PREVENTIVE MEDICINE

QUALITY ASSESSMENT OF THE SCREENING TEST FOR PREDICTORS OF CORONARY HEART DISEASE

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ABSTRACT

Background. *Coronary heart disease (CHD) ranks first among the causes of death, morbidity, and disablement. The development of innovative methods for predicting CHD will reduce these burden.*
The aim of the work. *To assess the quality of the screening test for predictors of coronary heart disease using statistical quality control of a verifiable diagnostic test (VDT) (with binary outcomes).*
Materials and methods. *In 2008–2013, 70 cases of CHD were registered in a group of 7959 initially healthy men aged 18–66 years old who were the members of locomotive crews. Statistical analysis identified CHD predictors: arterial hypertension; psychosocial stress; hyperglycemia; dyslipidemia; excessive alcohol consumption; I-III degree of obesity; age 34–66 years; microalbuminuria; thickening of the intima-media complex/atherosclerotic plaque (IMC/ASP); pulse wave velocity (PWV) > 12 m/s; left ventricular hypertrophy; grade I-II grade of retinopathy; atherosclerosis of aorta. DiagStat software (Russian Federation) determined their predictive ability when used in screening tests to predict CHD. We demonstrated the use of this method to assess the predictive ability of risk factors for any disease.*
Results. *CHD predictors have high to moderate specificity for the absence of CHD in individuals who test negative for the above-listed factors. IMC/ASP, microalbuminuria, PWV > 12 m/s, grade III obesity moderately increase the posterior odds of developing CHD versus its absence in comparison with the prior odds after receiving a positive result of the verifiable diagnostic test for these factors. Age 34–66 years moderately increases the posterior odds in favor of the absence of CHD versus its occurrence compared with the prior odds after receiving a negative result of the verifiable diagnostic test.*
Conclusion. *When assessing the result of the verifiable diagnostic test, we should focus on both the probability of occurrence and the absence of CHD in the presence or absence of a predictor in the patient. Since the determination of PWV > 12 m/s, atherosclerosis of aorta, microalbuminuria, stress, and excessive alcohol consumption among workers of locomotive crews is not mandatory, it is necessary to conduct a targeted search for them.*

Key words: *coronary heart disease, risk factors, prognosis, screening study, verifiable diagnostic test, prevention*

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ОЦЕНКА КАЧЕСТВА СКРИНИНГ-ТЕСТА ПРЕДИКТОРОВ ИШЕМИЧЕСКОЙ БОЛЕЗНИ СЕРДЦА

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РЕЗЮМЕ

Введение. *Ишемическая болезнь сердца (ИБС) занимает первые позиции среди причин смерти, заболеваемости, профессиональной непригодности. Разработка инновационных методов прогнозирования ИБС позволит сократить эти потери.*

Цель работы. *Оценить качество скрининг-теста предикторов ишемической болезни сердца методом статистического контроля качества проверяемого диагностического теста (ПДТ) (с бинарными исходами).*

Материалы и методы. *В 2008–2013 гг. в группе изначально здоровых 7959 мужчин 18–66 лет – работников локомотивных бригад – зарегистрировали 70 случаев ИБС. С помощью статистического анализа идентифицировали предикторы ИБС: артериальная гипертензия; психосоциальный стресс; гипергликемия; дислипидемия; чрезмерное потребление алкоголя (ЧПА); ожирение I–III степени; возраст 34–66 лет; микроальбуминурия (МАУ); утолщение комплекса интима-медиа/атеросклеротическая бляшка (ТИМ/АСБ); скорость распространения пульсовой волны (СРПВ) > 12 м/с; гипертрофия левого желудочка; ретинопатия I–II степени; атеросклероз аорты (Ат.АО). В программе DiagStat (Россия) выяснили их предсказательную способность при использовании в скрининг-тестах для прогнозирования ИБС. Показано применение этого метода для оценки предсказательной способности факторов риска любого заболевания.*

Результаты. *Предикторы ИБС обладают высокой и умеренной специфичностью в отношении отсутствия возникновения ИБС у лиц, имеющих отрицательный результат на наличие этих факторов. ТИМ/АСБ, МАУ, СРПВ > 12 м/с, ожирение III степени умеренно повышают апостериорные шансы возникновения ИБС против её отсутствия в сравнении с априорными шансами после получения положительного результата ПДТ этих факторов. Возраст 34–66 лет умеренно повышает апостериорные шансы в пользу отсутствия ИБС против её возникновения в сравнении с априорными шансами после получения отрицательного результата ПДТ.*

Заключение. *При оценке результата ПДТ следует ориентироваться как на вероятность возникновения, так и на отсутствие ИБС при наличии или отсутствии у пациента предиктора. Так как определение СРПВ > 12 м/с, Ат.АО, МАУ, стресса, ЧПА у работников локомотивных бригад в обязательном порядке не предусмотрено, необходимо проводить их целенаправленный поиск.*

Ключевые слова: *ишемическая болезнь сердца, факторы риска, прогнозирование, скрининг-исследование, проверяемый диагностический тест, профилактика*

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INTRODUCTION

Statistical data indicate that cardiovascular disease (CVD) morbidity and mortality remain leading causes worldwide and in the Russian Federation [1, 2]. The largest share in the mortality structure from diseases of the circulatory system falls on coronary heart disease (CHD) [3], with acute forms predominating [4]. The widespread use of modifiable risk factors (RF) for CVD has placed cardiovascular causes and CHD in the first positions in the ranking of ten leading causes of death in the world [5, 6]. Despite the fact that chronic CHD is characterized by a stable long-term course, CHD occupies the first positions among the causes of death, temporary and permanent loss of working capacity of the population [7-9]. These problems are also relevant for railway medicine, since cases of this disease are regularly registered among locomotive crew workers (LCW). CHD is included in the list of diseases that do not allow LCWs to work in the profession, and is the leading cause of professional unsuitability. The share of professional unsuitability due to CHD reaches 40–50 %. Admission by the medical expert commission to train work does not guarantee the absence of this latent CVD in LCW and the safety of railway traffic, does not prevent early retirement from the profession and economic losses associated with the health of workers [10-14]. Therefore, it is important for such professional groups of clinically asymptomatic individuals to undergo primary examination – screening testing to prevent CVD. Screening examination helps to detect the disease at an early stage and completely cure or prevent it. The disease should be understood as any clinical outcome under study that has a latent period and forms long before the appearance of clinical manifestations [13]. Despite their obvious usefulness, screening methods have varying effectiveness, since they do not exclude diagnostic error or the formation of a false opinion about the absence of the disease. Therefore, a screening test should meet an acceptable level of prediction [15] and comply with the World Health Organization (WHO) principles for conducting a screening study [16]: the course and treatment of the actual disease should be known; case finding should be carried out continuously, and the diagnostic costs should be justified. An ideal screening test should detect the disease before its manifestation, not give false-positive or false-negative results, and reduce disability and mortality. The party performing the screening study should have an idea of how effective a particular diagnostic test is in predictive performance in order to compare its capabilities and the expected benefit of conducting the screening study. In this study, the predictive performance of previously established predictors of coronary heart disease [17] is assessed, their exposure (concentration, dose) capable of causing coronary heart disease in the observation group and the range of probability of the coronary heart disease in the presence or absence of the predictor in the patient are shown. A method for assessing the quality of coronary heart disease predictors is proposed, and its application is shown, since no other scientific publications on this topic could be found.

THE AIM OF THE STUDY

To determine the predictive performance of coronary heart disease predictors using statistical quality control of a verifiable diagnostic test (with binary outcomes).

MATERIALS AND METHODS

According to the criteria of the recommendations on arterial hypertension (AH) of the Russian Medical Society on Arterial Hypertension and the All-Russian Scientific Society of Cardiologists (ARSC) for 2008 and 2011 and in accordance with the regulatory order [10, 18, 19], from 2008 to 2013, all LCWs of the Trans-Baikal Railway (TBR) annually for 6 years during medical expert commissions underwent underwent annual screening for CVD, target organ damage (TOD) and CVD. The following risk factors were determined: age; hypertension; dyslipidemia – total cholesterol > 5.0 mmol/l, and/or low-density lipoprotein cholesterol (LDL) > 3.0 mmol/l, and/or high-density lipoprotein HDL < 1.0 mmol/l, and/or triglycerides > 1.7 mmol/l; hyperglycemia > 5.5 mmol/l; family history of early CVD; excessive alcohol consumption (EAC); psychosocial stress; smoking; overweight – body mass index (BMI) ≥ 25.0 kg/m^2. According to BMI gradations, obesity stages I–III were distinguished: BMI = 30.0–34.9, 35.0–39.9, and ≥ 40.0 kg/m^2, respectively. The following were identified from the TOD: left ventricular hypertrophy (LVH) by electrocardiography (Sokolov–Lyon sign > 38 mm, Cornell product > 2440 mm×ms) and echocardiography (left ventricular mass index ≥ 125 g/m^2); aortic atherosclerosis (AA) by radiography and/or ultrasound diagnostics (USD); thickening of the intima-media complex (IMC) > 0.9 mm or atherosclerotic plaques (ASP) by USD of the brachiocephalic arteries [18]; reduced glomerular filtration rate; microalbuminuria (MAU); hypercreatininemia; retinopathy stages I–II; pulse wave velocity (PWV) > 12 m/s; ankle-brachial index < 0.9; type 2 diabetes mellitus (T2DM) [10, 12]. Lipid and carbohydrate metabolism parameters were determined and assessed according to the above criteria [18] and were included in the sample as qualitative variables – "yes" or "no". According to the order [10], the LCWs had no CVD at baseline except for hypertension stage I, 1–2 stages. They dropped out of the study in case of death, dismissal, or if their health did not meet the criteria of the order [10]. The observation was approved by the local Ethics Committee of the Chita State Medical Academy of the Ministry of Health of the Russian Federation (protocol No. 30 dated November 09, 2011) and was conducted using official laboratory and instrumental diagnostic methods, on licensed equipment by certified specialists. The study design, collected material on 22 items at the beginning and end of the observation are shown in Figure 1 and Table 1. Comparison of the collected data

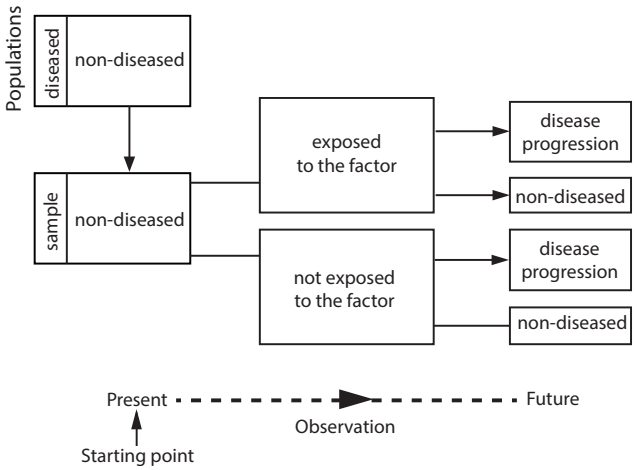

FIG. 1.
Prospective cohort design of locomotive crews members of the Trans-Baikal Railway [20]

at the beginning and end of the observation showed that CVD risk factors are cumulative, increasing over time both in the population and within individuals. [12].

