABC analysis), and ranking of prescribed drugs by degree of importance (VEN analysis). A frequency analysis is a type of quantitative assessment that reflects how often specific medicines or pharmacological groups are prescribed, and their proportion within the total number of prescriptions, arranged from highest to lowest frequent. The trade names (TN) of medicines and their Anatomical Therapeutic Chemical (ATC) classification system ATC/DDD Index 2025 [13] were used the frequency analysis of prescriptions to evaluate the main trends in pharmacotherapy of patients with T2DM complicated by DFS.

According to an expert approach of VEN analysis [14], medicines were divided into three categories: vital (V), essential (E), and non-essential (N), taking into consideration the compliance of patients' pharmacotherapy with current standards and clinical protocols: Order of the Ministry of Health of Ukraine No. 356 [15], Resolution of the Cabinet of Ministers of Ukraine No. 333 [16], Order of the Ministry of Health of Ukraine No. 971 [17], WHO Model List of Essential Medicines [18], the National Institute for Health and Care Excellence (NICE) guideline [19], Order of the Ministry of Health of Ukraine No. 1513 [20], AWaRe classification [21]. ABC analysis is the categorisation of medicines into three groups (high-cost, medium-cost, and low-cost) depending on the share of expenses for their use in the total amount of medicines costs over a certain period of time. According to the methodology group "A" should be formed by the most expensive drugs (80% of total costs), group "B" – medium-cost (15%) and group "C" – low-cost (5%). ABC analysis is based on the Pareto principle: 20% of the total number of prescribed medicines allows covering 80% of costs, while 80-85% of prescribed medicines require 20% of the funds raised. Indicators such as prescription frequency (PF), average retail price (ARP) per package, percentage of total costs, and cumulative cost percentage were used for ABC classification [14]. Statistical processing of the numerical data was performed using Excel software suite (Microsoft, USA), tabulating the data and expressing them in percents. The research was conducted following the principles set out in the Declaration of Helsinki [22] and Ethics and Data Protection [23]. Ethical approval for the publication of this case report was obtained from the Ethics Committee of Ivan Horbachevsky Ternopil National Medical University (protocol No. 83 dated November, 2025).

Thus, an integrated pharmacoeconomic evaluation combining frequency, ABC, and VEN analyses was applied to assess the rationality and economic structure of pharmacotherapy in inpatients with T2DM complicated by DFS. This approach helped to identify the most frequently prescribed medicines, determine their contribution to total treatment costs, and assess their clinical significance in accordance with treatment priorities. In addition, it provided a clear basis for optimising therapeutic strategies, ensuring both clinical and economic efficiency in the treatment of patients with T2DM complicated by diabetic foot syndrome.

Results and Discussion

Analysis of patients (n = 80) demographics by age and sex revealed that males accounted for 66.25% of the cohort, while females represented 33.75%. The mean age was 61-70 years and above 70 years, respectively. Gender distribution indicated that men with T2DM were more prone to developing DFS compared to women. Pharmacoeconomic frequency analysis of prescriptions identified 43 TNs of medicines, which were stratified into three groups based on PF: Group 1 – PF ≥ 40%, Group 2 – PF 20-40%, and Group 3 – PF < 20%. The analysis showed that only one medicine (Ceftriaxone, powder for solution for injection 1.0, vial) had a PF > 40% (Table 1). Group 2 included five drugs, three of which belonged to the pharmacological group J 01 (antimicrobials for systemic use). The largest number of medicines (37 drugs, mean PF 3.20%) was assigned to Group 3.

Table 1. TOP-10 medicines by PF in pharmacotherapy T2DM complicated with DFS

No.	INN	ATC-index	Trade name / Dosage form	PF, %
1.	Ceftriaxone	J01D D04	Ceftriaxone / powder for solution for injection, 1.0 g No. 1 vial	46.70%
2.	Cefazolin	J01D B04	Cefazolin-BChPhF / powder for solution for injection, 1.0 g No. 1 vial	18.60%
3.	Piperacillin and β-lactamase inhibitor	J01C R05	Tazpen / powder for solution for injection and infusion, 4.0/0.5 g No. 1 vial	16.30%
4.	Metformin	A10B A02	Metformin-Teva / film-coated tablets, 1.0 g No. 30 (15x2)	16.30%

Continued Table 1

No.	INN	ATC-index	Trade name / Dosage form	PF, %
5.	Metronidazole	J01X D01	Metronidazole / tablets, 250 mg No. 20 (10x2)	11.60%
6.	Metronidazole	D06B X01	Metrogyl Gel / gel for external use, 10 mg/g, 30 g tube	11.60%
7.	Insulin (human)	A10A B01	Actrapid NM / solution for injection, 100 IU/mL, 10 mL No. 1 vial	9.30%
8.	Arginine hydrochlorid	B05X B01	Tivortin / infusion solution, 42 mg/mL, 100 mL bottle	9.30%
9.	Electrolytes in combination	B05BB04	Reosorbilact / infusion solution, 200 mL vial	4.60%
10.	Insulin aspart	A10AB05	Novorapid Flexpen / solution for injection, 100 IU/mL, 3 mL No. 5, prefilled pen	4.60%

