ORIGINAL ARTICLE

CONTENTS

Study of the influence of medication properties and lifestyle of patients with coronary heart disease on adherence to treatment

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ABSTRACT

Aim: To investigate how lifestyle factors of patients with CHD and comorbid conditions, along with medicines properties, influence treatment adherence.
Materials and Methods: include the results of a survey conducted among patients with CHD and comorbid conditions at the Department of Cardiology of the P.L. Shupyk National Healthcare University of Ukraine from June to September 2024 (n = 101). The study employed methods of analysis, synthesis, deduction, induction, comparison, statistical and bibliographic research.
Results: The study revealed a significantly low adherence rate of 13.9% [CI 95% 13.9 ± 0.002; $p<0.0001$] to risk factor modification and prescribed pharmacotherapy in secondary prevention of CHD. It confirmed a statistically significant influence of patient preferences with CHD and comorbid conditions on effective pharmacotherapy ($\chi 2 = 3.350{,}232$, $p = 0.067$). Patients receiving consultations from both doctors and pharmacists were 22 times more likely (OR = 22.67) to adhere to pharmacotherapy compared to those consulting only doctors. The study found that only 7.8% [CI 95% 7.8 ± 0.05; $p<0.0001$] of surveyed patients with CHD and comorbid conditions such as hypertension, diabetes mellitus and chronic kidney disease utilized the "Affordable Medicines" program.
Conclusions: The decline in the socioeconomic status of the population during the war in Ukraine negatively affects adherence to clinical guidelines for risk factor modification and secondary prevention of CHD, as evidenced by observational studies EUROASPIRE IV and V. The study identified that 42.8% of respondents prefer original medicines when selecting medications, but financial constraints prevent prolonged use as part of prescribed pharmacotherapy, adversely affecting treatment adherence. The effectiveness of a multidisciplinary approach in enhancing treatment adherence among patients with CHD and comorbid conditions was confirmed, demonstrating a 22-fold higher adherence rate compared to consultations with doctors alone.

KEY WORDS: Coronary heart disease, treatment adherence, pharmaceutical care, multidisciplinary team, generic medicines, original medicines

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INTRODUCTION

Cardiovascular diseases (CVD) are the leading cause of mortality worldwide, accounting for 9.7% of the global disease burden [1]. Globally, Ukraine ranks fourth in CVD mortality after Tajikistan, Azerbaijan and Uzbekistan [2]. The primary cause of CVD-related deaths in Ukraine is ischemic heart disease (CHD) [3]. The ongoing war in Ukraine has evidently worsened the socioeconomic conditions of the population [4], reducing access to medications and placing additional strain on the national healthcare system [5].

According to the National Health Service of Ukraine (NHSU), the statistics for issuing temporary disability certificates in specialized medical care for cardiologists in the "general illness or injury" category indicate nearly a twofold increase in the number of signed certificates in 2023 (0.57 million) compared to 2022 (0.29 million). In the first half of 2024 alone, this number increased by an additional 0.24 million compared to 2023 [6]. Consequently, there has been a rise in unplanned hospitalizations, along with increased prescriptions of medications, which partially contribute to the effectiveness of pharmacotherapy [7] in the treatment strategy for the CHD patients.

Clinical guidelines from the European Society of Cardiology (ESC) [8, 9], the American Heart Association (AHA) [10], and the Ukrainian Unified Clinical Protocol on Stable Coronary Heart Disease [11] emphasize the modification of risk factors and effective pharmacotherapy to achieve better clinical outcomes and improve the quality of life for patients with CHD. Observational findings from the EUROASPIRE V study (n=3562) [12] highlight suboptimal treatment adherence among CHD patients with comorbid conditions such as arterial hypertension (AH), diabetes mellitus (DM) and chronic kidney disease (CKD). Specifically,

adherence rates were reported as 64.9% for antihypertensive medicines, 61.3% for lipid-lowering medicines and 76.5% for hypoglycemic agents among CHD patients [12].

Given the above, it is considered appropriate to define the term "treatment adherence" as "the degree to which a patient's behavior corresponds with clinical recommendations (prescriptions), including the timing, dosage, and frequency of medication intake prescribed by healthcare providers over a specified period" [13]. It has been determined that adherence to pharmacotherapy is influenced by: health care providers (doctors, nurses, pharmacists, state health insurance programs); patients (socioeconomic status, knowledge of the correct use of medicines, polypharmacy, personal biases in the use of medicines, etc.) and properties with characteristics inherent in medicines (price, quality, shelf life, adverse reactions, polypharmacy, pharmacokinetic and pharmacodynamic properties, method of use, release form, etc.) [13].

Therefore, a likely reason for the lack of adherence to treatment due to the deterioration of the socioeconomic status of the population may be the use of original and generic medicines. The use of original medicines leads to the impact of high costs and additional burden on the budgets of health care systems and patients' households. In turn, the use of generic medicines, on the contrary, reduces the burden on the budgets of national health care systems and households of patients with chronic diseases. Such medicines are bioequivalent to the original ones.

According to European data on the use of medicines [14], the consumption of generic medicines in Europe is 70% by volume and 14% by value. The use of generic medicines expands and improves the population's access to medicines. And the redistribution of budget expenditures of national health systems from original to generic medicines leads to significant savings. WHO emphasizes that the average monthly burden of medicine consumption on the family budget of patients should be no more than 10-25% of the total monthly family budget [15]. Therefore, in order to address the issues of the relationship between the deterioration of the socioeconomic status of the population during the war in Ukraine with low adherence to pharmacotherapy of patients with ischemic heart disease and further obtaining better clinical outcomes, the study of a number of factors influencing the choice of medicines within the same molecule by International Nonproprietary Name (INN) in the pharmacotherapy of ischemic heart disease with comorbid conditions is being updated.

According to the current Ukrainian legislation, original (innovative) medicinal products are understood as those medicinal products that are for the first time in the world "registered on the basis of a complete registration dossier" with evidence of efficacy, safety and quality. Generic medicinal products have the same "qualitative and quantitative composition of active substances, dosage form" compared to the original medicinal product (reference medicinal product) and proven bioequivalence with the original medicinal product "as a result of relevant studies" [16]. According to the Law of Ukraine "On Medicinal Products", all medicinal products are prescribed by the INN [16].

Thus, in connection with the decline in the socioeconomic status of the population of Ukraine and the increase in unplanned hospitalizations, in particular of patients with ischemic heart disease [5], the issue of studying factors influencing adherence to pharmacotherapy in patients with ischemic heart disease with comorbid conditions, related to lifestyle and medicines properties, is becoming more relevant.

