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Prevalence of a combination of hypertension and dyslipidemia among the adult population of a large East Siberian region

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Aim. To study the prevalence of a combination of two major cardiovascular risk factors, hypertension (HTN) and lipid metabolism disorders, among the Krasnoyarsk Krai population as a whole, as well as among men and women in different age groups.

Material and methods. We analyzed the data from a random representative sample of 1603 residents of the Krasnoyarsk city and Berezovsky district aged 25-64 years within the ESSE-RF epidemiological study. Statistical processing was performed using IBM SPSS 22 and Microsoft Office Excel 2007. The proportion of people with hypertension and dyslipidemia and 95% confidence intervals was calculated. The significance of differences in the prevalence of hypertension and dyslipidemia was tested using the chi-squared test with Yates' correction. Differences were considered significant at $p \leqslant 0,05$.

Results. The prevalence of a combination of HTN and any dyslipidemia was 40%, HTN + hypercholesterolemia — 31,6%, HTN + high low density lipoprotein cholesterol (LDL-C) — 32,3%, HTN + hypertriglyceridemia — 16,4%, HTN + reduced high density lipoprotein cholesterol (HDL-C) — 10,8%. This characteristic increased with age. The prevalence of a combination of HTN with hypercholesterolemia, with an increased LDL-C level, as well as HTN with any dyslipidemia in women aged 55-64 years was significantly higher than in men.

Conclusion. The prevalence of a combination of HTN with any dyslipidemia in the Krasnoyarsk Krai among the adult population aged 25-64 years was 40% and increased with age. In women aged 55-64 years, the prevalence of a combination of HTN with hypercholesterolemia, with an increased LDL-C level, as well as HTN with any dyslipidemia was significantly higher than in men.

Keywords: hypertension, dyslipidemia, lipitension, cardiovascular risk factors, epidemiology.

Relationships and Activities: none.

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Introduction

Epidemiology statistics indicate that >90% of hypertensive (HTN) patients in North America, Europe and the Middle East and >80% in Australia, Latin America and Asia have at least one additional cardiovascular risk factor [1]. In particular, the prevalence of dyslipidemia (DLP) among persons with HTN is ~1,2-1,5 times higher than in the general population [2-5].

In medical literature, the term dyslipidemic hypertension first appeared in the context of familial DLP [6], although later it received a broader interpretation. Dalal JJ, et al. (2012) proposed the term lipitension to denote the simultaneous presence of HTN and DLP and reported the need for "active identification, diagnosis, and management of these two risk factors together, as global cardiovascular risk factors" [7].

To date, a sufficient amount of epidemiological data has been accumulated in favor of the fact that the combination of HTN and lipid metabolism disorders not only sums up the risk of unfavorable cardiovascular outcomes (primarily of an atherosclerotic nature), but can also multiply this risk by 2-3 or more times. This is confirmed by a number of well-known works, such as the Framingham study [8], the Multiple Risk Factor Intervention Trial (MRFIT) [9], and the Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (INTERHEART) study [10]. The average prevalence of a combination of HTN and DLP in the general population is 15-31%, while significant differences are found depending on age, sex (in young and middle age, it is more often recorded among men), ethnicity (less often in Spaniards, more often among African Americans) [7, 11-13].

It should be emphasized that, in contrast to epidemiological observational studies, not all lipid metabolism parameters demonstrated their significant causal relationship with the development of atherosclerotic cardiovascular diseases, primarily coronary artery disease, when using such a sensitive genetic approach as the Mendelian randomization (MR). Thus, the last large-scale study by Zanetti D,

et al. (2020) using MR techniques showed the pathogenetic role of low-density lipoprotein cholesterol (LDL-C), triglycerides (TG), lipoprotein(a) and apolipoprotein B. However, as before, the role of high-density lipoprotein cholesterol (HDL-C) was not confirmed, which, according to the authors, is a simple biochemical marker rather than a true risk factor [14].