Note: INN – International Nonproprietary Names
Source: compiled by the authors

Regarding ATC/DDD Index 2025 [13], eight pharmacological groups were identified in prescriptions. As illustrated in Figure 1, the leading ATC groups were: A10 – Drugs used in diabetes (23%; leading drug – Metformin-Teva, film-coated tablets), J01 – Antibacterials for systemic use (21%; leading drug – Ceftriaxone, powder for injection solution), B01A – Antithrombotic agents (18.6%; leading drug – Tivortin, infusion solution).

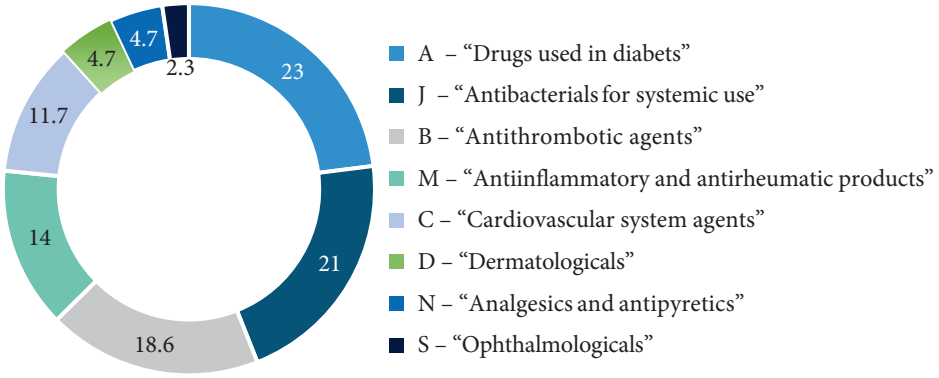

Figure 1. PF by ATC classification groups (%)
Source: compiled by the authors

Other pharmacological groups included agents for etiological therapy of DFS or pathogenetic therapy of comorbidities: M01 – Anti-inflammatory and antirheumatic products (14%), C – Cardiovascular system agents (11.7%), D – Dermatologicals (4.7%), and N02B – Analgesics and antipyretics (4.7%). Analysis of prescription forms revealed an equal distribution between oral (film-coated tablets) and parenteral formulations (injection and infusion solutions) at a 1:1 ratio. Oral administration was preferred for mild infections (occasionally with topical therapy), while moderate and severe infections typically required initial parenteral therapy with a subsequent switch to oral administration once clinical stability was achieved. Further analysis of antibiotics' prescription within the J01 group demonstrated that Ceftriaxone accounted for the highest PF (46.7%) and indicates compliance with the Ministry of Health of Ukraine's treatment guidelines for DFS [15], and simultaneous non-compliance with the requirements of rational pharmacotherapy [20] (Table 2).

Table 2. PF and expenses for antibacterial therapy T2DM complicated with DFS

No.	INN	ATC-index	Trade name / Dosage form	PF	AVR, UAH	Expenses, UAH
1.	Ceftriaxone	J01DD04	Ceftriaxone / powder for solution for injection, 1.0 g, No. 1 vial	20	44.00	880.00
2.	Cefazolin	J01DB04	Cefazolin-BHFZ / powder for solution for injection, 1.0 g, No. 1 vial	8	24.00	192.00
3.	Piperacillin and β-lactamase inhibitor	J01CR05	Tazpen / powder for solution for injection and infusion, 4.0/0.5 g, No. 1 vial	7	300.0	2,100.00
4.	Metronidazole	J01XD01	Metronidazole / tablets, 250 mg, No. 20 (10×2)	5	58.50	292.50
5.	Meropenem	J01DH02	Diapenem / powder for solution for injection and infusion, 1.0 g, No. 10 vials	1	3,600.00	3,600.00
6.			Meropenem / powder for solution for injection, 1.0 g, No. 1 vial	1	370.00	370.00

Continued Table 2

No.	INN	ATC-index	Trade name / Dosage form	PF	AVR, UAH	Expenses, UAH
7.	Levofloxacin	J01MA12	Supralev / infusion solution, 500 mg/100 mL, 100 mL vial	1	60.00	60.00
8.			Levofloxacin-Teva / film-coated tablets, 0.5 g, No. 10	1	228.00	228.00
9.	Ciprofloxacin	J01MA02	Ciprofloxacin-Astrafarm / film-coated tablets, 0.5 g, No. 10	1	97.00	97.00

Note: INN – International Nonproprietary Names; ARP – average retail price
Source: compiled by the authors

No evidence of polypharmacy was observed: the maximum number of prescribed drugs per patient was five, while the minimum was one, consistent with the therapeutic specificity of T2DM patients with DFS. Cost analysis revealed that expenditures on Tazpen (powder for injection and infusion solution) and Diapenem (powder for injection and infusion solution) significantly exceeded the median cost (UAH 303.00), potentially creating an additional financial burden under budget-reimbursed treatment schemes for DFS. The next stage of the study involved conducting a VEN-analysis of medicines prescribed to patients with DFS. To evaluate the rationality of anti-bacterial agents' prescriptions, information on the inclusion them in key national and international regulatory and clinical documents was systematised (Table 3).

