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The frequency and profile of drug treatment in subjects with dyslipidemias and cardimetabolic diseases in an urban russian population older then 55 years

Aim — To analyze frequency and profile of the lipid-lowering therapy (LLT) in patients with dyslipidemia (DLP) and cardiometabolic diseases (CMD) in a population sample aged 55–84 years at the current time (2015–2017).

Material and methods — Despite guidelines on DLP treatment and the availability of effective and safe lipid-lowering drugs, control of DPL in primary and secondary prevention of cardiovascular diseases (CVD) is insufficient. Knowledge of the level of pharmaceutical correction of DLP in the Russian population is limited; it requires an LLT assessment in various regions and in a wide age range, and a regular monitoring taking into account changing approaches to the correction of DLP. A random population of men and women aged 55–84 years (n=3896) was evaluated in Novosibirsk in 2015–2017 (project HAPIEE). A joint DLP category was established as low-density lipoprotein cholesterol (LDL–C) ≥3.0 mmol/l, or total cholesterol (TC) ≥5.0 mmol/l, or triglycerides (TG) ≥1.7 mmol/l, or LLT. The combined group of DLP and CMD included ischemic heart disease (IHD), type 2 diabetes mellitus (DM2), and DLP. Regular LLD treatment for the recent 12 months, excluding the dosage of medicines, was assessed using the Anatomic Therapeutic Chemical (ATC) classification. The conditional control of serum lipids was taken as the achievement of LDL–C <3.0 mmol/l, TC <5.0 mmol/l, and TG <1.7 mmol/l.

Results — In the study sample, the total prevalence of DLP and CMD was 88% (82.8% for men and 91.3% for women, p<0.001). 48.3% of patients in the IHD group, 35.0% in the DM2 group, 29.4% in the DLP group, and 32.8% in the CMD group took LLT. Control of serum lipids was achieved in 18.3% (37.9% of patients on LLT) of patients with IHD; 9% (25.6% of patients on LLT) of patients with DM2; 7.3% (24.8% of patients on LLT) of patients with DLP; and 9.0% (27.6% of patients on LLTсреди) in the DLP and CMD group. Women with DM2 and DLP more frequently achieved lipid control than men (p<0.001). 98.7% of study participants took statins as LLT.

Conclusion — In the sample of urban population aged 55–84 years in 2015–2017, 90% of patients had DLP or CMD, and at least ¾ of them required blood lipid control. The lipid control was achieved in every fifth IHD patient and in approximately 40% of those who took LLT. For DM2 or DLP patients, the lipid control was achieved in every tenth patient and in approximately 25% of those receiving LLT. Frequency of lipid control in IHD patients was comparable for men and women; in DM2 and DLP, men less frequently achieved the lipid control than women. About 70% of patients in the combined DLP and CMD group and more than 50% of IHD patients did not take LLT, which considerably contributed to the insufficient lipid control in primary and secondary prevention of atherosclerotic CVDs in this population.

Keywords — Dyslipidemia; lipid-lowering therapy; population; HAPIEE cohort

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Introduction

Cardiovascular diseases (CVDs), mainly atherosclerotic forms, cause more than 4 million deaths in Europe annually [1]. In Russia, cardiovascular mortality is responsible for about 850,000 deaths a year. In 2018 and 2019, the mortality rate was 579.6 and 573.7 per 100,000 people, respectively [2, 3]. Currently, epidemiological, placebo-controlled clinical trials, along with Mendelian randomization, produce strong evidence of the causal role of low-density lipoprotein cholesterol (LDL–C) and apolipoprotein B (ApoB) containing lipoproteins in the development of atherosclerotic CVDs with cumulative effect. The contribution of decreased levels of LDL–C and ApoB lipoproteins to the proportional reduction of cardiovascular risk is also noted [4–7]. The 2019 ESC Guidelines on Management of Dyslipidaemias set the target levels of LDL–C in patients at very high, high, moderate, and low cardiovascular risk less than 1.4, 1.8, 2.6, and 3.0 mmol/L, respectively [4].

Despite regular updating of the guideline for managing patients with dyslipidemia (DLP) [4, 8–14] and the availability of effective and safe lipid-lowering drugs with key statin position, DLP control is not sufficient for the primary and secondary prevention of CVDs [15–17].

The most consistent evaluation of the implementation of CVD prevention guidelines, including for DLP, was performed in EUROASPIRE I–V [15, 18, 19], NHANES [20–24], ECCE-RF [25–27].

There is significant heterogeneity between countries in the efficacy of DLP treatment [15], including a shift of the global epicenter of suboptimal cholesterol levels from countries with higher per capita incomes in northwestern Europe, North America, and Australia to southeastern Asia and Oceania [28]. The data on the rates of prescribing drug therapy and DLP control in the Russian population mainly relate to clinical analysis. Population studies should take into account the profiles of lipid-lowering therapy (LLT) in different regions, cover a wide age range, and include regular monitoring assessments due to changing approaches to DLP correction.

This article continues a series of papers studying the profile of drug treatment of cardiometabolic diseases (CMDs) in the modern Russian population on the example of a Novosibirsk population sample [29, 30].

Objective

To analyze the rates and profile of LLT in patients with DLP and CMDs in a population sample of 55–84-year-old patients in the contemporary period (2015–2017).

Material and Methods

Data of the «Health, Alcohol, and Psychosocial factors In Eastern Europe, HAPIEE international project, Novosibirsk» population cohort served as a basis for the study. The basic random sample of 45–69-year-old men and women was formed among residents of two districts having typical civil infrastructure, demographic indicators, and migration levels for the Novosibirsk urban region. After being formed on the basis of electoral lists using a random number table, the sample was stratified into five-year age groups. The design and protocol of the project were as published earlier [31]. At baseline, 9,360 people were examined in 2003–2005 (98% subject were Caucasian, 61% response), the screenings were repeated in the cohort in 2006–2008 and 2015–2017. The object of this study was a sample of subjects of the third screening performed in 2015–2017 (n = 3,898, age 55–84, response 60.1%). The analysis included 3,896 patients with the required data set. The study was approved by the ethics committee of the Research Institute for Internal and Preventive Medicine, Branch of the Institute of Cytology and Genetics of the Siberian Branch of the Russian Academy of Sciences. All patients signed informed consent to be included in the study.