AIM

The aim of the article is to study the factors influencing the lifestyle of patients with ischemic heart disease with comorbid conditions and medicines properties on adherence to treatment.

MATERIALS AND METHODS

The materials and methods of this study were the results of a survey of patients with ischemic heart disease with comorbid conditions, conducted at the Department of Cardiology of the P.L. Shupyk National University of Health Care of Ukraine. The empirical study took place from June to September 2024 in the process of an online survey using Google Form of 101 patients (66 women, 35 men) with ischemic heart disease and concomitant hypertension, diabetes, CKD from 13 regions of Ukraine. Patients were previously given verbal consent to fill out online questionnaires. In the introduction to the questionnaire, patients were provided with the definitions of "original medicines" and "generic medicines" in accordance with current Ukrainian legislation [16]. The questionnaire contained three blocks of questions: "socioeconomic", "determination of adherence to treatment", "patient perception of original and generic medicines". In this study, we analyze the influence of "socioeconomic" factors, factors of "patient perception of medicines", determine the relationship of their influence on "adherence to pharmacotherapy" of CVD, in particular CHD with concomitant hypertension, diabetes, CKD.

The "socioeconomic" block of questions examined gender, age, education, professional employment, monthly burden on the family budget of patients (ratio of monthly income to expenses for medicines). Patients were asked to choose the level of income according to the data of the Ministry of Finance of Ukraine (subsistence minimum (2920 UAH), minimum (8000 UAH) and average salary (14577 UAH) and above) [17]. It should be noted that the USD exchange rate of the National Bank of Ukraine is 41.24 UAH [18]. This block included questions to determine the lifestyle of patients and their self-assessment of their health. The block "patients' perception of medicines" included questions to determine factors that influence the choice of medicines by INN; the number of medicines used daily; reasons for discontinuation of pharmacotherapy. It is proposed to define statements regarding the general characteristics of original and generic medicines to further identify factors influencing patients' choice of medicines by INN and awareness regarding original and generic medicines.

The "adherence to pharmacotherapy" block contained four questions determined by the standardized Morisky-4 treatment adherence scale (MMAS-4) [19]:

1) Have you ever forgotten to take medications prescribed for cardiovascular diseases (CVD) and associated conditions such as arterial hypertension (AH), diabetes mellitus (DM), or chronic kidney disease (CKD)?

2) Have you ever made mistakes in taking medications prescribed for cardiovascular diseases (CVD) and associated conditions such as arterial hypertension (AH), diabetes mellitus (DM), or chronic kidney disease (CKD)?

3) Have you ever stopped taking medications prescribed for cardiovascular diseases (CVD) and associated conditions such as arterial hypertension (AH), diabetes mellitus (DM), or chronic kidney disease (CKD) on your own if you felt better?

4) Have you ever stopped taking medications prescribed for cardiovascular diseases (CVD) and associated conditions such as arterial hypertension (AH), diabetes mellitus (DM), or chronic kidney disease (CKD) on your own if you felt worse?

Patients were asked to select "yes/no" answers. A "yes" answer was scored as 1 point, a "no" answer as 0 points. Patients were considered compliant with pharmacotherapy when they did not score points for four answers.

Patients were also asked to rate their own health on a scale from 0 to 10, where 10 is the highest health indicator, in order to further establish the relationship between adherence to pharmacotherapy and self-assessment of health status.

It was determined that the sample size required for statistical analysis should be 96 respondents. For calculations, the acceptable margin of error for marketing research (10%), the variation for the sample – 50% and the confidence coefficient (standard deviation) CI – 1.96 (probability p = 0.95). The difference in indicators was considered significant at a CI level of 95% ($p<0.0001$).

To test the hypotheses about the significance of the differences between frequencies, the $\chi 2$ criterion with a likelihood adjustment was used. The φ (phi) criterion was determined, intended for the relationships of four-way (2x2) tables. For multi-way tables, the Cramer V criterion was used. The values of both criteria vary from 0 to 1. Both criteria are based on the $\chi 2$ criterion.

The results were visualized in Microsoft Office Excel spreadsheets, where the accumulation, adjustment, systematization of the original information, etc. took place. Statistical processing was performed using the STATISTICA.13 and IBM SPSS Statistics programs.

The empirical study was conducted in accordance with the Declaration of Helsinki of the World Health Organization "Ethical Principles of Medical Research Involving Human Subjects as Research Subjects".

RESULTS

According to the results of the study, it was determined that the average age of patients was 54.22 ± 4 years, more than two-thirds of the respondents had higher education (77.2%), the rest had vocational education (22.8%). Professional employment was observed in 73.3% of respondents (working or working pensioners), other respondents (unemployed and pensioners) were 26.7%. Exclusion criteria: oncological diseases, concomitant rheumatic diseases, dyscirculatory encephalopathy of more than II degree, patients with mental disorders and myocardial infarction more than a year.

The results of the analysis of changes in the lifestyle of patients after the diagnosis and their relationship with adherence to pharmacotherapy (Fig. 1) indicate that 1.9% [CI 95% 1.9 ± 0.03; $p<0.0001$] of patients who were committed to pharmacotherapy gave up smoking. The largest proportion of respondents who were committed to pharmacotherapy "clearly followed the recommendations of doctors" and was 13.9% [CI 95% 13.9 ± 0.002; $p<0.0001$]. At the same time, 10.9% [CI 95% 1.9 ± 0.06; $p<0.0001$] of patients who were committed to pharmacotherapy started to follow a diet. Compliance with the sleep regimen was determined by 7.9% [CI 95% 7.9 ± 0.05; $p<0.0001$] and changes in the daily schedule were determined by 6.9% [CI 95% 6.9 ± 0.05; $p<0.0001$] of patients who

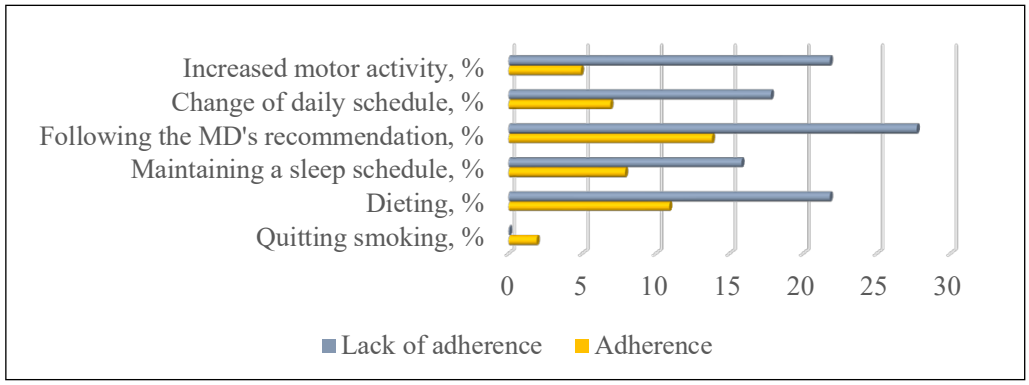

Fig. 1. Relationship between adherence to pharmacotherapy and changes in patients' lifestyle after diagnosis.