The same MR approach using meta-regression analysis has shown that a long-term (lifelong) genetic decrease in both LDL-C and systolic blood pressure (BP), and to an even greater extent, their combination, lead to a significant decrease in cardio-vascular risk [15]. Moreover, the first data appeared in favor of the fact that there may be a causal relationship between the LDL-C level and HN [16]. It is not surprising that the European Atherosclerosis Society experts, among all lipid metabolism parameters, recognize LDL as the most important, "primary driver of atherogenesis" [17, 18].

Since the discussion of combined antihypertensive and lipid-lowering therapy seems logical in the presence of HTN and DLP combination, it is extremely important to reveal the actual prevalence of lipitension in the population of one of the largest Russian regions. In this regard, the aim of the study was to investigate the prevalence of a combination of two major cardiovascular risk factors (HTN and lipid metabolism disorders) among the Krasnoyarsk Krai population as a whole, as well as among men and women in different age groups.

Material and methods

The work was carried out within the ESSE-RF epidemiological study [19] on a random representative sample of 1603 residents of the Krasnoyarsk and Berezovsky rural district of Krasnoyarsk Krai aged 25-64 years. This study was performed in accordance with the Helsinki declaration. The medical ethics committee approved this study. All patients signed informed consent.

A questionnaire was drawn up for each participant. Blood pressure was measured twice on the right arm with a 5-minute interval in a sitting position. Fasted blood samples were taken from the ulnar vein. Hypertension was considered as the systolic BP ⩾140 and/or diastolic BP ⩾90 mm Hg or BP >140/90 mm Hg with a receiving antihypertensive therapy.

Venous blood samples were centrifuged, serum was frozen and delivered to the federal center, where biochemical parameters were evaluated. By enzymatic methods on an Abbot Architect c8000 Clinical Chemistry Analyzer using Abbot Diagnostic (USA) kits, the following lipid profile parameters were studied: total cholesterol (TC), LDL-C, HDL-C and TG. Hypercholesterolemia (HC) was diagnosed with total cholesterol ⩾5,0 mmol/L. The increased LDL-C and TG levels were ⩾3 mmol/L and ⩾1,7 mmol/L, respectively, while a decrease in the HDL-C level was recorded at <1,0 mmol/L and <1,2 mmol/L in men and women, respectively.

Statistical processing was carried out in the programs IBM SPSS 22 and Microsoft Office Excel 2007. The proportion of those with HTN and DLP among the total number of participants and 95% confidence intervals (CI) was calculated. The significance of differences between the groups was tested using the chi-squared test with Yates' correction. Differences were considered significant at p⩽0,05.

Results

The study included 652 (39,4%) men and 951 (60,6%) women. The combination of HTN and any DLP was observed in 40% (37,6%; 42,5%) of participants. At the same time, with an increase in age, there is a natural and significant increase in the prevalence of lipitension both in the general population (from 10,7% in patients aged 25-34 years to 66,6% in those aged 55-64 years) and among women (Table 1). In men, the studied indicator reaches a plateau in the 45-54 age group. There was also a tendency towards a lower prevalence of lipitension among women compared with men aged 25-54 years, with the exception of a significant increase in the 55-64 age group (72,5 vs 58,1%).

The prevalence of different variants of HTN + DLP combination, depending on sex and age, is shown in Figure 1.

The combination of HTN and HC (HTN + HC) is recorded in 31,6% (29,33%; 33,97%) of the general population and clearly increases with age from 6,6 to 55,4% (Figure 1A). Sex differences in HTN + HC prevalence remain insignificant until the age of 55-64 years, where this combination is significantly more common in women (65,9% vs 40,2% in men).

The combination of HTN and increased LDL-C levels have the similar characteristics (Figure 1B).