The earlier-published protocol and methodology of the cross-sectional study [31] used standardized questionnaires to provide an epidemiological assessment of CVDs and their risk factors (history and management of arterial hypertension (AH) and diabetes mellitus (DM), history of CVDs, and other chronic diseases, smoking, alcohol consumption, social and demographic characteristics) and objective measurements (anthropometric measurements, blood pressure (BP), electrocardiography (ECG), blood serum levels of lipids and glucose).

BP was measured three times using an Omron M-5 tonometer on the right hand in a sitting position after 5-minute rest. The mean value of three measurements was calculated. AH was established using the 2018 ESC/ESH Guideline criteria [32] when systolic or diastolic BP was ≥140/90 mmHg and/or if antihypertensive drugs had been used within the previous two weeks. Waist-to-hip ratio (WHR) and body mass index (BMI) was calculated using the formula:

$$\text{BMI} = \text{body weight (kg)} / \text{height}^2 \text{ (m)}.$$

A person who smoked one or more cigarettes a day was classified as a smoker. The Graduated Frequency Questionnaire (GFR) was used to assess alcohol consumption. Five groups were identified by the

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frequency of consumption: abstainers, less than once a month, 1–3 times a month, 1–4 times a week, 5 or more times a week. Twelve-lead ECG was recorded using the Minnesota code (MC). Blood samples were collected on an empty stomach. The blood serum levels of total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL–C), and glucose were estimated by the enzymatic method using a KoneLab 300i analyzer. LDL–C was calculated using the Friedewald formula (FF). The European Association for the Study of Diabetes (EASD) formula (2007) was used to transfer fasting serum glucose to plasma glucose (PG):

$$PG = -0.137 + 1.047 \times \text{serum glucose (mmol/L)}.$$

The combined category of DLP was established with LDL-C ≥3.0 mmol/L or TC≥5.0 mmol/L or TG≥1.7 mmol/L or during LLT based on the approach commonly used in population-based studies and using the guidelines for the management of dyslipidemia and the prevention of CVDs during the study period [8, 10, 13, 14]. The population-based screening used missing data to determine the categories of total cardiovascular risk fully and to differentiate the target levels of LDL–C following the current guidelines [4]. Given this fact and in order to provide comparability with several major epidemiological studies, we decided to use a single category of 'conditional' blood lipid control. The conditional lipid control was achieving the following levels: LDL-C <3.0 mmol/L, TC<5.0 mmol/L, TG<1.7 mmol/L.

Coronary artery disease (CAD) taking account of the epidemiological criteria subject to a positive Rose angina questionnaire score (MC classes 1, 4, and 5), a history of myocardial infarction (MI), acute coronary syndrome, or coronary revascularization (documented hospitalization). The unified category of CVDs was established in the presence CAD according to the specified criteria or a history of stroke/transient ischemic attack (documented hospitalization). DM type 2 was established with a known history of Dm type, treated or untreated, or fasting PG≥7 mmol/L [35]. For this analysis, a combined group of patients with DLP and CMDs (DCMDs) was also identified, which included patients with CAD or DM type 2 or DLP.

Regular use of LLT was defined as a daily administration for the past 12 months irrespective of the drug dosage. The drugs were coded according to the Anatomical Therapeutic Chemical Classification System (ATC) [36]. The following drugs were analyzed: statins (St; C10AA); fibrates (C10AB); essential fatty acids (Omega-3 triglycerides including other esters and acids, C10AX); bile acid sequestrants (C10AS); nicotinic acid and derivatives (C10AD); cholesterol absorption inhibitors, including ezetimibe (C10AX09); proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors, including alirokumab (C10AX14). Three cardiologists carried out the coding. The reproducibility of drug class coding was assessed using the double-blind method (in a 10% random subsample); the kappa coefficient was 0.84.

The study included 3,896 patients: The stage one analysis included 3,430 patients with DLP and/or CMDs. 1,125 of these were administered LLT and included in the stage two analysis. The specific drug was indicated by 478 (50%) patients. Further, we analyzed the proportion of conditional blood lipid control in patients with individual diseases (CAD, DM type 2, DLP) and in the combined group of patients with DLP and CMDs.

Statistical analysis was carried out using SPSS v.13.0. The data were presented as the means, standard deviations (M (SD)), and proportions (n (%)). The rate of a trait in the groups was compared using Pearson's chi-square and the Cochran-Mantel-Haenszel test. ANOVA was used for quantitative comparisons. The Mann-Whitney test was used for non-normal distributions. The differences were statistically significant with $p<0.05$.

Results

The characteristics of the study sample (55–84 years old) are presented in Table 1.

The mean age of the examined patients, which did not differ significantly between male and female patients, was 69.3 (6.89) years. The distribution of the patients between 10-year groups was the following: 55–64 years (32.1%), 65–74 years (40%), and 75 years and older (27.2%). As compared with females, the male patients had higher BP, PG, WHR, incidence of CAD and CVDs, smoking, and more regular alcohol consumption. Female patients had higher BMI, serum lipid levels, incidence of AH and administration of antihypertensive therapy than male patients, a similar prevalence of DM type 2, and more frequent administration of sugar-reducing therapy; a greater proportion of female patients had low levels of education and were single.

The incidence of DLP was 83.1%. Among patients with DLP, the proportion of combinations of LDL–C > 3 mmol/L with increased levels of TC or TG was 75.5%; isolated increase in LDL–C or TC; or TG was from 2.4% to 1.3%; other combinations amounted to about 14%. The frequency of the combined category of DLP and CMDs was 88%; this was higher in female patients than in male patients. LLT was administered in 32.8%

Table 1. Characteristics of the study population sample (male and female patients, 55–84 years, Novosibirsk, n = 3,896)

