

UNSATISFACTORY CARDIOVASCULAR RISK CONTROL – OPPORTUNITIES FOR FAMILY MEDICINE NEZADOSTNO OBVLADOVANJE DEJAVNIKOV TVEGANJA ZA SRČNO- ŽILNE BOLEZNI – PRILOŽNOST ZA DRUŽINSKO MEDICINO

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Abstract

Although theoretically very effective and apparently quite straightforward, cardiovascular prevention leaves much to be desired in practice. Several reasons, including ethical, conceptual, psychological, and operative pitfalls (lifestyle changes are mostly ignored; drug therapy is too often prescribed with no good reason, and performed in an episodic or on/off way) are presented in this essay. Discussed are the grounds of these aberrations and suggested are some intuitive solutions, best achievable in family practice.

Key words: cardiovascular diseases, prevention, family medicine

Pregledni znanstveni članek
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Izvelek

Preprečevanje srčno-žilnih bolezni je teoretično zelo učinkovito in na videz precej enostavno, vendar pa je treba v praksi na tem področju še marsikaj storiti. Prispevek opisuje razloge takšnega stanja, tj. etične, konceptualne in psihološke dejavnike ter težave pri izvajanju. Zdravljenje z zdravili prevečkrat predpišemo brez pravega razloga, poteka pa občasno in neredno. Prispevek obravnava vzroke teh slabosti in predlaga nekaj rešitev, ki jih najlaže ponudi družinska medicina.

Ključne besede: srčno-žilne bolezni, preprečevanje, družinska medicina

Medical research has markedly improved the knowledge of etiology and prevention of cardiovascular conditions, particularly coronary heart disease (CHD), so that these disorders could virtually be eliminated. Indeed, several years ago, the global community was seemingly approaching the eradication of atherosclerosis, the leading cause of cardiovascular morbidity and mortality. Unfortunately, in reality the expectations had not been met: nowadays the decrease in CHD in economically developed countries is stagnant (1), the prevalence of CDH is probably increasing (2), while in developing and transitional countries it is escalating (3). This gloom picture is often attributed to unavailability of or to a delay in using modern invasive procedures and new medications, particularly in patients with heart attack or stroke.

Although this segment of management should not be neglected (e.g. prompt and accurate diagnosis, early initiation of treatment in family practice, faster transportation, better organization and distribution of adequately staffed and well equipped interventional units), the bulk of the problem lies at the other end of the clinical spectrum – in unsatisfactory prevention. The EURASPIRE III results (4) show that during the past decade the prevalence of obesity among coronary patients in Europe has increased from 25% to 38%, and that of diabetes from 17.4% to 28%, while smoking and hypertension rates remained unchanged, i.e. approx. 20 % and 60%, respectively.

Which are the obstacles on the path to effective primary prevention of CHD, i.e. to adequate protection of apparently healthy, younger people against adverse

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cardiovascular events? In this paper some of the most important issues are presented from the family physician's standpoint, partly skewed by the Croatian experience in the field.

- 1) Low perception of deferred risk. Any patient will seek urgent medical attention for acute, painful events, such as fibrinous pericarditis or coronary spasm. On the other hand, chronic conditions, such as arterial hypertension, hyperlipoproteinemia or glucose intolerance, are much less alarming and often painless. The management, especially primary prevention, consisting of adequate nutrition, avoidance of weight gain, exercise and/or smoking cessation, is mostly neglected or at best performed in an episodic way. The reasons are probably psychological (5): in spite of good theoretical knowledge of the problem, practical execution leaves much to be desired because human perception of deferred risk is considerably inferior to the appreciation of imminent danger. For this reason people unwillingly fasten seatbelts, and put them on more for the fear of being fined than for the statistically tiny, but individually immense risk of getting injured in the case of a car crash. More than twenty years ago our study showed that declaratively appropriate and cost-effective measures for managing arterial hypertension are seldom implemented in daily practice (6). There is a wide gap between words and deeds, which needs to be bridged both by physicians, patients and the population at large.
- 2) Ethical issues. From the middle of the past century the human rights movement has been rapidly expanding, this development being expected and understandable after incredible crimes against human dignity committed not only during World War II but also previously and subsequently alike (7). Patient autonomy is respected whenever possible, and the traditional, paternalistic doctor-patient relationship is replaced by a kind of negotiating, mutually agreeable partnership, with informed consent as one of its cornerstones. It seems, however, that modern society is moving towards the other extreme: while striving for human rights, the dues tend to be neglected. Although these components of moral judgment should stay in balance – more rights beget more obligations – the ethics of rights is overwhelming the ethics of responsibilities (8). It is increasingly overlooked that individual rights are limited by the rights of the neighbours and the community at large, so that current moral judgment is focusing more closely on individual than on collective interest. Personal