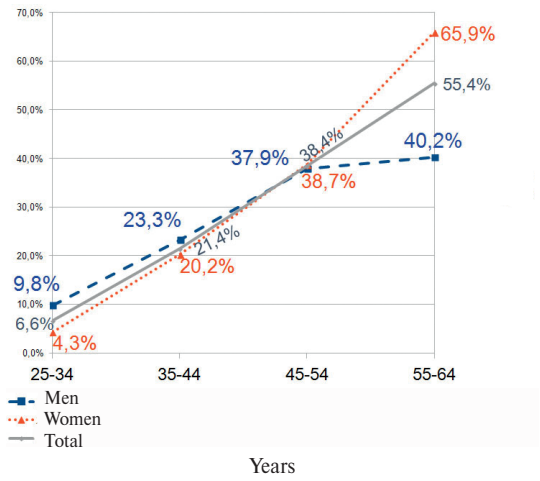
Table 1

Prevalence of a combination of HTN and any DLP in the Krasnoyarsk Krai population, depending on sex and age (%)

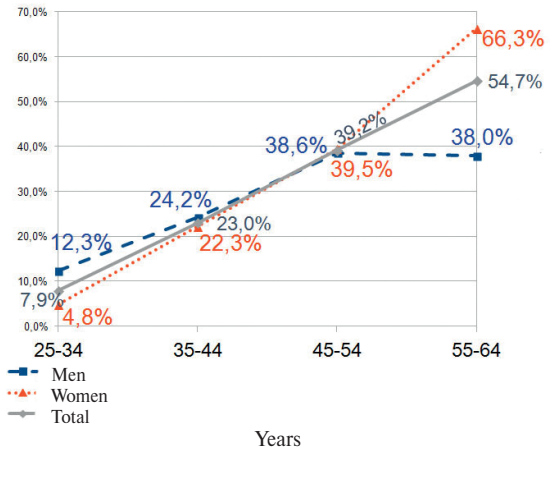
Age group	Men		Women		Total	
	%	95% CI	%	95% CI	%	95% CI
25-34 years old	16,0	10,3-21,6	6,9	3,7-10,2	10,7	7,6-13,7
35-44 years old	35,0	26,5-43,5	23,8	17,8-29,9	28,1	23,1-33,1
45-54 years old	57,9	49,9-66,0	44,3	38,2-50,4	49,2	44,3-54,2
55-64 years old	58,1	50,9-65,3	72,5	67,0-78,0	66,6	62,1-71,0

Notes: age differences are significant (p<0,001 for all). Sex differences are insignificant in the 35-44 age group (p=0,112), but significant in the other age groups: p=0,003 in the 25-34 age group, p=0,001 in the 45-54 age group and p=0,002 in the 55-64 age group.