Parameter	Total sample	Male	Female	p
Examined patients	3,896	1,499 (38.42)	2,397 (61.58)	–
Age, years	69.29 (6.89)	69.04 (6.95)	69.46 (6.85)	0.061
SBP, mm Hg	145.72 (21.31)	146.88 (20.64)	145.0 (21.69)	0.007
DBP, mm Hg	83.63 (11.37)	85.79 (11.82)	82.28 (10.87)	<0.001
HR, bpm	71.75 (11.41)	71.34 (12.16)	72.01 (10.91)	0.084
BMI, kg/m2	29.47 (5.49)	27.76 (4.59)	30.55 (5.73)	<0.001
WHR	0.90 (0.08)	0.95 (0.07)	0.87 (0.07)	<0.001
TC, mmol/L	5.46 (1.19)	5.17 (1.14)	5.65 (1.19)	<0.001
LDL-C, mmol/L	3.46 (1.06)	3.28 (0.99)	3.58 (1.08)	<0.001
HDL-C, mmol/L	1.32 (0.39)	1.24 (0.38)	1.38 (0.38)	<0.001
TG, mmol/L	1.49 (0.92)	1.44 (0.89)	1.52 (0.94)	<0.005
PG, mmol/L	6.34 (1.81)	6.41 (1.83)	6.29 (1.8)	0.041
AH, n (%)	3,137 (80.9)	1,162 (78.0)	1,975 (82.6)	<0.001
Treatment of AH (in patients with AH), n (%)	2,399 (77.4)	723 (62.8)	1,676 (86.1)	<0.001
DM, n (%)	803 (20.8)	299 (20.1)	504 (21.2)	0.463
Treatment of DM (in patients with DM), n (%)	470 (59.3)	141 (47.6)	329 (66.2)	<0.001
CAD, n (%)	573 (14.9)	261 (17.5)	312 (13.2)	<0.001
CVDs, n (%)	769 (19.9)	337 (22.6)	432 (18.2)	0.001
Menopause, n (%)	–	–	1,924 (81.5)	–
Smoking, n (%)				
• smokers	714 (18.6)	572 (38.5)	142 (6.0)	<0.001
• former smokers	515 (13.4)	410 (27.6)	105 (4.4)	
• non-smokers	2619 (68.1)	504 (33.9)	2115 (89.5)	
Frequency of alcohol consumption, n (%)				
• 5 times a week	47 (1.2)	40 (2.7)	7 (0.3)	<0.001
• 1–4 times a week	413 (10.7)	326 (21.9)	87 (3.7)	
• 1–3 times a month	835 (21.7)	444 (29.9)	391 (16.6)	
• less than once a month	1609 (41.8)	413 (27.8)	1196 (50.6)	
• abstainers	944 (24.5)	263 (17.7)	681 (28.8)	
Education, n (%)				
• primary	246 (6.3)	86 (5.7)	160 (6.7)	<0.001
• vocational	1063 (27.3)	335 (22.3)	728 (30.4)	
• secondary	1252 (32.1)	478 (31.9)	774 (32.3)	
• higher	1335 (34.3)	600 (40.0)	735 (30.7)	
Family status, n (%)				
• single	1535 (39.9)	230 (15.5)	1305 (55.1)	<0.001
• married	2319 (60.2)	1258 (84.5)	1061 (44.9)	

The data are expressed as M (SD) or n (%); p-value is used for sex-related comparisons. SBP – systolic blood pressure; DBP – diastolic blood pressure; HR – heart rate; BMI – body mass index; WHR – waist-hip ratio; TC – total cholesterol; LDL-C – low-density lipoprotein cholesterol; HDL-C – high-density lipoprotein cholesterol; TG – triglycerides; PG – plasma glucose; AH – arterial hypertension; DM – diabetes mellitus; CAD – coronary artery disease; CVD – cardiovascular disease.

of patients with DCMDs; female patients received this more often than male patients. About 50% of patients with DCMDs did not receive LLT, while another 17.1% did not provide information about LLT. Among patients receiving LLT, about 50% reported taking lipid-correcting drugs without specifying any specific one. Conditional blood lipid control was achieved in 9% of patients with DCMDs; this was more frequent in female patients than male patients (Table 2).

Patients with DCMDs received the following LLT: statins (98.7%), fibrates or essential fatty acids (EFA;<1%). Other classes of LLT were not administered by the subjects. Combined LLT was used in 0.4% of patients with DCMDs.

Table 3 shows the frequency of LLT and blood lipid control in patients with CAD, DM type 2, and DLP. The proportion of patients taking LLT was higher (48.3%) in the CAD group than in the other groups (p<0.001). Blood lipid control was also nearly two-fold in the CAD group compared to the other groups. This trend remained in patients receiving LLT (37.9% in the CAD group versus 25.6% and 24.8%; p<0.001). Among

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Table 2. Frequency of lipid-lowering therapy and distribution of the main drug classes in patients with dyslipidemia and cardiometabolic diseases (CAD and/or DM type 2 and/or DLP)

Parameter	Total	Male	Female	p
Examined number	3 896	1 499	2 397	–
DLP and cardiometabolic diseases	3 430 (88.0)	1 241 (82.8)	2 189 (91.3)	<0.001
LLT in patients with DLP and cardiometabolic diseases (total)	1 125 (32.8)	263 (21.2)	862 (39.4)	
No LLT	1 718 (50.1)	631 (50.8)	1 087 (49.6)	<0.001
No data on LLT	578 (17.1)	347 (28.0)	240 (11.0)	
LLT with the drug indicated	478 (42.5)	132 (50.2)	346 (40.1)	0.004
Non-differentiated LLT	647 (57.5)	131 (49.8)	516 (59.9)	
Blood lipid control (in patients with DLP and cardiometabolic diseases, total)	310 (9.0)	94 (7.6)	216 (9.9)	<0.001
Blood lipid control (in recipients receiving LLT)	310 (27.6)	94 (35.7)	216 (25.1)	<0.001
Classes of LLT drugs in patients who specified the drugs (n = 478)				
Lipid lowering therapy, n	478	132	346	–
Statins	472 (98.7)	132 (100)	340 (98.3)	0.128
Fibrates	1 (0.2)	0 (0.0)	1 (0.3)	0.536
Essential fatty acids	7 (0.7)	0	7 (2.0)	0.100
Bile acid sequestrants	0	0	0	–
Nicotinic acid and derivatives	0	0	0	–
Cholesterol absorption inhibitors	0	0	0	–
Proprotein convertase subtilisin/kexin type 9 enzyme inhibitors	0	0	0	–
Combined LLT	2 (0.4)	2 (1.5)	0	0.381

p – value is specified for sex-related comparison. The data are expressed n (%) – unless otherwise is specified.
CAD – coronary artery disease; DM – diabetes mellitus; DLP – dyslipidemia; LLT – lipid-lowering therapy.

