

# The Pharmacoeconomic Analysis of the Treatment Regimens of Patients Having Cardiovascular Diseases with Drugs of the Antithrombotic Action

A. S. Nemchenko, V. N. Nazarkina, Yu. Ye. Kurylenko

*Department of Organization and Economic of Pharmacy, National University of Pharmacy, Kharkiv, Ukraine*

## Abstract

**Aim:** The aim of our study is to conduct the pharmacoeconomic analysis of the treatment regimens of patients having cardiovascular diseases (CVDs) with antithrombotic drugs, namely clopidogrel and acetylsalicylic acid, in Ukraine. **Materials and Methods:** The results of a randomized, blind Clopidogrel versus Aspirin in Patients at Risk of Ischemic Event study (clopidogrel,  $n = 9599$  and acetylsalicylic acid,  $n = 9588$ ) and materials of unified clinical protocols in the specialty “Cardiology” and data of the “Available medicines” reimbursement program in Ukraine were used in the work. **Results and Discussion:** Based on available clinical studies of the effectiveness of using drugs with the antithrombotic action in patients with CVD, the direct and indirect costs for further analysis of the total cost of the disease were calculated. It was found that the direct cost of the treatment with clopidogrel was 2.16 times higher than the cost of the treatment with acetylsalicylic acid. The total cost of the treatment of one patient with clopidogrel was 20.35% higher than with acetylsalicylic acid. The analysis by the “cost-effectiveness” method showed that the cost-effectiveness ratio (CER) for acetylsalicylic acid was 13837.33 UAH/529.76 USD and for clopidogrel was 17366.66 UAH/664.88 USD. The cost of an incremental CER additional unit per one saved life when treating with clopidogrel is 5788.71 UAH/221.62 USD. **Conclusion:** Summing up the results of the study conducted, it has been found that the therapy with clopidogrel is more expensive; however, this drug is included in the reimbursement program in Ukraine, and therefore, the state partially compensates the patient for the expenses of it. Despite the fact that the therapy with acetylsalicylic acid should be carried out on a permanent basis in patients with CVD, it is necessary to include it in the “Available medicines” reimbursement program. The inclusion of drugs with acetylsalicylic acid in the list of reimbursed drugs will improve the health of patients with CVD and will help to save public funds that may be lost due to disability of the patient.

**Key words:** Cardiovascular diseases, pharmacoeconomic analysis, the “Available medicines” reimbursement program

## INTRODUCTION

Cardiovascular diseases (CVDs) occupy a leading place in the world among other nosologies in the number of deaths of the working-age population [Table 1].<sup>[1]</sup>

Thus, in the structure of the main causes of mortality of the population on the CVD in aggregate make up 48.28%, for the comparison of HIV / AIDS, cancer trachea and lower respiratory tract infections totaled 24.87%, which is 23.41% lower than that of the CVD. Each year, more than 18.5 million people die in the CVD from around the world. In Europe, approximately 3 million people die each year from CVD, and in the USA, more than 1 million

people die; moreover, more than half of the deaths are persons under 65 years of age.

According to the Ministry of Health of Ukraine, annually more than two million people diagnosed with CVD are registered for the first time with a family physician; of them, every

### Address for correspondence:

A. S. Nemchenko, Department of Organization and Economic of Pharmacy, National University of Pharmacy, Kharkiv, Ukraine.  
E-mail: asnemchenko@ukr.net

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second person is of working age. Therefore, the “Available medicines” reimbursement program was introduced in Ukraine; its goal is to provide all segments of the population with the necessary qualitative and effective drugs for the treatment of nosologies such as CVD, bronchial asthma, and type II diabetes.<sup>[2]</sup> The pharmacotherapy of CVD is rather expensive and prolonged due to the peculiarity of the disease course and the presence of concomitant nosologies in the patient. The data of unified clinical protocols in the specialty “Cardiology” indicate that the treatment with antithrombotic drugs is necessary throughout the life of patients with chronic conditions of CVD; they are also used for prevention in the early stages of the disease.<sup>[3]</sup>

Therefore, the aim of our study is to conduct pharmacoeconomic analysis of the use of drugs with the antithrombotic action, namely clopidogrel and acetylsalicylic acid, which are used in the treatment of CVD. To achieve the goal, the following tasks were outlined: To search for the data of scientific literature on clinical studies concerning the use of drugs with the antiplatelet action and to perform the analysis by the pharmacoeconomic methods selected.