Table 3. Analysis of the availability of anti-bacterial agents on the lists of rational pharmacotherapies of DFS

No.	INN	National List of Essential Medicines of Ukraine, 2023	State Formulary of Medicinal Products (edit), 2025	WHO Model List of Essential Medicines, 2025	NICE guideline, 2019	AWaRe classification, 2021
1.	Ceftriaxone	+	+	+	+	C
2.	Cefazolin	+	+	+	-	A
3.	Piperacillin and β-lactamase inhibitor	-	+	-	+	B
4.	Metronidazole	+	+	+	+	A
5.	Meropenem	-	+	+	-	B
6.	Levofloxacin	-	+	+	-	C
7.	Ciprofloxacin	+	+	+	+	B

Source: compiled by the authors

According to the obtained data, 100% of prescribed anti-bacterial agents were listed in the State Formulary of Medicinal Products [17]. Ceftriaxone, cefazolin, and metronidazole are consistently included in the National List of Essential Medicines [16], State Formulary of Medicinal Products [17], WHO Model List of Essential Medicines [18], reflecting their essential status and wide relevance in empiric and targeted antimicrobial therapy. However, according to AWaRe classification [21], ceftriaxone and levofloxacin are included in the "Reserve" category, so their use must be restricted and carefully monitored. Meropenem, although not included in all lists due to its classification as a broad-spectrum carbapenem, appears within the AWaRe "Watch" category, highlighting its importance for resistant infections but recommending restricted use. According to the NICE guideline [19], four of these agents (ceftriaxone, piperacillin-β-lactamase inhibitor, metronidazole, ciprofloxacin) are recommended for use in moderate to severe infections associated with DFS, confirming their clinical appropriateness. According to the WHO AWaRe classification [21], cefazolin and metronidazole are categorised in the "Access" group, due to their lower resistance risk. Three antibiotics (piperacillin-β-lactamase inhibitor, meropenem, and ciprofloxacin) are classified in the "Watch" group and reserved for specific indications and require stewardship oversight to prevent overuse and resistance development.

Based on the full (100%) inclusion of Ceftriaxone, Metronidazole, and Ciprofloxacin in all regulatory acts their prescriptions were classified as justified and assigned to the "V" (vital) category. However, the low PF of Ciprofloxacin (2.30%) may indicate either its empirically low clinical efficacy or high microbial resistance in wound infections in patients with T2DM complicated by DFS. Moreover, the high PF of Piperacillin and beta-lactamase inhibitors (16.30%) remains controversial, as these drugs are absent from the WHO Model List of Essential Medicines [18] and, accordingly, from the National List of Essential Medicines [16]. Similarly, prescriptions for Cefazolin, Meropenem, and Levofloxacin require further discussion, as they are not included in the NICE guideline [19].

According to the research, ten medicines were classified as "vital". Among them, three medicines (30%) were antibiotics, active against gram-positive wound pathogens, while six medicines (60%) belonged to the A10 pharmacological group (antidiabetic agents) aimed at pathogenetic correction in T2DM patients. One medicine, Reosorbilact (infusion solution) from the B05 group (blood substitutes

and perfusion solutions), was identified as essential for improving microcirculation, arterial and venous blood flow, and correcting metabolic acidosis. 19 medicines (44%) of the prescriptions were assigned to the "essential" category. Most of these were included in the National List of Essential Medicines [16] and the State Formulary of Medicinal Products [17], however were not always recommended in DFS treatment protocols [15]. These medicines largely contribute to maintaining the quality of life in patients with chronic comorbidities with high disease burden indices, such as arterial hypertension, diabetes mellitus, and venous thromboembolism. Antimicrobial agents predominated in this category (36.8%), followed by B01A antithrombotic drugs (26.3%), reflecting the cardiovascular comorbidity profile of T2DM patients. Ultimately, 32.6% of prescribed medicines were classified as "non-essential". These agents were absent in the National List of Essential Medicines [16] and primarily used for symptomatic management of conditions not directly affecting DFS progression. The majority of these medicines belonged to the M01A pharmacological group (nonsteroidal anti-inflammatory and antirheumatic drugs), particularly Dexketoprofen (35.8%).