Table 3. Frequency of LLT and blood lipid control in patients with CAD, DM type 2 and DLP

Parameter	CAD	DM type 2	DLP (without CAD / DM type 2)	p
Examination / answered the question about LLT	573/549	803/734	2197/1718	–
Receive LLT, n (%)	277 (48.3)	281 (35.0)	646 (29.4)	
No LLT, n (%)	272 (47.5)	453 (56.4)	1072 (48.8)	<0.001
No data on LLT, n (%)	24 (4.2)	69 (8.6)	479 (21.8)	
LLT with the drug indicated, n (%)	150 (54.2)	120 (42.7)	246 (38.1)	<0.001
Non-differentiated LLT, n (%)	127 (45.8)	161 (57.3)	400 (61.9)	
Blood lipid control, n (%)				
per a disease group, total	105 (18.3)	72 (9.0)	160 (7.3)	<0.001
among patients receiving LLT	105 (37.9)	72 (25.6)	160 (24.8)	<0.001
among patients who indicated an LLT drug	86 (57.3)	56 (46.7)	113 (45.9)	0.046
in non-differentiated LLT	19 (15.0)	16 (9.9)	47 (11.8)	0.307

CAD – coronary artery disease; DM – diabetes mellitus; DLP – dyslipidemia; LLT – lipid lowering therapy.

patients who named a specific drug, blood lipid control was better in those with (57.3%); the DM type 2 and DLP groups differed insignificantly (46.7% and 45.9%, respectively). Almost 50% of the subjects did not receive LLT.

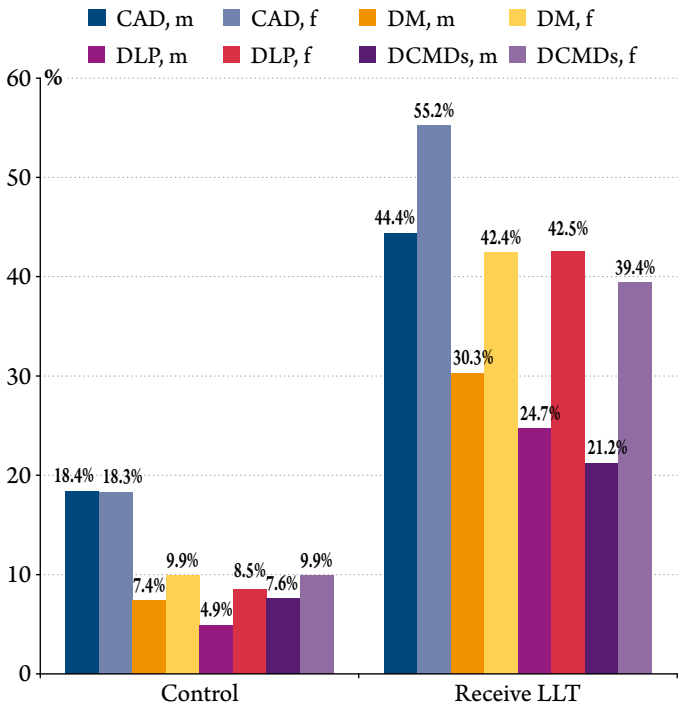
Although blood lipid control was similar in male and female patients with CAD, it was better in female patients than in male patients in the other groups (Figure 1).

Discussion

The total prevalence of DLP and CMDs (CAD, DM type 2, and DLP) was 88% in the sample of male and female 55–84-year-old residents of Novosibirsk. Among patients with CAD, about 50% received LLT in the CAD group, 35% in the DM type 2 group, 29% in the DLP group, and 33% in the combined DLP+CMDs group. Conditional blood lipid control was achieved in 18% of the patients with CAD and 10% of patients in the DM type 2 and DLP groups. Among patients taking LLT, blood lipid levels were controlled by 38% of patients with CAD and 25% in the DM type 2 and DLP groups. Blood lipid control was achieved in female patients more often than in male patients.

DLP management was assessed in different countries in the EUROASPIRE I–V [19], NHANES [20, 24],

Figure 1. Frequency of lipid-lowering therapy (LLT) and conditional blood lipid control in male and female patients with CAD, DM type 2, dyslipidemia, and the combined group of dyslipidemia and cardiometabolic diseases (DCMDs)



Control, p (m, f)	p=0.813	p≤0.001	p≤0.001	p≤0.001
Receive LLT, p (m, f)	p=0.013	p≤0.001	p≤0.001	p≤0.001

The category 'Patients receiving LLT' is the proportion of patients who receive LLT in a particular disease group (CAD, DM type 2, DLP, and DCMDs); 'Blood lipid control' is the proportion of patients who achieved conditional targets of blood lipid control in a particular disease group (CAD, DM type 2, DLP and DCMDs).

ESSE-RF [25, 27] trials. The EUROASPIRE trial of secondary CVD prevention in Europe was performed in 18–80-year-old patients in 6 months – 2 years after coronary complication; stage V was contacted in 130 sites in 27 countries in 2016–2017 [15, 19]. According to the EUROASPIRE V study, LLT was administered in about 84%, of whom 33% did not achieve the target levels of LDL–C <2.6 mmol/L. Based on EUROASPIRE IV (2014–2015) [18], 74.9% of obese and overweight patients received LLT in the Russian EUROASPIRE sample versus 86.6% in the European sample. Effective blood lipid control was achieved only in 15.9% of Russian patients receiving hypolipidemic drugs.

According to NHANES trial (USA; 2013–2014) [20], the rates of using statins in patients with atherosclerotic CVDs (21 years and older), elevated LDL–C ≥190 mg/dL (21 years and older), 40–75-year-old patients with DM type 2 and 40–75-year-old patients with risk of developing atherosclerotic CVD ≥7.5% were 64.6%, 65.5%, 46.2%, and 30.3%, respectively. When comparing the stages of the NHANES trial conducted in 1999–2000 and 2015–2016, the incidence of LLT among patients with atherosclerotic CVDs (in 40–85-year-old patients, which was comparable to our age groups) increased from 37.1% to 69.2% [22], accompanied by a decrease in LDL–C, non-LDL cholesterol, and TG by 23%, 21%, and 28%, respectively. In the ESSAY-RF trial (2012–2014), LLT was administered by approximately 7% of 25–64-year-old patients at high and very high risk; target levels of LDL–C were achieved in 14.4% of male patients and 4.8% of female patients [26, 27]. Statins were most commonly used by patients with a history of MI (40% of male patients and 28% of female patients), LLT was received by 23% of male patients and 13% of female patients in the CAD group; in the DM type 2 group, about 12% of male and female patients received LLT [27].

