



# Updated European guidelines for the prevention of cardiovascular diseases. Analytic review

Mamedov M. N.<sup>1</sup>, Mitchenko E. I.<sup>2</sup>, Serpitis P.<sup>3</sup>, Kamilova U. K.<sup>4</sup>,  
Tsinamdzgvrishvili B. V.<sup>5</sup>, Seisembekov T. Z.<sup>6</sup>, Podpalov V. P.<sup>7</sup>, Olimzoda N. Kh.<sup>8</sup>,  
Istrati V.<sup>9</sup>, Mirrakhimov E. M.<sup>10</sup>, Annaev B. Kh.<sup>11</sup>, Alekperov E. Z.<sup>12</sup>

- <sup>1</sup> National Medical Research Center for Therapy and Preventive Medicine of the Ministry of Healthcare of the Russian Federation, Moscow, Russia.
- <sup>2</sup> National Research Center «Institute of Cardiology named after N.D. Strazhesko» of the Academy of Medical Sciences of Ukraine, Kiev, Ukraine.
- <sup>3</sup> Vilnius University Hospital «Santaros Clinics», Vilnius, Lithuania.
- <sup>4</sup> Republican specialized Scientific-Practical Medical Center of Therapy and Medical Rehabilitation, Tashkent, Uzbekistan.
- <sup>5</sup> Ivane Javakhishvili Tbilisi State University, Tbilisi, Georgia.
- <sup>6</sup> Astana Medical University, Nur-Sultan, Kazakhstan.
- <sup>7</sup> Vitebsk State Medical University, Vitebsk, Belarus.
- <sup>8</sup> Tajik State Medical University, Dushanbe, Tajikistan.
- <sup>9</sup> Moldovan State Medical University, Chisinau, Moldova.
- <sup>10</sup> Kyrgyz State Medical Academy named after I.K. Akhunbaev, Bishkek, Kyrgyzstan.
- <sup>11</sup> Hospital with scientific and clinical center of Cardiology, Ashgabat, Turkmenistan.
- <sup>12</sup> Research Institute of Cardiology named after J. Abdullayev, Baku, Azerbaijan.

*The review article presents the analysis of the main issues of updated European guidelines for the prevention of cardiovascular diseases (CVD). Previous European guidelines were dedicated to the risk stratification and the prevention of risk factors (RFs), when 2021 European Society of Cardiology guidelines on CVD prevention focuses on the personalized and stepwise intervention in clinical practice. Estimation of 10-year fatal and nonfatal CVD risk with SCORE2 is recommended in patients aged from 40 to 69 years, and SCORE-OP - for people aged ≥70 years. Four risk scales are proposed for countries depending on their risk group: low, moderate, high, very high. It is recommended to take into account not only gender and age, but also ethnicity and geographic factors during the development of prophylaxis strategy. It is also essential to personalize treatment by using stepwise method. After initial RF treatment and the achievement of RF treatment goals, the individual residual risk for recurrent CVD should be considered. The presence of comorbidities should be considered during treatment – the treatment of one pathology*

*should not negatively affect the course of other diseases. Lifestyle management is the key method in atherosclerosis-related CVD prevention. Population level approaches is one of the main points in CVD prevention and include complex measures at the governmental and regional levels for various population segments.*

**Keywords:** *prophylaxis, RFs, cardiovascular diseases.*

## INFORMATION ABOUT AUTORS

**Mekhman N. Mamedov\***, MD, doctor of medical sciences, professor, head of the Department of Secondary Prevention of Chronic Non-infectious Diseases of the National Medical Research Center for Therapy and Preventive Medicine of the Ministry of Healthcare of the Russian Federation, Moscow, Russia.

**Elena U. Mitchenko**, MD, doctor of medical sciences, professor, head of the Department of Dyslipidemia of the National Research Center «Institute of Cardiology named after N. D. Strazhesko» of the Academy of Medical Sciences of Ukraine, Kiev, Ukraine.

