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CV RISK – A new relative cardiovascular risk score

Dumitru Zdrenghea[a,b], Gabriel Guşetu[a,b,*], Mihnea Zdrenghea[a,b], Gabriel Cismaru[a,b], Bogdan Caloian[a,b], Georgeta Vaidean[c], Dana Pop[a,b]

[a] University of Medicine and Pharmacy "Iuliu Hatieganu", Cluj-Napoca, Romania
[b] Clinical Rehabilitation Hospital, Cardiology Department, Cluj-Napoca, Romania
[c] Fairleigh Dickinson University, Department of Chemistry and Pharmaceutical Science, New York, United States

A B S T R A C T

Background and aims: Nowadays it is recommended to use risk scores to evaluate the magnitude of cardiovascular risk in healthy people, most popular being SCORE (Europe) and Framingham and ASCVD (US). Unfortunately, they are not enough motivating in young and old population, don't consider protective factors and cannot be used in cardiovascular patients always included in very high risk category. To improve the evaluation everytime of individual cardiovascular risk we described a new score – CVRISK (cardiovascular relative individual risk).
Methods: It uses 15 items and can be used also in cardiovascular patients. The first seven items are clinical – age and gender, heredity, smoking, hypertension, obesity, psychosocial stress, previous cardiovascular disease. For items refer to laboratory data – LDL-C, HDL-C, TG, fasting plasma glucose (diabetes mellitus). The last two are protective factors – physical activity and healthy diet.
Results: Every item has a number of risk points and protective factors decrease with 25% and 15% the calculated risk. The risk can be automatically calculated after the introduction of the required data through an algorithm available at www.cvrisk.ro. Here, the calculated risk is compared with optimal and maximal risk. Thus the user is motivated to initiate or to continue preventive measures also suggested at www.cvrisk.ro, to improve cardiovascular health.
Conclusion: CVRISK is not a substitute of current risk scores, but a complimentary tool to appreciate and modulate the individual cardiovascular risk. It can be useful to prevent CV disease or to improve its evolution. Individuals themselves can calculate it in order to maintain or improve their health.

Background

Nowadays, it is definitely well recognized that degenerative cardiovascular disease, mainly atherosclerosis, depends on unmodifiable and modifiable risk factors [1,2].

Risk scores, mainly SCORE (Europe) [1,3], Framingham [4] and ASCVD (US) [5,6], are used to evaluate the magnitude of cardiovascular (CV) risk.

According to these scores, subjects are included in low, moderate, high and very high-risk categories [1,7] and several preventive measures are recommended to reduce CV risk factors.

CV patients are always in the very high-risk category, while diabetes mellitus and chronic kidney disease are also known to increase CV risk.

The INTERHEART study [8] has proved that atherosclerosis and ischemic heart disease depend, in all geographical regions, on the same risk factors. Different prevalence of ischemic heart disease results from different prevalence of risk factors. The study has identified six main risk factors (RF), namely high cholesterol (apoB/apoA ratio), smoking, hypertension (HTN), obesity, diabetes mellitus, psychosocial stress. It has also identified three protective factors: rich fruits and vegetables diet (Mediterranean), physical activity and moderate alcohol consumption.

All CV risk scores have however a few limitations.

They don't consider the population under 30 and no difference is made in the population over 65 years [1,4]. Also, obesity and psychosocial stress are not included in the calculation of the risk [1,4].

The protective factors are not included in these those scores, even if they can decrease significantly the incidence and prevalence of ischemic heart disease [1,3–5].

That's why the absolute risk scores (SCORE, Framingham, ASCVD) are not motivating for young and old people. For example, in a subject 75 years old, a ten years risk of 15% (very high) to die by CV disease) means not much, because general mortality in the same period is much higher.

To be noted that all in use scores cannot be applied in CV patients, because they are already in the very high-risk category [1,3–5]. Therefore, the patients are not motivated to submit secondary preventive measures.

It would be necessary to have a CV risk score which considers all main risk factors and protective ones, and that could also be used in

* Corresponding author at: 46-50 Viilor Street, 2nd Floor, Room 221, Clinical Rehabilitation Hospital, Cardiology Dept., University of Medicine and Pharmacy "Iuliu Hatieganu", Cluj-Napoca 400347, Romania.
E-mail addresses: dzdrenghea@yahoo.com (D. Zdrenghea), gusetu@gmail.com (G. Guşetu), m.zdrenghea@yahoo.com (M. Zdrenghea), gabi_cismaru@yahoo.com (G. Cismaru), bogdan912@yahoo.com (B. Caloian), gvaidean@fdu.edu (G. Vaidean), pop67dana@gmail.com (D. Pop).