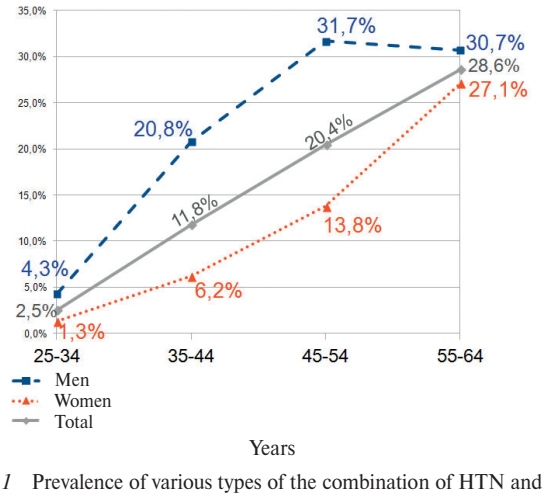
A) HTN + HC



B) HTN + increased LDL-C



C) HTN + HTG



D) HTN + reduced HDL-C

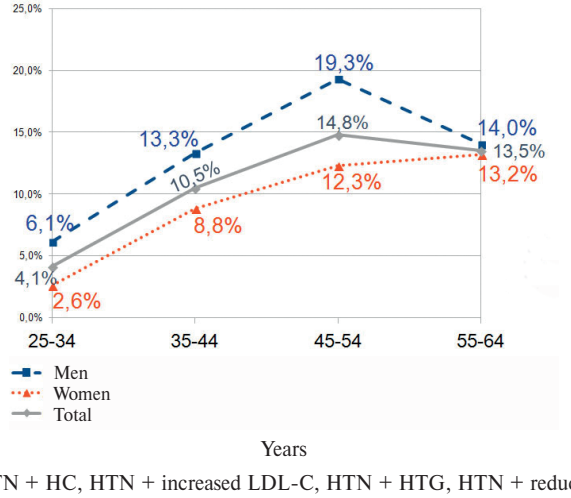


Figure 1 Prevalence of various types of the combination of HTN and DLP (HTN + HC, HTN + increased LDL-C, HTN + HTG, HTN + reduced HDL-C) in the Krasnoyarsk Krai population, depending on sex and age (%).

Notes: *A*) Age differences are significant (p<0,001). Sex differences are significant only in the 55-64 age group (p<0,001), but insignificant in other age groups. *B*) Age differences are significant (p<0,001). Sex differences are significant in the 25-34 (p=0,011) and 55-64 age groups (p<0,001). *C*) Age differences are significant (p<0,001). Sex differences are significant in the 35-44 and 45-54 age groups (p<0,001). *D*) Age differences are significant (p<0,001). Sex differences are not significant in any of the age groups.

The prevalence of this variant of lipitension in general population is 32,3% (29,3%; 34,0%) and naturally increases with age from 7,9 to 54,7%. In addition, if at the age of 25-34 years, the HTN + increased LDL-C combination is more common among men (12,3 vs 4,8%), then in the older age group of 55-64 years — among women (66,3 vs 38,0%).

The combination of HTN + hypertriglyceridemia (HTG) is recorded in the general population relatively less often — in 16,4% (14,6%; 18,3%), but also steadily increases with age — from 2,5 to 28,6% (Figure 1C). In men, this indicator reaches a plateau at the age of 45-54 years and exceeds this in women in the age range of 25-54 years. In women, in contrast to men, the prevalence of HTN + HTG combination is steadily increasing from 25 to 64 years old and practically equals with men aged 55-64 years.

Finally, the combination of HTN with a reduced HDL-C levels is observed in 10,8% (9,3%; 12,4%) in the general population. It tends to grow up to the 45-54 age group (from 4,1 to 14,8%), and at an older age does not change significantly (Figure 1D). At the same time, sex differences in any of the age groups were not significant.

It is noteworthy that the prevalence of individual DLP markers differs in persons with HTN and those with a normal BP level. So, in hypertensive patients, an increased LDL-C and HTG levels are more often recorded in the 25-34 and 35-64 age groups, respectively, while a decreased HDL-C level at the age