**Pranas Serpitis**, doctor of medical sciences, professor, head of the Cardiology Department of the Emergency Medicine Center of the Vilnius University Hospital «Santaros Clinics», Vilnius, Lithuania.

**Umida K. Kamilova**, MD, doctor of medical sciences, professor of the Republican specialized Scientific-Practical Medical Center of Therapy and Medical Rehabilitation, Tashkent, Uzbekistan.

**Bezhan V. Tsinamdzgvrishvili**, MD, doctor of medical sciences, professor, head of the Cardiology Center named after M.D. Tsinamdzgvrishvili, head of the Department of Internal Medicine of the Ivane Javakhishvili Tbilisi State University, the president of the Georgian Society of Hypertension, Tbilisi, Georgia.

**Telman Z. Seisembekov**, MD, doctor of medical sciences, professor of the Department of Internal Medicine №2 of Astana Medical University, Nur-Sultan, Kazakhstan.

**Vladislav P. Podpalov**, MD, doctor of medical sciences, professor of the Department of Internal Medicine №1 of Vitebsk State Medical University, Vitebsk, Belarus.

**Nasim K. Olimzoda**, MD, doctor of medical sciences, professor of Tajik State Medical University, Dushanbe, Tajikistan.

**Valery Istrati**, MD, doctor of medical sciences, Moldovan State Medical University, Chisinau, Moldova.

**Erkin M. Mirrakhimov**, MD, doctor of medical sciences, professor, head of the Department of Internal Medicine of Kyrgyz State Medical Academy named after I. K. Akhunbaev, Bishkek, Kyrgyzstan.

**Begench H. Annaev**, MD, PhD, Hospital with scientific and clinical center of Cardiology, Ashgabat, Turkmenistan.

**Elman Z. Alekperov**, MD, doctor of medical sciences, leading researcher of the Department of myocardial infarction of Research Institute of Cardiology. named after J. Abdullayev, Baku, Azerbaijan.

## FOR CITATION

Mamedov M. N., Mitchenko E. I., Pranas Serpitis, Kamilova U. K., Tsinamdzgvrishvili B. V., Seisembekov T. Z., Podpalov V. P., Olimzoda N. Kh., Istrati V., Mirrakhimov E. M., Annaev B. Kh., Alekperov E. Z. Updated European guidelines for the prevention of cardiovascular diseases. Analytic review. International Heart and Vascular Disease Journal. 2022. 10[33]. DOI 10.24412/2311-1623-2022-33-3-9

**Conflict of interest:** none declared.



Received: 20.09.2021

Accepted: 28.10.2021

Cardiovascular diseases associated with atherosclerosis are the main cause of mortality worldwide. The disease burden of cancer in Europe has been increasing over the last years. However, coronary artery disease

\* Corresponding author. Tel. +7(926) 228-3309. E-mail: mmamedov@mail.ru



(CAD) and ischemic stroke are still the main causes of death [1]. According to the World Health Organization (WHO), Western Europe countries have low and medium cardiovascular risk (CVR), while countries of Eastern Europe and the former Soviet Union remain at high and very high risk that requires active interventions, including primary prevention measures [2].

Cardiovascular events prophylaxis by the reduction of cardiovascular risk is the main priority in primary prevention [3]. Previous European guidelines focused on risk stratification and RF (RF) prevention, while 2021 updated European Society of Cardiology recommendations places a strong emphasis on personalization and stepwise intervention in clinical practice [4].

Here we present the main updates on cardiovascular complications (CVC) risk assessment and the principles of preventive interventions based on analyzed clinical guidelines. According to the new guidelines, it is necessary to assess CVR not only in apparently healthy people, but also in older people with diagnosed cardiovascular diseases, as well as in people with diabetes mellitus (DM) that allows to personalize preventive measures. This approach should also be applied in patients with other diseases, including DM, chronic kidney disease (CKD), chronic obstructive pulmonary disease (COPD).