De la Sierra et al. [17] showed in a literature review that the prevalence of hypercholesterolemia was 50–84% among patients with DM type 2, 64–74% of patients with CAD, 40–70% of patients with MI, and 60–80% of patients with peripheral artery disease. Serum lipid control during LLT varied significantly from 15% to 65%.

Due to differences in the groups of patients with symptomatic CVDs and population sample, differences in patient age, and study designs, caution should be taken when comparing our findings with clinical trials and population-based studies. For this reason, our comparisons, which are limited by a judgment on the direction and order of differences in the rates of administering LLT, are compared with similar age groups where possible. Our findings that more than 50% of the examined patients with CAD and about 70% of patients with DLP do not receive LLT are consistent with the outpatient clinical studies and registers (ARGO, REKVAZA) [37, 38]. The frequency of LLT was consistently around 2 times lower in our sample than in the EUROASPIRE V subjects with coronary complications and had clear indications for LLT. The frequency of LLT was 1.5 times lower in the main CMD groups in Novosibirsk than in the NHANES trial (in similar age groups). The frequency of LLT in patients with CAD and DM type 2 was higher in the Novosibirsk sample than in the ESSE-RF trial in 13 Russian regions due to the younger age of patients in the ESSE study (25–64 years) [27].

LLT in the study population included statins in 99% of cases. Fibrates and EFA formed a cumulative 1%, while combined LLT was extremely rare (0.4%). It should

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be noted that the proportion of high-intensity statin ezetimibe combination in the EUROASPIRE V trial in 2016–2017 was only 2.7%; here, PCSK9 inhibitors were administered in 15 patients of all patients with coronary disease in 130 centers in 27 countries [15]. This was due to the limited distribution of these drugs at the time of the study, which was also a relevant factor for our sample.

The frequency of LLT was higher in female patients than in male patients in our population sample for all CMDs of interest. Blood lipid control, which was comparable for male and female CAD patients receiving LLT (18%), was achieved more often by female patients than male patients with DM type 2 and DLP. Higher adherence to LLT and better blood lipid control among female patients in our sample differ from NHANES (67% of male patients and 56% of female patients with DLP received LLT and 63% and 51%, respectively, controlled blood lipid levels) [39] and EUROASPIRE V (85.6% of male patients and 80.3% of female patients received LLT; 69.6% and 51%, respectively, controlled LDL–C at<2.6 mmol/L) [15]. In the essay-RF study, LLT only prevailed in female patients in the high and moderate risk groups, while the opposite was true in the very high-risk group; moreover, male patients achieved target levels of TC more often than female patients (14.4% and 4.8%, respectively) [27]. Opposite sex-related dependencies may be due to better care of female patients without CVDs than in male patients; however, monitoring of risk factors is more regular in male patients in the group of high risk with established CVDs and following MI [15].

Limitations

The present study has several limitations. Blood lipid levels were measured only once, which may affect the identification of DLP. However, this limitation is minimized by standardized blood collection (8-hour fasting, as well as the same staff and storage protocol) and unified analysis protocol using a single KoneLab 300i autoanalyzer and the same Thermo Fisher kits in the certified laboratory of the Research Institute for Internal and Preventive Medicine. Self-assessment of LLT profile and specific drugs named by approximately 50% of patients receiving LLT may also be responsible for errors. However, the very fact of receiving LLT can be considered in most cases as taking statins; the performance of ATC coding by three certified cardiologists in 10% of the sample using a double-blind method (kappa coefficient was 0.84) eliminated significant errors. Although doses and regimens could not be taken into consideration in the study population, and it was not possible to identify high-intensity or low- and medium-intensity treatment with statins, this did not affect the assessment of the frequency of administering and profile of LLT. Due to a lack of available population screening data to establish complete criteria for risk groups and apply differentiated target levels of LDL–C, the conditional blood lipid control category was used (LDL–C<3.0 mmol/L, TC<5.0 mmol/L, and TG<1.7 mmol/L). While this approach allows the achievement of target levels for low-risk groups to be determined assuming underestimation of lipid control deficit in higher-risk groups, the blood lipid profile was not adequately controlled. Moreover, the epidemiological approach ensured comparability with several population-based trials, including those with a long-term follow-up. The results of the analysis, which are limited to the Novosibirsk sample, are not extrapolated to other regions of the Russian Federation. At the same time, the study of a typical urban population was characterized by a country-specific epidemiological profile, medical care practices, and comparable cardiovascular mortality rates. Thus, the results indicated on the example of a specific Russian population that LLT is not sufficiently used. The analysis in the sample of mainly elderly age limits the generalization of results; however, the greater prevalence of CMDs in elderly patients permits a clearer presentation of the LLT profile in the more robust population.

Although there are a series of works analyzing LLT in the Russian outpatient clinical studies [16, 37, 38, 40], only sporadic population-based Russian data on LLT were published in 2012–2014 [27]; for this reason, we carried out monitoring at the population level for the current period. The analysis confirmed the inadequate frequency of LLT and inadequate control of blood lipid levels among patients receiving LLT (70% of patients with CMDs and >50% of elderly patients with CAD). While the frequency of blood lipid control is virtually independent of sex in the elderly CAD study sample, male patients with DM type 2 and DLP are more likely to have ineffective control than female patients.

Conclusion

In the population sample of 55–84-year-old patients examined in a typical Russian city in 2015–2017, almost 90% of the subjects had dyslipidemia or cardiometabolic disease; about 75% of these should have controlled blood lipid levels. Blood lipid control was achieved in about 20% of patients with coronary artery disease; about 40% of patients were receiving lipid-lowering therapy. Among patients with type 2 diabetes or dyslipidemia, lipid levels were controlled in about 10% of the population, with about 25% of patients receiving lipid-lowering therapy. The frequency of blood lipid

control was equally inadequate in male and female patients with coronary artery disease; male patients with diabetes mellitus type 2 and dyslipidemia achieved blood lipid control less frequently than female patients.

About 70% of patients with dyslipidemia and cardiometabolic disease, as well as more than 50% of patients with coronary artery disease, did not receive lipid-lowering therapy; this significantly contributed to the inadequate control of blood levels of atherogenic lipids during the primary and secondary prevention of atherosclerotic cardiovascular diseases.