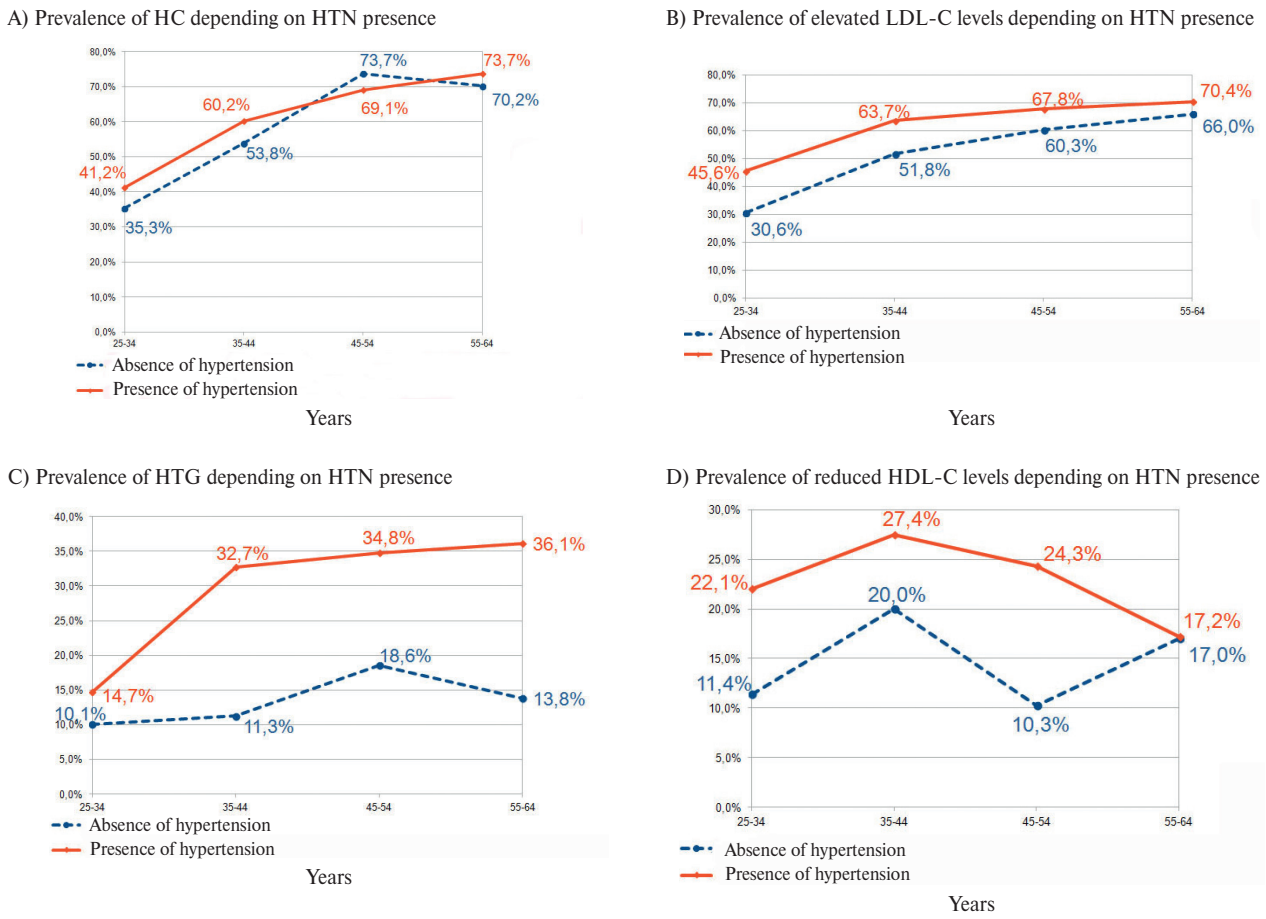


Figure 2 Prevalence of various DLP markers depending on the presence/absence of hypertension (%).
Notes: *A*) Differences are insignificant. *B*) Differences are significant in the 25-34 age group (p=0,025). *C*) Differences are significant in 35-64 age group (p<0,001). *D*) Differences are significant in the 25-34 (p=0,031) and 45-54 age groups (p=0,001).

of 25-34 and 45-54 years old. There were no significant differences in the increased total cholesterol level (Figure 2).

Discussion

Thus, in the Krasnoyarsk Krai, not only HTN (49,4%) [20] has a high prevalence, but also its combination with DLP, which, according to study results, was 40%. This indicator was higher than in the US epidemiological studies (15-31%) [11-13], but lower than in Lithuania [5].

The combination of HTN with the most important parameter of lipid metabolism disorders (increased LDL-C) is recorded in 1/3 of the adult population, in ~40% of people aged 45-54 years and in more than half of the Krasnoyarsk Krai population aged 55-64 years old. This combination is comparable in its prevalence to the United States [12], but lower in comparison with the Lithuanian [5] and Malaysian populations [21].

