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Assessment of risk factors for atherosclerosis in individuals of different categories of cardiovascular risk using the Aterostop calculator

Aim	To analyze first results of using the Aterostop calculator for a comprehensive evaluation of the risk for cardiovascular diseases (CVD).
Material and methods	A cross-sectional study analyzed major and additional risk factors in 460 subjects without apparent disease and in patients with documented CVD of atherosclerotic origin using the application (calculator) Aterostop developed in the National Medical Research Center of Cardiology in Moscow, Russia.
Results	45.4% of evaluated persons belonged to the categories of very high and extreme risk. Age and frequencies of smoking, arterial hypertension, and diabetes mellitus (DM) increased with the increase in risk; the growth of DM was exponential. 129 (28%) individuals used lipid-lowering medications at the time of study. Their plasma levels of low-density lipoprotein cholesterol (LDL–C) were significantly lower than in those who did not received this treatment. However, achieving the target level was inversely proportional to the risk: the greatest proportion of individuals who reached the LDL–C target was in the category of low risk and the smallest proportion was in the category of extreme risk (75% vs. 3.7%, respectively).
Conclusion	The results obtained with the calculator Aterostop were consistent with earlier reports of insufficient effectiveness of primary and secondary prevention of atherosclerotic CVDs, which requires more tight and fruitful cooperation of the physician and the patient.

Keywords	Atherosclerosis; risk of cardiovascular diseases; risk factors; cholesterol
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Introduction

Cardiovascular diseases (CVDs) are the main cause of mortality in Europe [1]. In Russia, in particular, cardiovascular mortality caused by atherosclerosis remains high. CVDs are associated with a high prevalence of disability and significant material costs. Atherosclerosis is associated with risk factors (RFs), such as advanced age, increased total cholesterol (TC) levels, low-density lipoprotein cholesterol (LDL–C), non-high-density lipoprotein cholesterol (non-HDL–C), decreased high-density lipoprotein cholesterol (HDL–C), diabetes mellitus (DM), arterial hypertension (AH), chronic kidney disease (CKD), smoking, as well as a family history of CVDs of atherosclerotic origin [2]. The risk of developing CVDs is particularly high when several RFs are present. The primary basis for the prevention and treatment of CVDs of atherosclerotic origin consists in managing existing RFs.

An innovative application for the complex assessment of cardiovascular risk, Aterostop, developed by the Russian National Cardiology Research Center [3] is based on the new guidelines of the National Atherosclerosis Society [4]. The application, which is implemented as a browser-based web version and a mobile app for Android and iOS devices, can be used to assesses risk, assess the achievement of target plasma levels of LDL–C and provide recommendations for adjusting lipid-lowering therapy. Intended for both physician and patient use, the application significantly increases levels of awareness concerning personal cardiovascular risk and possible measures for reducing it.

Objective

Analyze the first results of using the Aterostop calculator (app) to estimate cardiovascular risk, the prevalence of main RFs, the degree of their correction, LDL–C plasma levels, as well as collecting information on the achievement of LDL–C target levels according to the risk category in a sufficiently large sample of patients

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in the context of primary and secondary prevention of atherosclerosis.

Material and methods

The Aterostop calculator (app) consists of a form to be filled in by a user whose fields describe medical history and several quantitative measures. The algorithm underlying the app's functionality uses the data obtained from the form to calculate the risk category for a particular patient, evaluate the achievement of the target LDL–C level and provide recommendations on how to achieve it (if necessary). The app is implemented as a publicly-available, cross-platform Internet resource (URL: https://aterostop.ru/calc/) as well as in the form of a free mobile app (Aterostop) for any Android or iOS devices, available for download from the Google Play Store and Apple App Store, respectively. After processing the anonymized information, the application allows the distribution of atherosclerosis phenotypes and cardiovascular risk factors to be monitored at the population level. Alerts concerning changes to treatment regimens are only provided according to a physician's advice. The app has a clear and simple interface.

The application algorithm is implemented as follows: the necessary patient data are specified, intermediate parameters are calculated according to certain formulas, and then the final parameters are calculated. Based on the final parameters, a text statement is provided to the patient, which includes a report on cardiovascular risk, the achievement of target plasma levels of LDL–C, and any changes in lipid-lowering therapy.