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REFERENCES

1. Townsend N, Nichols M, Scarborough P, Rayner M. Cardiovascular disease in Europe – epidemiological update 2015. European Heart Journal. 2015;36(40):2696–705. DOI: 10.1093/eurheartj/ehv428
2. Federal State Statistics Service. Russian statistical yearbook 2019. Statistical handbook. -M.: Rosstat;2019. - 708 p. [Russian: Федеральная служба государственной статистики. Российский статистический ежегодник. 2019. Статистический сборник. – М.:Росстат; 2019. –708с. Доступно на: https://rosstat.gov.ru/storage/mediabank/Ejegodnik_2019.pdf]. ISBN 978-5-89476-473-3
3. Federal State Statistics Service. Natural movement of the population in the context of the subjects of the Russian Federation. 2019. [Russian: Федеральная служба государственной статистики. Естественное движение населения в разрезе субъектов российской федерации. 2019. Доступно на: https://www.gks.ru/free_doc/2019/demo/edn10-19.htm] [Internet] 2019.
4. Mach F, Baigent C, Catapano AL, Koskinas KC, Casula M, Badimon L et al. 2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk. European Heart Journal. 2020;41(1):111–88. DOI: 10.1093/eurheartj/ehz455
5. Rodriguez F, Maron DJ, Knowles JW, Virani SS, Lin S, Heidenreich PA. Association Between Intensity of Statin Therapy and Mortality in Patients With Atherosclerotic Cardiovascular Disease. JAMA Cardiology. 2017;2(1):47–54. DOI: 10.1001/jamacardio.2016.4052
6. Ference BA, Ginsberg HN, Graham I, Ray KK, Packard CJ, Bruckert E et al. Low-density lipoproteins cause atherosclerotic cardiovascular disease. 1. Evidence from genetic, epidemiologic, and clinical studies. A consensus statement from the European Atherosclerosis Society Consensus Panel. European Heart Journal. 2017;38(32):2459–72. DOI: 10.1093/eurheartj/ehx144
7. Baigent C, Keech A, Kearney PM, Blackwell L, Buck G, Pollicino C et al. Efficacy and safety of cholesterol-lowering treatment: prospective meta-analysis of data from 90 056 participants in 14 randomised trials of statins. The Lancet. 2005;366(9493):1267–78. DOI: 10.1016/S0140-6736(05)67394-1
8. Graham IM, Catapano AL, Wong ND. Current guidelines on prevention with a focus on dyslipidemias. Cardiovascular Diagnosis and Therapy. 2017;67(Suppl 1):S4–10. DOI: 10.21037/cdt.2017.04.04
9. Piepoli MF, Hoes AW, Agewall S, Albus C, Brotons C, Catapano AL et al. 2016 European Guidelines on cardiovascular disease prevention in clinical practice: The Sixth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of 10 societies and by invited experts) Developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR). European Heart Journal. 2016;37(29):2315–81. DOI: 10.1093/eurheartj/ehw106
10. Catapano AL, Graham I, De Backer G, Wiklund O, Chapman MJ, Drexel H et al. 2016 ESC/EAS Guidelines for the Management of Dyslipidaemias: The Task Force for the Management of Dyslipidaemias of the European Society of Cardiology (ESC) and European Atherosclerosis Society (EAS) Developed with the special contribution of the European Assocciation for Cardiovascular Prevention & Rehabilitation (EACPR). Atherosclerosis. 2016;253:281–344. DOI: 10.1016/j.atherosclerosis.2016.08.018
11. Grundy SM, Stone NJ, Bailey AL, Beam C, Birtcher KK, Blumenthal RS et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation. 2019;139(25):e1082–143. DOI: 10.1161/CIR.0000000000000625
12. Kukharchuk V.V., Ezhov M.V., Sergienko I.V., Arabidze G.G., Bubnova M.G., Balakhonova T.V. et al. Diagnostics and correction of lipid metabolism disorders in order to prevent and treat of atherosclerosis Russian recommendations VII revision. Atherosclerosis and dyslipidemia. 2020;1(38):7–40. [Russian: Кухарчук В.В., Ежов М.В., Сергиенко И.В., Арабидзе Г.Г., Бубнова М.Г., Балахонова Т.В. и др. Диагностика и коррекция нарушений липидного обмена с целью профилактики и лечения атеросклероза. Российские рекомендации, VII пересмотр. Атеросклероз и дислипидемии. 2020;1(38):7-40]. DOI: 10.34687/2219-8202.JAD.2020.01.0002
13. Ezhov M.V., Sergienko I.V., Aronov D.M., Arabidze G.G., Akhmedzhanov N.M., Bazhan S.S. et al. Diagnostics and correction of lipid metabolism disorders for the prevention and treatment of atherosclerosis. Revision VI. Atherosclerosis and Dyslipidemias. 2017;3(28):5–22. [Russian: Ежов М.В., Сергиенко И.В., Аронов Д.М., Арабидзе Г.Г., Ахмеджанов Н.М., Бажан С.С. и др. Диагностика и коррекция нарушений липидного обмена с целью профилактики и лечения атеросклероза. Российские рекомендации VI пересмотр. Атеросклероз и дислипидемии. 2017;3(28):5-22]
14. Jellinger PS, Handelsman Y, Rosenblit PD, Bloomgarden ZT, Fonseca VA, Garber AJ et al. American association of clinical endocrinologists and american college of endocrinology guidelines for management of dyslipidemia and prevention of cardiovascular disease. Endocrine Practice. 2017;23(Suppl 2):1–87. DOI: 10.4158/EP171764.APPGL
15. De Backer G, Jankowski P, Kotseva K, Mirrakhimov E, Reiner Ž, Rydén L et al. Management of dyslipidaemia in patients with coronary heart disease: Results from the ESC-EORP EUROASPIRE V survey in 27 countries. Atherosclerosis. 2019;285:135–46. DOI: 10.1016/j.atherosclerosis.2019.03.014