The ABC analysis (Table 4) revealed that group "A" included 15 trade names (34.9%), dominated by antidiabetic agents (40%), blood and haematopoietic drugs (33.3%), and systemic antibacterials (20%). It reflects that the management of T2DM with complications, along with haematological support, is consuming a significant portion of healthcare resources. In contrast, group "B", representing only 15% of expenditures, includes medicines with a moderate cost impact, suggesting they are essential but not as financially demanding. It comprised 13 medicines (30.2%) with an equal share of antidiabetic and antimicrobial agents (23% each), reflecting etiological and pathogenetic treatment approaches. It suggests that these drugs support both disease management and infection control, but at a lower overall expense. Group "C" (5% of expenditures) consisted of 15 medicines (34.9%), mainly cardiovascular agents (26.7%) and anti-bacterial agents (20%). Their budgetary burden is minimal, indicating that either they are low-cost generics or have lower consumption volumes.

Table 4. Generalised results of integrated frequency/ABC/VEN analysis

ABC / VEN analysis	V			E			N		
	Number of medicines	Cost, UAH	Share, %	Number of medicines	Cost, UAH	Share, %	Number of medicines	Cost, UAH	Share, %
A	6	8,260.00	30.34	7	11,833.00	43.47	2	1,658.00	6.09
B	2	733.50	2.69	4	1,125.30	4.13	7	2,299.00	8.45
C	2	312.00	1.15	8	602.50	2.22	5	329.20	1.46
Total	10	9,305.50	34.18	19	13,560.80	49.82	14	4,355.20	16.00

ABC-analysis			VEN-analysis		
Class	Number of medicines	Share, %	Group	Number of medicines	Share, %
A	15	34.89	V	10	23.26
B	13	30.22	E	19	44.19
C	15	34.89	N	14	32.56
Total	43	100	Total	43	100

Source: compiled by the authors

The integration of antibacterial prescribing patterns with essential medicines lists and stewardship frameworks provides a deeper understanding of the rationality of antimicrobial therapy in patients with DFS. The results indicated a disproportionate cost burden for vital and essential medicines, emphasising the need for economic strategies to optimise resource allocation and improve access to cost-effective pharmacotherapy for DFS in patients with T2DM. The results of the frequency analysis indicated the predominance of etiological and pathogenetic therapy, consistent with the recommendations of regulatory documents [15, 19, 20]. The high concordance of frequently prescribed antibiotics (such as ceftriaxone, cefazolin, metronidazole, and piperacillin-tazobactam) with national and international essential medicines lists underscores the alignment of local prescribing practices with evidence-based standards. This suggests that the antimicrobial choices made in the study setting adhere to globally recognised therapeutic principles and emphasise the availability and affordability of core antibacterial agents.

The VEN analysis revealed that "non-essential" drugs were mainly prescribed for concomitant minor conditions. Their clinical efficacy is often poorly supported by evidence, and in some cases, these medicines are costly relative to their limited therapeutic benefit. Importantly, inclusion in the "N" category does not necessarily mean the drug is absent from the formulary system or essential medicines list; in many cases, drugs for minor illnesses appear on essential medicines lists but are considered lower priority for procurement compared to others. Overall, the VEN analysis helped to derive the following equation for drug distribution in prescriptions by clinical importance: E > V > N. The quantitative predominance of "essential" over "vital" medicines remains a subject of debate due to the

complexity of the pathology (patients were treated not only for the primary disease but also for chronic comorbidities) and the nature of DFS therapy. A positive finding was the relatively small share of "non-essential" drugs, indicating a preference for targeted, evidence-based pharmacotherapy (V + E > N by twofold) among healthcare professionals.

The ABC analysis revealed a shift toward a higher proportion of high-cost "A" medicines, indirectly suggesting a potentially irrational allocation of funds for DFS pharmacotherapy. In the study, the ABC-equation was A = C > B, indicating about the demand in the cost optimisation and a reduction in the share of expensive drugs through greater use of Ukrainian generic medicines. For practical implications for budget optimisation, it would be appropriate to prioritise negotiations for group "A" and "V"/"E" medicines to reduce procurement costs, especially high-cost antidiabetic and antimicrobial agents. Secondly, promote generics in the "E" group to maintain access while lowering expenses. And finally, rationalise or restrict "N" medicines, particularly those in group "A", to prevent wasteful spending healthcare costs.