The age of the LCWs at the beginning of the observation was 35.7 ± 10.6 years, at the end of the observation – 38.6 ± 10.3 years. 53.4 % (n = 4251) of the LCWs in the observation group were under 40 years of age (fig. 2).

The dynamics of cardiovascular risk according to the SCORE scale by observation years in the LCW of the Trans-Baikal Railway is presented in Figure 3.

Predicted probability of 10-year prediction of fatal cases of atherosclerosis-associated diseases according to the SCORE scale in the year of their prediction and the same year of death occurring among LCWs of the Trans-Baikal Railway is shown in Figure 4.

The structure of the identified SVDs in 2008–2013 is shown in Figure 5. In 2008, 7959 LCWs of the Trans-Baikal Railway were observed, in 2009 – 7851, in 2010 – 7141, in 2011 – 6817, in 2012 – 6016, in 2013 – 5722.

TABLE 1

OCCURRENCE OF RISK FACTORS, TARGET ORGAN LESIONS IN LOCOMOTIVE CREW MEMBERS OF THE TRANS-BAIKAL RAILWAY AT THE BEGINNING AND AT THE END OF THE OBSERVATION [12]

Risk factors, target organs	Start of observation		End of observation		%#/%*	McNemar's test	
	n*	%*	n*	%*		χ^2	p
Arterial hypertension	1401	17.6	2033	25.5	1.4	2381.6	0.00
Overweight (BMI = 25.0–29.9 kg/m^2)	2602	32.7	3135	39.4	1.2	580.4	0.00
Obesity stage I (BMI = 30.0–34.9 kg/m^2)	923	11.6	1215	15.3	1.3	4104.4	0.00
Obesity stage II (BMI = 35.0–39.9 kg/m^2)	167	2.1	234	2.9	1.4	7114.4	0.00
Obesity stage III (BMI ≥ 40.0 kg/m^2)	16	0.2	24	0.3	1.5	7868.3	0.00
Smoking	4600	57.8	4918	61.8	1.1	293.7	0.00
Dyslipidemia	700	8.8	2534	31.8	3.6	2278.1	0.00
Left ventricular hypertrophy	446	5.6	597	7.5	1.3	5895.1	0.00
Psychosocial stress	1249	15.7	1635	20.5	1.3	3084.3	0.00
Family history of early CVD	597	7.5	906	11.4	1.5	5038.6	0.00
Retinopathy stages I–II	533	6.7	337	4.2	0.6	6470.7	0.00
Hyperglycemia	80	1.0	445	5.6	5.6	6636.4	0.00
Aortic atherosclerosis	8	0.1	458	5.8	58.0	6674.0	0.00
Excessive alcohol consumption	48	0.6	71	0.9	1.5	7697.6	0.00
IMC/ASP	8	0.1	24	0.3	3.0	7876.3	0.00
PWV > 12 m/s	0	0	19	0.2	-	7899.2	0.00
Creatininemia	24	0.3	116	1.5	5.0	7590.7	0.00
Microalbuminuria	3	0.04	8	0.1	2.5	7929.0	0.00
Decreased glomerular filtration rate	0	0	6	0.1	-	7938.0	0.00
Ankle-brachial index < 0.9	0	0	5	0.1	-	7941.0	0.00
Diabetes mellitus type 2	24	0.3	45	0.6	2.0	7798.0	0.00

Note. * – start of observation; # – end of observation.

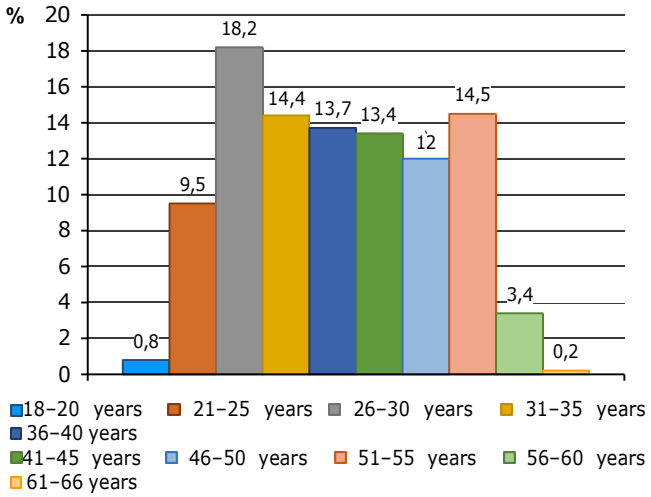

FIG. 2.
Age structure of respondents

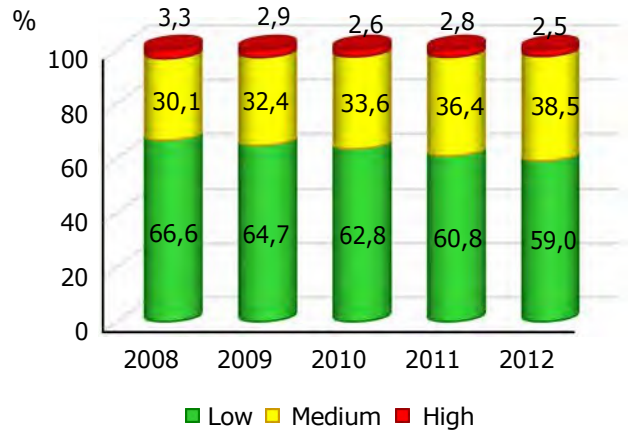

FIG. 3.
Cardiovascular risk assessment using the SCORE scale in the observation group

In 2008–2013, medical expert commissions of 14 non-governmental healthcare institutions of the Trans-Baikal Railway diagnosed 70 chronic cases of coronary heart disease, which were confirmed during inpatient examination at the Railway Clinical Hospital at Chita station, as well as by the Central Medical Expert Commission of Russian Railways (Moscow) in the case of their complex resolution. The diagnostics were carried out in accordance with the clinical recommendations of the All-Russian Society of Cardiology (ARSC) in 2009, the Ministry of Health and Social Development of Russia in 2013, and the ESC (European Society of Cardiology) in 2013 [12, 21–23].

Considering the identified risk factors, the individual cardiovascular risk was calculated annually using the SCORE scale as the most adapted to the Russian population and recommended by the State Research Center for Preventive Medicine for individuals aged 40 and older. LCWs aged under 40 were classified as having a low cardiovascular risk. In the SCORE scale, the overall cardiovascular risk is expressed as the absolute risk of cardiovascular mortality in the next 10 years. Since the absolute overall cardiovascular risk is highly dependent on age, it can be low in young patients even with a combination of high blood pressure (BP) and other RF [24]. Individuals aged under 40, regardless of the RF presence (except for very high levels of individual factors), have a low absolute risk of fatal cardiovascular complications in the next 10 years of life. For young people (under 40), not the absolute, but the relative total cardiovascular risk is determined. A person under 40 years of age without RF (non-smoker, with normal BP and total cholesterol levels in the blood) has a 12-fold lower relative total cardiovascular risk compared to a person with the specified RF [12, 25]. We did not analyze further or identify special age groups in the assessment and stopped studying the SCORE indicators in order to save our resources when this scale showed low predictive abilities in this category of workers (fig. 4).

At the end of the LCW observation, the above-listed CHD predictors were determined in a 2 × 2 contingency table, in a multivariate stepwise analysis, and in a survival analysis (in the Cox proportional hazards regression model and in the Kaplan – Meier models), and their relative risk was established [17]. As a result of the performed multivariate analysis, all CHD predictors were divided into three categories, since they showed statistical heterogeneity in the analytical models. The first category included IMC/ASP, hypertension, and retinopathy, which showed a statistically significant assessment in all

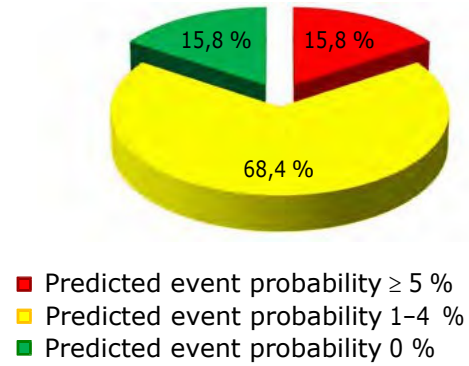

FIG. 4.
Predicted probability of 10-year prediction of fatal cases of atherosclerosis-associated diseases according to the SCORE scale in the year of their prediction and the same year of death coming among locomotive crew members of the Trans-Baikal Railway: sudden cardiac death – 15 cases, cerebral stroke – 4 cases; mean age of the deceased – 46.3 ± 9.2 years