responsibility for careless and hazardous life-style is left out in the cold, but in the case of misfortune instead of silent suffering the health problem is suddenly and vociferously socialized, requesting costly treatment at the expense of solidarity. These inconsistencies in ethics should be corrected if adequate and coherent attitudes towards health care in the community are to be contemplated.

- 3) Decisive role of risk factors. A number of large-scale investigations, from the Framingham cohort to the recent INTERHEART case-control study (9, 10), have clearly demonstrated that CHD is uncommon without a concurrent or antecedent exposure to one or several major risk factors. With the clustering of these factors the probability of CHD complications increases exponentially (Table 1).

Comparable data have been obtained in Croatia as well (11,12). Unfortunately, these clear and simple facts, explaining over 90% of the global coronary risk (9), often go unknown or ignored. A straightforward evaluation of cumulative individual risk, emanating from these studies, is widely disseminated (charts, calculators etc.) and easily accessible to family practitioners. Although it is scientifically sound to investigate additional, novel risk factors, improvement in population levels of several "conventional" risk factors remains the main goal of scientific elucidation and practical enforcement.

- 4) Desirable risk factor levels are uncommon indeed. Alas, this is true for all the populations evaluated, either rich or poor, developed, transitional or developing (12,13). In an analysis of the NHANES-3 data, Vasan et al. (10) have shown that less than 1% of men aged 35-74 years were non smokers, having systolic blood pressure ≤ 120 mm Hg, diastolic blood pressure ≤ 80 mm Hg, LDL cholesterol ≤ 2.6 mmol/l, HDL cholesterol ≥ 1.5 mmol/l, and fasting glucose level ≤ 6 mmol/l or 2-h postprandial glucose level ≤ 7.8 mmol/l. The same was true for women aged 55 to 74 years (10). Stamler et al. (13) have demonstrated years ago that age-adjusted risk of CHD mortality was 77-92% lower for women and men with no major risk factors in relation to the rest of the cohort. Even all-cause mortality rates were 40-58% less for those with no major risk factors compared with the rest of the series, and the estimated life expectancy gain ranged from 5.8 to 9.5 years (13). In a Croatian sample including 5,840 persons aged 18-65 years, 31.1% of the male examinees had BMI ≥ 30 , 31.9% had blood pressure $>140/90$ mm Hg, and the 75th percentiles of serum cholesterol and triglycerides were 6.6 and 2.6 mmol/l, respectively (11)!

Table 1. Exponential increase in the probability of acute myocardial infarction with the aggregation of risk factors [according to (9)].

Tabela 1. Eksponentni porast verjetnosti miokardnega infarkta pri agregiranih dejavnikih tveganja.

Risk factor Dejavnik tveganja		Odds ratio Razmerje obeto
1	Smoking kajenje	2.9
2	Diabetes mellitus diabetes mellitus	2.4
3	Arterial hypertension arterijska hipertenzija	1.9
4	Apo B/A 3 rd vs. 1 st tertile koncentracije ApoB/A tretji vs. prvi tercil	3.3
Clustering of the risk factors Kopičenje dejavnikov tveganja	1+2+3	13.0
	1+2+3+4	42.3
	The former + obesity prejšnji + debelost	68.5
	The former + psychosocial factors prejšnji + psihosocialni dejavniki	182.9
	Combination of the former six factors + lack of physical activity + inadequate alcohol intake (more than moderate or total abstinence) kombinacija prejšnjih šestih dejavnikov + pomanjkanje telesne dejavnosti + neustrezno pitje alkohola (več kot zmerno ali popolna abstinenca)	333.7

Table 2. A comparison of control and high risk 14-year-old pupils in Split, Croatia [according to (14)].