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young and old population, as well as in CV patients. The option to evaluate CV risk even when laboratory data are not available would increase the popularity and usefulness of such a score.

More people would feel more motivated to apply preventive measures by a score that would allow to gage in evolution, the relative risk to develop a CV disease.

Of course such a score, if not validated through population studies, can be considered more a tool to evaluate ideal cardiovascular health [9,10] than a true CV RISK score

The hypothesis

Considering all the above things, our new CV RISK (cardiovascular relative individual risk) score is trying to address all these unmet needs. It evaluates using 13 items, the individual relative risk to acquire or to die through CV disease during lifetime.

We included the six RF proved to be important in the INTERHEART study, but we replaced ApoB/ApoA ratio with LDL-C or total cholesterol (TC). We also considered two protective factors: physical activity and a healthy diet. We added HDL-C and TG which can modulate CV risk and also age and gender, heredity and the presence of CV disease [1,2,11,12].

We decided to attribute 1 point of risk to every item, even not present, to reinforce that CV disease can appear even when RF are missing. An exception – no CV disease received 0 points. The protective factors result in percent decrease of calculated risk.

The first seven items are clinical and result in a rough evaluation of CV RISK. When the remaining four laboratory items are available it is possible to more accurately calculate the total CV RISK.

Attributing points of risk to every item we considered the current literature data [1,2], especially INTERHEART study [8] and not our own studies.

Because every factor is evaluated by subjects or patients themselves, and not by a doctor, the evaluation being partially subjective, we simplified the calculation of the points of risk and the percent reduction of CV risk through protective factors. We made it easier to calculate and more motivating for the subjects. We considered this is not an important error because CV RISK doesn't compare everyone with the others, but with himself, over time.

We will describe separately every item (Table1).

Age and gender

CV disease is prevalent in men up to 65 years of age, and in women above 75 [1,2]. Considering this, but also the low incidence of ischemic heart disease in young people, we used a combined item for gender and age, attributing 1p for men under 40 and women under 50, 2p between 40–65 (men) and 50–75(women) and 3p above this age (see Table 2).

Heredity

The influence of heredity is difficult to quantify, but genetic component is suggested when CV disease appears under 55 (men) or 65 (women) [13,14]. To simplify, we considered 60 years of age for both genders. If parents didn't develop CV disease before 60, the value of risk is 1p; if they did, it's 2p.

Psychosocial stress

It is difficult to define and recognize and usually it is not included in CV risk scores. We think it is important even if subjective, and INTERHEART demonstrated that a too tempestuous lifestyle is a true CV risk factor [15,16]. We ask subjects to appreciate whether they are stressed during daily activity (2p) or not (1p).

Table 1
CV RISK calculation chart.

1	Age and gender	< 40 yr (M); < 50 yr (F)	**1p**
		40–65 yr (M); 50–75 yr (F)	**2p**
		> 65 yr (M); > 75 yr (F)	**3p**
2	Heredity	parents without CVD < 60 yr	**1p**
		parents with CVD < 60 yr	**2p**
3	Smoking (any)	No	**1p**
		Yes	**2p**
4	BP	< 140/90 mmHg	**1p**
		≥140/90 mmHg	**2p**
5	Obesity	BMI < 30 Kg/m^2	**1p**
		BMI ≥ 30 Kg/m^2	**2p**
6	Stress	No	**1p**
		Yes	**2p**
7	CVD	Without CVD	**0p**
		With CVD	**10p**
8	LDL-C (TC)		
	Primary prevention : without CVD		
		< 100 mg/dl; (< 175 mg/dl)	**1p**
		100–160 mg/dl; (175–250 mg/dl)	**2p**
		> 160 mg/dl; (> 250 mg/dl)	**3p**
	Secondary prevention: with CVD		
		< 70 mg/dl; (< 155 mg/dl)	**1p**
		70–130 mg/dl; (155–200 mg/dl)	**2p**
		> 130 mg/dl; (> 200 mg/dl)	**3p**
9	HDL	≥40 mg/dl (M); ≥45 mg/dl (F)	**1p**
		< 40 mg/dl (M); < 45 mg/dl (F);	**2p**
10	TG	< 150 mg/dl	**1p**
		≥150 mg/dl	**2p**
11	DM	No	**1p**
		Yes	**2p**
12	Physical activity	Yes	**−25%**
13	Healthy diet	Yes	**−15%**

Abbreviations: BMI, body mass index; BP, blood pressure; CVD, cardiovascular disease; DM, diabetes mellitus; F, female; HDL-C, HDL cholesterol; LDL-C, LDL cholesterol; M, male; TC, total cholesterol; TG, triglycerides;
Clinical **CV Risk**: items 1–7 (± 12, 13) Total **CV Risk**: items 1–11 (± 12, 13).