The updated scale predicts not only fatal, but also non-fatal events that increases CVR numerical expressions.

For the first time non-high-density lipoprotein cholesterol instead of total cholesterol is used for the calculation of CVR, which requires the analysis of full lipid panel.

For the assessment of 10-year CVR in people aged 40-69 years SCORE2 scale is recommended, and SCORE2-OP is recommended in people  $\geq 70$  years. Moreover, the cut-off for CVR varies in three age categories (<50, 50-69,  $\geq 70$  years) [5,6]. Scales are calibrated to four clusters of countries depending on CVD risk group: low, moderate, high, and very high.

It has been established that psychosomatic stress is associated with atherosclerosis-related CVD risk [7]. Social factors also play a pivotal role in the prognosis and CVD development [8].

Family history should be enquired about routinely, and a positive family history of premature CVD should be considered in CVD risk assessment [9] Current data does not support the use of genomic risk scores in CVD risk assessment in primary prevention. CVR

prevalence varies in different age groups. For example, 2.5% has low CVD risk at <50 years, 5% — at 50-69 years, 7.5% - at 70 years. According to the new guidelines, patients with low CVR do not require RFs correction, patients with high CVR need correction, and in patients with very high CVR the correction of RFs is mandatory [4].

Not only gender and age, but also, ethnic, and geographic factors should be considered during the development of prophylaxis strategy.

Treatment goals also need to be personalized using a stepwise approach. The term residual risk was introduced for patients with established CVD that is defined as the risk assessed after initial lifestyle changes and RF correction [4].

One of widely discussed issues of updated guidelines is comorbidities and CVD risk. This can be explained by the fact that the number of patients with non-cardiovascular comorbidities is constantly increasing. Adverse effects of prescribed medications should be considered during treatment strategy development in patients with comorbidities. The management of comorbid diseases should be personalized and not focus on the disease separately. The updated document addresses the principles for the prevention of complications in a number of comorbidities.

Cancer and CVD have common RFs. High risk of CVC in patients with cancer can be explained not only by chemotherapy-induced cardiotoxicity, but also by the presence of RFs [10].

CKD is independent CVD RF, and CVD is the main cause of death in patients with CKD [11]. In all CKD patients, appropriate screening for CVD and changes in albuminuria monitoring is recommended. A reduction in albuminuria by approximately 30% upon starting renin-angiotensin-aldosterone system (RAAS) inhibition is associated with improved cardiovascular and kidney outcomes.

COPD is the main CVD RF including stroke and heart failure (HF) [12]. Patients with COPD tend to have atrial fibrillation (AF), ventricular tachycardia, and sudden cardiac death. All patients with COPD should be screened for CVD. Medications for COPD treatment are safe for patients with CVD.

Non-alcoholic fatty liver disease is associated with other cardiometabolic RF, therefore, screening for other cardiometabolic RFs is recommended for this group of patients.

Migraine, especially with aura, is independent RF for ischemic stroke and CAD [13]. Vascular risk of subjects with migraine may be magnified by cigarette smoking and by the use of combined hormonal contraceptives.

Sleep duration that varies significantly up or down from the optimum of 7 h are associated with increased CV risk [4].

The risk of psychosomatic diseases increases by 2.2 times in patients with CVD that negativity affect their prognosis [14]. For the other hand, symptoms of anxiety and depression are associated with the development of CVD and with a worse prognosis in those with existing CVD (CAD, arterial hypertension (AH), AF, HF).

Preeclampsia and pregnancy-related hypertension are associated with a higher risk of CVD. Polycystic ovary syndrome confers a significant risk for future development of DM [4].

Erectile dysfunction (ED) is associated with future cardiovascular events and mortality in men of reproductive age. CVD risk should be assessed in men with ED [4].