Tabela 2. Primerjava kontrolne skupine in skupine 14-letnih učencev z visokim tveganjem, Split, Hrvaška, glede na (14).

Parameter Parameter	Control children Kontrolna skupina otrok (n=139)	Children of parents having AMI <45 years Otroci staršev z AMI<45 let	
		History only samo anamneza (n= 97)	Additional risk factors Dodatni dejavniki tveganja (n= 50)
Relative weight (%)* Relativna telesna teža	99.5±11.2	103.8±15.2 [†]	110.1±16.7 [‡]
Plasma cholesterol (mmol/l) Plazemski holesterol	4.4±0.6	5.2±1.1 [†]	5.4±1.2 [‡]
Systolic blood pressure (mm Hg) Sistolični krvni tlak	114.3±8.5	116.6±15.3 [†]	122.9±17.0 [‡]
Diastolic blood pressure (mm Hg) Diastolični krvni tlak	73.6±7.3	74.3±12.7 [†]	79.7±13.3 [‡]

*Body mass in kg as % of ideal weight for age/gender; [†]p<0.05; [‡]p<0.001 vs. control group.

5) Early detection of persons at higher risk for CHD is of paramount importance. The child is recycling the genetic (inner) and micro-social (outer) characteristics of man. Because of risk factors clustering among the offspring of people suffering from premature atherosclerotic events, these “stigmatized” individuals should be identified, screened, and evaluated early in childhood or at school age. The yield is high and the number of persons to be assessed is low; the cost of intervention is almost negligible, and lifestyle interventions (e.g. dietary habits, exercise and/or antismoking programs) may have a durable and decisive impact on prognosis. Marked differences were demonstrated between school-age children of parents with premature CHD (offspring aged 14.2 ± 4.8 , parents 39.9 ± 4.2 years) and their control school-age peers (aged 14.2 ± 0.6 years) (14) (Table 2).

The probability of adverse prognosis was even higher in the presence of additional risk factors; e.g. the prevalence of arterial hypertension among these high-risk children was 46.4%, and that of smoking was even higher, i.e. 51.3% (14). These data send us the following vivid message:

- a) The incidence of early atherosclerotic complications at young age is low (<5% of the CHD patients), and the prevalence in those patients' offspring among their peers is even lower (<1%);
 - b) Some conventional risk factors (e.g. smoking, obesity) are detectable at a glance, while others, such as hyperlipoproteinemia and hypertension, are confidently and cheaply identified in those selected individuals;
 - c) Simple measures, such as dietary advice or smoking cessation programs, and rare, specific interventions (e.g. statins in heterozygous familial hypercholesterolemia) substantially improve the cardiovascular prognosis in these individuals.
- 6) General measures are underestimated and largely ignored. The effectiveness of well structured counseling on lifestyle modifications has been ascertained beyond any reasonable doubt (15). However, just a minor portion of persons at increased risk quit smoking, decrease body mass and salt intake, adopt a “Mediterranean” diet or engage in adequate exercise for any longer period of time (16, 17). There are several formal reasons for this situation; some pertain to fluid diagnostic criteria (e.g. for the metabolic syndrome) or overlapping guidelines (e.g. misunderstandings

about global cardiovascular risk assessment by the Framingham and SCORE tables, although the former is obviously related to morbidity, and the latter to mortality) (18). However, fundamental are socio-economic and cultural barriers^{5,17} which may be overcome by early gentle and persistent education about healthy lifestyles, extending from family to school and involving the whole community. Additional effects may be obtained through legislation and law enforcement (e.g. higher smoking taxation and/or banning).