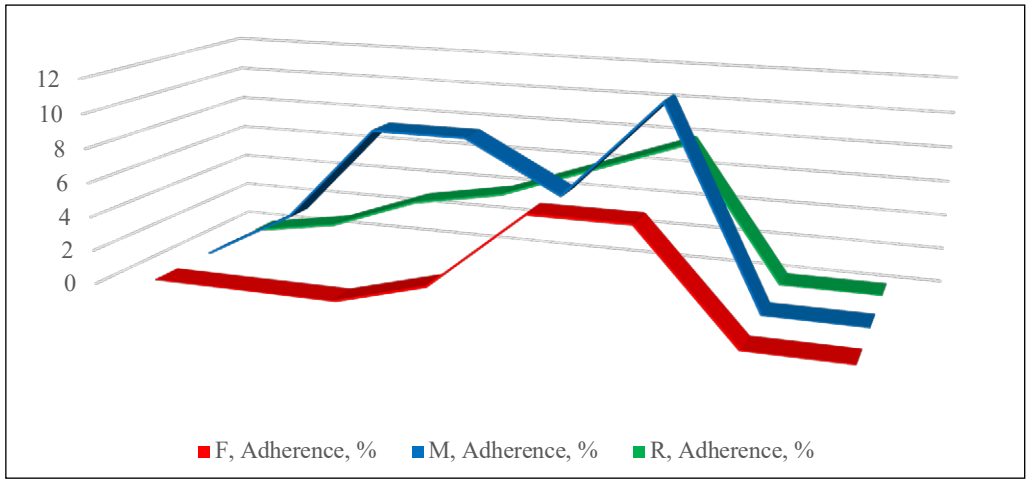

Fig. 2. Relationship between adherence to pharmacotherapy and self-assessment of health status among the surveyed respondents (R).

were committed to pharmacotherapy, respectively. 17.8% [95% CI 17.8 ± 0.07; p<0.0001] of respondents did not change their lifestyle and were not compliant with pharmacotherapy.

The relationship between adherence to pharmacotherapy and self-assessment of the health status of the surveyed respondents (Fig. 2) was analyzed on a scale from "0 – 10", where "10" is the highest health indicator. The results of the observation show that the surveyed patients assessed their own health status from 3 (3.9% [CI 95% 3.9 ± 0.04; p < 0.0001]) to 10 (1.9% [CI 95% 1.9 ± 0.03; p < 0.0001]). At the same time, the largest proportion of patients adhering to pharmacotherapy was observed in the group with a self-assessment of their own health status "8" - 7.9% [CI 95% 7.9 ± 0.05; p < 0.0001]. Adherent to pharmacotherapy patients with self-assessment of their own health status "7" were 5.9% [CI 95% 5.9 ± 0.04; p<0.0001]. There is a tendency for decreased adherence to pharmacotherapy with worsening self-assessment of health status of their own. Within the patients with self-assessment of their own health status "3", "9" and "10" there was a lack of adherence to pharmacotherapy.

We tested the hypothesis of the influence of self-assessment of health status on adherence to pharmacotherapy (Fig. 2). According to the calculations of the Pearson Chi-square criterion, this thesis had to be refuted: = 9.726, p=0.246, fd=5, α=0.211. Chi-square is not statistically significant. Therefore, there is no relationship - p=0.115 between adherence to pharmacotherapy and self-assessment of the health status of the surveyed respondents (Table 1).

We present descriptive data on the factors influencing the choice of medicines in the prescribed pharmacotherapy. It was determined that (Fig. 3) the most significant factors were those related to doctor's prescriptions (73.3%), the cost of medicines (27.68%), and the choice of original medicines in the use of pharmacotherapy (13.8%). At the same time, 12.1% of respondents trust the recommendations of friends and relatives in the use of medicines. 7.8% of respondents pay attention to the availability of the "Affordable Medicines" program. It should be noted that the largest share of patients who are committed to pharmacotherapy is observed in the group for whom the cost of medicines is important – 21.78% [CI 95% 21.78 ± 0.07; p<0.0001]. In the group that adheres to medical prescriptions, 18.8% [CI 95% 18.8 ± 0.07; p<0.0001] of respondents are committed to pharmacotherapy. Some of the respondents (3.9% [CI 95% 3.9 ± 0.04; p<0.0001]) who are committed to pharmacotherapy follow the advice of pharmacists. Other patients (1-2%) are committed to pharmacotherapy, trust data from the Internet, advice from

Table 1. Calculations of the Relationship between Adherence to Pharmacotherapy and Self-assessment of Patients' Health Status Using Pearson's Chi-square Criterion Adjusted for Likelihood

Contingency Tables					
	Absent Present		Adherence		Total
Health condition	3,00	Count	4	0	4
		Expected count	3,1	,9	4,0
	4,00	Count	7	1	8
		Expected count	6,3	1,7	8,0
	5,00	Count	14	3	17
		Expected count	13,3	3,7	17,0
	6,00	Count	14	4	18
		Expected count	14,1	3,9	18,0
	7,00	Count	21	6	27
		Expected count	21,1	5,9	27,0
	8,00	Count	10	8	18
		Expected count	14,1	3,9	18,0
	9,00	Count	7	0	7
		Expected count	5,5	1,5	7,0
	10,00	Count	2	0	2
		Expected count	1,6	,4	2,0
Total		Count	79	22	101
		Expected count	79,0	22,0	101,0

Chi-square Criteria			
	Value	fd	Asymptotic Significance (2-sided)
Pearson Chi-square	9,626[a]	7	0,211
Likelihood Ratio	11,599	7	0,115
Valid Observations Count	101		

		Value	Approximate Significance
Nominal/Nominal	Phi	0,309	0,211
	Cramér's V	0,309	0,211
	Contingency Coefficient	0,295	0,211
Valid Observations Count		101	

friends and relatives, pay attention to the originality of the medicine, the presence of the "Affordable Medicines" program, and the "manufacturer of the medicines".