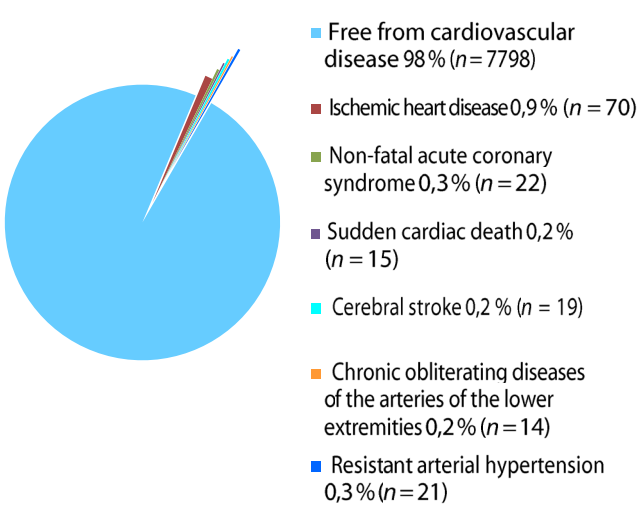

FIG. 5.
Structure of diagnosed cardiovascular diseases in 2008–2013

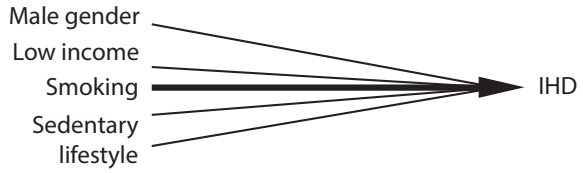

FIG. 6.
Assessment of the influence of various potential risk factors on coronary heart disease [26]

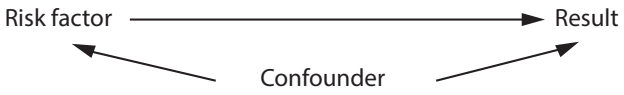

FIG. 6.
Confounder interaction scheme [26]

five models used. These factors were assessed as the main independent predictors capable of being realized in CHD without the participation of other predictors. Such predictors of coronary heart disease as age 34–66 years, AA, obesity stage III, which had a statistically significant result in 4 statistical models, were hypothetically assessed as interacting RFs, realized in coronary heart disease with the participation of other factors as part of a complex variable consisting of 2 or more similar independent factors. The remaining predictors of coronary heart disease, which had a statistically significant result in less than 4 models used, were assessed as confounders, factors influencing the final outcome and the main influencing variable [17, 26] (fig. 6, 7; Table 3). The results of this part of the work were published [12, 17]. Since the predictors of coronary heart disease differ in their statistical characteristics and, therefore, can have different effects on the disease development, we decided to determine their predictive ability using the method of statistical quality control of the verified diagnostic test (VDT) [27] in the DiagStat software (Russian Federation) [28] to clarify the issue of the informativeness and appropriateness of their use in screening examinations. We also decided to show how this method can be used to assess the predictive ability of predictors of any disease.

The main requirement for disease diagnostic methods is that they should have sufficient sensitivity and high specificity. However, when disease factors are tested for a screening test, it is necessary to remember and understand that they are individual, differ from each other in their statistical characteristics and have the ability to interact with each other [17, 26, 29]. In medical and biological issues, three types of factor interaction are described: additivity – summation; synergism – mutual enhancement of the effect; antagonism – mutual weakening of the effects of predictors [30]. Patient examination methods that are usually used as screening tests do not have these qualities. Therefore, these features of environmental factors during their assessment of the VDT quality can manifest themselves in the analysis, and the results interpretation of the study of disease predictors using this technique may differ from the assessment of the VDT quality of diagnostic methods for detecting the disease.

The VDT predictive value is assessed by the accuracy and predictive value indicators, comparing its result with the gold standard – a diagnostic reference test that almost accurately determines the presence or absence of a disease in the patient being examined. The gold standard may be one or several tests for determining the disease. A diagnostic test (T) should be understood as a factor being examined for diagnostic ability (as in this case) or a method for identifying an important disease, which can have two values for the patient being examined: T^+ – a positive result or T^- – a negative result. The disease can be realized in two binary outcomes – "yes" or "no" (CHD^+ and CHD^-). To evaluate the VDT, it is necessary to compare the exposed and unexposed VDT groups by the frequency of disease occurrence in them – in this case, coronary heart disease. For this purpose, a 2 × 2 contingency table is formed. The frequencies of opposite values of the studied binary outcome of both groups are entered in absolute figures. The exposed and unexposed VDT groups are marked in the rows, and the possible outcomes are indicated in the columns. Each study object is included in only one of the groups and has only one of the possible outcomes. Positive results and negative results of the VDT form 4 combinations of the disease outcome: $T+CHD^+$ – true "positive"; $T+CHD^-$ – false "positive"; T^-CHD^+ – false "negative"; T^-CHD^- – true "negative". Their number in the 2 × 2 cross-classification is designated as a, b, c and d, respectively. The methodology for assessing the VDT is shown in Table 2 [27]. All designations in the text, tables and figures

are given in the original terminology of the methodology and the DiagStat program [27, 28].

The indicators of the accuracy and predictive value of the VDT reflecting its ability to determine and predict the outcome under study form two pairs of indicators and counter-indicators, by which the VDT quality is assessed when comparing them. Four conditional probabilities of the indicator of the VDT accuracy form two pairs of opposites – sensitivity (Se) and counter-sensitivity (coSe), specificity (Sp) and counter-specificity (coSp). Their statistical estimates are measured by proportions (f), which can be shown as a percentage, or as the ratio of a part to a whole or the ratio of the constituent parts of a set to its total volume [31, 32]. Four indicators of the VDT predictive value form two pairs of opposites: the positive predictive value (PPV) and its counter-positive predictive value (coPPV); the negative predictive value (NPV) and its counter-negative predictive value (coNPV). Their qualities and capabilities are indicated in the note to table 3 [27].

When checking the VDT quality, it is necessary to have data on the prevalence of the disease *(Prev)* in the tested population. These data are automatically generated in the DiagStat software [28] when entering the study parameters as the proportion of people with the disease (CHD) among all those examined in the group: $f(CHD^+) = (a + c) / n$.

There is an interdependence between the indicators of VDT accuracy and VDT predictive value, which is determined by the likelihood ratios that form two opposite pairs: the likelihood ratio for the CHD "positives" (LR[+]), the likelihood ratio for the CHD "negatives" (LR[–]), and their antipodes. Likelihood ratios and their inversion results are estimated in terms of probabilities and odds – "for" or "against" [27].

The quality of screening tests for CHD predictors was assessed using the DiagStat software (Russia). If the 100 (1 – α)% confidence interval (CI) for the studied CHD predictor θ did not include the uninformative value θ_{ni}, then the estimated unknown value in this CI of the predictor θ_{uk} had a statistically significant difference from its uninformative value θ_{ni} at the significance level α. This means that $\theta_{uk} \neq \theta_{ni}$ and is statistically significant at the level α. When the 100 (1 – α)% CI of the θ indicator included the uninformative value θ_{ni}, the unknown value θ_{uk} of the CHD predictor estimated by this CI did not statistically significantly differ from θ_{ni} at the level α, and a conclusion was made about the insignificance of the result, $\theta_{uk} = \theta_{ni}$, according to the VDT assessment methodology [27].

The value $Se_{ni} = coSe_{ni} = 0.5$ is uninformative for the sensitivity Se and counter-sensitivity coSe. If they are equal, then the VDT cannot be considered accurate in identifying "positives" in individuals with a disease, in this case, coronary heart disease. By analogy, the value $Sp_{ni} = coSp_{ni} = 0.5$ is considered uninformative for the specificity Sp and counter-specificity coSp [27].

TABLE 2

TABLE OF CROSSED CLASSIFICATION MATRIX 2 × 2 FOR CORONARY HEART DISEASE

Object groups	Gold standard (infallible test for disease detection)		Total objects in the group
	Result		
	CHD [+]	CHD [–]	
Exposed Test [+]	True "positive" T^+CHD^+ a	False "positive" T^+CHD^- b	T^+ $P(T^+)$ a + b
	Prevalence of "positives" in the outcome		
	$P(T^+CHD^+)$	$P(T^+CHD^-)$	
Unexposed Test [–]	False "negative" T^-CHD^+ c	True "negative" T^-CHD^- d	T^- $P(T^-)$ c + d
	Prevalence of "negatives" in the outcome		
	$P(T^-CHD^+)$	$P(T^-CHD^-)$	
Total objects in the outcome	Prevalence of outcome (disease) in the observation group		1 *n*
	CHD^+ $Prev = P(CHD^+)$ a + c	CHD^- $(1 – Prev = P(CHD^-))$ b + d	

Note. (here and in Table 3). [+] – positive result of the gold standard (GS) or the VDT compared with it; [–] – negative result of the gold standard or the VDT compared with it; CHD^+ – presence of CHD in the patient according to the GS, CHD– – absence of CHD in the patient according to the GS; T+ – "positive", positive result of the VDT; T– – "negative", negative result of the VDT; Prev, (P) – prevalence of the disease.

If the PPV CI overlaps "overlaps" the CHD Prev, then such a "positive" is considered an uninformative value: PPV_{ni} = Prev [27].

According to the method used, if the "negative" NPV does not increase the probability of the probability of absence of CHD (coPrev), then such a value is also considered uninformative: NPVni = coPrev [27]. The PPV and NPV graphs of the test should differ from Prev, located in the center of the scale grid, that is, the effect of the test on the population prevalence of the disease should be noticeable, and the stronger it is, the more significant the deviation of the test curve from Prev.

According to the methodology for the likelihood ratio for the CHD LR[+] "positives" and the CHD LR[–] "negatives", the values $LR[+]_{ni}$ = 1 and $LR[-]_{ni}$ = 1 are considered uninformative [27]. The practical usefulness of the VDT quality indicators is determined by verbal scales that make it possible to qualitatively evaluate the quantitative result in the proportion values for Se and Sp from 0 to 1.0 [27]. Evaluation in values: 0–0.5 – useless; 0.5–0.7 – low; 0.7–0.9 – moderate; 0.9–1.0 – high. LR[+] and LR[–] in verbal scales are evaluated in the following ranges: 1–3 – insignificant assessment; 3–10 – mediocre; 10–33 – moderate; 33–100 – high; 100–1000 – very high; > 1000 – perfect score.