Controversial results are also observed when comparing the principles of the WHO AWaRe classification with the medical prescriptions of the studied group of patients. Under this framework, "Access" antibiotics are intended to be broadly accessible, as they constitute first-line therapeutic options associated with a relatively low resistance potential. It is recommended that these agents comprise a minimum of 60% of all antibiotic use in inpatient settings and 95% in ambulatory practice [21]. In the case of the authors, ceftriaxone was the first-line antibiotic, with a prescription rate exceeding 40%, leading to the conclusion that healthcare costs are irrational. This is also confirmed by WHO data [21] and the study by K. Myroniuk-Konstantynovych *et al.* [24], where the share of antibiotics of "Access" category accounted for only 59.1% of total antibiotic consumption in outpatient settings and merely 39.8% in hospitals, in Ukraine in 2024, reflecting a substantial departure from the recommended global targets established by the WHO. This imbalance emphasises a concerning overuse of "Watch" and "Reserve" group antibiotics, which risks accelerating antimicrobial resistance and highlights the urgent need for improved antibiotic stewardship in the country. This observation aligns with global concerns regarding antibiotic overuse in DFS management, as highlighted by A. Jodheea-Jutton *et al.* [9] that antimicrobial therapy constitutes a substantial proportion of DFS-related costs and that irrational antibiotic use accelerates resistance while inflating healthcare expenditures. The results further confirmed their conclusion that optimising antimicrobial selection is central to improving both clinical outcomes and cost-effectiveness in DFS care.

Comparative analysis with the study by N. Rahayuningsih *et al.* [25] revealed similar trends in antibiotic-driven cost structures. Their cost-effectiveness analysis of antibiotic use in DFS patients in Indonesia demonstrated that broad-spectrum antibiotics significantly increased treatment costs without proportional improvements in outcomes when not guided by severity stratification and microbiological data. Likewise, the current study identified high-cost antibiotics (piperacillin – tazobactam, meropenem) as contributors to the "A" cost group, despite relatively low prescription frequencies. This reinforces the notion that even limited use of high-cost antimicrobials can disproportionately burden hospital budgets, particularly in resource-constrained health systems [26]. In contrast to studies focusing predominantly on pharmacotherapy costs, S. Russo *et al.* [27] evaluated the cost-effectiveness of platelet-rich plasma versus standard of care for DFS management in the United States. Their findings demonstrated that although platelet-rich plasma's therapy entails higher upfront costs, it may reduce long-term expenditures by accelerating wound healing and decreasing complications. While the present study did not assess advanced wound-healing technologies, the heavy reliance on prolonged systemic pharmacotherapy observed in the cohort may indirectly reflect limited access to such adjunctive interventions. This comparison suggests that investment in cost-effective non-pharmacological or biologic therapies could potentially reduce reliance on expensive antimicrobial regimens and improve overall economic efficiency in DFS management.

The systematic review by E. Sutrisno *et al.* [10] further contextualised the present findings by comparing conservative treatment strategies with amputation-related costs in gangrene associated with T2DM. Their analysis demonstrated that although conservative pharmacotherapy may appear costly in the short term, it is generally more cost-effective than surgical interventions, particularly amputations, when clinical outcomes are favourable. In this context, the high share of expenditures allocated to "vital" and "essential" medicines in the present study may be interpreted positively, as it reflects an emphasis on limb preservation strategies. However, the presence of a considerable proportion of "non-essential" medicines, including non-steroidal anti-inflammatory drugs, suggests the need for further rationalisation to ensure that resources are concentrated on interventions with direct impact on DFS outcomes. From a broader health-system perspective, the findings are consistent with those of A.M. Alshammari *et al.* [28], who reported that diabetes-related hospital costs are primarily driven by complications and inpatient pharmacotherapy. The hospital-centric cost analysis in Saudi Arabia identified medications and prolonged hospital stays as major cost drivers, emphasising the importance of formulary management and prescribing optimisation. Similarly, the present study's results of the ABC analysis demonstrated that approximately one-third of medicines accounted for the majority of expenditures, underscoring the relevance of targeted procurement strategies and price negotiations for high-cost, high-priority drugs, particularly those in the "A/V" and "A/E" categories.

The economic implications of alternative treatment modalities were further illustrated by K. Tochaiwat *et*

al. [29]. The paper reported favourable cost-effectiveness outcomes for high-power laser therapy compared to conventional treatment for diabetic foot ulcers in Thailand. Their results confirmed that innovative therapies may reduce total treatment costs by shortening healing time and decreasing medication use. In contrast, the pharmacotherapy-heavy approach observed in present study may contribute to prolonged treatment duration and sustained drug expenditures. This was further supported by L. Ge *et al.* [30], who found that specialised multidisciplinary management programmes significantly reduce costs and improve outcomes in diabetic foot ulcer treatment. This comparison highlighted the potential benefits of integrating pharmacoeconomic evidence into clinical decision-making when selecting DFS treatment strategies. Ultimately, A. Shankar [31] emphasised that effective diabetic foot care requires alignment between clinical guidelines, health policy, and economic evaluation. The present findings directly address this intersection by demonstrating partial alignment of prescribing practices with essential medicines lists and clinical guidelines, while simultaneously revealing deviations from antimicrobial stewardship principles, particularly under the WHO AWaRe framework. The overrepresentation of "Watch" and "Reserve" antibiotics observed in this study mirrors national trends reported for Ukraine and signals an urgent need for stewardship interventions to improve rational antibiotic use and long-term cost containment.