## MATERIALS AND METHODS

For further research, the method of the pharmacoeconomic analysis for the treatment of patients with CVD was developed [Figure 1].

The second stage of the pharmacoeconomic analysis included the search for the results of clinical trials in specialized scientific databases (Cochrane, PubMed, and MEDLINE) on the safety and efficacy of the antiplatelet therapy in patients with CVD.

**Table 1: The main causes of mortality in the world\***

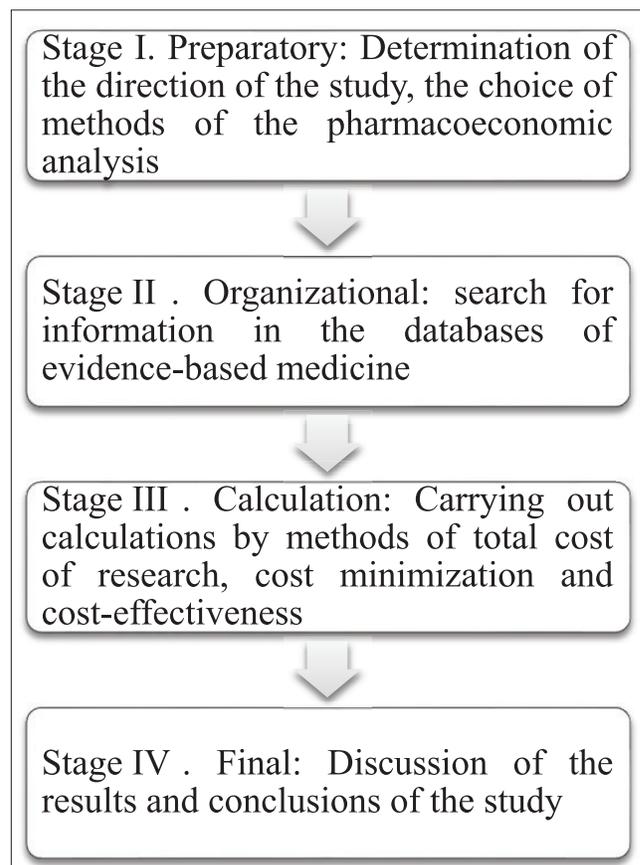
The causes of mortality	Percentage
Coronary heart disease	23.47
Cerebral accident and other diseases associated with cerebral circulation disorders	21.57
Infections of the lower respiratory tract	13.26
Diabetes	9.58
Chronic obstructive pulmonary disease	6.41
Diarrheal diseases	6.85
HIV/AIDS	6.47
Cancer of the trachea, bronchi, and lungs	5.14
Hypertensive disease	3.24
Road traffic accidents	4.03
In total	100

\*The data are given at the beginning of 2018

Thus, the following studies were analyzed: Clopidogrel in Unstable Angina to Prevent Recurrent Events (CURE), CURE-percutaneous coronary intervention, Clopidogrel for the Reduction of Events during Observation trial, Clopidogrel as Adjunctive Reperfusion Therapy, and Clopidogrel and Aspirin versus Aspirin Alone for the Prevention of Atherothrombotic Events; however, a randomized, blind Clopidogrel versus Aspirin in Patients at Risk of Ischemic Events study (CAPRIEs) was selected for calculations. In this study, they compared monotherapy with clopidogrel and acetylsalicylic acid in patients at risk for ischemic manifestations [Figure 2].