On the basis of the calculation results, the estimated likelihood of life-threatening cardiovascular complication (CVC) in the following ten years is displayed. The second module of the results includes the recommended treatment of dyslipidemia and prevention of CVCs, while the third module assesses achievement of the target LDL–C levels and proposes options for adjusting lipid-lowering therapies. The fourth module includes the calculation of additional measures: body mass index (BMI) including an indication of underweight or overweight status, as well as a calculation of glomerular filtration rate using the CKD-EPI formula with an indication of CKD stage.

The 10-year likelihood of life-threatening CVCs is displayed as follows: low risk (<1%); moderate risk (1–4%); high risk (5–9%); very high risk (10–45%); extreme risk (>45%). The corresponding target levels of LDL–C are: ≤3.0 mmol/L; ≤2.6 mmol/L; ≤1.8 mmol/L; ≤1.4 mmol/L; ≤1.4 mmol/L; best possible ≤1.0 mmol/L.

The data entered by the users into the Aterostop app in 2019–2020 was evaluated in September 2020. Questionable data, such as blank and incomplete modules, were detected during the enrollment. A total of 460 male and female subjects were included in the final analysis. The study was conducted according to the Declaration of Helsinki of the World Medical Association.

The obtained data were processed with the Statistica software suite (Statsoft, US). The data collected were represented by various scales, continuous and binary variables. The main analysis tools were descriptive statistics, including hypothesis testing using statistical tests and diagrams. The normality of the distribution of quantitative variables was tested using the Shapiro-Wilk test. For the intergroup comparisons, the T-test was used for the normal distribution of variables, while the Mann-Whitney test was used for non-normal distribution. Depending on the type of distribution, the quantitative data are presented as the mean and standard deviation (M±DM) or the median and inter-quartile range (Me [Q1; Q3]). The absolute and relative frequencies were calculated to analyze the qualitative data. The differences were statistically significant at $p < 0.05$.

Results

A total of 460 male and female subjects were included in the analysis. The distribution across cardiovascular risk categories was as follows: low risk (n=96), moderate risk (n=100), high risk (n=55), very high risk (n=135), and extreme risk (n=74). The categories of very high and extreme risks included 45.4% of the subjects (Figure 1).

The subjects were from 19 to 90 years old; the median age was 53.5 [39; 65] years. The data on the age composition is presented by risk categories presented in Figure 2. These are consistent with the known provision that older age is directly related to increased cardiovascular risk.

The subjects of different sex were represented equally: 49.6% of males and 50.4% of females. In the sex-specific analysis according to the risk categories, there were predictably more female subjects in the low-risk group (Figure 3).

Smoking, AH and DM comprise the main RFs for the development of CVDs of atherosclerotic origin. A gradual increase in the prevalence of these RFs is shown according to the risk categories in Figure 4; as for DM, it was characterized by exponential growth.

The sex-specific analysis showed that the prevalence of smoking was higher in male subjects in all risk categories, excluding the low-risk group (Figure 5).

Average waist circumference (WS), which should not normally exceed 102 cm for males and 88 cm for females, was 94.1±13.3 cm in males and 86.1±16.9 cm for females. The mean values of the other additional RF and BMI were increased in all risk categories except low risk: 24.1, 27.9,