The prevalence of two types of lipitension (HTN + elevated total cholesterol and HTN + elevated LDL-C) increases with age. Moreover, at a young age, sex differences are either insignificant, or there is a slight superiority towards men, but at an older age, these combinations are much more common in women.

The most logical (but not the only) explanation for such dynamics is the cardioprotective profile of female sex hormones in reproductive age and testosterone-estrogen imbalance during and after menopause [22, 23].

The combination of HTN + HTG and HTN + low HDL-C in the Krasnoyarsk Krai population tend to prevail among men aged 25-54 years, and then level out in men and women in the 55-64 age group. The listed features are generally comparable with the average Russian data according to the ESSE-RF study [2], except that the HTN + low HDL-C combination within the general Russian population continues to be more often recorded in men compared with women and in the older age group (55-64 years old).

Unfortunately, dietary changes and adequate exercise, being important components of the cardiovascular prevention, are still inferior to active drug therapy in their ability to improve the prognosis with

already existing lipitension. Thus, in 3 large-scale prospective cohort studies with a 32-year follow-up, strict adherence to dietary recommendations led to a decrease in cardiovascular risk by 14-21%, and this indicator was even lower in the presence of HTN and HC [24]. Even more limited results are found in a systematic review by Patnode CD, et al. (2017) including 88 randomized clinical trials, where a significant but weakly expressed association of a healthy diet and/or physical activity with a decrease in systolic BP by 1,26 mm Hg, diastolic BP by 0,49 mm Hg, LDL-C by 2,58 mg/dl, and total cholesterol by 2,85 mg/dl was registered; moreover, there was no significant association with the HDL-C and TG levels [25].

Therefore, with the combination of hypertension and DLP, it seems logical to prescribe combined antihypertensive and lipid-lowering therapy, primarily statins. Evidence of this approach is provided by a number of randomized controlled trials, as well as two large meta-analyzes [26, 27], which demonstrated an improvement in long-term cardiovascular prognosis in such patients (with an additional 21% risk reduction compared with antihypertensive therapy only). The tactics with early initiation of not only antihypertensive, but also lipid-lowering therapy is supported by the meta-analysis with 327037 participants [28]. In addition, the use of fixed-dose combinations of statins and antihypertensive drugs in patients with lipitension contributes to an increase in medical adherence in actual clinical practice and a significant improvement in clinical outcomes, as evidenced by the recently published meta-analysis by Weisser B, et al. [29].

Conclusion

The prevalence of a combination of HTN with any DLP type in the Krasnoyarsk Krai among the adult population of 25-64 years is 40% and increases with age. The combination of HTN with the most important parameter of lipid metabolism disorders (increased LDL-C) is recorded in 1/3 of the adult population (32,3%), in ~40% of those aged 45-54 years and in more than half of the population aged 55-64 years. A combination of HTN and an increased total cholesterol level has similar statistics. In men, the prevalence of HTN and both elevated LDL-C and total cholesterol levels gradually increasing, reaches its plateau in the 45-54 age group. In women, compared with men, the combination of HTN with an increased level of LDL-C and total cholesterol is less common at a younger age, leveled out in the 45-54 age group, and prevails in the 55-64 age range. In order to effectively reduce the burden of HTN and hyperlipidemia, a wider and earlier introduction of combined antihypertensive and lipid-lowering therapy (primarily statins) should be considered.

Relationships and Activities: none.