RESULTS AND DISCUSSION

The results of the quality assessment of the VDT predictors of CHD are shown in Table 3 and Figures 8–23. All CHD predictors had low VDT sensitivity (Se), except for the predictors of hypertension, BMI ≥ 25, and age 34–66 years. According to the method used [27], Se has the ability to "sense" the presence of the disease (CHD) and shows the frequency of "positives" among individuals with CHD. This interpretation of the indicator is used when assessing the VDT of the patient examination method. When assessing environmental factors using this method, it should be understood that Se shows the prevalence of the factor that caused the disease among individuals who have experienced this outcome (Tables 2, 3). That is, Se, when working with predictors, determines and shows the exposure (accumulation, dose) of the factor [29], capable of causing the expected disease in a specific population. This information is important for determining the scope of preventive measures and medical care in a specific society. The range of probability of a disease event is shown by the PPV and NPV indicators. The prognostic CI of the «positives» of the PPV predictors: hypertension, PWV > 12 m/s, age 34–66 years, LVH, MAU, AA, IMC/ASP, obesity stage III, retinopathy, "do not overlap" the central zone of the population prevalence of CHD Prev, which indicates the informativeness of their values. Figures 9–14, 16, 21, 22 confirm this conclusion visually. The CI predictive value of the PPV "positives" predictors: EAC, hyperglycemia, BMI ≥ 25.0, obesity stages I–II, dyslipidemia – cover the zone of population prevalence of CHD Prev and have no informative value (figs. 8, 15, 18–20, 23). In this regard, when assessing these predictors, one should focus on the CI predictive value of the NPV "negatives", showing the ranges of the probability of the CHD absence in individuals who do not have these predictors, as well as the proportion of individuals in the population (Sp) without these factors, guaranteeing the CHD absence in this probability range at the level of the controlled society. The CI of "negatives" and "positives" of the predictor psychosocial stress overlap the zone of prevalence of CHD Prev and have no informative value. This factor (confounder) is associated with and contributes to the CHD formation, but does not have an independent prognostic effect on CHD (fig. 7, 17) [17]. The quantitative assessment of the increase in the odds of a disease event or absence of a disease in the group of "positives" LR[+] and in the group of "negatives" LR[–] is shown by the VDT likelihood ratios. The predictors IMC/ASP, MAU, PWV > 12 m/s, BMI > 40.0, in contrast to other CHD predictors, statistically significantly moderately increase the posterior odds in favor of the CHD development after a positive VDT result is obtained in a patient. The predictor age in the range of 34–66 years statistically significantly moderately increases the posterior odds in favor of the absence of coronary heart disease versus the development of coronary heart disease after a negative VDT result is obtained in a patient. In our study, most of the CHD predictors did not reach the level of statistical significance Se, and, therefore, this indicator does not accurately determine the prevalence (exposure) of risk factors in the group of individuals who developed CHD, which indicates a higher real statistically significant concentration of RF required for the development of this disease in the group of LCWs of the Trans-Baikal Railway. To determine the exact value of the concentration of these RF causing CHD in the RLB population, clarifying population studies are needed on a larger sample or a sample of similar size, but with a longer observation period.

We did not compare the obtained VDT results of CHD predictors with the data of VDT coronary angiography or CT coronary angiography, which are considered the gold standard for CHD diagnosing due to the lack of publications on the assessment of the latter using the VDT method. At the same time, it is not possible to compare predictors of the disease and methods of diagnosing the disease, since they belong to different categories and have different qualities. Predictors form the preclinical course and progress the disease until clinical manifestations appear; methods of diagnosing the disease do not have this quality, as well as a number of other properties of RF.

Graphical assessment of the VDT statistical quality control method of the CHD predictors as screening tests is the final stage of the methodology [27, 28] and a useful tool for visualizing the obtained estimates and the influence of predictors on the population prevalence of the disease. The extent to which the predictor under study is invasive and dangerous is visible on the graphs.

TABLE 2

TABLE OF CROSSED CLASSIFICATION MATRIX 2 × 2 FOR CORONARY HEART DISEASE

CHD predictors	*Se*	*Sp*	The probability of CHD developing				Likelihood ratio	
			PPV (+), %		*NPV (–), %*		*LR[+]*	*LR[–]*
			PPV	*coPPV*	*NPV*	*coNPV*		
EAC	~~**0.03**~~	**0.99**	$_{0.1}$ 2.7 $_{9.9}$	$_{90.1}$ 97.3 $_{99.9}$	$_{98.8}$ **99.1** $_{99.3}$	$_{0.7}$ **0.9** $_{1.2}$	3.0	1.0
Arterial hypertension	**0.80**	**0.75**	$_{2.0}$ **2.9** $_{3.9}$	$_{96.1}$ **97.1** $_{98.0}$	$_{99.5}$ **99.7** $_{99.9}$	$_{0.1}$ **0.3** $_{0.5}$	~~**3.2**~~	~~**3.6**~~
Retinopathy stages I–II	~~**0.23**~~	**0.96**	$_{2.5}$ **5.0** $_{8.5}$	$_{91.5}$ **95.0** $_{97.5}$	$_{99.0}$ **99.3** $_{99.5}$	$_{0.5}$ **0.7** $_{1.0}$	~~**5.7**~~	1.3
LVH	~~**0.29**~~	**0.93**	$_{1.9}$ **3.5** $_{5.7}$	$_{94.3}$ **96.5** $_{98.1}$	$_{99.0}$ **99.3** $_{99.5}$	$_{0.5}$ **0.7** $_{1.0}$	~~**3.9**~~	1.3
Stress	~~**0.19**~~	**0.79**	$_{0.4}$ 0.9 $_{1.6}$	$_{98.4}$ 99.1 $_{99.6}$	$_{98.7}$ 99.1 $_{99.3}$	$_{0.7}$ 9.3 $_{1.3}$	0.9	1.0
IMC/ASP	~~**0.05**~~	**0.99**	$_{2.8}$ **15.4** $_{37.4}$	$_{62.6}$ **84.6** $_{97.2}$	$_{98.8}$ **99.1** $_{99.4}$	$_{0.6}$ **0.9** $_{1.2}$	**19.6**	1.1
Microalbuminuria	~~**0.03**~~	**0.99**	$_{1.2}$ **20.0** $_{58.5}$	$_{41.5}$ **80.0** $_{98.8}$	$_{98.8}$ **99.1** $_{99.4}$	$_{0.6}$ **0.9** $_{1.2}$	**27.0**	1.0
Aortic atherosclerosis	~~**0.21**~~	**0.94**	$_{1.5}$ **3.3** $_{5.8}$	$_{94.2}$ **96.7** $_{98.5}$	$_{98.9}$ **99.2** $_{99.5}$	$_{0.5}$ **0.8** $_{1.1}$	~~**3.6**~~	1.2
PWV > 12 m/s	~~**0.04**~~	**0.99**	$_{1.8}$ **14.3** $_{38.7}$	$_{61.3}$ **85.7** $_{98.2}$	$_{98.8}$ **99.1** $_{99.4}$	$_{0.6}$ **0.9** $_{1.2}$	**18.6**	1.0
Dyslipidemia	0.45	~~**0.68**~~	$_{0.8}$ 1.3 $_{2.0}$	$_{98.0}$ 98.7 $_{99.2}$	$_{98.9}$ **99.3** $_{99.5}$	$_{0.5}$ **0.7** $_{1.1}$	1.4	1.2
Hyperglycemia	~~**0.10**~~	**0.94**	$_{0.5}$ 1.6 $_{3.5}$	$_{96.5}$ 98.4 $_{99.5}$	$_{98.8}$ **99.1** $_{99.4}$	$_{0.6}$ **0.9** $_{1.2}$	1.7	1.0
BMI ≥ 25,0	**0.74**	~~**0.42**~~	$_{0.8}$ 1.1 $_{1.6}$	$_{98.4}$ 99.4 $_{99.2}$	$_{99.0}$ **99.4** $_{99.7}$	$_{0.3}$ **0.6** $_{1.0}$	1.3	1.6
BMI = 30,0–34,9	~~**0.26**~~	**0.85**	$_{0.8}$ 1.6 $_{2.6}$	$_{97.4}$ 98.4 $_{99.2}$	$_{98.9}$ **99.2** $_{99.5}$	$_{0.5}$ **0.8** $_{1.1}$	1.7	1.1
BMI = 35,0–39,9	~~**0.08**~~	**0.97**	$_{0.7}$ 2.5 $_{5.9}$	$_{94.1}$ 97.5 $_{99.3}$	$_{98.8}$ **99.1** $_{99.4}$	$_{0.6}$ **0.9** $_{1.2}$	2.8	1.1
BMI ≥ 40,0	~~**0.04**~~	**0.99**	$_{1.4}$ **11.5** $_{32.1}$	$_{67.9}$ **88.5** $_{98.6}$	$_{98.8}$ **99.1** $_{99.4}$	$_{0.6}$ **0.9** $_{1.2}$	**14.1**	1.0
Age 34-66 years	**0.99**	~~**0.38**~~	$_{1.0}$ 1.4 $_{2.0}$	$_{98.0}$ 98.6 $_{99}$	$_{99.0}$ **99.9** $_{100.0}$	$_{0.0}$ **0.03** $_{1.0}$	~~**1.6**~~	**27.5**

Note. Informative values are shown in bold, with the results that did not stand up to verbal assessment crossed out. The assessment results in tables and figures are shown as 99% CI. The Se (sensitivity – how often "positives" are observed in individuals with coronary heart disease, i.e. to what extent the test "feels" the presence of coronary heart disease) and Sp (specificity – how often "negatives" are observed in individuals without coronary heart disease, i.e. to what extent the test "feels" the absence of coronary heart disease) indicators are presented as shares, since they show the specific value of occurrence (accumulation) of RF among the population of individuals who have developed the outcome under study (coronary heart disease) (Se), and the specific value of the absence of this factor among individuals who have not developed coronary heart disease (Sp). The PPV (positive predictive value – the VDT ability to correctly predict coronary heart disease in a person with a "positive") and NPV (negative predictive value – the VDT ability to correctly predict the absence of coronary heart disease in a person with a "negative") indicators and their inversions coPPV (counter-positive predictive value – the VDT ability to erroneously predict the absence of coronary heart disease in a person with a "positive") and coNPV (counter-negative predictive value – the VDT ability to erroneously predict coronary heart disease in a person with a "negative") are presented in %, since they show the range of the probability of the occurrence or absence of a coronary heart disease event in the representatives of the sample. LR[+] – the ratio of the proportion of "positives" among persons with coronary heart disease to the proportion of "positives" among persons without coronary heart disease, shows an increase in the posterior odds in favor of the coronary heart disease presence versus its absence in the respondent in comparison with the a priori odds after receiving a positive VDT result; LR[–] – the ratio of the proportion of "negatives" among persons without coronary heart disease to the proportion of "negatives" among persons with coronary heart disease, shows an increase in the posterior odds in favor of the coronary heart disease absence versus its presence in the respondent in comparison with the a priori odds after receiving a negative VDT result; – independent effect of the factor; – interaction of the factor; – confounding effect.