Figure 1. Distribution of subjects (n=460) across risk categories

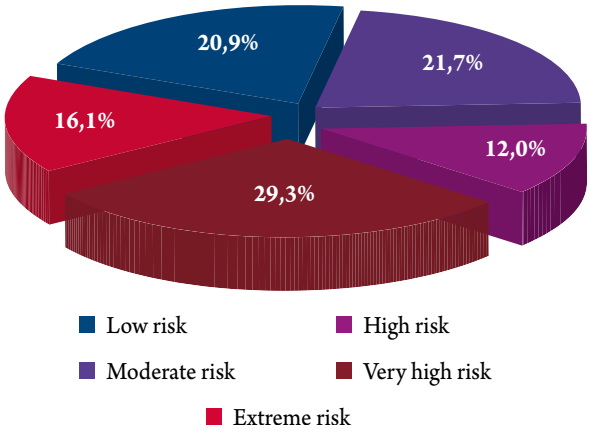


Figure 2. Mean age of the subjects according to risk categories

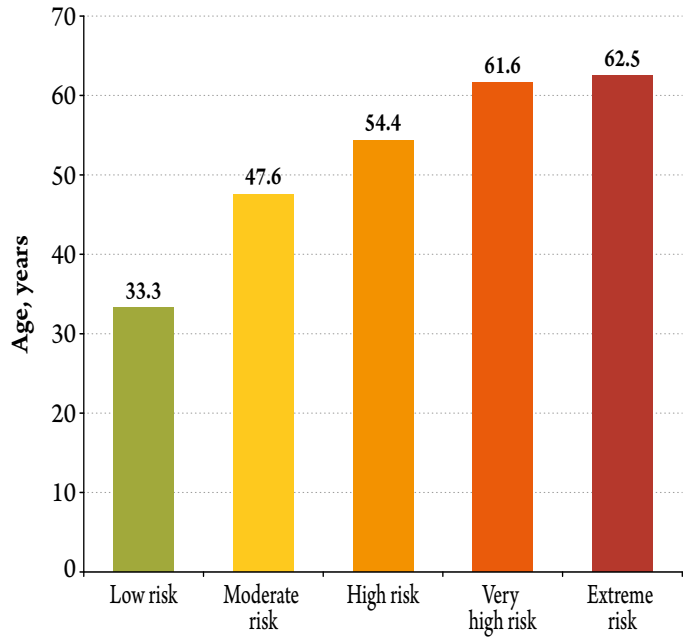
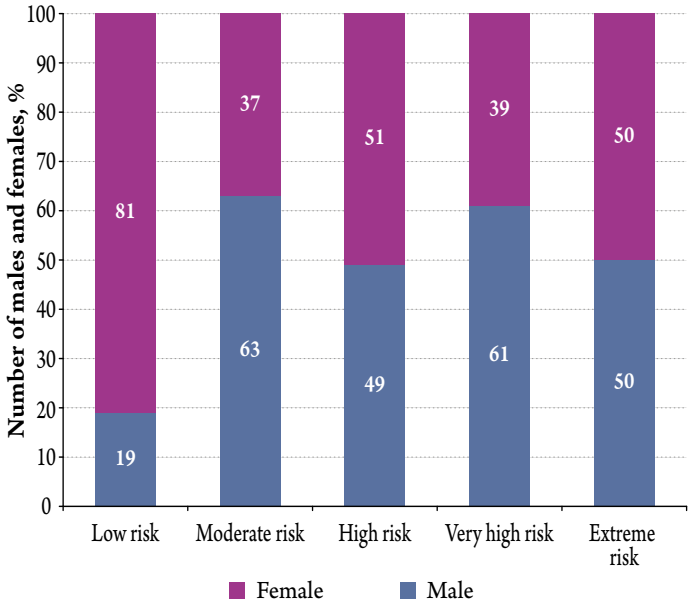


Figure 3. Distribution of subjects of different sexes according to risk categories



27.8, 28.9 and 30.2 kg/m² in the low-, moderate-, high-, very high- and extreme risk categories, respectively.

CVDs of the atherosclerotic origin or other diseases/pathological conditions contributing to their development are presented for all the subjects in Figure 6.

The frequencies of vascular surgeries were: transluminal balloon coronary angioplasty with stenting – 10.7%; coronary bypass – 3.3%; revascularization for peripheral atherosclerosis – 1.7%.

The data on blood lipid profile were of particular interest with respect to the described calculator. The mean levels of TC and LDL–C are shown according to the risk categories in Figure 7.

129 (28%) patients took lipid-lowering drugs at the time of using the calculator, 127 (27.6%) refused lipid-

Figure 4. Prevalence of major cardiovascular risk factors according to risk categories