The dependence of patients' adherence to prescribed pharmacotherapy on the participation of pharmacists in pharmacotherapy management was established. 80 valid questionnaires were selected to answer the question. The answers were used to determine the factors influencing the choice of medicines in prescribed pharmacotherapy (Fig. 4).

According to the results of the Chi-square, adjusted for likelihood = 28.633, $p<0.000$, the statistical significance of the difference in observed frequencies

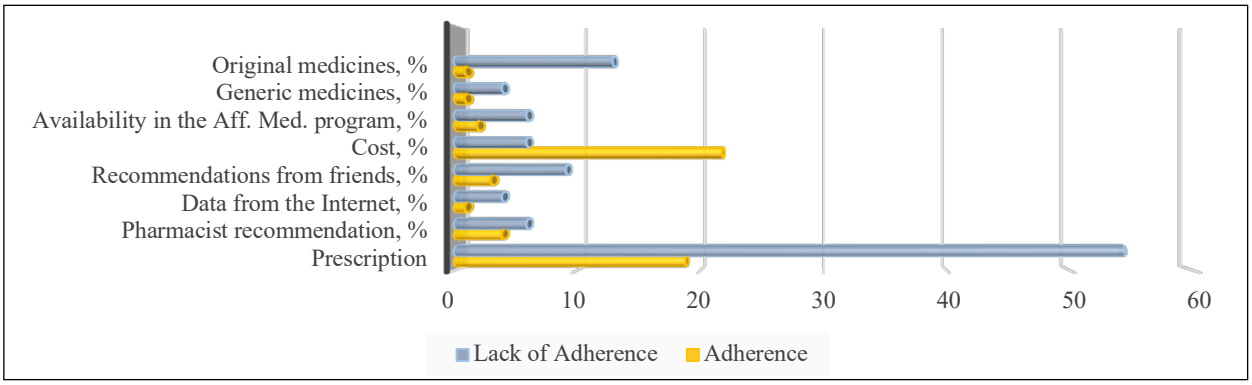

Fig. 3. Factors influencing the choice of medicines in the prescribed pharmacotherapy.

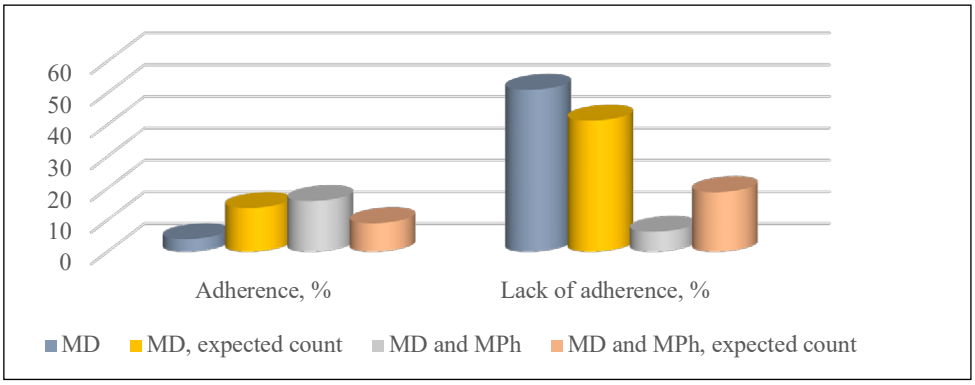

Fig. 4. Dependence of patient adherence to prescribed pharmacotherapy on pharmacists' participation in pharmacotherapy management.

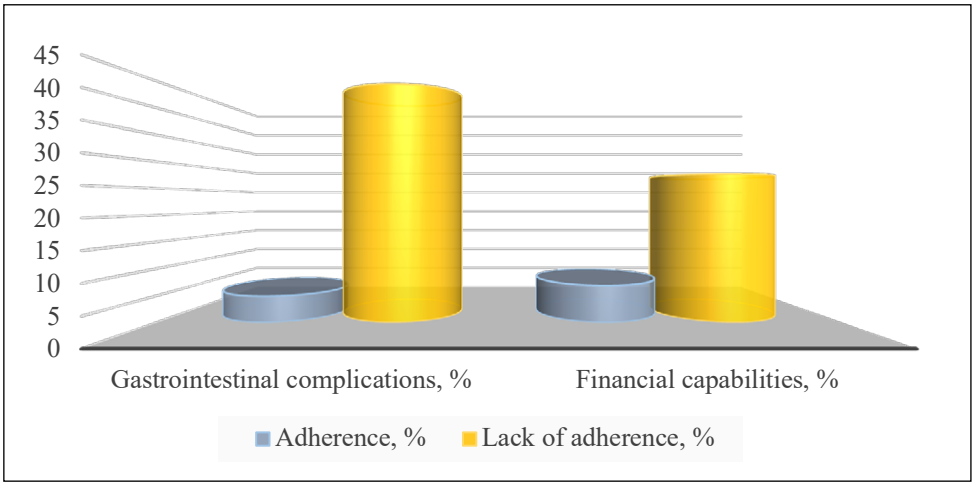

Fig. 5. Factors influencing the discontinuation of prescribed pharmacotherapy.

between patients who consulted only with doctors or doctors and pharmacists was established. The relationship is quite strong, the coefficient of association φ and Cramer = 0.607, p<0.000.

The odds ratio OR=22.67 was also determined. The data obtained indicate that patients with consultations with a doctor and a pharmacist have 22 times greater adherence to pharmacotherapy (Table 2) compared to patients who received consultations with a doctor only.

A relationship was established between adherence to pharmacotherapy and the use of medicines under the "Affordable Medicines" program. We selected 91 valid responses. It was determined that patients who use the "Affordable Medicines" program do not have adherence to pharmacotherapy compared to those patients who do not use the reimbursement program. This may be explained by the adherence of patients with ischemic heart disease and comorbid conditions to more effective, and therefore expensive, medicines that are not included in the "Affordable Medicines" program (Table 3). Chi-square adjusted for likelihood = 5.353 p = 0.021. The relationship is moderate φ and Cramer's coefficient 0.234, p =0.025.

It has been statistically proven that patients who do not use the "Affordable Medicines" program have a greater commitment to pharmacotherapy compared to those who use the reimbursement program.