Overall, the findings of this study were consistent with international evidence demonstrating that DFS management imposes a substantial economic burden, largely driven by pharmacotherapy costs and antimicrobial use. Compared with global studies, the Ukrainian context is characterised by a high reliance on systemic antibiotics and a cost structure dominated by a limited number of high-cost medicines. The integrated frequency/ABC/VEN approach proved effective in identifying priority areas for optimisation, including promotion of "Access" antibiotics, increased use of cost-effective generics, and restriction of non-essential medicines. These measures, combined with broader adoption of evidence-based adjunctive therapies, may enhance the cost-effectiveness of DFS management and improve patient outcomes within constrained healthcare budgets.

Conclusions

The pharmacoeconomic research was conducted using 80 inpatient medical records of patients with T2DM complicated by DFS with an analysis of 43 TNs of prescribed medicines. The distribution of prescriptions according to the ATC classification revealed that the leading pharmacological groups were A10 – Drugs used in diabetes (23%), J01 – Antibacterials for systemic use (21%), and B01A – Antithrombotic agents (18.6%). Analysis of dosage form types demonstrated an equal distribution between oral formulations (film-coated tablets) and parenteral formulations (injection and infusion solutions) at a 1:1 ratio. The frequency analysis involved dividing the drugs into three groups, which revealed a significantly uneven distribution of prescriptions, characterised by the dominance of ceftriaxone in Group 1.

According to the VEN analysis identified 10 medicines in the "vital" category: 30% were antibiotics, 60% belonged to group A10 "Antidiabetic drugs", and 10% belonged to group B05 "Blood substitutes and perfusion solutions". The "essential" category comprised 19 medicines (44% of all agents prescribed to patients with T2DM and DFS), with antimicrobials accounting for 36.8%. Due to the high prevalence of comorbidities in T2DM, medicines from group B01A "Antithrombotic agents" constituted 26.3% of this category. The "non-essential" category accounted for 32.6% of all prescribed medicines and was predominantly represented by group M01A "Nonsteroidal anti-inflammatory and antirheumatic drugs". Thus, "essential" medicines dominated over "vital" categories (E > V > N), indicating rational prescribing practices with limited use of low-priority drugs. The results of the ABC analysis demonstrated that Group A (accounting for 80% of expenditures) comprised 15 TNs of medicines (34.90%), Group B (15% of expenditures) included 13 TNs (30.2%), and Group C (5% of expenditures) comprised 15 TNs (34.9%). The ABC correlation was A = C > B, indicating a shift toward an increased share of high-cost "A" category medicines, and therefore the need for economic optimisation and broader implementation of cost-effective domestic generics to improve affordability and reduce the financial burden on healthcare systems and patients.

Based on the results of the integrated analysis, the following correlations were formulated: 73% of expenditures – E/A > V/A indicates the high cost of "vital" and "essential" medicines; 27% of expenditures – N/B > N/A > E/B > V/B > E/C > N/C > V/C indicates an irrational approach to DFS therapy, as there is a predominance of medicines lacking sufficient evidence of effectiveness and associated with considerable economic burden. The study results emphasised the critical role in optimisation of antimicrobial therapy in DFS management while drawing attention to the growing risk of antimicrobial resistance, underlining the necessity of evidence-based selection of antibiotics. Future research should focus on developing pharmacoeconomic models for individualised therapy, assessing cost-utility parameters, and exploring innovative strategies to enhance treatment effectiveness while ensuring sustainable healthcare financing.

Acknowledgements

None.

Funding

None.

Conflict of Interest

The authors declare no conflict of interest financial or otherwise.

References

[1] Armstrong DG, Tan TW, Boulton AJM, Bus SA. Diabetic foot ulcers: A review. JAMA. 2023;330(1):62–75. DOI: 10.1001/jama.2023.10578

[2] Carter MJ, DaVanzo J, Haught R, Nusgart M, Cartwright D, Fife CE. Chronic wound prevalence and the associated cost of treatment in Medicare beneficiaries: Changes between 2014 and 2019. J Med Econ. 2023;26(1):894–901. DOI: 10.1080/13696998.2023.2232256

[3] Zhang Y, Lazzarini PA, McPhail SM, van Netten JJ, Armstrong DG, Pacella RE. Global disability burdens of diabetes-related lower-extremity complications in 1990 and 2016. Diabetes Care. 2020;43(5):964–74. DOI: 10.2337/dc19-1614

[4] Del Core MA, Ahn J, Lewis RB, Raspovic KM, Lalli TAJ, Wukich DK. Republication of "The evaluation and treatment of diabetic foot ulcers and diabetic foot infections". Foot Ankle Orthop. 2023;8(3):24730114231193418. DOI: 10.1177/24730114231193418

[5] Petersen BJ, Linde-Zwirble WT, Tan TW, Rothenberg GM, Salgado SJ, Bloom JD, et al. Higher rates of all-cause mortality and resource utilization during episodes-of-care for diabetic foot ulceration. Diabetes Res Clin Pract. 2022;184:109182. DOI: 10.1016/j.diabres.2021.109182