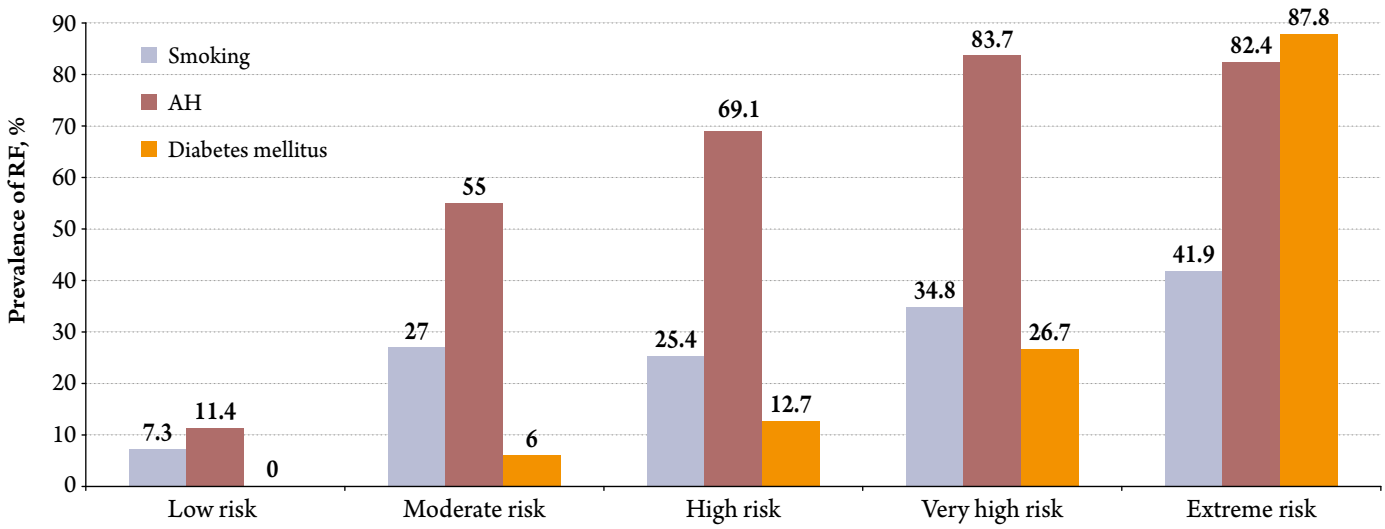


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Figure 5. Smoking among subjects of different sexes according to risk categories

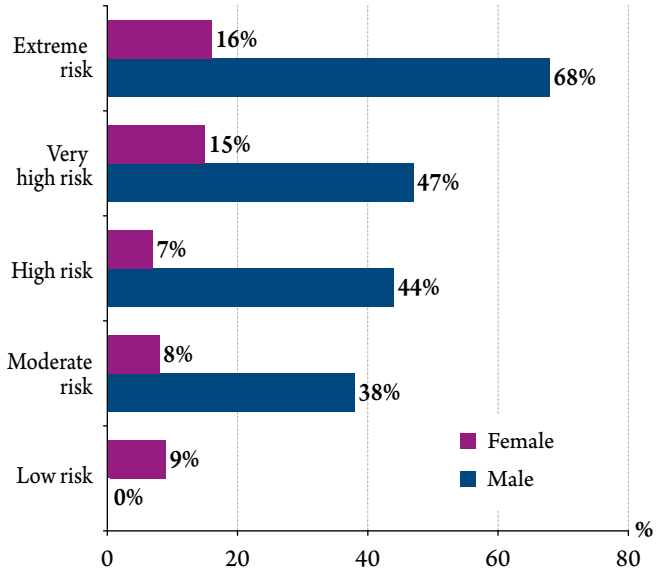
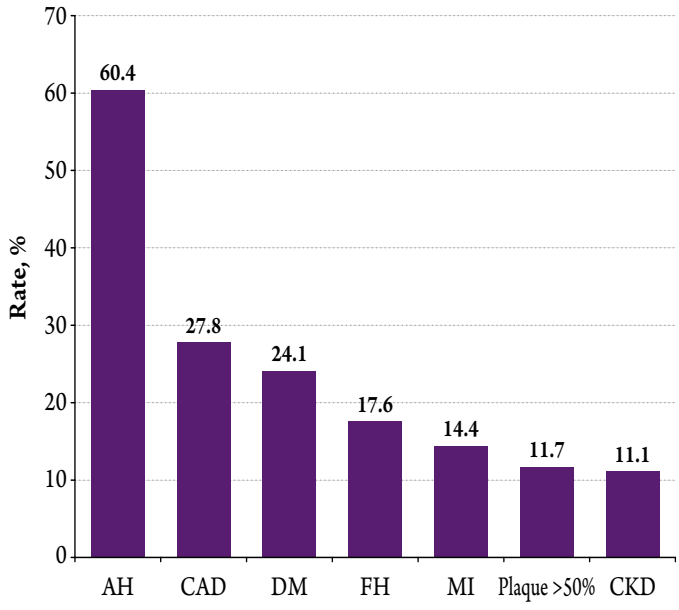
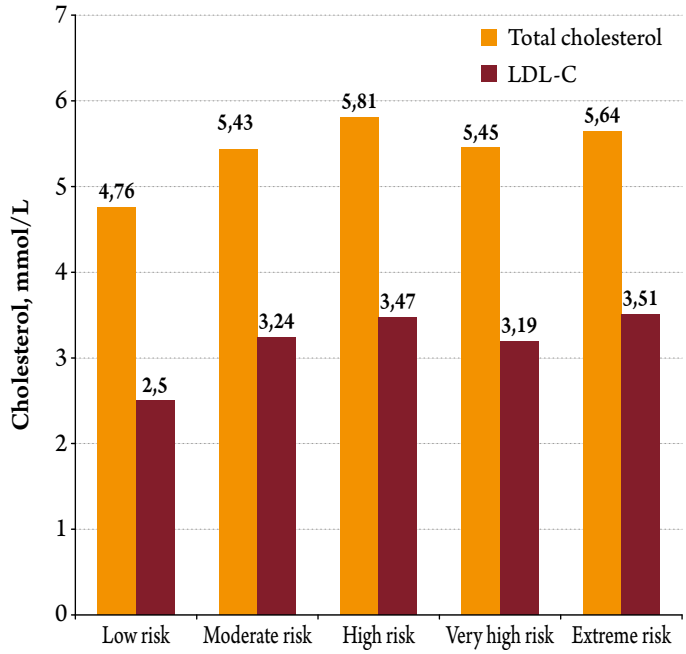