Table 2
Optimal and maximal **CV RISK** by age and gender.

Category	Optimal CV RISK		Maximal CV RISK	
	Clinical	Total	Clinical	Total
Without CVD				
< 40 yr (M); < 50 yr (F)	3.6p	6p	11p	20p
40–65 yr (M); 50–75 yr (F)	4.2p	6.6p	12p	21p
> 65 yr (M); > 75 yr (F)	4.8p	7.2p	13p	22p
With CVD				
< 40 yr (M); < 50 yr (F)	9.6p	12p	21p	30p
40–65 yr (M); 50–75 yr (F)	10.2p	12.6p	22p	31p
> 65 yr (M); > 75 yr (F)	10.8p	13.2p	23p	32p

Abbreviations: CVD, cardiovascular disease; F, female; M, male;
CV RISK – a New Relative Cardiovascular Risk Score.

Smoking

Smoking is first among modifiable risk factors [17,18], being easier to be influenced, even if the results at population level are not so good. It is easily detectable but not easily quantified. We accorded 1p for nonsmokers and former smokers and 2p for smokers of any type and

intensity.

Hypertension

It is the most prevalent risk factor in the whole world [19,20]. The definition of HTN is different in different guidelines but we consider the classical value of 140/90 mmHg, attributing 1p under this value and 2p above this value. The subjects with blood pressure less than 140/90 mmHg under treatment receive 2p.

Obesity

It is recognized as an independent CV risk factor [21], but when associated with the others (metabolic syndrome), it increases CV risk exponentially. For easier evaluation, we considered only body mass index, attributing 1p under and 2p above 30 kg/m^2.

Cardiovascular disease

Cardiovascular disease is not included in risk scores, CV patients being considered always and forever as very high-risk category [1]. We assigned 10 points for this clinical condition. This will increase substantially the number of points of risk, but an adequate control of RF and promotion of protective factors can much decrease the calculated risk. This way, in time, the patients are motivated to adopt secondary preventive measures and a healthy lifestyle.

All the above 7 items are included in the clinical module-clinical CV RISK, with a rough, but important, estimation of the risk to develop an ischemic heart disease.

Laboratory data

They are very important and included in CV RISK when they are available.

LDL-C (or TC) is one of the most important risk factors [22,23]. We considered, according to guidelines but simplified, and separately for primary and secondary prevention, the three levels of LDL-C (TC), attributing 1p, 2p, or 3p (see Table 1).

Diabetes mellitus is an increasingly important and prevalent CV risk factor, associated or not with the others as metabolic syndrome [24,25]. It is appreciated through serum fasting glucose (see table 1) or known disease, resulting 1p (no diabetes) or 2p of risk (with diabetes).

HDL-C, when decreased, (less than 40 mg/dL in men and less than 45 mg/dL in women) increase CV risk. We attributed 1p above and 2p under these values.

Triglycerides (TG). They are an independent or associated risk factor mainly in subjects with metabolic syndrome [26,27]. A value under 150 mg/dL was noted with 1p and above with 2p.

Availability of all above 11 items offers the possibility of a more accurate calculation of CV risk-total CVRISK.

Protective factors

Physical activity performed every day at least 30 min, at least 5 times/week reduced CV risk and mortality in both healthy people and CV patients, with approximatively 25–30% [1,28,29]. That is why we considered such an activity reduces the number of calculated risk points with 25%.

Healthy diet

It is a well known protective factor [30,31]. We considered a simplified form of Mediterranean diet (daily use of fruits and vegetables, not quantified in servings, use of vegetable oil and not of animal fat. In this case the number of points of risk is reduced by15%, probably less in reality, but very important to motivate people to adopt a healthy lifestyle.

We renounced to introduce alcohol consumption as a protective factor [32] for two reasons. High alcohol consumption has many negative consequences, including cardiac ones. Also, some recent studies had have doubt on any beneficial effect of moderate alcohol consumption [33].

Evaluation of the hypothesis

It is possible to calculate Clinical CVRISK (when only the 7 clinical items are available), or Total CVRISK, when all 11 items are available), the number of risk points being reduced in both cases by 15% in case of a healthy diet and another 25% in case of regular physical activity.