Lifestyle change is an important point in atherosclerosis-related CVD risk prevention. Traditionally, it includes physical activity, healthy diet, and bad habits reduction [15].

Regular physical activity is the basis of CVD prevention. All adults are recommended to perform aerobic physical activity and reduce sedentary lifestyle [16].

Healthy diet reduces the risk of cardiovascular and other chronic diseases. A shift from an animal- to a more plant-based food pattern can reduce the frequency of CVD [17].

The achievement and maintenance of optimal body mass through lifestyle changes positively affect major RFs such as: blood pressure (BP), lipid and glucose metabolism. Pharmacotherapy and bariatric surgery can be recommended in high-risk individuals when lifestyle changes are ineffective [4].

Smoking cessation reduce CVD risk and is one of the key strategies in its primary and secondary prophylaxis. The following medications can be recommended: nicotine replacement therapy, varenicline, and bupropion individually or in combination [18].

Interdisciplinary approach can be recommended for the correction of psychosomatic disorders. Stress reduction and life quality improvement positively affect CVD outcomes [7].

The reduction of low-density lipoproteins (LDL) cholesterol followed by the maintenance of target level, reduces the risk of cardiovascular events. Lowering LDL cholesterol with statins, ezetimibe, and, if needed, PCSK9 inhibitors, decreases the risk of CVD proportionally to the absolute achieved reduction in LDL cholesterol [19]. When LDL cholesterol goals according to level of risk cannot be attained, LDL cholesterol should be reduced by  $>50\%$ .

When AH is suspected, the diagnosis should be confirmed by repeated office BP measurement or 24-hour BP monitoring. Lifestyle interventions are indicated for all patients with AH and can delay the need for drug treatment or complement the BP-lowering effect during treatment. BP-lowering drug treatment is recommended in adults when office BP is  $\geq 40/90$  mmHg and in all adults when BP is  $\geq 160/100$  mmHg. BP treatment goals are lower in updated guidelines compared with previous recommendations for all patient groups, including older patients. A simple drug treatment algorithm should be used to treat most patients, based on combinations of a renin-angiotensin system (RAS) blocker with calcium channel blockers or thiazide/thiazide-like diuretics. Beta-blockers and mineralocorticoid receptor antagonists may also be used where there is a guideline-directed indication [20]. Patients with high or very high risk can be recommended with statin therapy for primary prevention. Antiplatelet therapy is indicated for secondary prevention in patients with AH.

A multifactorial approach, including lifestyle changes, is critical for patients with type 2 DM. It is known that the management of hyperglycemia reduces the risk of microvascular complications and, to a lesser extent, the risk of CVD. Glycemic targets should be relaxed in older patients. New antihyperglycemic drugs are particularly important for patients with type 2 DM with existing CVD and HF or renal failure [21].

Intensive treatment of hyperglycemia in patients with type 1 DM reduces the risk of micro- and macrovascular complications and premature mortality. The target of 6.5 - 7.5% (48-58 mmol/mol) of HbA1c is recommended. Metformin is not recommended in patients with type 1 DM to lower CVD risk. Dapagliflozin can be recommended for use in patients with type 1 DM, although it increases the risk of diabetic ketoacidosis. Other RFs reduction, in particular smoking, BP, and cholesterol levels, remains an important measure to lower CVD risk in type 1 DM.

All patients with established CVD regardless of their clinical state require mono- or dual antithrombotic therapy. The updated guidelines present new data on antithrombotic therapy schemes for atherosclerosis-related CVD risk prevention. The management of CVD RFs associated with particular disease (CAD, HF, cerebrovascular disease, peripheral artery disease) require multifactorial approach [22, 23].