Taking into account the data of the CAPRIE study, the average duration of therapy – 1.9 years – was taken for further calculations. The number of patients participated in the study was 19185; of them, 9599 patients took clopidogrel and 9588 patients received acetylsalicylic acid.<sup>[4-10]</sup>

The third stage included the choice of methods of pharmacoeconomic analysis, first of all, the mandatory “total cost of the disease,” taking into account direct and indirect costs, separately for each of the drugs, as well as the calculation by the methods of “cost minimization” (CMA indicator) and “cost-effectiveness” (the cost-effectiveness ratio [CER] and incremental CER [ICER]).



**Figure 1:** The method of the pharmacoeconomic analysis for the treatment of patients with cardiovascular diseases

At the last fourth stage, the general conclusions on the results of the study were highlighted, and recommendations on the pharmacoeconomic analysis conducted were given.

## RESULTS

We calculated direct costs – the cost of treatment regimens during the hospital stay and indirect costs – the costs arising from the inability of the patient to be useful to the society [Table 2]. The cost of treatment regimens was calculated using the materials of the Register of Wholesale and Retail Prices for Drugs as of 04.05.2018, and their recalculation

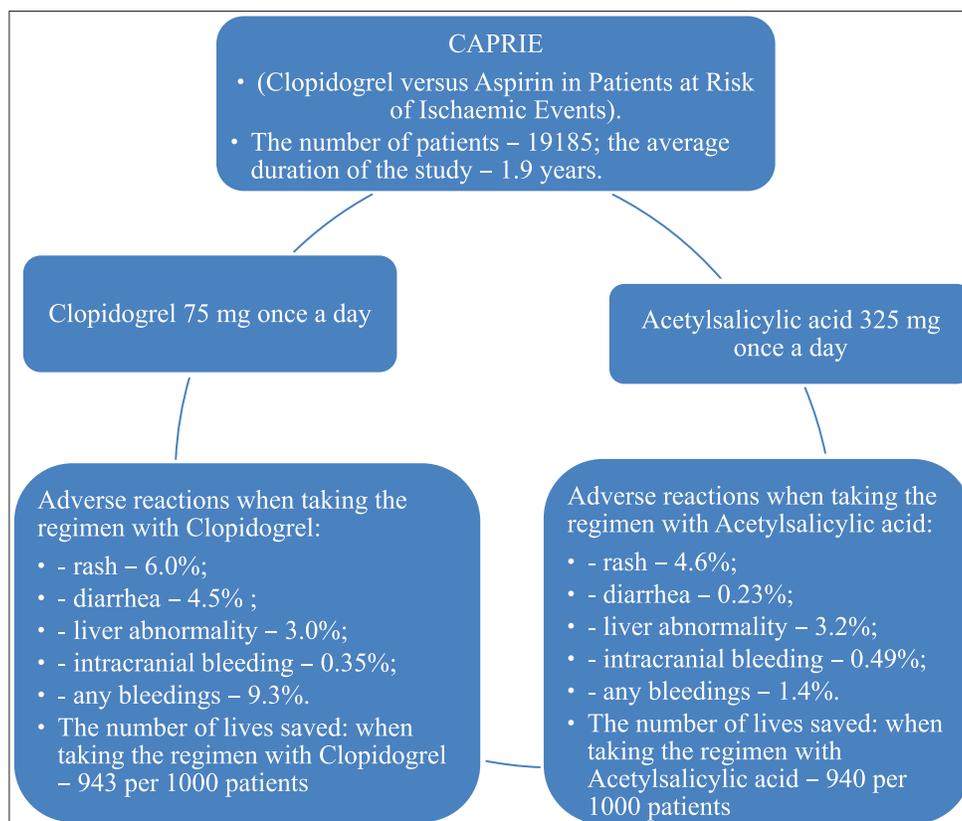
was done in dollar equivalent at the official exchange rate of the National Bank of Ukraine (1 USD = 26.12 UAH, as of June 01, 2018).<sup>[11,12]</sup> According to the data of unified clinical protocols and guidelines, it was found that the average length of patients' staying in the hospital was 28 bed days, and the average cost was 105.28 USD.<sup>[13]</sup> For the calculations, the data of the State Statistics Committee of Ukraine, namely the average salary as of May 01, 2018, and the nominal Gross Domestic Product (GDP) for 2017, were taken.<sup>[14]</sup>

According to the calculations, it was found that the direct cost of the treatment of one patient with clopidogrel was 2.16 times higher than the cost of the treatment with acetylsalicylic acid.