Both Clinical and Total CVRISK are expressed in points of risk, which can be compared with optimal risk for every subject or CV patient (minimum points of risk when there are no risk factors and a healthy lifestyle) and with maximal risk (maximum number of points obtained when all risk factors are present and also an unhealthy lifestyle).

The CV RISK can be automatically calculated after the introduction of the required data, through an algorithm available at www.cvrisk.ro.

For a better evaluation of CVRISK it is possible to calculate the unfavorable risk as ratio between calculated risk and optimal risk. Its negative prognostic value is in direct relationship with a value higher than 1.

Depending on the RF contributing to unfavorable risk, we recommend specific preventive measures, including medical advice (very high values of risk factors - HTN, dyslipidemia, etc.).

Every patient can calculate the CVRISK over time referring to the initial calculated in order to continue preventive measures (when the number of points of risk is low or decreasing), or to adopt additional preventive measures (when the number of points of risk is high or increasing).

It is recommended for CVRISK to be calculated in healthy individuals after 40 years old (but optionally also before), every one or two years. In CV patients of any age CVRISK is recommended every six months or at least yearly.

Consequences of the hypothesis

CVRISK is not a surrogate of current risk scores, but a complimentary tool to assess and refine the individual CV risk and ideal cardiovascular health.

It can be useful to prevent CV disease or to improve its evolution. Individuals themselves can calculate it in order to maintain or improve their health.

Declaration of Competing Interest

No conflict of interests.

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References

[1] Piepoli MF, Hoes AW, Agewall S, et al. 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(29):2315–81.

[2] Arnett DK, Blumenthal RS, Albert MA, et al. ACC/AHA guideline on the primary prevention of cardiovascular disease. J Am Coll Cardiol 2019;2019. https://doi.org/10.1016/j.jacc.2019.03.010.

[3] Conroy RM, Pyorala K, Fitzgerald AP, Sans S, Menotti A, De Backer G. Estimation of