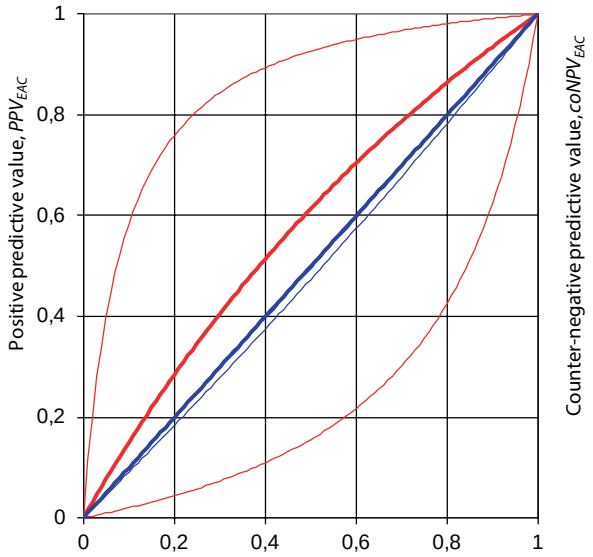

FIG. 8.
PPV_{EAC} and $coNPV_{EAC}$ versus $Prev_{CHD}$ diagram: EAC – excessive alcohol consumption; CHD – coronary heart disease

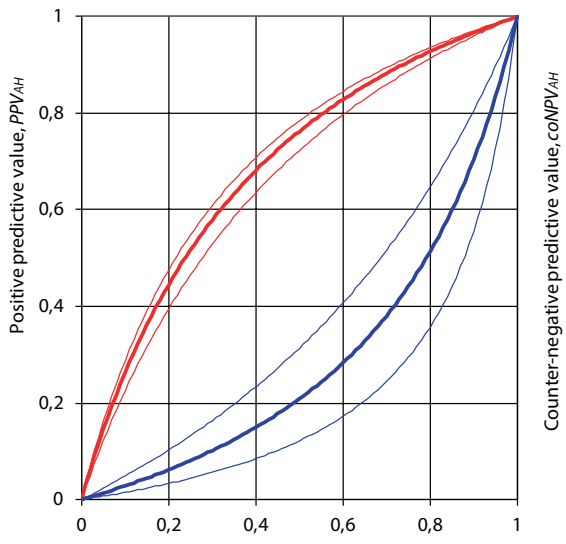

FIG. 9.
PPV_{AH} and $coNPV_{AH}$ versus PrevCHD diagram: AH – arterial hypertension; CHD – coronary heart disease

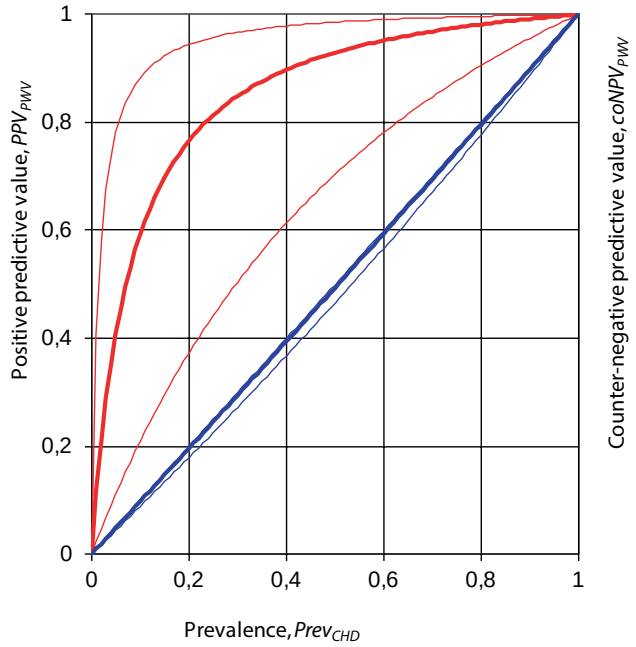

FIG. 10.
PPV_{PWV} and coNPVPWV versus $Prev_{CHD}$ diagram: PWV – pulse wave velocity; CHD – coronary heart disease

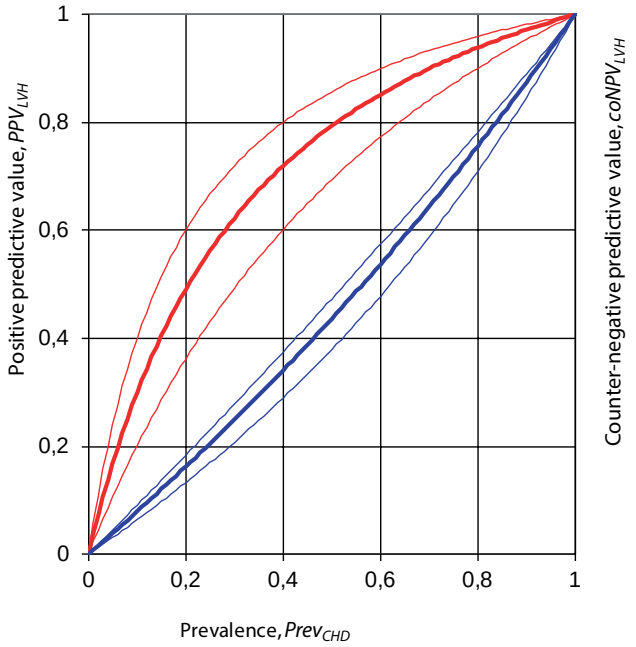

FIG. 12.
PPV_{LVH} and coNPV$_{LVH}$ versus $Prev_{CHD}$ diagram: LVH – left ventricular hypertrophy; CHD – coronary heart disease

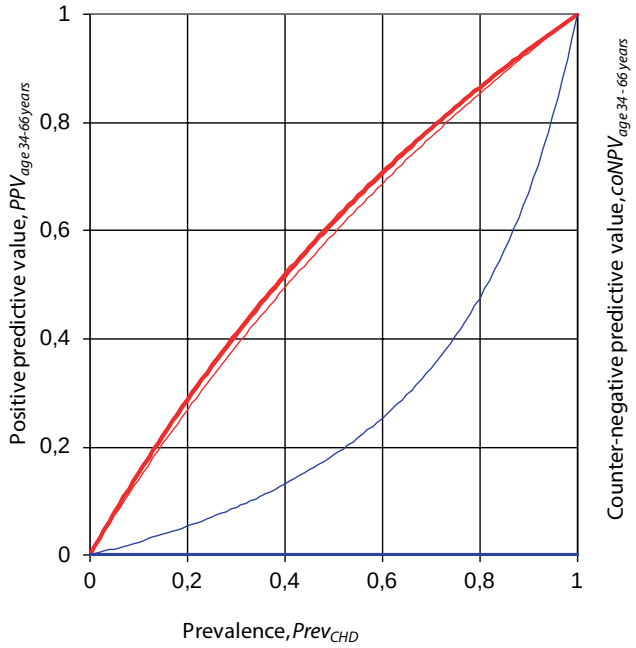

FIG. 11.
$PPV_{age\ 34–66}$ and coNPV$_{age\ 34–66}$ versus $Prev_{CHD}$ diagram: CHD – coronary heart disease

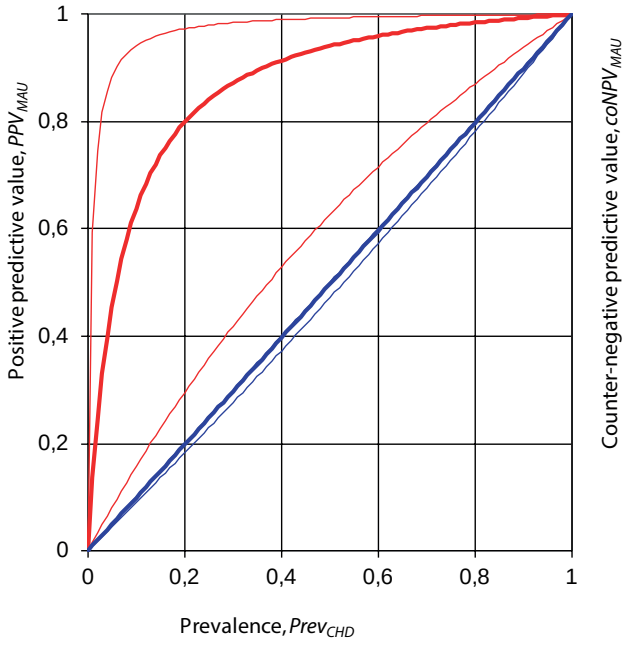

FIG. 13.
PPV_{MAU} and coNPV$_{MAU}$ versus $Prev_{CHD}$ diagram: MAU –microalbuminuria; CHD – coronary heart disease

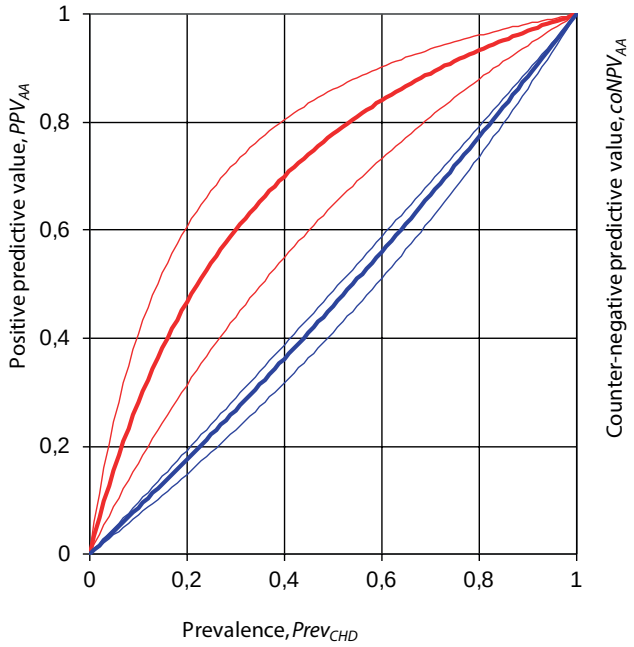

FIG. 14.
PPV_{AA} and $coNPV_{AA}$ versus $Prev_{CHD}$ diagram: AA – atherosclerosis of aorta; CHD – coronary heart disease