**Table 2:** The total cost of cardiovascular diseases treatment regimens

International non-proprietary name	Clopidogrel	Acetylsalicylic acid
Dosage regimens	75 mg once a day	325 mg once a day
The wholesale and retail price of drugs, UAH	62.09	4.89
The cost of a daily dose, UAH	6.20	0.31
The total cost of the treatment of a patient for 1.9 years, UAH/USD	3585.69/137.28*	179.09/6.86*
Direct costs		
The cost of therapy regimens+the cost of bed days per one patient, UAH/USD	6333.57/242.48*	2929.09/112.14*
Indirect costs		
Expenses for payment of incapability days+loss of GDP due to disability per one patient, UAH/USD	10078.14/385.84*	10078.14/385.84*
Total costs per one patient, UAH/USD	16411.71/628.32*	13007.23/497.98*

\*US dollar exchange rate as of 01.06.2018. GDP: Gross domestic product



**Figure 2:** Characteristics of the results of Clopidogrel versus Aspirin in Patients at Risk of Ischemic Event clinical trial

**Table 3:** The results of the pharmaco-economic analysis of therapy with clopidogrel and acetylsalicylic acid by the method of “cost-effectiveness”

The name of the drug	Clopidogrel	Acetylsalicylic acid
Total costs per 1000 patients, UAH/USD	16411718.4/628320*	13007237.6/497980*
The number of lives saved per 1000 patients, (Ef)	943	940
The CER USD per one saved life, UAH/USD	17366.66/664.88*	13837.33/529.76*

\*US dollar exchange rate as of 01.06.2018. GDP: Gross domestic product, CER: Cost-effectiveness ratio

The total amount for pharmacotherapy with clopidogrel is 16411.71 UAH/628.32 USD and with acetylsalicylic acid is 13007.23 UAH/497.98 USD. Thus, if the cost-effectiveness indicator CMA (by the method of “cost minimization”) is calculated, the treatment with acetylsalicylic acid is less expensive by 3404.48 UAH/130.34 USD (by 26.0%) than with clopidogrel.

Next, the “cost-effectiveness” analysis (CEA) requiring the calculation of CER and ICER was conducted [Table 3].

It should be noted that when receiving the regimen with clopidogrel, the number of additionally saved lives is 3.

Thus, it has been found that CER for acetylsalicylic acid is 13837.33 UAH/529.76 USD, and for the drug clopidogrel, it is 17366.66 UAH/664.88 USD, i.e., 25.5% higher. The cost of an ICER additional unit per one saved life when treating with clopidogrel is 5788.71 UAH/221.2 USD.<sup>[15]</sup>

## DISCUSSION

According to open scientific sources, 3525 studies of the clinical efficacy of clopidogrel and acetylsalicylic acid in patients with various types of CVD, and concomitant diseases were assessed. Thus, 12 studies, or (0.35%) of the total, in which clopidogrel or acetylsalicylic acid were used as monotherapy, were performed, comparing the effectiveness of these drugs placebo was shown in 312 (8.85%), research, and study medication were treated with other drugs in 3201 (90.80%) studies, respectively. The duration of studies ranged from a month to 5 years. At present, there is no consensus what drug is better to use in the treatment of patients with CVD: Clopidogrel or acetylsalicylic acid under the conditions of tolerance of both drugs.

## CONCLUSION

Summing up the results of our study conducted, it has been found that the treatment with clopidogrel is more expensive by 3404.48 UAH/130.34 USD than the treatment with acetylsalicylic acid. However, considering the economic factor, the treatment with clopidogrel is more costly, but this drug is included in the reimbursement program in Ukraine, and therefore, the partial cost to the patient is compensated

by the state. Despite the fact that the therapy of patients with CVD using acetylsalicylic acid should be carried out on a permanent basis, it is advisable to include this drug to the “Available medicines” reimbursement program.<sup>[16]</sup> Thanks to the inclusion of drugs with acetylsalicylic acid, the availability of drugs for all segments of the population will increase; it will improve the epidemiological situation and the rational use of budget funds for the treatment of CVD in the context of further reforming of the health-care system.