[6] Centers for Disease Control and Prevention. National diabetes statistics report [Internet]. 2024 May 15 [cited 2025 May 10]. Available from: https://www.cdc.gov/diabetes/php/data-research/index.html

[7] McDermott K, Fang M, Boulton AJM, Selvin E, Hicks CW. Etiology, epidemiology, and disparities in the burden of diabetic foot ulcers. Diabetes Care. 2023;46(1):209–21. DOI: 10.2337/dci22-0043

[8] Cortes-Penfield NW, Armstrong DG, Brennan MB, Fayfman M, Ryder JH, Tan TW, et al. Evaluation and management of diabetes-related foot infections. Clin Infect Dis. 2023;77(3):e1–13. DOI: 10.1093/cid/ciad255

[9] Jodheea-Jutton A, Hindocha S, Bhaw-Luximon A. Health economics of diabetic foot ulcer and recent trends to accelerate treatment. Foot. 2022;52:101909. DOI: 10.1016/j.foot.2022.101909

[10] Sutrisno E, Sodik JJ, Fakih TM. Cost-effectiveness analysis and medication use for gangrene treatment in type 2 diabetes patients: A systematic literature review. Pharmacia. 2025;72:e144858. DOI: 10.3897/pharmacia.72.e144858

[11] Bakaliuk TH, Makarchuk NR, Seniuk KM, Stelmakh HO, Sverstiuk AS. Evaluation of the effectiveness of rehabilitation for diabetic foot syndrome. Zaporozhye Med J. 2023;25(2):115–21. DOI: 10.14739/2310-1210.2023.2.267251

[12] Kostiuk IA, Kosiachenko KL. Integrated ABC/VEN-analysis of medicinal prescribing in pharmacotherapy of bronchial asthma in children. Curr Issues Pharm Med Sci. 2019;12(2):190–5. DOI: 10.14739/2409-2932.2019.2.171074

[13] World Health Organization. ATC/DDD Index 2025 [Internet]. [cited 2025 May 10]. Available from: https://atcddd.fhi.no/atc_ddd_index/

[14] Parii VD, Gryshchuk SM. Methods for conducting ABC analysis, VEN analysis, frequency analysis, integrated frequency/VEN/ABC analysis. In: Parii VD, editor. Health care economics: Textbook. Zhytomyr: Buk-Druk Publishing House LLC; 2021. P. 197–213.

[15] Order of the Ministry of Health of Ukraine No. 356. Clinical Protocol for the Management of Patients with Diabetic Foot Syndrome [Internet]. 2009 May 22 [cited 2025 May 10]. Available from: https://www.content.net.ua/registration/content/ua1622/pages/f12705.html

[16] Resolution of the Cabinet of Ministers of Ukraine No. 333. National List of Essential Medicines [Internet]. 2009 March 25 [cited 2025 May 10]. Available from: https://zakon.rada.gov.ua/laws/show/333-2009-%D0%BF#n15

[17] Order of the Ministry of Health of Ukraine No. 971. On Approval of the Seventeenth Edition of the State Formulary of Medicinal Products and Ensuring its Availability [Internet]. 2025 June 13 [cited 2025 May 10]. Available from: https://www.dec.gov.ua/materials/chynnyj-vypusk-derzhavnogo-formulyara-likarskyh-zasobiv/

[18] The selection and use of essential medicines, 2025: WHO Model List of Essential Medicines, 24th list [Internet]. 2025 September 5 [cited 2025 September 10]. Available from: https://www.who.int/publications/i/item/B09474

[19] National Institute for Health and Care Excellence guideline. Diabetic foot problems: Prevention and management [Internet]. 2015 August 26 [cited 2025 May 10]. Available from: https://www.nice.org.uk/guidance/ng19/resources/diabetic-foot-problems-prevention-and-management-pdf-1837279828933

[20] Order of the Ministry of Health of Ukraine No. 1513. On Approval of the Medical Standard "Rational Use of Antibacterial and Antifungal Medicines for Therapeutic and Prophylactic Purposes" [Internet]. 2023 August 23 [cited 2025 May 10]. Available from: https://moz.gov.ua/uk/decrees/nakaz-moz-ukraini-vid-23082023--1513-pro-zatverdzhennja-standartu-medichnoi-dopomogi-racionalne-zastosuvannja-antibakterialnih-i-antifungalnih-preparativ-z-likuvalnoju-ta-profilaktichnoju-metoju

[21] World Health Organization. AWaRe classification of antibiotics for evaluation and monitoring of use [Internet]. 2021 September 30 [cited 2025 May10]. Available from: https://www.who.int/publications/i/item/2021-aware-classification

[22] The World Medical Association. Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects [Internet]. [cited 2025 May 10]. Available from: https://www.wma.net/what-we-do/medical-ethics/declaration-of-helsinki/