ten-year risk of fatal cardiovascular disease in Europe: the SCORE project. Eur Heart J 2003;24(11):987–1003.
[4] Lee MS, Flammer AJ, Li J, Lennon RJ, Delacroix S, Kim H. Comparison of time trends of cardiovascular disease risk factors and framingham risk score between patients with and without acute coronary syndrome undergoing percutaneous intervention over the last 17 years: from the mayo clinic percutaneous coronary intervention registry. Clin Cardiol 2015;38(12):747–56.
[5] Preiss D, Kristensen SL. The new pooled cohort equations risk calculator. Canad J Cardiol 2015;31(5):613–9.
[6] American College of Cardiology, American Heart Association. ASCVD Risk Estimator. Available at: https://tools.acc.org/ldl/ascvd_risk_estimator/index.html#!/calulate/estimator.
[7] Goff Jr DC, Lloyd-Jones DM, Bennett G, et al. 2013 ACC/AHA guideline on the assessment of cardiovascular risk: a report of the American College of Cardiology/American Heart Association TaskForce on Practice Guidelines. J Am Coll Cardiol 2014;63:2935–59.
[8] Yusuf S, Hawken S, Ounpuu S, Dans T, Avezum A, Lanas F. 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.
[9] Shah AM, Claggett B, Folsom AR, Lutsey PL, Ballantyne CM, Heiss G. Ideal cardiovascular health during adult life and cardiovascular structure and function among the elderly. Circulation 2015;132(21):1979–89.
[10] Lloyd-Jones DM, Hong Y, Labarthe D, Mozaffarian D, Appel LJ, Van Horn L. Defining and setting national goals for cardiovascular health promotion and disease reduction: the American Heart Association's strategic Impact Goal through 2020 and beyond. Circulation 2010;121(4):586–613.
[11] Catapano AL, Graham I, De Backer G, et al. 2016 ESC/EAS guidelines for the management of dyslipidaemias. Eur Heart J 2016;37(39):2999–3058.
[12] Grundy SM, Stone NJ, Bailey AL, et al. AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA guideline on the management of blood cholesterol. A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol 2018. https://doi.org/10.1016/j.jacc.2018.11.003.
[13] Banerjee A. A review of family history of cardiovascular disease: risk factor and research tool. Int J Clin Pract. 2012;66:536–43.
[14] Bachmann JM, Willis BL, Ayers CR, Khera A, Berry JD. Association between family history and coronary heart disease death across long-term follow-up in men: the cooper center longitudinal study. Circulation 2012;125:3092–8.
[15] Rosengren A, Hawken S, Ounpuu S, Sliwa K, Zubaid M, Almahmeed WA. Association of psychosocial risk factors with risk of acute myocardial infarction in 11119 cases and 13648 controls from 52 countries (the INTERHEART study): case-control study. Lancet 2004;364(9438):953–62.
[16] Eaker ED, Sullivan LM, Kelly-Hayes Sr M, D'Agostino RB, Benjamin EJ. Marital status, marital strain, and risk of coronary heart disease or total mortality: the Framingham Offspring Study. Psychosom Med 2007;69:509–13.
[17] Teo KK, Ounpuu S, Hawken S, Pandey MR, Valentin V, Hunt D. Tobacco use and risk of myocardial infarction in 52 countries in the INTERHEART study: a case-control study. Lancet 2006;368(9536):647–58.
[18] Prescott E, Hippe M, Schnohr P, Hein HO, Vestbo J. Smoking and risk of myocardial infarction in women and men: longitudinal population study. BMJ 1998;316:1043–7.
[19] Williams B, Mancia G, Spiering W, Agabiti Rosei E, Azizi M, Burnier M. 2018 ESC/ESH Guidelines for the management of arterial hypertension. Eur Heart J. 2018;39(33):3021–104.
[20] Whelton PK, Carey RM, Aronow WS, Casey Jr. DE, Collins KJ, Dennison Himmelfarb C. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: executive summary: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation 2018;138(17):e426–83.
[21] Yusuf S, Hawken S, Ounpuu S, Bautista L, Franzosi MG, Commerford P. Obesity and the risk of myocardial infarction in 27,000 participants from 52 countries: a case-control study. Lancet 2005;366(9497):1640–9.
[22] McQueen MJ, Hawken S, Wang X, Ounpuu S, Sniderman A, Probstfield J. Lipids, lipoproteins, and apolipoproteins as risk markers of myocardial infarction in 52 countries (the INTERHEART study): a case-control study. Lancet 2008;372(9634):224–33.
[23] Neaton JD, Blackburn H, Jacobs D, Kuller L, Lee DJ, Sherwin R, et al. Serum cholesterol level and mortality findings for men screened in the Multiple Risk Factor Intervention Trial. Multiple Risk Factor Intervention Trial Research Group. Arch Intern Med 1992;152:1490–500.
[24] Gerstein HC, Islam S, Anand S, Almahmeed W, Damasceno A, Dans A, et al. Dysglycaemia and the risk of acute myocardial infarction in multiple ethnic groups: an analysis of 15,780 patients from the INTERHEART study. Diabetologia 2010;53(12):2509–17.
[25] Introduction: Standards of Medical Care in Diabetes-2019. Diabetes Care. 2019;42(Suppl 1):S1-s2.
[26] Chapman MJ, Ginsberg HN, Amarenco P, et al. Triglyceride-rich lipoproteins and high-density lipoprotein cholesterol in patients at high risk of cardiovascular disease: evidence and guidance for management. Eur Heart J 2011;32:1345–61.
[27] Sarwar N, Danesh J, Eiriksdottir G, Sigurdsson G, Wareham N, Bingham S, et al. Triglycerides and the risk of coronary heart disease: 10,158 incident cases among 262,525 participants in 29 Western prospective studies. Circulation 2007;115:450–8.
[28] Held C, Iqbal R, Lear SA, Rosengren A, Islam S, Mathew J. Physical activity levels, ownership of goods promoting sedentary behaviour and risk of myocardial infarction: results of the INTERHEART study. Eur Heart J 2012;33(4):452–66.
[29] Lollgen H, Bockenhoff A Knapp. Physical activity and all-cause mortality: an updated meta-analysis with different intensity categories. Int J Sports Med 2009;30:213–24.
[30] Iqbal R, Anand S, Ounpuu S, Islam S, Zhang X, Rangarajan S. Dietary patterns and the risk of acute myocardial infarction in 52 countries: results of the INTERHEART study. Circulation 2008;118(19):1929–37.
[31] Sofi F, Abbate R, Gensini GF, Casini A. Accruing evidence on benefits of adherence to the Mediterranean diet on health: an updated systematic review and meta-analysis. Am J Clin Nutr. 2010;92:1189–96.
[32] Leong DP, Smyth A, Teo KK, McKee M, Rangarajan S, Pais P. Patterns of alcohol consumption and myocardial infarction risk: observations from 52 countries in the INTERHEART case-control study. Circulation 2014;130(5):390–8.
[33] Holmes TMV, Dale CE, Zuccolo L, et al. Association between alcohol and cardiovascular disease: mendelian randomisation analysis based on individual participant data. BMJ 2014;349:g4164–218.