## REFERENCES

1. Official website of the Ministry of Health of Ukraine. Available from: <http://moz.gov.ua/article/reform-plan/jak-transformuetsja-sistema-ohoroni-zdorovja>.
2. Government Program “Available Drugs”. Available from: <http://liky.gov.ua/#portf>.
3. Unified clinical protocols on the specialty “Cardiology” Available from: <http://medstandart.net/byspec/43>.
4. CAPRIE Steering Committee. A randomised, blinded, trial of clopidogrel versus aspirin in patients at risk of ischaemic events (CAPRIE). CAPRIE steering committee. *Lancet* 1996;348:1329-39.
5. Cannon CP; CAPRIE Investigators. Effectiveness of clopidogrel versus aspirin in preventing acute myocardial infarction in patients with symptomatic atherosclerosis (CAPRIE trial). *Am J Cardiol* 2002;90:760-2.
6. Mehta SR, Yusuf S; Clopidogrel in Unstable angina to prevent Recurrent Events (CURE) Study Investigators. The clopidogrel in unstable angina to prevent recurrent events (CURE) trial programme; rationale, design and baseline characteristics including a meta-analysis of the effects of thienopyridines in vascular disease. *Eur Heart J* 2000;21:2033-41.
7. Bhatt DL, Fox KA, Hacke W, Berger PB, Black HR, Boden WE, *et al.* Clopidogrel and aspirin versus aspirin alone for the prevention of atherothrombotic events. *N Engl J Med* 2006;354:1706-17.
8. Steinhubl SR, Berger PB, Mann JT 3<sup>rd</sup>, Fry ET, DeLago A, Wilmer C, *et al.* Early and sustained dual oral antiplatelet therapy following percutaneous coronary intervention: A randomized controlled trial. *JAMA* 2002;288:2411-20.
9. Sabatine MS, Cannon CP, Gibson CM, López-Sendón JL, Montalescot G, Theroux P, *et al.* Effect of clopidogrel pretreatment before percutaneous coronary

intervention in patients with ST-elevation myocardial infarction treated with fibrinolytics: The PCI-CLARITY study. *JAMA* 2005;294:1224-32.

10. Vandvik PO, Lincoff AM, Gore JM, Guterman DD, Sonnenberg FA, Alonso-Coello P, *et al.* Primary and secondary prevention of cardiovascular disease: Antithrombotic therapy and prevention of thrombosis, 9<sup>th</sup> ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest* 2012;141:e637S-68S.
11. Official Site of the National Bank of Ukraine. Available from: <https://bank.gov.ua/control/uk/allinfo>.
12. Register of Whole Sale and Retail Prices for Medicines. Available from: [http://moz.gov.ua/uploads/2/10157-dn\\_20190201\\_265\\_dod.pdf?fbclid=IwAR2vzjn9f-ioN3Q\\_umZPHh52kADLbZDwc6IOWM9FLHHJTCsV IK3629dm3eQ](http://moz.gov.ua/uploads/2/10157-dn_20190201_265_dod.pdf?fbclid=IwAR2vzjn9f-ioN3Q_umZPHh52kADLbZDwc6IOWM9FLHHJTCsV IK3629dm3eQ).
13. The Cost of Medical Services in In-Patient Departments of Ukraine. Available from: <https://likarni.com/kliniki/kyev/prebyvanije-v-dnevnom-stacionare>.
14. Official Site of the State Statistics Service of Ukraine. Available from: <http://database.ukrcensus.gov.ua/PXWEB2007/>.
15. Storozhakov GI, Tronina OA, Modern aspects of the use of the drug clopidogrel for the treatment and prevention of atherothrombosis. *Cardiology news* 2011;1:29-36.
16. Drozdov VN, Kim VA, Efficacy and safety of using acetylsalicylic acid. *RPC* 2010;6:212-215.

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