Figure 6. Prevalence of cardiovascular diseases of atherosclerotic origin and other diseases/pathological conditions in the study population (n=460)



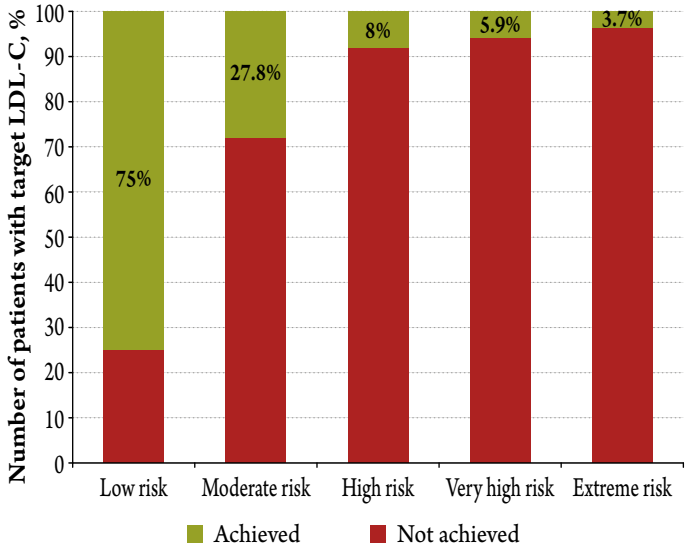
AH – arterial hypertension; CAD – coronary artery disease; DM – diabetes mellitus; FH – familial hypercholesterolemia; MI – myocardial infarction; CKD – chronic kidney disease.

Figure 7. Mean plasma levels of total cholesterol and low-density lipoprotein cholesterol according to risk categories



LDL-C, low-density lipoprotein cholesterol.

Figure 8. Achievement of target plasma levels of low-density lipoprotein cholesterol according to risk categories



lowering therapy, while 204 (44.3%) did not provide data. The comparison of blood lipid profiles in subjects receiving and not receiving the lipid-lowering therapy showed significantly lower LDL–C levels in the treated subjects irrespective of sex (Table 1). However, the analysis of the LDL–C target achievement carried out according the risk categories showed that the degree of the target achievement was inversely proportional to the risk: there was the largest number of individuals who achieved the LDL–C target level in the low-risk group, and the smallest number in the extreme-risk category (Figure 8).

Discussion

In Russian clinical practice, there are no examples of implementing complex cardiovascular risk calculation algorithms that provide objective information based on large population studies, which can be used independently

Table 1. Comparison of the mean plasma levels of total cholesterol and low-density lipoprotein cholesterol with/without lipid-lowering therapy

Measure	Male		Female	
	Therapy (–) (n=60)	Therapy (+) (n=71)	Therapy (–) (n=67)	Therapy (+) (n=58)
Total cholesterol, mmol/L	5.31 ± 1.12	5.1 ± 1.32	5.58 ± 1.21	5.05 ± 1.33*
Triglycerides, mmol/L	1.6 [1.0; 2.13]	1.81 [1.34; 2.2]	1.7 [1.15; 2.73]	1.7 [1.27; 2.0]
LDL-C, mmol/L	3.49 ± 1.21	2.99 ± 1.26*	3.37 ± 1.61	2.82 ± 1.12**
HDL-C, mmol/L	1.16 ± 0.37	1.18 ± 0.36	1.63 ± 0.57	1.61 ± 0.63