- 7) Drug therapy is hastily prescribed in primary prevention. Potent drugs are too often prescribed on the ground of a single laboratory result or blood pressure reading. Such interventions are frequently superfluous because of false positive findings (e.g. white coat hypertension, biological variation, laboratory flaw) or could be postponed while waiting for the results of effective lifestyle modifications. Moreover, wide implementation of pharmacotherapy in primary prevention bears several burdens:
 - a) Individual prognosis in a low-risk population is only marginally, although statistically significantly, improved by the use of highly effective modern drugs (e.g. statins, ACE inhibitors): the medication must be taken by several hundreds of low-risk individuals for years to benefit just a few;
 - b) The expected side-effects (e.g. angioedema with ACE inhibitors, myopathy with statins), although rare, (incidence rate well below 0.1%) become alarming when legions of apparently healthy individuals are exposed to the intervention;
 - c) The probability of adequate intake of this medication is inversely proportional to subjective ailments, motivation, and the number of people exposed. Noncompliance becomes the rule rather than an exception, particularly if the subjects are inadequately informed and motivated;
 - d) This approach is extremely expensive, and could absorb up to 25-50% of all the funds available to health service (19). Pharmacoeconomic analyses are invaluable in addressing these issues, but other variables, such as political feasibility and social acceptability, must be kept in mind as well (20). For instance, what about the proposed wide prescribing of statins to children over eight years of age if their LDL cholesterol is above 4.9 mmol/l (or just > 4.1 mmol/l in the case of positive family history or two additional risk factors) (21)?

- 8) Only well tolerated, highly effective medications should be prescribed in primary prevention. Which kind of evidence is good enough in this respect? Because of extremely high cost of large randomized clinical trials, conducted under time constraint and based upon logically plausible presumptions, “soft” goals, i.e., “surrogate end-points”, such as amelioration of a clinical sign or a laboratory result, are investigated instead of “hard” endpoints (e.g. death, stroke, acute myocardial infarction). Although attractive, such trials are often misleading, as shown by a large, randomized and controlled clinical study on antiarrhythmic agents following myocardial infarction (22) carried out several years ago; and recently by the attempts to control the atherosclerotic process by elevating HDL cholesterol levels (23). It is self-evident that results of unconvincing clinical trials should not be implemented in practice. However, even the messages given by large, well-designed, randomized clinical trials with hard end-points (mostly hospital-based and including very sick inpatients) must not be literally extrapolated to family practice i.e. to mostly ambulatory and less sick, outpatients, since two opposite extremes of the same nosologic spectrum are at stake. Then, again, the treatment may have worse effects than the disease itself, as argued in paragraph 7.
- 9) Pharmacotherapy is underused in secondary CHD prevention. In contrast to primary prevention which shows a tendency to overprescribe pharmacotherapy, in secondary prevention, protective drugs are quantitatively and qualitatively underprescribed for

individuals at substantially higher risk. Again, the reasons are manifold, from differences in opinions and attitudes encountered in various countries and even regions, to the neglect of convincing scientific evidence. This is sometimes due to fear of possible adverse effects, which, considering a favorable risk/benefit ratio in this case, are quite acceptable (24,25). However, there are differences in the level of therapeutic gain between the available interventions because of unequal intrinsic efficacy and dissimilar patient characteristics. This concept is best illustrated with the number of patients who require treatment to prevent one event (NNT). The relative cost/effectiveness reasoning is clearly illustrated in the following example. Suppose that a country may afford about eight million € to give simvastatin, one of the best known statins, in a daily dose of 20 mg to 25,000 people with increased CHD risk. If such treatment is given to high-risk individuals (4S study criteria) it can save some 190 lives per year; if the treatment is offered to medium-risk individuals (HPS study criteria), it can save about 90 persons, and if the treatment is offered to lower-risk individuals (WOSCOPS or ASCOT-LLA criteria) some 69 deaths can be prevented with the same investment (19). Many coronary patients may need a complicated drug regimen of variable therapeutic gain (Table 3), consisting possibly of aspirin (acetylsalicylic acid), a β -adrenergic blocker, a statin, an ACE inhibitor, a diuretic, an aldosterone antagonist (e.g. eplerenone), a nitrate, some digoxin, a fish-oil formulation, and other ingredients (26).