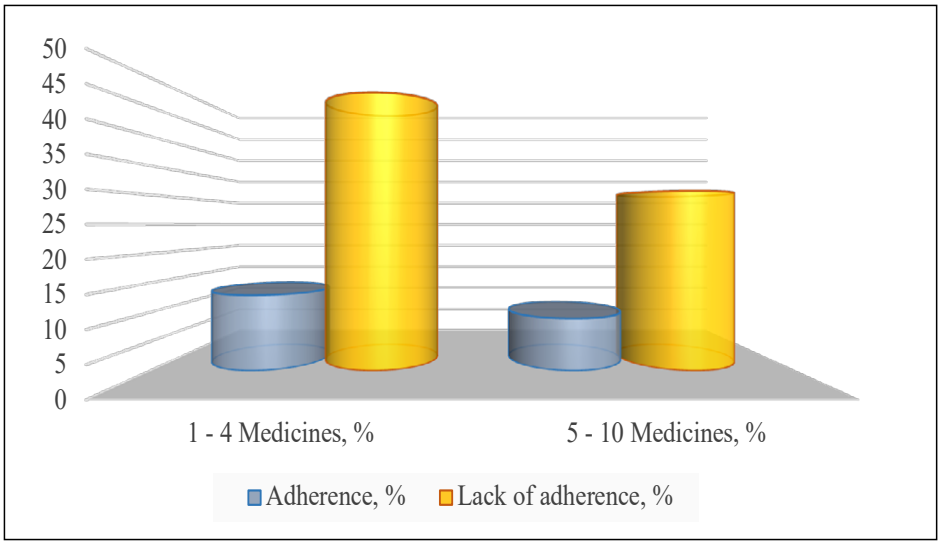

Fig. 6. Relationship between adherence to pharmacotherapy and the amount of daily medication consumption.

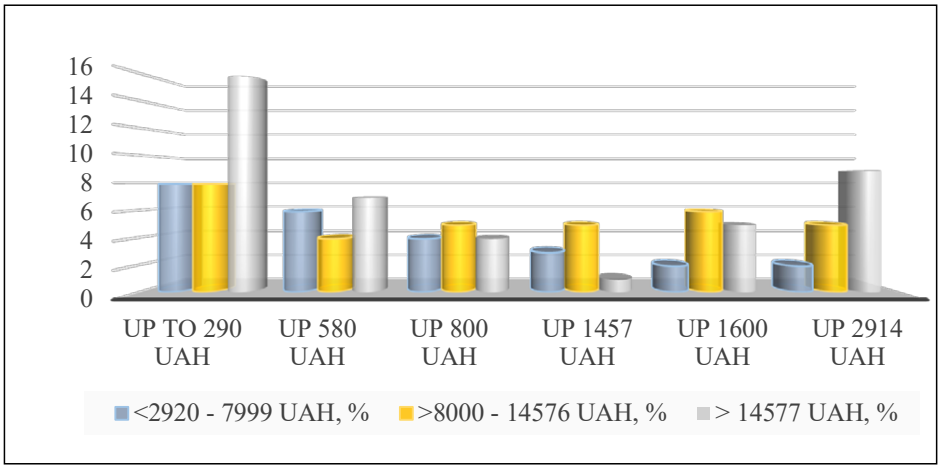

Fig. 7. Relationship between average monthly income of patients and average monthly expenses for medicines.

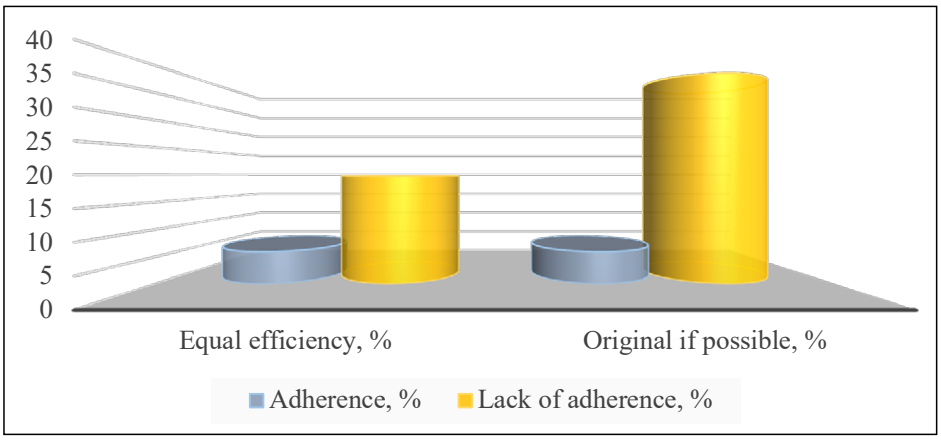

Fig. 8. Relationship between patient preferences and adherence to pharmacotherapy.

This situation is explained by the desire to use more effective medicines. In both groups, patients noted that they have a preference for original medicines. However, financial capabilities do not allow all patients to use effective medicines in pharmacotherapy all the time. For Chi-square calculations we selected 91 valid responses. $\chi 2$ adjusted for probability is not statistically significant, $\chi 2=3.350.232$, $p=0.067$. There is no relationship, $p = 0.069$. Therefore, patients who currently use the "Affordable Medicines" program do not have the opportunity to use a number of medicines and have low commitment to pharmacotherapy. The observation of adherence to original medicines due to their effectiveness, and therefore price, indicates that all patients can purchase generic medicines for long-term use if necessary (Table 4).

It was found that the main reasons for discontinuation of pharmacotherapy (Fig. 5) were gastrointestinal complications (49.4%) and financial capabilities of patients (34.6%). The proportion of respondents who

Table 2. The Dependence of Patient Adherence to Prescribed Pharmacotherapy on Pharmacist Involvement in Pharmacotherapy Management

Consolidated Observation Report						
	Observations					
	Valid		Missing		Total	
	N	Percentage	N	Percentage	N	Percentage
Pharmacotherapy Management* Adherence	80	100,0%	0	0,0%	80	100,0%

Cross-tabulation of Pharmacotherapy Management Adherence*					
			Adherence		Total
			Lack of Adherence	Presence of Adherence	
Pharmacotherapy Management	Doctor Only	Count	51	4	55
		Expected Count	41,3	13,8	55,0
	Doctor and Pharmacist	Count	9	16	25
		Expected Count	18,8	6,3	25,0
Total		Count	60	20	80
		Expected Count	60,0	20,0	80,0

Chi-square Criteria					
	Value	Dg.	Asymptotic Significance (2-sided)	Exact Significance (2-sided)	Exact Significance (1-sided)
Pearson Chi-square	29,498[a]	1	0,000		
Continuity Correction[b]	26,550	1	0,000		
Likelihood Ratio	28,633	1	0,000		
Fisher's Exact Test				0,000	0,000

Symmetric Measures[c]			
		Value	Approximate Value
Nominal/Nominal	Phi (Φ)	0,607	0,000
	Cramér's V	0,607	0,000

Risk Estimate			
	Value	95% Confidence Interval	
		Lower	Upper
Odds Ratio for Pharmacotherapy Management (Doctor / Doctor + Pharmacist)	22,667	6,148	83,574
Number of Valid Observations	80		

were supportive of pharmacotherapy and who noted gastrointestinal complications was 4.9% [CI 95% 4.9 ± 0.04; p<0.0001]. Another proportion of patients who were supportive of pharmacotherapy (6.9% [CI 95% 6.9 ± 0.05; p<0.0001]) focused on financial capabilities, which became a burden for the whole family. Patients noted that "other family members pay for the treatment". Some respondents (4%) with a lack of adherence to pharmacotherapy noted that they take "a large number of medications,""have other burdens," "take dietary supplements," "are worried about their liver," "clearly follow the doctor's recommendations, but forget to take medications on time."