References

1. Williams B, Masi S, Wolf J, et al. Facing the Challenge of Lowering Blood Pressure and Cholesterol in the Same Patient: Report of a Symposium at the European Society of Hypertension. Cardiol Ther. 2020;9(1):19-34. doi:10.1007/s40119-019-00159-1.
2. Chazova IE, Zhernakova YuV, Oshchepkova EV, et al. on behalf of study participants. Prevalence of cardiovascular risk factors in Russian population of patients with arterial hypertension. Kardiologiia. 2014; 54(10):4-12. (In Russ.) doi:10.18565/cardio.2014.10.4-12.
3. Liu X, Yu S, Mao Z, et al. Dyslipidemia prevalence, awareness, treatment, control, and risk factors in Chinese rural population: the Henan rural cohort study. Lipids Health Dis. 2018;17(1):119. doi:10.1186/s12944-018-0768-7.
4. Opoku S, Gan Y, Fu W, et al. Prevalence and risk factors for dyslipidemia among adults in rural and urban China: findings from the China National Stroke Screening and prevention project (CNSSPP). BMC Public Health. 2019;19(1):1500. doi:10.1186/s12889-019-7827-5.
5. Kutkiene S, Petrulioniene Z, Laucevicius A, et al. Cardiovascular risk assessment of dyslipidemic middle-aged adults without overt cardiovascular disease over the period of 2009-2016 in Lithuania. Lipids Health Dis. 2018;17(1):233. doi:10.1186/s12944-018-0883-5.
6. Williams RR, Hunt SC, Hopkins PN, et al. Familial dyslipidemic hypertension. Evidence from 58 Utah families for a syndrome present in approximately 12% of patients with essential hypertension. JAMA. 1988; 259(24):3579-86. doi:10.1001/jama.259.24.3579.
7. Dalal JJ, Padmanabhan TNC, Jain P, et al. LIPITENSION: Interplay between dyslipidemia and hypertension. Indian J Endocrinol Metab. 2012;16(2):240-5. doi:10.4103/2230-8210.93742.
8. Castelli WP, Anderson K. A population at risk. Prevalence of high cholesterol levels in hypertensive patients in the Framingham Study. Am J Med. 1986;80(2A):23-32. doi:10.1016/0002-9343(86)90157-9.
9. Neaton JD, Wentworth D. Serum cholesterol, blood pressure, cigarette smoking, and death from coronary heart disease. Overall findings and differences by age for 316,099 white men. Multiple Risk Factor Intervention Trial Research Group. Arch Intern Med. 1992;152(1):56-64. doi:10.1001/archinte.1992.00400130082009.
10. Yusuf S, Hawken S, Ounpuu S, et al., INTERHEART Study Investigators. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. Lancet. 2004;364(9438):937-52. doi:10.1016/S0140-6736(04)17018-9.
11. Eaton CB, Feldman HA, Assaf AR, et al. Prevalence of hypertension, dyslipidemia, and dyslipidemic hypertension. J Fam Pract. 1994;38(1):17-23.
12. Johnson ML, Pietz K, Battleman DS, et al. Prevalence of comorbid hypertension and dyslipidemia and associated cardiovascular disease. Am J Manag Care. 2004;10(12):926-32.
13. Wong ND, Lopez V, Tang S, et al. Prevalence, treatment, and control of combined hypertension and hypercholesterolemia in the United States. Am J Cardiol. 2006;98(2):204-8. doi:10.1016/j.amjcard.2006.01.079.