Table 3. *Reduced number of events among 1,000 coronary patients treated for one year [according to (26)].*
 Tabela 3. *Zmanjšano število zapletov pri 1000 koronarnih bolnikih po enem letu zdravljenja (26).*

Intervention Ukrep	Fatal and non-fatal complications prevented Preprečene smrtno nevarni ali manj nevarni zapleti	Mortality decrease	
		Deaths prevented Preprečeni smrtni izidi	NNT/ 1 year* NNT/ 1 leto
Beta-blockers Blokatorji beta	42	21	48
Smoking cessation Prenehanje kajenja	61	15	67
Statins Statini	37	7	143
Acetylsalicylic acid Acetilsalicilna kislina	19	7	143
ω -3 fatty acids Omega-3 maščobne kisline	<6	<3	>330

*NNT: number needing treatment (i.e. how many people should receive treatment to benefit one)

Hence, individual selection of the most appropriate regimen in terms of efficacy, tolerability and cost is compelling. One should keep in mind that overtreatment usually leads not only to noncompliance but also to omission of vital interventions in favour of marginal ones.

10) The pivotal role of family medicine. In this review, organizational, financial and political pitfalls have been intentionally skipped for the sake of brevity. In order to lower the prevalence of coronary risk factors in the population, instead of sophisticated technology, invasive procedures and expensive medications, many education efforts coupled with human understanding, persuasion, and common sense are desperately needed. These issues can best be addressed in a personalized, family practice. Hypertension, smoking or weight gain embody many behavioural components that are not easily addressed by formal medical therapy alone. Family medicine has a unique opportunity for behavioral modification at the individual and public health levels, based on empathy, role modeling, and personal skills in communication and education.

It should be remembered that specialist training in family medicine was introduced in Croatia half a century ago (27) and that at the time, Croatian family practice professionals were among the world's leading experts in the field. Instead of treating diseases, family medicine helps sick individuals by enhancing the quality of their life; instead of depersonalized, industrialized services, it offers human understanding, instead of high technology that benefits a few, it delivers efficient care to many, and instead of fee for service, it ensures comprehensive care. After identifying the level of coronary risk, family physician must give pertinent, evidence-based information to a patient (or a small group of patients). He/she must answer the patients' questions, allow time for data interpretation, and, after a while, schedule a discussion about their views, problems, and steps to be taken. Such a task takes a lot of time, dedication and commitment to be effective. Family physicians must be adequately remunerated for their services and unburdened of huge capitation rates (presumably not more than 1,500 under care in Croatia) and cumbersome administration, setting aside two hours per day for preventive and educational purposes. That such amendments are feasible was recently shown in the field of minor surgery (28). Intrinsic to family medicine are certain attitudes that are not readily taught at medical schools: the need to compromise, humility, tolerance and acceptance of different values (29). The most important teaching

method is acting as a role model, in other words being an exemplar of *decorum* (i.e. a propriety of appearance and behaviour) that manifest one's inner virtues, e.g. in order for a physician in the field of preventive cardiology to be persuasive, he/she must not be an authoritative, obese smoker.

Preventive programs should be cost-effective. However, humanism is about quality and not quantity. It is hardly defined and measured in a quantitative manner. Fine qualitative research, followed by quantitative studies, should be done to convince the politicians of the benefits and advantages of investing in family practice (29). In this perspective, we foresee the solution for the stagnant or worsening circumstances in preventive cardiology.

Finally, we would mention some additional relevant problems emerging in everyday practice, which a competent family physician must be able to solve individually, on the spot:

- At which level a risk factor becomes a disease (e.g. millimeters of mercury for blood pressure or millimoles per liter for cholesterol, glucose or uric acid)?
- Which are the pros and cons of labeling a newly discovered, at-risk but apparently healthy, symptomless person as sick (e.g. hypertension, hyperlipidemia)?
- Should the patient be scared, encouraged or something else?
- When it is appropriate to refer a patient for a specialist consultation?
- How to overcome the apparent conflict between general measures – which as a rule are ignored –, and drug therapy which is accepted and even requested, mostly for episodic, on/off and ineffective treatment? In other words: how to bridge the gap between scientific evidence and crude reality?

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