Population-level approaches are important for CVD prevention. Prospective studies have shown the effectiveness of multifactorial prevention the governmental and regional levels [24]. Population-level approaches for CVD prevention include approaches to increase regular physical activity, healthy diet adherence, tobacco and alcohol use cessation. These skills should be developed from school age. Daily physical activity at school should be practiced for at least 3 hours a week. Overall, global progress to increase physical activity has been slow, largely due to lack of awareness and investment. Adolescence is the most vulnerable period for the uptake of smoking, with life-long consequences. Previous prevention campaigns reduced tobacco use in girls much less than in boys. High taxes on all tobacco products are the most effective policy measure to reduce smoking uptake by the young. Within the 10 voluntary targets of World Health Organization to reach in 2025 is a 30% relative reduction in mean population salt intake. Structural measures such as: product reformulation, limitations on marketing to children, taxes on unhealthy foods,

and nutrition labelling will improve healthy food choices. The measures for the reduction of harmful use of alcohol are cost-effective (increasing alcoholic beverage minimum unit pricing, restricting access to alcoholic beverages, and implementing comprehensive restrictions on advertising and the promotion of alcoholic beverages) [4].

Environment, air pollution, and climate change issues are significant factors in CVD and other chronic disease prevention. Environmental exposure has taken on new urgency, as air pollution, in addition to its health effects, has also been ascribed as a major contributor to climate changes, notably through the burning of fossil fuels leading to increasing emissions of carbon dioxide.

## Conclusion

Thus, personalized approach to CVD prevention with the implementation of CVD risk score and a stepwise treatment-intensification approach is more complex compared with general prevention strategy, however, it addresses patients' diversity and individual characteristics in clinical practice.

Principles of lifestyle changes, psychosocial factors, behavioral and biological parameters, as well as the social status of the patient should be considered during the development of individual strategy for CVD prevention and rehabilitation.

**Conflict of interest:** None declared.

## References

1. Kotseva K., De Backer G., De Bacquer D., Ryden L., Hoes A., Grobbee D., Maggioni A., Marques-Vidal P., Jennings C., Abreu A., Aguiar C., Badariceni J., Bruthans J., Cifkova R., Davletov K., Dilic M., Dolzhenko M., Gaita D., Gotcheva N., Hasan-Ali H., Jankowski P., Lionis C., Mancas S., Milicic D., Mirrakhimov E., Oganov R., Pogossova N., Reiner Z., Vucic D., Wood D. Primary prevention efforts are poorly developed in people at high cardiovascular risk: A report from the European Society of Cardiology EURObservational Research Programme EUROASPIRE V survey in 16 European countries. *Eur J Prev Cardiol.* 2020;2047487320908698. doi: 10.1177/2047487320908698
2. World Health Organization. Gender and health. [https://www.who.int/health-topics/gender#tab=tab\\_1](https://www.who.int/health-topics/gender#tab=tab_1) (4 June 2021).
3. Piepoli M.F., Hoes A.W., Agewall S., Albus C., Brotons C., Catapano A.L., Cooney M.T., Corra U., Cosyns B., Deaton C., Graham I., Hall M.S., Hobbs F.D.R., Lochen M.L., Lollgen H., Marques-Vidal P., Perk J., Prescott E., Redon J., Richter D.J., Sattar N., Smulders Y., Tiberi M., van der Worp H.B., van Dis I., Verschuren W.M.M., Binno S., ESC Scientific Document Group. 2016 European Guidelines on cardiovascular disease prevention in clinical practice: The Sixth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of 10 societies and by invited experts) Developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR). *Eur Heart J.* 2016;37:2315–2381. Doi: 10.1093/eurheartj/ehw106
4. Visseren F.J., Mach F., Smulders Y., Carballo D., Koskinas K.S., Bäck M., Benetos A., Biffi A., Boavida J., Capodanno D., Cosyns B., Crawford C., Davos C.H., Desormais I., Angelantonio E.D., Franco O.H., Halvorsen S., Hobbs R., Hollander M., Jankowska E.A., Michal M., Sacco S., Sattar N.,