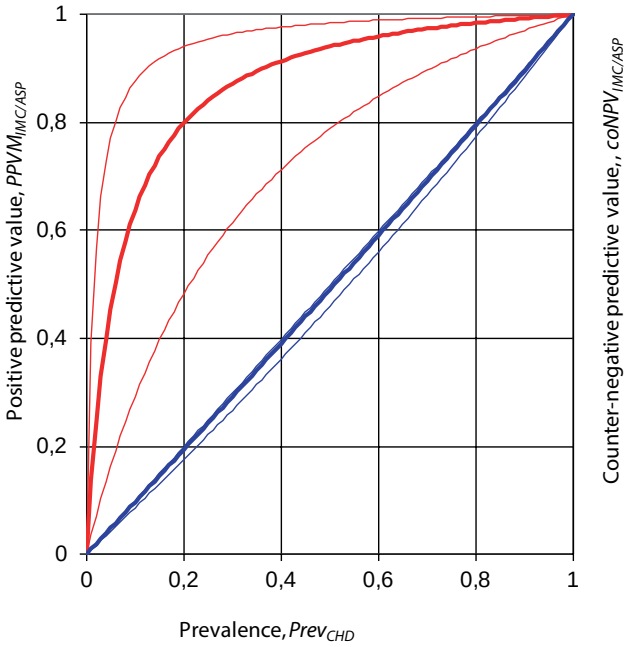

FIG. 16.
$PPV_{IMC/ASP}$ and $coNPV_{IMC/ASP}$ versus $Prev_{CHD}$ diagram: IMC – intima-media thickness; ASP – atherosclerotic plaque; CHD – coronary heart disease

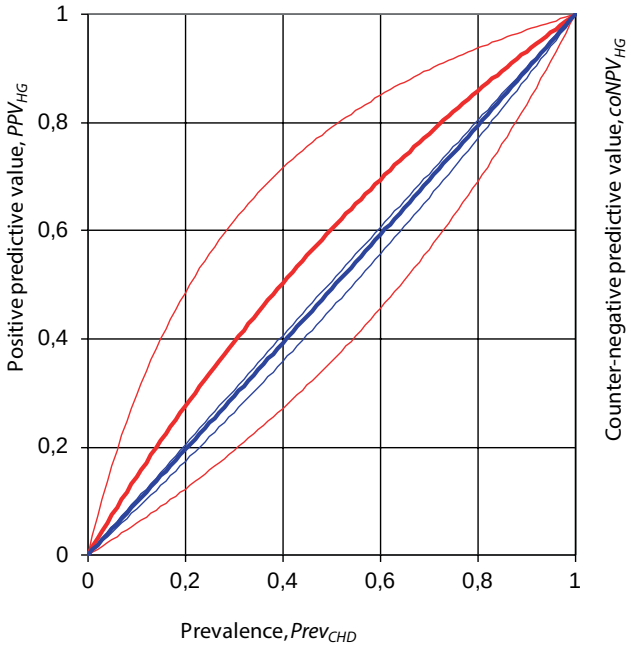

FIG. 15.
PPV_{HG} and $coNPV_{HG}$ versus $Prev_{CHD}$ diagram: HG – hyperglycemia; CHD – coronary heart disease

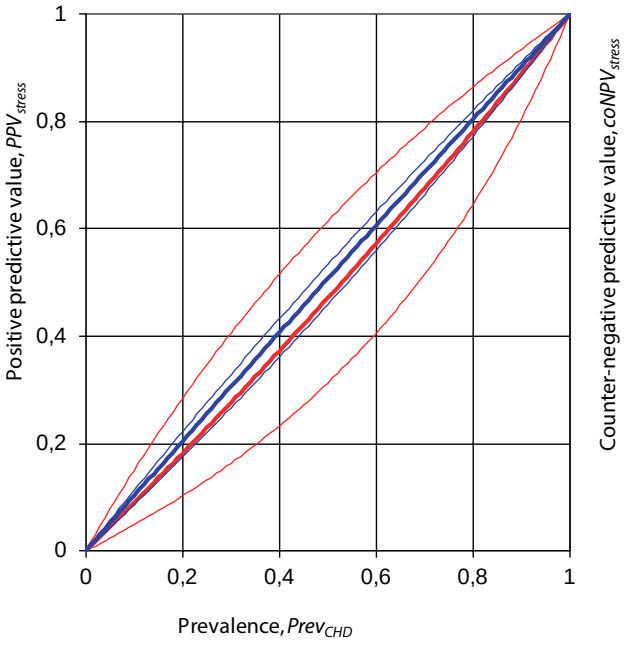

FIG. 17.
PPV_{stress} and $coNPV_{stress}$ versus $Prev_{CHD}$ prevalence: CHD – coronary heart disease

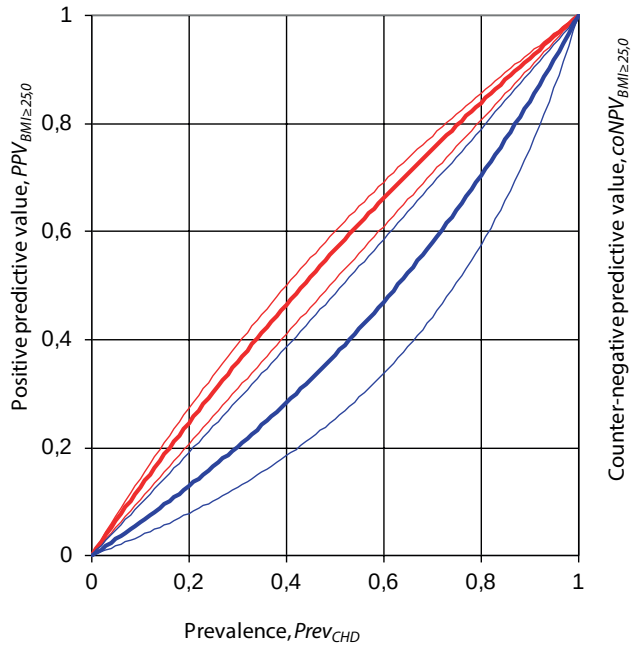

FIG. 18.
$PPV_{BMI \geq 25,0}$ and $coNPV_{BMI \geq 25,0}$ versus $Prev_{CHD}$ diagram: BMI – body mass index; CHD – coronary heart disease

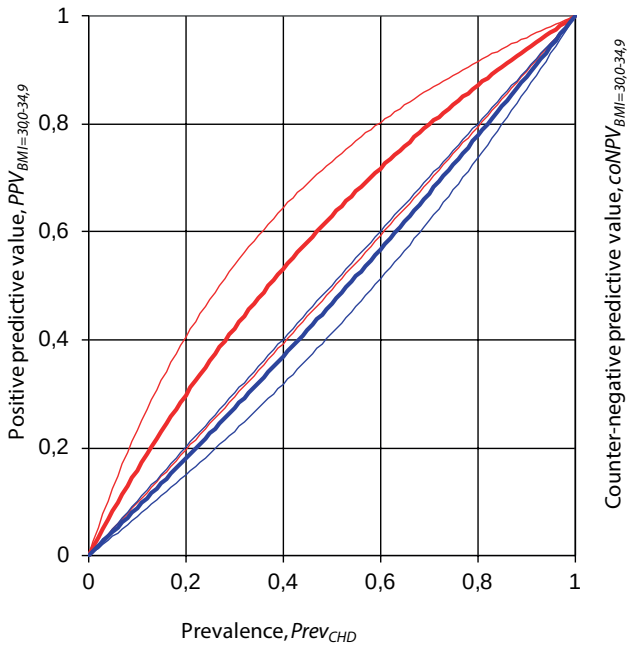

FIG. 20.
$PPV_{BMI = 30,0–34,9}$ and $coNPV_{BMI = 30,0–34,9}$ versus $Prev_{CHD}$ diagram: BMI – body mass index; CHD – coronary heart disease

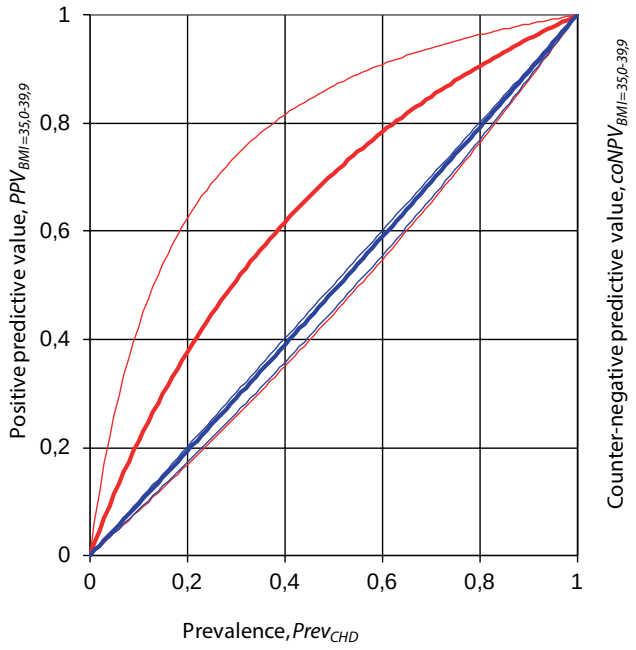

FIG. 19.
$PPV_{BMI = 35,0–39,9}$ and $coNPV_{BMI = 35,0–39,9}$ versus PrevCHD diagram: BMI – body mass index; CHD – coronary heart disease