To establish the relationship between the reasons for discontinuation of pharmacotherapy for patients and its impact on adherence (side effects, high cost),

Table 3. The Relationship between Adherence to Pharmacotherapy and the Use of Medications under the "Affordable Medicines" Program

Consolidated Observation Report						
"Affordable Medicines" Program * Adherence to Pharmacotherapy	Observations					
	Valid		Massing		Total	
	N	Percentage	N	Percentage	N	Percentage
	91	100,0%	0	0,0%	91	100,0%

Cross-tabulation of "Affordable Medicines" Program * Adherence

			Adherence		Total
			Lack of Adherence	Presence of Adherence	
"Affordable Medicines" Program	Do not apply	Count	37	16	53
		Expected Count	41,4	11,6	53,0
	Apply	Count	34	4	38
		Expected Count	29,6	8,4	38,0
Total		Count	71	20	91
		Expected Count	71,0	20,0	91,0

Chi-square Criteria

	Value	df	Asymptotic Significance (2-sided) p-value	Exact Significance (2-sided) p-value	Exact Significance (1-sided) p-value
Pearson Chi-square	4,990[a]	1	0,025		
Continuity Correction[b]	5,353	1	0,021		
Likelihood Ratio				0,039	0,022

Symmetric Measures[c]

		Value	p-value
Nominal/ Nominal	Phi (Φ)	0,234	0,025
	Cramér's V	0,234	0,025

81 valid responses were filtered (single responses "absence of symptoms", "communication with a doctor", "taking dietary supplements", etc. were excluded). All responses were divided into 4 groups – gastrointestinal problems, side effects, financial problems, responses where respondents mentioned both problems (side effects, finances) and others.

It was found that there is no significant difference between the problems experienced by people and their adherence to pharmacotherapy. In general, patients react equally to the listed problems. The indicator of the adjusted for likelihood $\chi 2$ is not statistically significant.

The relationship of adherence to pharmacotherapy between the number of daily medications used was analyzed (Fig. 6). It was determined that 60.4% of respondents take one to four medications daily, the remaining 39.6% of patients have to take five to ten medications daily. The relationship of adherence to pharmacotherapy in the group of respondents who take from 1 to 4 medications daily was established – 12.9% [CI 95% 12.9 ± 0.06; $p < 0.0001$]. Respondents who are adherent to treatment with daily intake of 5 to 10 drugs are 8.9% [CI 95% 8.9 ± 0.001; $p < 0.0001$].

It was determined that adherence to pharmacotherapy does not depend on the number of medications taken. The indicator adjusted for the probability of $\chi 2$ is not statistically significant.

It was found that 31.6% of respondents spend up to 290 UAH per month on medications – 7.9% [CI 95% 7.9 ± 0.05; $p<0.0001$] with an average monthly income from the minimum subsistence minimum (2920 UAH) to the average salary (14576 UAH) and 15.8% [CI 95% 7.9 ± 0.05; $p<0.0001$] with an average

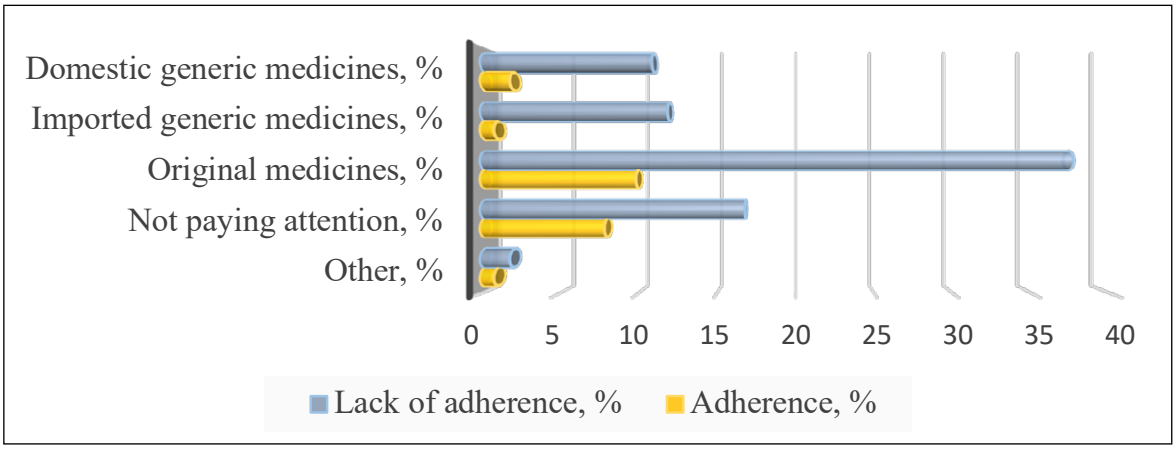

Fig. 9. Relationship between adherence to pharmacotherapy and factors influencing the choice of medicines by INN.

monthly income higher than the average salary (>14577 UAH) (Fig. 7). Another 37.1% of respondents spend from 1457 UAH to 2914 UAH per month. It was determined that 24.23% of respondents had a monthly income from the minimum subsistence minimum (2920 UAH) to the minimum wage (7999 UAH). The surveyed patients with an average monthly income from the minimum wage (7999 UAH) to the average wage (14576 UAH) accounted for 31.8%. The remaining respondents had a monthly income of more than the average wage (14576 UAH) – 43.93%. It should be noted that due to the deterioration of the socioeconomic status of the population, not all patients were able to complete the survey using modern electronic devices.

The relationship between adherence to pharmacotherapy and medicines costs has been statistically proven: the higher the price, the higher the adherence to pharmacotherapy (invested in treatment, need for taking medicines). According to the results of the calculated $\chi 2$, adjusted for plausibility = 19.476, $p = 0.002$, $fd = 5$, at a given level of hope $\alpha = 0.05$, there is. The strength of the relationship is moderate (Table 5). $\chi 2 = 0.445$, $p = 0.000$ and $\varphi = 0.445$ $p = 0.000$. However, the survey results indicate that such patients eventually cancel pharmacotherapy used in CHD with comorbid conditions due to the lack of funds.