* – p=0.01; ** – p=0.02. LDL-C – low density lipoprotein cholesterol; HDL-C – high density lipoprotein cholesterol.

to screen likely CVDs and their complications. The well-known Systematic COronary Risk Estimation (SCORE) score, which is used to predict fatal CVCs in the general population occurring in the following ten years, takes into account five clinical and demographic characteristics: sex, age (40 years and older), smoking status, TC and systolic blood pressure (BP) [5]. Comprising the prototype of the Aterostop calculator, the approaches are essentially comparable. However, the main drawback of the SCORE assessment, which is intended for the European population at least 40 years old without documented CVDs, is its low coverage. Aterostop was developed as a comprehensive estimation of cardiovascular risk with determination of LDL–C target levels and possible adjustment of individual lipid-lowering therapy. This is achieved by using some additional data (family and personal histories of hypercholesterolemia and CVDs, plasma levels of TC and LDL–C), assessing the probability of familial hypercholesterolemia, quantifying the 1-year risk of life-threatening CVCs and determining the target LDL–C level and its achievement/non-achievement, according to which criteria the lipid-lowering therapy is adjusted.

This study showed that Aterostop could provide valuable practical information at individual and higher (cohort) levels. The study showed that almost 50% of those who used the calculator had a documented CVD of atherosclerotic origin. The risk naturally increased with age, confirming once again that age is one of the most stable determinants of cardiovascular risk. Significant sex-specific differences (with a female predominance) were observed only in the low-risk category. The ratio between the sexes was more similar in other risk categories, possibly due to the onset of menopause and the loss of estrogen protection in females. For example, the mean age was 54.4 years in the high-risk group, which is associated with the cessation of periods and the onset of menopause for most females.

The main RFs, such as smoking, AH and DM, demonstrated a linear frequency increase as the cardiovascular risk grows, with exponential growth for DM. The sex-specific analysis found that smoking rates were significantly higher among male subjects in all risk categories, except for the low-risk category, which included no smoking males. Our findings are consistent with the ESC-EORP EUROASPIRE V register that summarizes the surveys of patients with verified coronary atherosclerosis conducted in 27 countries. According to this register, most patients continued unhealthy lifestyles, including smoking, unhealthy diet and hypodynamy; most patients also failed to achieve the target levels of BP [6].

The increased mean WS (86.1 cm) in female subjects indicated more women with abdominal obesity and probable metabolic syndrome. Given the BMI values, obesity was typical of most categories except for the low-risk group.

As mentioned above, nearly 50% of the analyzed individuals had CVDs of atherosclerotic origin, mainly consisting of coronary artery disease, including myocardial infarction. Although the incidence of severe hereditary lipid disorder, familial hypercholesterolemia, was also high, this diagnosis should be confirmed by a trained specialist (lipidologist) and/or DNA analysis.

The blood lipid profile was of particular interest. The target plasma level of LDL–C depends on the risk category, i.e., the lower is LDL–C, the higher is the risk. However, the obtained data showed no such trend. Moreover, mean LDL–C (3.19–3.51 mmol/L) was higher in all risk categories from moderate risk to extreme risk than in the low-risk group (2.5 mmol/L), i.e., lipid-lowering therapy was inadequate or absent. Although the comparison of lipid composition in subjects both with and without lipid-lowering therapy showed significantly lower plasma levels of LDL–C in the treated subjects of both sexes, the analysis showed that the percentage of those who achieved target LDL–C decreased as the risk increased, even though all patients in the very high and extreme risk groups should have received lipid-lowering drugs. Compared to the data of the Russian part of the DYSIS study published in 2012 [7], the percentage of persons who achieved the target plasma levels of LDL–C (according to the risk categories) calculated using Aterostop was relatively lower: <1.8 mmol/L (12.2 and 8%, respectively) and <2.6 mmol/L (30.3 and 27.9%, respectively). However, the target LDL–C level of <3.0

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mmol/L, which is now recommended for the low-risk category, was achieved by a larger percentage of subjects than in the DYSIS sample (75 and 53.4%, respectively).

Conclusion

PThe results obtained using the Aterostop cardiovascular risk calculator mainly confirm previous findings demstrating failings in primary and secondary prevention of cardiovascular diseases of atherosclerotic origin, implying the need for a closer and more communicative relationship between the physician and the patient.

No conflict of interest is reported.

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