14. Zanetti D, Gustafsson S, Assimes TL, et al. Comprehensive Investigation of Circulating Biomarkers and their Causal Role in Atherosclerosis-related Risk Factors and Clinical Events. Circ Genom Precis Med. 2020;13(6):e002996. doi:10.1161/CIRCGEN.120.002996.
15. Ference BA, Bhatt DL, Catapano AL, et al. Association of Genetic Variants Related to Combined Exposure to Lower Low-Density Lipoproteins and Lower Systolic Blood Pressure With Lifetime Risk of Cardiovascular Disease. JAMA. 2019;322(14):1381-91. doi:10.1001/jama.2019.14120.
16. Go TH, Kwak KI, Jang JY, et al. Inference of a causal relation between low-density lipoprotein cholesterol and hypertension using mendelian randomization analysis. Clin Hypertens. 2021;27(1):7. doi:10.1186/s40885-021-00162-6.
17. Ference BA, Ginsberg HN, Graham I, 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. Eur Heart J. 2017;38(32):2459-72. doi:10.1093/eurheartj/ehx144.
18. Boren J, Chapman MJ, Krauss RM, et al. Low-density lipoproteins cause atherosclerotic cardiovascular disease: pathophysiological, genetic, and therapeutic insights: a consensus statement from the European Atherosclerosis Society Consensus Panel. Eur Heart J. 2020;41(24):2313-30. doi:10.1093/eurheartj/ehz962.
19. Boitsov SA, Chazov EI, Shlyakhto EV, et al. Scientific and Organizing Committee of the Russian Federation essay. Epidemiology of cardiovascular diseases in different regions of Russia (ESSE-RF). The rationale for and design of the study. The Russian Journal of Preventive Medicine. 2013;16(6):25-34. (In Russ.)
20. Artyukhov IP, Grinshtein YuI, Petrova MM, et al. Prevalence of arterial hypertension in the Krasnoyarsk Krai (Siberia, Russia). BMC Cardiovasc Disord. 2017;17(1):138. doi:10.1186/s12872-017-0559-5.
21. Mohamed-Yassin MS, Baharudin N, Daher AM, et al. High prevalence of dyslipidaemia subtypes and their associated personal and clinical attributes in Malaysian adults: the REDISCOVER study. BMC Cardiovasc Disord. 2021;21(1):149. doi:10.1186/s12872-021-01956-0.
22. Gheorghe G, Toth PP, Bungau S, et al. Cardiovascular Risk and Statin Therapy Considerations in Women. Diagnostics (Basel). 2020;10(7):483. doi:10.3390/diagnostics10070483.
23. Pucci G, Alcidi R, Tap L, et al. Sex- and gender-related prevalence, cardiovascular risk and therapeutic approach in metabolic syndrome: A review of the literature. Pharmacol Res. 2017;120:34-42. doi:10.1016/j.phrs.2017.03.008.
24. Shan Z, Li Y, Baden MY, et al. Association Between Healthy Eating Patterns and Risk of Cardiovascular Disease. JAMA Intern. Med. 2020;180(8):1090-100. doi:10.1001/jamainternmed.2020.2176.
25. Patnode CD, Evans CV, Senger CA, et al. Behavioral Counseling to Promote a Healthful Diet and Physical Activity for Cardiovascular Disease Prevention in Adults Without Known Cardiovascular Disease Risk Factors: Updated Systematic Review for the U.S. Preventive Services Task Force [Internet]. Rockville (MD): Agency for Healthcare Research and Quality (US); 2017. Report No: 15-05222-EF-1. Available from: https://www.ncbi.nlm.nih.gov/books/NBK476368/. (accessed 31.03.2021).
26. Sundstrom J, Gulliksson G, Wiren M. Synergistic effects of blood pressure-lowering drugs and statins: systematic review and meta-analysis. BMJ Evid Based Med. 2018;23(2):64-9. doi:10.1136/bmjebm-2017-110888.
27. Wang Y, Jiang L, Feng SJ, et al. Effect of Combined Statin and Antihypertensive Therapy in Patients with Hypertension: A Systematic Review and Meta-Analysis. Cardiology. 2020;145(12):802-12. doi:10.1159/000508280.
28. Wang N, Fulcher J, Abeysuriya N, et al. Intensive LDL cholesterol-lowering treatment beyond current recommendations for the prevention of major vascular events: a systematic review and meta-analysis of randomised trials including 327 037 participants. Lancet Diabetes Endocrinol. 2020;8(1):36-49. doi:10.1016/S2213-8587(19)30388-2.
29. Weisser B, Predel HG, Gillessen A, et al. Single Pill Regimen Leads to Better Adherence and Clinical Outcome in Daily Practice in Patients Suffering from Hypertension and/or Dyslipidemia: Results of a Meta-Analysis. High Blood Press Cardiovasc Prev. 2020;27(2):157-64. doi:10.1007/s40292-020-00370-5.