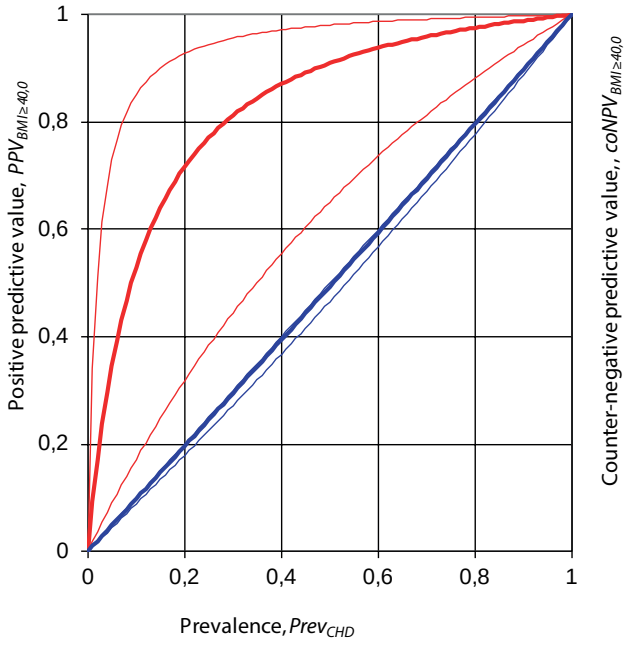

FIG. 21.
$PPV_{BMI \geq 40,0}$ and $coNPV_{BMI \geq 40,0}$ versus PrevCHD diagram: BMI – body mass index; CHD – coronary heart disease

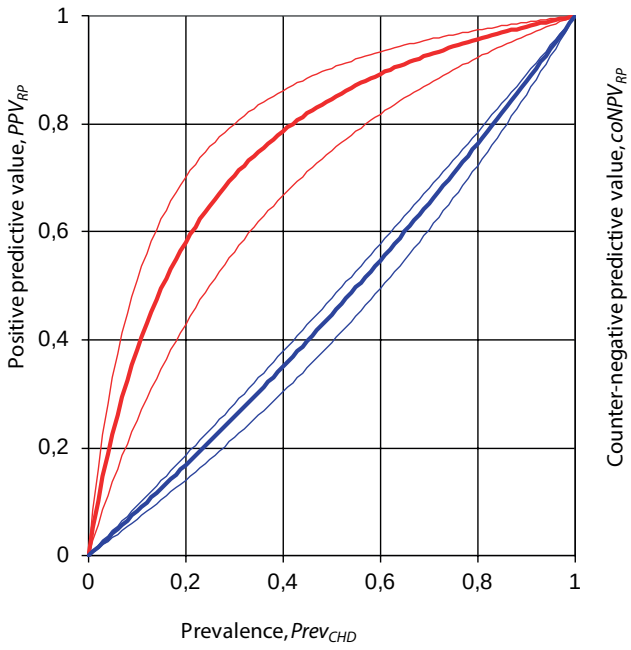

FIG. 22.
PPV_{RP} and $coNPV_{RP}$ versus $Prev_{CHD}$ diagram: RP – retinopathy; CHD – coronary heart disease

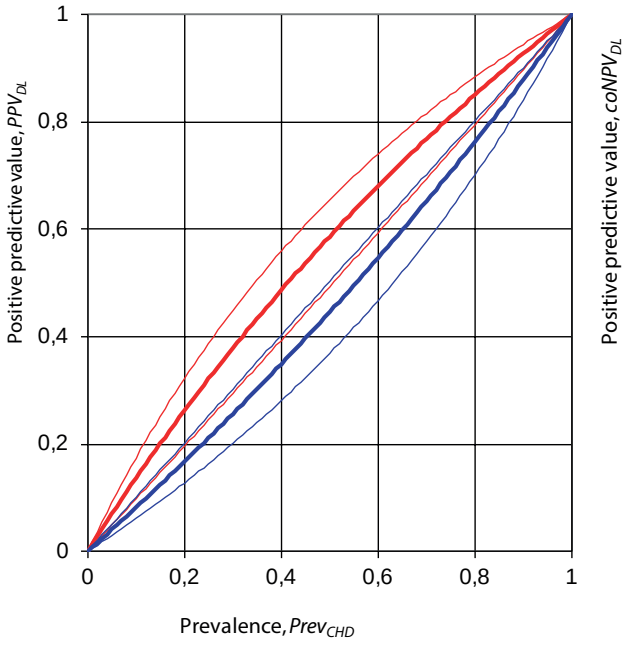

FIG. 23.
PPV_{DL} and $coNPV_{DL}$ versus $Prev_{CHD}$ diagram: DL – dyslipidemia; CHD – coronary heart disease

CONCLUSION

CHD predictors have high and moderate specificity in relation to the absence of CHD occurrence in individuals with a negative result for the presence of factors of this disease. When assessing the CHD probability, one should focus on the probability of both occurrence and absence of the outcome in the presence or absence of a factor of this disease in a patient and consider only estimates that are statistically significant. The obtained data can be used in the formation of the selection (medical screening) of safety-critical operator occupations with increased medical requirements for candidates, for example, LCW, driving a locomotive "alone" without an assistant driver. Modifiable risk factors of the disease should be modified in order to improve the medical indicators of the employee. When recruiting employees, all factors of the disease should be taken into account. Predictors of IMC/ASP, MAU, PWV > 12 m/s, BMI > 40.0, unlike other CHD predictors, statistically significantly moderately increase the a posteriori odds in favor of the CHD occurrence against its absence in comparison with the a priori chances after receiving a positive VDT result in a patient. The predictor age in the range of 34–66 years statistically significantly moderately increases the posterior odds in favor of the CHD absence versus its occurrence in comparison with the prior odds after the patient receives a negative VDT result.

Since the definition of predictors PWV > 12 m/s, AA, MAU, EAC, stress in LCWs is not mandatory provided for by regulatory documents, it is necessary to conduct a targeted search for them, especially if EAC screening is implemented among LCWs in order to prevent other CVDs, a predictor of which is this factor [12, 33, 34]. EAC test: latent daily single alcohol consumption above the WHO safe limit, i.e. more than 2 standard doses of alcohol per day with 1 dose of 13.7 g (18 ml of ethanol), is detected by performing the diagnostic algorithm for chronic alcohol intoxication [12, 35]. Other CHD predictors in LCWs should also be identified in order to carry out therapeutic and preventive measures for workers exposed to these factors in view of the available diagnostic methods and in order to prevent their cumulation in the population and in a specific worker.

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Conflicts of interest
No potential conflict of interest relevant to this article reported.

REFERENCES

1. Glushhenko VA, Irklienko EK. Cardiovascular morbidity – one of the most vital problems of modern health care. *Medicine and Health Care Organization*. 2019; 4(1): 56-63. (In Russ.). [Глущенко В.А., Ирклиенко Е.К. Сердечно-сосудистая заболеваемость – одна из важнейших проблем здравоохранения. *Медицина и организация здравоохранения*. 2019; 4(1): 56-63].

2. Alekseeva AV. Some aspects of the accessibility of medical care for children. *Children's Medicine of the North-West*. 2018; 7(1): 18-25. (In Russ.). [Алексеева А.В. Некоторые аспекты доступности медицинской помощи детскому населению. *Детская медицина Северо-Запада*. 2018; 7(1): 18].

3. Zubko AV, Sabgayda TP, Semyonova VG, Muzykantova NN. Mortality associated with preventable causes of deaths from cardio-vascular diseases in the pre-COVID period and during the pandemic in Russia. *Social'nye aspekty zdorov'a naselenia*. 2023; 69(1): 6. (In Russ.). [Зубко А.В., Сабгайда Т.П., Семенова В.Г., Музыкантова Н.Н. Потери российского населения от предотвратимых причин сердечно-сосудистой смертности в периоды до и во время пандемии. *Социальные аспекты здоровья населения*. 2023; 69(1): 6]. doi: 10.21045/2071-5021-2023-69-1-6

4. Samorodskaya IV, Klyuchnikov IV. Dynamics of mortality rates from chronic and acute coronary heart disease in the regions of the Russian Federation in 2013–2021. *Clinical Medicine (Russian Journal)*. 2023; 101(7-8): 395-403. (In Russ.). [Самородская И.В., Ключников И.В. Динамика показателей смертности от хронических и острых форм ишемической болезни сердца в регионах Российской Федерации в 2013–2021 годах. *Клиническая* медицина. 2023; 101(7-8): 395-403]. doi: 10.30629/0023-2149-2023-101-7-8-395-403

5. Tsybusov AP. The formation of a healthy lifestyle is a current and urgent task of domestic healthcare. *Medical Almanac*. 2017; (2): 10-13. (In Russ.). [Цыбусов А.П. Формирование здорового образа жизни – актуальная и неотложная задача отечественного здравоохранения. *Медицинский альманах*. 2017; (2): 10-13].

6. Bichurin DR, Atmaikina OV, Cherepanova OA. Cardiovascular diseases. A regional aspect. *International Research Journal*. 2023; 134(8). (In Russ.). [Бичурин Д.Р., Атмайкина О.В., Черепанова О.А. Сердечно-сосудистые заболевания. Региональный аспект. *Международный научно-исследовательский журнал*. 2023; 134(8)]. doi: 10.23670/IRJ.2023.134.103

7. Abrosimov VN, Zhukova LA, Glotov SI, Alekseeva EA. *Coronary heart disease*: *Textbook*. Ryazan: Ryazan State Medical University; 2015. (In Russ.). [Абросимов В.Н., Жукова Л.А., Глотов С.И., Алексеева Е.А. *Ишемическая болезнь сердца: учебное пособие*. Рязань: РязГМУ; 2015].

8. Goma TV. *Cardiac ischemia. Angina pectoris: Textbook*. Irkutsk: Irkutsk State Medical University; 2022. (In Russ.). [Гома Т.В. *Ишемическая болезнь сердца. Стенокардия напряжения: учебное пособие.* Иркутск: ИГМУ; 2022.].

9. Barbarash OL, Karpov YuA, Kashtalap VV, Boshchenko AA, Ruda MM, Akchurin RS, et al. 2020 Clinical practice guidelines for stable coronary artery disease. *Russian Journal of Cardiology*. 2020; 25(11): 201-250. (In Russ.). [Барбараш О.Л., Карпов Ю.А., Кашталап В.В., Бощенко А.А., Руда М.М., Акчурин Р.С., и др. Стабильная ишемическая болезнь сердца. Клинические рекомендации 2020. *Российский кардиологический журнал*. 2020; 25(11): 201-250]. doi: 10.15829/1560-4071-2020-4076

10. *On approval of the list of medical contraindications for work directly related to the movement of trains and shunting work: Order of the Ministry of Health and Social Development of the Russian Federation No. 796 d.d. 19.12.2005*. 2015. (In Russ.). [*Об утверждении перечня медицинских противопоказаний к работам, непосредственно связанным с движением поездов и маневровой работой: Приказ Минздравсоцразвития РФ № 796 от 19.12.2005*. 2015]. URL: http://base.consultant.ru [date of access: February 12, 2024].