ISSN 0022-9040. Kardiologiia. 2021;61(12). DOI: 10.18087/cardio.2021.12.n1558

16. Shlyakhto E.V., Zvartau N.E., Villevalde S.V., Yakovlev A.N., Soloveva A.E., Alieva A.S. et al. Cardiovascular risk management system: prerequisites for developing, organization principles, target groups. Russian Journal of Cardiology. 2019;24(11):69–82. [Russian: Шляхто Е.В., Звартау Н.Э., Виллевальде С.В., Яковлев А.Н., Соловьева А.Е., Алиева А.С. и др. Система управления сердечно-сосудистыми рисками: предпосылки к созданию, принципы организации, таргетные группы. Российский кардиологический журнал. 2019;24(11):69–82]. DOI: 10.15829/1560-4071-2019-11-69-82
17. de la Sierra A, Pintó X, Guijarro C, Miranda JL, Callejo D, Cuervo J et al. Prevalence, Treatment, and Control of Hypercholesterolemia in High Cardiovascular Risk Patients: Evidences from a Systematic Literature Review in Spain. Advances in Therapy. 2015;32(10):944–61. DOI: 10.1007/s12325-015-0252-y
18. Pogosova N.V., Oganov R.G., Boytsov S.A., Ausheva A.K., Sokolova O.Yu., Kursakov A.A. et al. Monitoring the Secondary Prevention of Coronary Artery Disease in Europe and Russia: Results of the Russian Part of the International Multicenter Study EUROASPIRE IV. Kardiologiia. 2015;55(12):99–107. [Russian: Погосова Н.В., Оганов Р.Г., Бойцов С.А., Аушева А.К., Соколова О.Ю., Курсаков А.А. и др. Мониторинг вторичной профилактики ишемической болезни в России и Европе: результаты российской части международного многоцентрового исследования EUROASPIRE IV. Кардиология. 2015;55(12):99-107]
19. Kotseva K, De Backer G, De Bacquer D, Rydén L, Hoes A, Grobbee D et al. Lifestyle and impact on cardiovascular risk factor control in coronary patients across 27 countries: Results from the European Society of Cardiology ESC-EORP EUROASPIRE V registry. European Journal of Preventive Cardiology. 2019;26(8):824–35. DOI: 10.1177/2047487318825350
20. American Heart Association. Prevalence and Number of US Adults Eligible for and Currently Using Statin Therapy by Race/Ethnicity (NHANES 2011-2014) – Health Metrics. 2018. [Internet] 2018. Available at: https://aha2017chme.wpengine.com/prevalence-and-number-of-us-adults-eligible-for-and-currently-using-statin-therapy-by-race-ethnicity-nhanes-2011-2014/
21. Gu Q, Paulose-Ram R, Burt VL, Kit BK. Prescription cholesterol-lowering medication use in adults aged 40 and over: United States, 2003-2012. NCHS data brief. 2014;177:1–8. PMID: 25536410
22. Vega GL, Grundy SM. Current trends in non–HDL cholesterol and LDL cholesterol levels in adults with atherosclerotic cardiovascular disease. Journal of Clinical Lipidology. 2019;13(4):563–7. DOI: 10.1016/j.jacl.2019.05.012
23. Mefford MT, Rosenson RS, Deng L, Tanner RM, Bittner V, Safford MM et al. Trends in Statin Use Among US Adults With Chronic Kidney Disease, 1999–2014. Journal of the American Heart Association. 2019;8(2):e010640. DOI: 10.1161/JAHA.118.010640
24. Carroll MD, Fryar CD, Nguyen DT. Total and High-density Lipoprotein Cholesterol in Adults: United States, 2015-2016. NCHS data brief. 2017;290:1–8. PMID: 29155686
25. Muromtceva G.A., Kontsevaya A.V., Konstantinov V.V., Artamonova G.V., Gatagonova T. M., Duplyakov D.V. et al. The prevalence of noninfectious disease risk factors in the Russian population in 2012-2013. Results of the ESSE-RF study. Cardiovascular Therapy and Prevention. 2014;13(6):4–11. [Russian: Муромцева Г.А., Концевая А.В., Константинов В.В., Артамонова Г.В., Гатагонова Т.М., Дупляков Д.В. и др. Распространенность факторов риска неинфекционных заболеваний в российской популяции в 2012–2013 гг. Результаты исследования ЭССЕ-РФ. Кардиоваскулярная терапия и профилактика. 2014;13(6):4-11]. DOI: 10.15829/1728-8800-2014-6-4-11
26. Meshkov A.N., Ershova A.I., Deev A.D., Metelskaya V.A., Zhernakova Yu.V., Rotar O.P. et al. Distribution of lipid profile values in economically active men and women in Russian Federation: results of the esse-rf study for the years 2012-2014. Cardiovascular Therapy and Prevention. 2017;16(4):62–7. [Russian: Мешков А.Н., Ершова А.И., Деев А.И., Метельская В.А., Жернакова Ю.В., Ротарь О.П. и др. Распределение показателей липидного спектра у мужчин и женщин трудоспособного возраста в Российской Федерации: результаты исследования ЭССЕ-РФ за 2012-2014гг. Кардиоваскулярная терапия и профилактика. 2017;16(4):62-7]. DOI: 10.15829/1728-8800-2017-4-62-67
27. Shalnova S.A., Deev A.D., Metelskaya V.A., Evstifeeva S.E., Rotar O.P., Zhernakova Yu.V. et al. Awareness and treatment specifics of statin therapy in persons with various cardiovasular risk: the study ESSE-RF. Cardiovascular Therapy and Prevention. 2016;15(4):29–37. [Russian: Шальнова С.А., Деев А.Д., Метельская В.А., Евстифеева С.Е., Ротарь О.П., Жернакова Ю.В. и др. Информированность и особенности терапии статинами у лиц с различным сердечно-сосудистым риском: исследование ЭССЕ-РФ. Кардиоваскулярная терапия и профилактика. 2016;15(4):29-37]. DOI: 10.15829/1728-8800-2016-4-29-37
28. NCD Risk Factor Collaboration (NCD-RisC), Taddei C, Zhou B, Bixby H, Carrillo-Larco RM, Danaei G et al. Repositioning of the global epicentre of non-optimal cholesterol. Nature. 2020;582(7810):73–7. DOI: 10.1038/s41586-020-2338-1
29. Malyutina S.K., Shapkina M.Yu., Ryabikov A.N., Mazdorova E.V., Avdeeva E.M., Shcherbakova L.V. et al. Characteristics of main drug therapy types in subjects with atrial fibrillation in population. Cardiovascular Therapy and Prevention. 2018;17(1):43–8. [Russian: Малютина С.К., Шапкина М.Ю., Рябиков А.Н., Маздорова Е.В., Авдеева Е.М., Щербакова Л.В. и др. Характеристика основных видов медикаментозной терапии у лиц с фибрилляцией предсердий в популяции. Кардиоваскулярная терапия и профилактика. 2018;17(1):43-8]. DOI: 10.15829/1728-8800-2018-1-43-48
30. Malyutina S.K., Mazdorova E.V., Shapkina M.Yu., Avdeeva E.M., Maslacov N.A., Simonova G.I. et al. The profile of drug treatment in subjects aged over 50 years with hypertension in an urban russian population. Kardiologiia. 2020;60(3):21–9. [Russian: Малютина С.К., Маздорова Е.В., Шапкина М.Ю., Авдеева Е.М., Маслацов Н.А., Симонова Г.И. и др. Профиль медикаментозной терапии у лиц с артериальной гипертензией старше 50 лет в городской российской популяции. Кардиология. 2020;60(3):21-9]. DOI: 10.18087/cardio.2020.3.n948
31. Peasey A, Bobak M, Kubinova R, Malyutina S, Pajak A, Tamosiunas A et al. Determinants of cardiovascular disease and other non-communicable diseases in Central and Eastern Europe: Rationale and design of the HAPIEE study. BMC Public Health. 2006;6(1):255. DOI: 10.1186/1471-2458-6-255
32. Williams B, Mancia G, Spiering W, Agabiti Rosei E, Azizi M, Burnier M et al. 2018 ESC/ESH Guidelines for the management of arterial hypertension: The Task Force for the management of arterial hypertension of the European Society of Cardiology and the European Society of Hypertension. Journal of Hypertension. 2018;36(10):1953–2041. DOI: 10.1097/HJH.0000000000001940
33. Cardiovascular Survey Methods. Rose GA, editor -Genève: WHO;1984. - 188 p. ISBN 978-92-4-240056-4
34. Kalinina A.M., Shalnova S.A., Gambaryan M.G., Eganyan R.A., Muromtseva G.A., Bochkareva E.V. et al. Epidemiological methods for identifying the main chronic non-communicable diseases and risk factors during mass population surveys. Methodical guide. Edited by Prof. Boytsov S.A. - M.: GNICPM; 2015. - 96p. Av. at: https://gnicpm.ru/wp-content/uploads/2020/01/metodposobie_epid_metody_viyavleniya_hniz_pri_massovih_obsledovaniyah.pdf. [Russian: Калинина А.М., Шальнова С.А., Гамбарян М.Г., Еганян Р.А., Муромцева Г.А., Бочкарева Е.В. и др. Эпидемиологические методы выявления основных хронических неинфекционных заболеваний и факторов риска при массовых обследованиях населения. Методическое пособие. Под ред. проф. Бойцова С.А. - М.: ГНИЦПМ; 2015. - 96с. Доступно на: https://gnicpm.ru/wp-content/uploads/2020/01/metodposobie_epid_metody_viyavleniya_hniz_pri_massovih_obsledovaniyah.pdf]
35. Rydén L, Grant PJ, Anker SD, Berne C, Cosentino F, Danchin N et al. ESC Guidelines on diabetes, pre-diabetes, and cardiovascular diseases developed in collaboration with the EASD: The Task Force on diabetes, pre-diabetes, and cardiovascular diseases of the European Society of Cardiology (ESC) and developed in collaboration with the European Association for the Study of Diabetes (EASD). Europe-