- Tokgozoglu L., Tonstad S., Tsioufis K. P., Dis I. van, Gelder I. S. van, Wanner C., Williams B., ESC Scientific Document Group, 2021 ESC Guidelines on cardiovascular disease prevention in clinical practice: Developed by the Task Force for cardiovascular disease prevention in clinical practice with representatives of the European Society of Cardiology and 12 medical societies With the special contribution of the European Association of Preventive Cardiology [EAPC], *European Heart Journal*, Vol. 42, Issue 34, 7 September 2021, P. 3227–3337, <https://doi.org/10.1093/eurheartj/ehab484>
5. SCORE2 working group and ESC Cardiovascular risk collaboration. SCORE2 risk prediction algorithms: new models to estimate 10-year risk of cardiovascular disease in Europe. *Eur Heart J*. 2021;42:2439–2454. Doi: 10.1093/eurheartj/ehab309
  6. SCORE2-OP working group and ESC Cardiovascular risk collaboration. SCORE2-OP risk prediction algorithms: estimating incident cardiovascular event risk in older persons in four geographical risk regions. *Eur Heart J*. 2021;42:2455–2467. Doi: 10.1093/eurheartj/ehab312
  7. Crawshaw J., Auyeung V., Norton S., Weinman J. Identifying psychosocial predictors of medication non-adherence following acute coronary syndrome: A systematic review and meta-analysis. *J Psychosom Res*. 2016;90:10–32. Doi: 10.1016/j.jpsychores.2016.09.003
  8. Schultz W.M., Kelli H.M., Lisko J.C., Varghese T., Shen J., Sandesara P., Quyyumi A.A., Taylor H.A., Gulati M., Harold J.G., Mieres J.H., Ferdinand K.C., Mensah G.A., Sperling L.S. Socioeconomic Status and Cardiovascular Outcomes: Challenges and Interventions. *Circulation*. 2018;137:2166–2178. Doi: 10.1161/CIRCULATIONAHA.117.029652
  9. Musunuru K., Kathiresan S. Genetics of Common, Complex Coronary Artery Disease. *Cell*. 2019;177:132–145. Doi: 10.1016/j.cell.2019.02.015
  10. Armenian S.H., Xu L., Ky B., Sun C., Farol L.T., Pal S.K., Douglas P.S., Bhatia S., Chao C. Cardiovascular Disease Among Survivors of Adult-Onset Cancer: A Community-Based Retrospective Cohort Study. *J Clin Oncol*. 2016;34:1122–1130. Doi: 10.1200/JCO.2015.64.0409
  11. GBD Chronic Kidney Disease Collaboration. Global, regional and national burden of chronic kidney disease, 1990–2017: a systematic analysis for the Global Burden of Disease Study. 2017. *Lancet*. 2020;395:709–733. Doi: 10.1016/S0140-6736(20)30045-3
  12. Chen W., Thomas J., Sadatsafavi M., FitzGerald J.M. Risk of cardiovascular comorbidity in patients with chronic obstructive pulmonary disease: a systematic review and meta-analysis. *Lancet Respir Med*. 2015;3:631–639. Doi: 10.1016/S2213-2600(15)00241-6
  13. Kurth T., Winter A. C., Eliassen A. H., Dushkes R., Mukamal K. J., Rimm E. B., Willett W. C., Manson J. E., Rexrode K. M. Migraine and risk of cardiovascular disease in women: prospective cohort study. *BMJ*. 2016;353:i2610. Doi: 10.1136/bmj.i2610
  14. Jha M.K., Qamar A., Vaduganathan M., Charney D.S., Murrough J.W. Screening and Management of Depression in Patients With Cardiovascular Disease: JACC State-of-the-Art Review. *J Am Coll Cardiol*. 2019;73:1827–1845. Doi: 10.1016/j.jacc.2019.01.041