The relationship between patient preferences and adherence to pharmacotherapy has been determined (Fig. 8). The results of the analysis show that 47.5% of the surveyed patients prefer to use original medicines, of which the proportion of those who are committed to pharmacotherapy is 9.9% [CI 95% 9.9 ± 0.06; p<0.0001]. The remaining part of the respondents (25%) does not pay attention to the manufacturer of the medicine and the proportion of those who are committed to pharmacotherapy in this group is 7.9% [CI 95% 7.9 ± 0.05; p<0.0001]. The opinions of the respondents regarding the use of domestic and generic medicines in pharmacotherapy were equally divided by 12.8%. At the same time, in the indicated groups of patients, 1.9% [CI 95% 1.9 ± 0.03; p<0.0001] and 0.9% [CI 95% 0.9 ± 0.19; p<0.0001] are inclined to use foreign medicines. The remaining 2.8% of respondents use in pharmacotherapy those medicines that are offered in pharmacies.

According to the results of the analysis of the factors influencing the choice of medicines by INN and patients' awareness of original and generic medicines, it was determined that a larger proportion of respondents have an understanding of the main differences between these medicines (Fig. 9). Patients noted that original and generic medicines have the same effectiveness (25.7%). At the same time, patients in this group who are committed to pharmacotherapy were 2.8% [CI 95% 2.8 ± 0.05; p<0.0001]. The proportion of respondents who, if possible, have a desire to receive pharmacotherapy with original medicines is 42.8%. Of these, 5.9% [CI 95% 5.9 ± 0.04; p<0.0001] are committed to pharmacotherapy. Almost all respondents noted that "original medicines are more expensive", and "generic medicines are cheaper". About 2% of respondents emphasized that "the quality of these medicines depends on the manufacturer", "generic medicines are fully controlled", "domestic medicines are not always effective".

DISCUSSION

The implementation of guidelines (clinical recommendations) for patients with ischemic heart disease for the prevention of cardiovascular diseases in clinical practice [8;9] was investigated in a series of EUROASPAIR III, IV, V surveys. In these studies, an objective assessment of the implementation of clinical recom-

Table 4. The Relationship Between Adherence to Pharmacotherapy and the Use of Generic Medicines

Consolidated Observation Report						
Observations Valid	Observations					
	Valid		Valid		Valid	
	Percentage	Percentage	Percentage	Percentage	Percentage	Percentage
Possibility * Preference	91	100,0%	0	0,0%	91	100,0%

Cross-tabulation of Generic Medicines * Preference					
			Preference		Total
			Generic	Original	
Possibility	No	Count	24	12	36
		Expected Count	19,8	16,2	36,0
	Yes	Count	26	29	55
		Expected Count	30,2	24,8	55,0
Total		Count	50	41	91
		Expected Count	50,0	41,0	91,0

Chi-square Criteria					
	Value	df	Asymptotic Significance (2-sided) p-value	Exact Significance (2-sided) p-value	Exact Significance (1-sided) p-value
Pearson Chi-square	3,306[a]	1	0,069		
Likelihood Ratio	3,350	1	0,067		
Fisher's Exact Test				0,086	0,054
Number of allowed observations	91				

Symmetric Measures[c]			
		Value	P-value
Nominal/ Nominal	Phi	0,191	0,069
	Cramér's V	0,191	0,069

mendations for patients with ischemic heart disease was carried out by surveying in EUROASPAIR IV, V (n = 16259, 27 countries) on lifestyle modification and pharmacotherapy management [20]. The data obtained as a result of the surveys indicate low rates of risk factor modification. Thus, among the surveyed patients with coronary heart disease (n = 16259) - 18.1% (n = 2950) followed a diet and 61.3% (n = 9963) led an active lifestyle after a coronary event. It was determined that out of 31% (n=4998) of surveyed smokers, 48.2% (n=2410) quit smoking after a coronary event [20].

According to the results of the analysis of the survey conducted by us (Fig. 1), in Ukraine it was found that 32.7% of the surveyed patients with ischemic heart disease follow a diet and began to move more (26.7%). 23.7% and 24.7% of patients with ischemic heart disease changed their sleep and daily schedule, respectively. There is also a very low level of patients with ischemic heart disease who have given up smoking (5.8%). These observations indicate that Ukrainian patients are more inclined to follow a diet, but continue to lead a sedentary lifestyle and cannot give up smoking. An interesting fact is that half of the respondents (50.6%) self-assessed their own health status from "5" to "7" (Fig. 2). In this survey, we did not investigate the mental state of the respondents, but according to statistics from the Ministry of Health of Ukraine, 70% of Ukrainians have mental health disorders (sleep disorders, anxiety, stress, depression, post-traumatic stress disorder, etc.) related to the war in the country [21]. It should be noted that factors of the mental state of the Ukrainian population negatively affect lifestyle changes and behavior correction and may explain the low level of lifestyle modification in patients with ischemic heart disease in Ukraine [20].

Observations of factors influencing the choice of medicines in the prescribed pharmacotherapy within

Table 5. Calculations of the Relationship between Adherence to Pharmacotherapy and Monthly Expenditures on Medicines Based on Pearson's Chi-square Adjusted for Likelihood

Contingency Table					
	Lack of Adherence Presence of Adherence		Adherence		Total
Expenditures, UAH	Up to 1457	Count	9	0	9
		Expected Count	7,0	2,0	9,0
	Up to 1600	Count	12	1	13
		Expected Count	10,1	2,9	13,0
	Up to 290	Count	26	4	30
		Expected Count	23,3	6,7	30,0
	Up to 2914	Count	7	10	17
		Expected Count	13,2	3,8	17,0
	Up to 580	Count	12	5	17
		Expected Count	13,2	3,8	17,0
	Up to 800	Count	11	2	13
		Expected Count	10,1	2,9	13,0
Total		Count	77	22	99
		Expected Count	77,0	22,0	99,0

Chi-square Criteria			
	Value	df	Asymptotic Significance (2-sided) p value
Pearson Chi-square	19,567[a]	5	0,002
χ^2 (Likelihood Ratio)	19,476	5	0,002

Measures of Association			
		Value	**p value**
Criterion	Phi	0,445	0,002
	Cramér's V	0,445	0,002

the limits of one molecule by INN indicate that the overwhelming number of surveyed patients with CHD (75.7%) trust the prescriptions and recommendations of doctors (Fig. 3). However, the decline in the socio-economic status of the population during the war in the country forces Ukrainian citizens to seek advice from pharmacists (13.6%) and acquaintances (12.1%) and to conduct independent data searches on the Internet (4.5%) to choose the cheapest medicines with proper efficacy and quality.