11. Prilutskaya YuA, Dvoretski LI. The strategy of management patients with non-ST elevation acute coronary syndrome. *Kardiologiia*. 2019; 59(9): 40-51. (In Russ.). [Прилуцкая Ю.А., Дворецкий Л.И. Стратегия ведения больных с острым коронарным синдромом без подъема сегмента ST. *Кардиология*. 2019; 59(9): 40-51]. doi: 10.18087/cardio.2019.9.n366

12. Lazutkina AYu. *Prediction of cardiovascular diseases and their outcomes among workers of locomotive crews of the Trans-Baikal Railway (results of a 6-year prospective observation)*: Abstract of the Thesis of Cand. Sc. (Med.). Chita; 2017. (In Russ.). [Лазуткина А.Ю. *Прогнозирование сердечно-сосудистых заболеваний и их исходов у работников локомотивных бригад Забайкальской железной дороги (результаты 6-летнего проспективного наблюдения):* автореф. дис. ... канд. мед. наук. Чита; 2017].

13. Boytsov SA, Drapkina OM. Modern content and improvement of high cardiovascular risk strategy in reducing mortality from cardiovascular diseases. *Terapevticheskii arkhiv*. 2021; 93(1): 4-6. (In Russ.). [Бойцов С.А., Драпкина О.М. Современное содержание и совершенствование стратегии высокого сердечно-сосудистого риска в снижении смертности от сердечно-сосудистых заболеваний. *Терапевтический архив.* 2021; 93(1): 4-6]. doi: 10.26442/00403660.2021.01.200543

14. Muraseyeva EV, Gorokhova SG, Prigorovskaya TS, Pfaf VF. On evaluating occupational fitness in railway workers with ventricular arrhythmias after coronary arteries stenting. *Russian Journal of Occupational Health and Industrial Ecology*. 2016; (4): 1-4. (In Russ.). [Мурасеева Е.В., Горохова С.Г., Пригоровская Т.С., Пфаф В.Ф. К вопросу оценки профпригодности работников железнодорожного транспорта с желудочковыми нарушениями ритма сердца после стентирования коронарных артерий. *Медицина труда и промышленная экология*. 2016; (4): 1-4].

15. Abram E. Screening and diagnostic tests. URL: http://emedicine.medscape.com/article/773832-overview#aw2aab6b5 [date of access: February 05, 2023].

16. Wilson JMG, Jungner G. Principles and practice of screening for disease. *WHO Chronicle*. 1968; 22(11): 473.

17. Lazutkina AYu, Gorbunov VV. *Continuum of coronary heart disease*. Khabarovsk: DVSMU; 2018. (In Russ.). [Лазуткина А.Ю., Горбунов В.В. *Континуум ишемической болезни сердца*. Хабаровск: ДВГМУ; 2018].

18. Diagnosis and treatment of arterial hypertension: recommendations of the Russian Medical Society for Arterial Hypertension and the All-Russian Scientific Society of Cardiology. *Cardiovascular Therapy and Prevention*. 2008; 7(6 Suppl 2): 1-32. (In Russ.). [Диагностика и лечение артериальной гипертензии: рекомендации РМОАГ и ВНОК. *Кардиоваскулярная терапия и профилактика*. 2008; 7(6 Прил. 2): 1-32.].

19. Cardiovascular prevention: recommendations of the All-Russian Scientific Society of Cardiology. *Cardio-*

vascular Therapy and Prevention. 2011; 10(6 Suppl 2): 1-64. (In Russ.). [Кардиоваскулярная профилактика: рекомендации ВНОК. *Кардиоваскулярная терапия и профилактика*. 2011; 10(6 Прил. 2): 1-64].

20. Petri MA, Sabin K. *Visual medical statistics; 2nd edition, revised and enlarged*. Moscow: GEOTAR Media; 2010. (In Russ.). [Петри М.А., Сэбин К. *Наглядная медицинская статистика; 2-е изд.*, перераб. и доп. М.: ГЭОТАР Медиа; 2010.].

21. *Diagnosis and treatment of stable angina: Recommendations of the All-Russian Scientific Society of Cardiology*. Moscow; 2009. (In Russ.). [*Диагностика и лечение стабильной стенокардии: рекомендации ВНОК*. М.; 2009].

22. *Diagnosis and treatment of chronic coronary heart disease: Clinical recommendations of the Ministry of Health of the Russian Federation and the Society of Specialists in Emergency Cardiology and the specialized commission on cardiology*. Moscow; 2013. (In Russ.). [*Диагностика и лечение хронической ишемической болезни сердца: клинические рекомендации Минздрава России и Общества специалистов по неотложной кардиологии и профильной комиссии по кардиологии*. М.; 2013].

23. Recommendations for the treatment of stable coronary heart disease. ESC 2013: European Society of Cardiology clinical guidelines. *Russian Journal of Cardiology*. 2014; 111(7): 7-79. (In Russ.). [Рекомендации по лечению стабильной ишемической болезни сердца. ESC 2013: клинические рекомендации Европейского общества кардиологов. *Российский кардиологический журнал*. 2014; 111(7): 7-79].

24. Recommendations for the diagnosis and treatment of arterial hypertension of the European Society of Hypertension (ESH) and the European Society of Cardiology (ESC). *Journal of Hypertension*. 2013; 31(7): 1281-1357. (In Russ.). [Рекомендации по диагностике и лечению артериальной гипертонии Европейского общества по гипертонии (ESH) и Европейского общества кардиологов (ESC). *Journal of Hypertension*. 2013; 31(7): 1281-1357].

25. Organization of medical examinations and preventive medical examinations of the adult population: Letter of the Ministry of Health of the Russian Federation No. 14-2/10/2-6432d.d. 08.29.2013. 2013. (In Russ.). [*Организация проведения диспансеризации и профилактических медицинских осмотров взрослого населения: Письмо Министерства здравоохранения РФ № 14-2/10/2-6432 от 29.08.2013*. 2013].

26. Rumyantsev PO, Saenko VA, Rumyantseva UV, Chekin SYu. Statistical methods for the analyses in clinical practice. Part 2. Survival analysis and multivariate statistics. *Problems of Endocrinology*. 2009; 55(6): 48-56. (In Russ.). [Румянцев П.О., Саенко В.А., Румянцева У.В., Чекин С.Ю. Статистические методы анализа в клинической практике. Часть II. Анализ выживаемости и многомерная статистика. *Проблемы эндокринологии*. 2009; 55(6): 48-56]. doi: 10.14341/probl200955648-56

27. Tishkov AV, Khromov-Borisov NN, Komashnya AV, Marchenkova FYu, Semenova EM, Eyubova NI, et al. *Statistical analysis of 2x2 tables in diagnostic studies*. Saint Petersburg: St. Petersburg State Medical University; 2013. (In Russ.). [Тишков А.В., Хромов-Борисов Н.Н., Комашня А.В., Марченкова Ф.Ю., Семенова Е.М., Эюбова Н.И., и др. *Статистический анализ таблиц 2 × 2 в диагностических исследованиях*. СПб.: СПбГМУ; 2013].

28. Khromov-Borisov NN, Tishkov AV, Komashnya AV, Marchenkova FYu, Semenova EM. *Statistical analysis of clinical studies: 2 × 2 table. Version 1.0*: Certificate of state registration of a computer program No. 2012616821. 2012. (In Russ.). [Хромов-Борисов Н.Н., Тишков А.В., Комашня А.В., Марченкова Ф.Ю., Семенова Е.М. *Статистический анализ клинических исследований: таблица 2×2. Версия 1.0:* Свидетельство о государственной регистрации программы для ЭВМ № 2012616821. 2012].

29. Last JM (ed.). *Epidemiological dictionary*. Moscow: 2009. (In Russ.). [Ласт Дж.М. (ред.). *Эпидемиологический словарь*. М.; 2009].

30. Zabolotskikh VV, Vasilyev AV, Tereshchenko YuP. Synergistic effects with simultaneous exposure to physical and chemical factors. *Izvestia of Samara Scientific Center of the Russian Academy of Sciences*. 2016; 18(5-2): 290-294. (In Russ.). [Заболотских В.В., Васильев А.В., Терещенко Ю.П. Синергические эффекты при одновременном воздействии физических и химических факторов. *Известия Самарского научного центра Российской академии наук*. 2016; 18(5-2): 290-294].

31. Yakovleva AV. *Economic statistics: textbook*. Moscow: Exam; 2005. (In Russ.). [Яковлева А.В. *Экономическая статистика: учебное пособие*. М.: Экзамен; 2005].

32. Tokarev YuA, Sherstobitova GI. *Theory of statistics: textbook*. Samara: SSTU; 2014. (In Russ.). [Токарев Ю.А., Шерстобитова Г.И. *Теория статистики: учебное пособие*. Самара: СГТУ; 2014].

33. Porsukov EA. Forensic diagnosis of sudden cardiac death on the background of alcoholic cardiomyopathy. *Russian Journal of Forensic Medicine*. 2019; 5(3): 42-44. (In Russ.). [Порсуков Э.А. Судебно-медицинская диагностика внезапной сердечной смерти на фоне алкогольной кардиомиопатии. *Судебная медицина*. 2019; 5(3): 42-44]. doi: 10.19048/2411-8729-2019-5-3-42-44

34. Shamray VYu, Makhmutova AM, Erubaeva BB. Comparative analysis of the main risk factors for stroke. *Neurosurgery and Neurology of Kazakhstan*. 2019; (2): 85-88. (In Russ.). [Шамрай В.Ю., Махмутова А.М., Ерубаева Б.Б. Сравнительный анализ основных факторов риска инсульта. Нейрохирургия и неврология Казахстана. 2019; (2): 85-88].

35. Petrov DV. *Diagnosis, treatment and prevention of alcohol use disorders*. Yaroslavl; 2002. (In Russ.). [*Петров Д.В. Диагностика, лечение и профилактика расстройств, вызванных употреблением алкоголя*. Ярославль; 2002].

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