[23] European Commission. Ethics and Data Protection [Internet]. 2021 July 5 [cited 2025 May 10]. Available from: https://ec.europa.eu/info/funding-tenders/opportunities/docs/2021-2027/horizon/guidance/ethics-and-data-protection_he_en.pdf
[24] Myroniuk-Konstantynovych K, Bondaruk I, Bevz T, Demchyshyn Y, Konstantynovych T. P12 Unjustified use of antibiotics in wartime conditions in Ukraine. JAC Antimicrob Resist. 2024;6(1):dlad143.016. DOI: 10.1093/jacamr/dlad143.016
[25] Rahayuningsih N, Pratiwi AL, Pebiansyah A. Cost-effectiveness analysis of antibiotic usage in diabetic foot ulcer patients in Dokter Soekardjo Tasikmalaya Hospital. Int J Appl Pharm. 2022;14(5):123–6. DOI: 10.22159/ijap.2022.v14s5.25
[26] Jais S, Oe M, Sanada H, Sasongko A, Haryanto H. Evaluating the cost-effectiveness of diabetic foot ulcer management by wound care specialists in Indonesia. Wound Repair Regen. 2024;32(1):80–9. DOI: 10.1111/wrr.13147
[27] Russo S, Landi S, Simoni S. Cost-effectiveness analysis for managing diabetic foot ulcer (DFU) in USA: Platelet-rich plasma (PRP) vs standard of care (SoC). Clinicoecon Outcomes Res. 2025;17:157–69. DOI: 10.2147/CEOR.S496616
[28] Alshammari AM, Elnaem MH, Ong SC. Evaluating the economic impact of diabetes mellitus: A hospital-centric cost analysis in Hail, Saudi Arabia. Clinicoecon Outcomes Res. 2025;17:473–84. DOI: 10.2147/CEOR.S521701
[29] Tochaiwat K, Singweratham N, Nawsuwan K. Cost-effectiveness analysis of diabetic foot ulcer treatment using high power laser compared to conventional treatment. J Health Sci Thailand. 2024;33(1):77–85.
[30] Ge L, Sun Y, Tan E, Liew H, Hoe J, Lin J, et al. Outcome evaluation and cost-effectiveness analysis for an integrated multidisciplinary diabetic limb salvage program: A combined observational and simulation study. BMJ Open Diabetes Res Care. 2025;13(1):e004688. DOI: 10.1136/bmjdrc-2024-004688
[31] Shankar A. Healthcare economics and policy in diabetic foot care. Int J Diabetes Endocrinol. 2025;10(4):85–97. DOI: 10.11648/j.ijde.20251004.12

Фармакоекономічна оцінка фармакотерапії пацієнтів із цукровим діабетом 2 типу з синдромом діабетичної стопи

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Анотація. Зростання поширеності цукрового діабету 2 типу, ускладненого синдромом діабетичної стопи, та призначення дорогих ліків, які не включені до протоколів лікування, значно підвищують витрати на охорону здоров'я та погіршують результати лікування пацієнтів, що робить оптимізацію фармакотерапії як клінічним, так і економічним пріоритетом. Метою дослідження було оцінити раціональність фармакотерапії для пацієнтів із синдромом діабетичної стопи за допомогою інтегрованого частотного/ABC/VEN аналізу. У дослідженні застосовувався частотний аналіз для оцінки фармакотерапевтичних схем та частоти призначення ліків за АТС-класифікацією, ABC-аналіз для класифікації ліків за рівнем витрат та VEN-аналіз для визначення їх терапевтичної значущості на основі рекомендацій національних та міжнародних рекомендацій щодо лікування цукрового діабету 2 типу. Результати показали, що в клінічній практиці переважали етіологічні та патогенетичні підходи до терапії. Протидіабетичні засоби становили найбільшу частку призначень (23 %), тоді як антибіотики були необхідними для лікування інфекційних ускладнень. Інтегрований частотний/ABC/VEN-аналіз показав, що «необхідні» ліки (44,19 %) переважали над категоріями «життєво важливим» (23,26 %) та «другорядними» (32,56 %), що свідчило про недостатньо раціональну практику призначення відповідно до рекомендацій щодо лікування. Висока частка витрат на охорону здоров'я була зосереджена в групі високовартісних ліків (34,89 %), що свідчило про неоптимальний розподіл ресурсів охорони здоров'я. Результати також підкреслили важливість вибору антибіотиків на основі доказів через зростаючий ризик резистентності до антимікробних препаратів. Дослідження створює платформу для підвищення економічної ефективності фармакотерапії у пацієнтів із синдромом діабетичної стопи шляхом підтримки раціонального призначення ліків, оптимізації витрат на охорону здоров'я та просування економічно ефективних українських аналогів

Ключові слова: інтегрований частотний/ABC/VEN-аналіз; лікарські призначення; антимікробні засоби; антибіотикорезистентність; оптимізація фармацевтичного забезпечення