an Heart Journal. 2013;34(39):3035–87. DOI: 10.1093/eurheartj/eht108
36. WHO Collaborating Centre for Drug Statistics Methodology. ATC Index with DDDs. [Internet] Available at: https://www.whocc.no/atc_ddd_index_and_guidelines/atc_ddd_index/
37. Boytsov S.A., Luk'yanov M.M., Yakushin S.S., Martsevich S.Yu., Vorobyov A.N., Zagrebelny A.V. et al. Cardiovascular diseases registry (RECVAZA): diagnostics, concomitant cardiovascular pathology, comorbidities and treatment in the real outpatient-polyclinic practice. Cardiovascular Therapy and Prevention. 2014;13(6):44–50. [Russian: Бойцов С.А., Лукьянов М.М., Якушин С.С., Марцевич С.Ю., Воробьев А.Н., Загребельный А.В. и др. Регистр кардиоваскулярных заболеваний (РЕКВАЗА): диагностика, сочетанная сердечно-сосудистая патология, сопутствующие заболевания и лечение в условиях реальной амбулаторно-поликлинической практики. Кардиоваскулярная терапия и профилактика. 2014;13(6):44-50]. DOI: 10.15829/1728-8800-2014-6-44-50
38. Akhmedzhanov N.M., Nebieridze D.V., Safaryan A.S., Vygodin V.A., Shuraev A.Yu., Tkacheva O.N. et al. Analysis of hypercholesterolemia prevalence in the outpatient practice (according to the ARGO study): part I. Rational Pharmacotherapy in Cardiology. 2015;11(3):253–60. [Russian: Ахмеджанов Н.М., Небиеридзе Д.В., Сафарян А.С., Выгодин В.А., Шураев А.Ю., Ткачева О.Н. и др. Анализ распространенности гиперхолестеринемии в условиях амбулаторной практики (по данным исследования АРГО): часть I. Рациональная фармакотерапия в кардиологии. 2015;11(3):253-60]. DOI: 10.20996/1819-6446-2015-11-3-253-260
39. Peters SAE, Muntner P, Woodward M. Sex Differences in the Prevalence of, and Trends in, Cardiovascular Risk Factors, Treatment, and Control in the United States, 2001 to 2016. Circulation. 2019;139(8):1025–35. DOI: 10.1161/CIRCULATIONAHA.118.035550
40. Ershova A.I., Meshkov A.N., Yakushin S.S., Loukianov M.M., Moseychuk K.A., Martsevich S.Yu. et al. Diagnosis and treatment of patients with severe hypercholesterolemia in real outpatient practice (according to the RECVASA registry). Rational Pharmacotherapy in Cardiology. 2014;10(6):612–6. [Russian: Ершова А.И., Мешков А.Н., Якушин С.С., Лукьянов М.М., Мосейчук К.А., Марцевич С.Ю. и др. Диагностика и лечение больных с выраженной гиперхолестеринемией в реальной амбулаторно-клинической практике (по данным регистра РЕКВАЗА). Рациональная фармакотерапия в кардиологии. 2014;10(6):612-6]. DOI: 10.20996/1819-6446-2014-10-6-612-616

ISSN 0022-9040. Kardiologiia. 2021;61(12). DOI: 10.18087/cardio.2021.12.n1558