It should be noted that 9.1% of the surveyed respondents use the "Affordable Medicines" program for medicines that are dispensed on reimbursement. Not all surveyed respondents were aware of the existence of this program, as indicated in the respondents' comments. The significant relationship between adherence to pharmacotherapy and monthly costs probably indicates that patients prefer the effectiveness of pharmacotherapy and the convenience of using medicines. It should be noted that the "Affordable Medicines" program does not contain fixed combinations, atorvastatin and rosuvastatin with proven efficacy and safety, which are proposed by the latest ESC/AHA clinical recommendations, the unified clinical protocol "Stable ischemic heart disease" [8-11] and are included in the list of "Essential medicines" (EML list) proposed by WHO [22, 23]. Our data coincide with the data of another study (n = 208) on the preferences of patients with CHD for original medicines, which are considered essential medicines and are not covered by insurance companies in foreign countries [24].

Therefore, efforts can be directed at regulating and improving the mechanisms for providing citizens with medicines dispensed under the "Affordable Medicines" program (prescribing of medicines for the long-term use, popularization among the population and health care providers).

It should also be noted that the analyzed data obtained as a result of the survey reveal barriers between the number of prescribed medicines and possible

complications from the gastrointestinal tract (Fig. 4, 5). A proportion of the surveyed patients (56.03%) have concerns about possible adverse reactions to the prescribed medicines. Practical experience indicates that the vast majority of respondents (77.2% of respondents have higher education) carefully study the instructions for medicines and pay attention to possible adverse reactions, conduct their own data search on the Internet after which they refuse to take some of the prescribed medicines or return to the doctor's appointment to change pharmacotherapy. Such actions lead to unplanned hospitalizations and an additional burden on the healthcare system.

Therefore, given the proportion of patients who trust the recommendations of doctors and pharmacists, efforts aimed at a multidisciplinary team approach to education and additional explanations on the use of medicines (frequency of adverse reactions, method of administration, prevention of possible drug interactions, including prediction of possible drug-food interactions) would be possible. Numerous international clinical studies have shown the high effectiveness of pharmacists' influence on adherence to pharmacotherapy in patients [25-27].

Analysis of the results of the study confirms the data of monitoring companies on the decline in the socioeconomic status of the population [4]. When choosing medicines in the prescribed pharmacotherapy, 27.68% of respondents pay attention to the pricing policy of medicines (Fig. 3), 27.2% may cancel the prescribed pharmacotherapy due to the high price of medicines (Fig. 4). According to the latest clinical recommendations [9,28,30], the surveyed patients in the prescribed pharmacotherapy can use direct oral anticoagulants (from 800 UAH), NGKTH inhibitors (from 850 UAH) [30], fixed combinations, etc. for simultaneous long-term administration. These groups of medicines in Ukraine are expensive in relation to the average budget of patients (Fig. 6), therefore, patients refuse the prescribed pharmacotherapy after the respondents "felt an improvement" in their health. The listed pharmacological groups of medicines have been included in the medical guarantee programs [31], however, in accordance with domestic legislation [32], there is no necessary number of registered medicines of the listed pharmacological groups in Ukraine for their further inclusion in the "Affordable Medicines" program.

According to the results of the EUROASPAIR V observational survey of patients with high cardiovascular risk (n=2759) in primary care, it was found that less than 47% of patients are adherent to pharmacotherapy with antihypertensive and lipid-lowering medicines, and another 65% of the surveyed patients adhere to hypoglycemic pharmacotherapy. Such data indicate low adherence to pharmacotherapy in secondary prevention of patients with high cardiovascular risk [33]. The results of our survey showed low adherence of 21.8% [21.8 ± 0.07; $p<0.0001$] to pharmacotherapy in patients with ischemic heart disease and concomitant hypertension, diabetes, CKD. However, of the 42.8% of respondents who preferred original medicines (Fig. 7), 5.9% [CI 95% 5.9 ± 0.04; $p<0.0001$] showed the highest adherence to treatment. The same proportion of respondents indicated that if possible they would be treated only with original medicines (Fig. 8), but generic medicines are used in pharmacotherapy.

Thus, the analysis of awareness regarding the use of original and generic medicines and the identified factors influencing the choice of pharmacotherapy allow us to draw the following conclusions. The surveyed patients are aware of the difference between original and generic medicines. However, the financial capabilities of a significant part of the modern Ukrainian population do not allow them to use original medicines. To resolve this issue, doctors, who are trusted by a large proportion of respondents, should explain in more detail to socially unprotected segments of the population the difference in the use of generic and original medicines and redistribute the prescription of medicines from original to generic. Pharmacists could also join the interaction in the patient-doctor-pharmacist team within the framework of providing pharmaceutical care in advising patients on the benefits of medicines, their clinical effectiveness and safety in the prescribed pharmacotherapy and finally convincing patients to adhere to clinical recommendations [34,35].

CONCLUSIONS

1. It was investigated that the decrease in the socioeconomic status of the population during the war in Ukraine negatively affects compliance with clinical recommendations for the modification of risk factors and secondary prevention of CHD within the use of medicines, which is confirmed by the results of observational studies EUROASPAIR IV, V.
2. A significantly low adherence of 13.9% [CI 95% 13.9 ± 0.002; $p<0.0001$] to the modification of risk factors and prescribed pharmacotherapy in the secondary prevention of CHD was established, which is emphasized in observational studies EUROASPAIR IV, V.
3. The reliability of the influence of preferences of patients suffering from CHD with comorbid conditions to effective pharmacotherapy was confirmed ($\chi 2 = 3.350.232$, $p = 0.067$).

4. It was determined that 42.8% of respondents prefer original medicines when choosing medicines, however, the financial capabilities of patients do not allow them to be used for a long time in the prescribed pharmacotherapy, which negatively affects adherence to treatment.
5. It was found that patients who receive consultations from a doctor and a pharmacist are 22 times more likely to adhere to pharmacotherapy than patients who receive consultations only from a doctor. Odds ratio OR=22.67.
6. It was found that 7.8% [CI 95% 7.8 ± 0.05; p<0.0001] of the surveyed patients suffering from ischemic heart disease with concomitant hypertension, diabetes, CKD use the "Affordable Medicines" program and do not have the opportunity to use a number of medicines proposed by clinical recommendations.
7. The integration of pharmacists into multidisciplinary teams is recommended as well.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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