  15. Rozanski A. Behavioral cardiology: current advances and future directions. *J Am Coll Cardiol*. 2014;64:100–110. Doi: 10.1016/j.jacc.2014.03.047
  16. Jakicic J.M., Kraus W.E., Powell K.E., Campbell W.W., Janz K.F., Troiano R.P., Sprow K., Torres A., Piercy K.L., 2018 Physical Activity Guidelines Advisory Committee. Association between Bout Duration of Physical Activity and Health: Systematic Review. *Med Sci Sports Exerc*. 2019;51:1213–1219. Doi: 10.1249/MSS.0000000000001933
  17. Guasch-Ferre M., Satija A., Blondin S.A., Janiszewski M., Emlen E., O'Connor L.E., Campbell W.W., Hu F.B., Willett W.C., Stampfer M.J. Meta-Analysis of Randomized Controlled Trials of Red Meat Consumption in Comparison With Various Comparison Diets on Cardiovascular RFS. *Circulation*. 2019;139:1828–1845. Doi: 10.1161/CIRCULATIONAHA.118.035225
  18. Anthonisen N.R., Skeans M.A., Wise R.A., Manfreda J., Kanner R.E., Connett J.E., Lung Health Study Research Group. The effects of a smoking cessation intervention on 14.5-year mortality: a randomized clinical trial. *Ann Intern Med*. 2005;142:233–239. Doi: 10.7326/0003-4819-142-4-200502150-00005
  19. Cholesterol Treatment Trialists' (CTT) Collaboration, Fulcher J., O'Connell R., Voysey M., Emberson J., Blackwell L., Mihaylova B., Simes J., Collins R., Kirby A., Colhoun H., Braunwald E., La Rosa J., Pedersen T.R., Tonkin A., Davis B., Sleight P., Franzosi M.G., Baigent C., Keech A. Efficacy and safety of LDL-lowering therapy among men and women: meta-analysis of individual data from 174,000 participants in 27 randomised trials. *Lancet*. 2015;385:1397–1405. Doi: 10.1016/S0140-6736(15)01350-5
  20. Ettehad D., Emdin C.A., Kiran A., Anderson S.G., Callender T., Emberson J., Chalmers J., Rodgers A., Rahimi K. Blood pressure lowering for prevention of cardiovascular disease and death: a systematic review and meta-analysis. *Lancet*. 2016;387:957–967. Doi: 10.1016/S0140-6736(15)01225-8
  21. Marx N., Davies M.J., Grant P.J., Mathieu C., Petrie J.R., Cosentino F., Buse J.B. Guideline recommendations and the positioning of newer drugs in type 2 diabetes care. *Lancet Diabetes Endocrinol*. 2021;9:46–52. Doi: 10.1016/S2213-8587(20)30343-0



22. Knuuti J., Wijns W., Saraste A., Capodanno D., Barbato E., Funck-Brentano C., Prescott E., Storey R.F., Deaton C., Cuisset T., Agewall S., Dickstein K., Edvardsen T., Escaned J., Gersh B. J., Svitil P., Gilard M., Hasdai D., Hatala R., Mahfoud F., Masip J., Muneretto C., Valgimigli M., Achenbach S., Bax J. J., ESC Scientific Document Group. 2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes. *Eur Heart J.* 2020;41:407–477. Doi: 10.1093/eurheartj/ehz425
23. Chiarito M., Sanz-Sanchez J., Cannata F., Cao D., Sturla M., Panico C., Godino C., Regazzoli D., Reimers B., De Caterina R., Condorelli G., Ferrante G., Stefanini G. G. Monotherapy with a P2Y12 inhibitor or aspirin for secondary prevention in patients with established atherosclerosis: a systematic review and meta-analysis. *Lancet.* 2020;395:1487–1495. Doi: 10.1016/S0140-6736(20)30315-9
24. World Health Organization. Disease burden and mortality estimates. [www.who.int/healthinfo/global\\_burden\\_disease/estimates/en](http://www.who.int/healthinfo/global_burden_disease/estimates/en) (4 June 2021).