

# COMPARISON OF CARDIOVASCULAR RISK SCREENING METHODS AND MORTALITY DATA AMONG HUNGARIAN PRIMARY CARE POPULATION: PRELIMINARY RESULTS OF THE FIRST GOVERNMENT-FINANCED MANAGED CARE PROGRAM

## PRIMERJAVA METOD PRESEJANJA OGROŽENOSTI SRČNO-ŽILNEGA SISTEMA IN PODATKOV O SMRTNOSTI MADŽARSKEGA PREBIVALSTVA Z OSNOVNO ZDRAVSTVENO OSKRBO: PREDHODNI REZULTATI PRVEGA PROGRAMA VODENE OSKRBE, KI GA JE FINANCIRALA VLADA

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### ABSTRACT

#### Keywords:

cardiovascular screening, mortality, Hungary, managed care, primary health care

**Introduction.** Besides participation in the primary prevention, screening as secondary prevention is an important requirement for primary care services. The effect of this work is influenced by the characteristics of individual primary care practices and doctors' screening habits, as well as by the regulation of screening processes and available financial resources. Between 1999 and 2009, a managed care program was introduced and carried out in Hungary, financed by the government. This financial support and motivation gave the opportunity to increase the number of screenings.

**Method.** 4,462 patients of 40 primary care practices were screened on the basis of SCORE risk assessment. The results of the screening were compared on the basis of two groups of patients, namely: those who had been pre-screened (pre-screening method) for known risk factors in their medical history (smoking, BMI, age, family cardiovascular history), and those randomly screened. The authors also compared the mortality data of participating primary care practices with the regional and national data.

**Results.** The average score was significantly higher in the pre-screened group of patients, regardless of whether the risk factors were considered one by one or in combination. Mortality was significantly lower in the participating primary practices than had been expected on the basis of the national mortality data.

**Conclusion.** This government-financed program was a big step forward to establish a proper screening method within Hungarian primary care. Performing cardiovascular screening of a selected target group is presumably more appropriate than screening within a randomly selected population. Both methods resulted in a visible improvement in regional mortality data, though it is very likely that with pre-screening a more cost-effective selection for screening may be obtained.

### IZVLEČEK

#### Ključne besede:

presejanje za srčno-žilno ogroženost, smrtnost, Madžarska, vodena oskrba, osnovno zdravstveno varstvo

**Uvod.** Poleg primarne preventivne je presejanje kot sekundarna preventiva pomemben člen pri storitvah osnovnega zdravstvenega varstva. Na uspešnost tovrstnega dela vplivajo značilnosti posameznih splošnih ambulant varstva in pripravljenost zdravnikov za izvajanje presejalnih pregledov kot tudi ureditev procesov presejanja in razpoložljivih finančnih virov. Med leti 1999 in 2009 je bil v Madžarski uveden in izpeljan program vodene oskrbe, ki ga je financirala vlada. Ta finančna podpora in spodbuda je omogočila priložnost za povečanje števila presejalnih pregledov.

**Metode.** 4462 pacientov iz 40 splošnih ambulant je bilo vključenih v presejalni pregled v sklopu ocene tveganja SCORE. Rezultate presejanja se je primerjalo na podlagi dveh skupin pacientov, in sicer tistih, ki so bili predhodno presejani (metoda predhodnega presejanja) za znane dejavnike tveganja v njihovi zdravstveni anamnezi (kajenje, indeks telesne mase, starost, zgodovina srčno-žilnih obolenj) ter tistih, ki so bili presejani naključno. Avtorji so primerjali tudi podatke sodelujočih splošnih ambulant o smrtnosti z regionalnimi in nacionalnimi podatki.

**Rezultati.** Povprečen rezultat je bil bistveno višji v predhodno presejani skupini pacientov, ne glede na to, ali so bili dejavniki tveganja upoštevani posamično ali v kombinaciji. Smrtnost je bila bistveno nižja pri sodelujočih splošnih ambulantah, kot je bilo pričakovati na podlagi nacionalnih podatkov o smrtnosti.

**Zaključek.** Ta program, ki ga je financirala država, je pomenil velik korak naprej k ustanovitvi ustrezne metode presejanja znotraj madžarskega sistema osnovne zdravstvene oskrbe. Izvajanje presejanja za ogroženost srčno-žilnega sistema pri izbrani skupini je očitno bolj primerno od naključnih pregledov. Obe metodi sta vidno prispevali k izboljšanju regionalnih podatkov o smrtnosti, čeprav je precej verjetno, da se s predhodnim presejanjem doseže bolj stroškovno učinkovita izbira presejanj.

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## 1 BACKGROUND

Cardiovascular diseases are among the leading causes of death worldwide. In Hungary, they are responsible for more than 60,000 cases of death annually (1). Screening can help detect patients with a high cardiovascular risk. Screening itself may not be enough; patients should also be informed and taught how to lead a healthier lifestyle. It is also necessary to treat them and provide follow-up (2).

Over previous decades, a number of methods for cardiovascular risk evaluation have been developed. EuroSCORE is the most accepted system in Europe and in Hungary. The SCORE system predicts the probability of a patient's cardiovascular mortality within ten years (3).

National cardiovascular screening programs usually focus on the whole population within selected age-categories. An example of this is the UK government's recommended national strategy to screen all adults aged 40-74 for cardiovascular risks. However, the financial demand of cardiovascular screening is huge, therefore, it is essential to find the appropriate method to choose the target population. One way focuses on a probably high-risk population (for example, smokers, obese people, etc.), which is identified by different pre-screening methods, such as using questionnaires (e.g. the Findris-questionnaire), or the data of patients' medical records (4).

Screening for cardiovascular diseases is usually the task of general practitioners on the basis of definite protocols, and it is financed by health insurance agencies or governments. As an initiative, between 1999 and 2009, a government-financed managed care project was introduced and carried out in Hungary (5). A part of this project included complex screening programs to improve morbidity and mortality of the population of participating regions.

### 1.1 Aims

- The main scope of this paper is to describe the cardiovascular screening program which was organized in Bács-Kiskun County, Central-Eastern Hungary, including the implementation and the appraisal of the project.

Other goals:

- Evaluation and comparison of the outcomes of the two different screening methods with a pre-screened and randomly selected population.
- Comparison of practice-based and regional/national mortality data.

## 2 SUBJECTS AND METHODS

### 2.1 Selection of Participants

The managed health care system (MHCS) was introduced and applied in Hungary between 1999 and 2009. The gradually expanding system finally covered 22% of the population and included the full spectrum of curative-preventive health care. To join the MHCS, general practitioners had to submit an application to the National Health Insurance Fund Administration (NHIFA). If the NHIFA accepted it, the patients belonging to each general practitioner got into the system automatically. The main points of acceptance were the public health status of a given region of the country and the rate of risk adjusted quote of a given region. Other key persons of the MHCS were case managers, who were interested in the optimization of patient paths. Case managers accomplished a provider and financing function. Case managers of Bács-Kiskun County worked in Kecskemét.

As mentioned above, each case manager had to organize a complex public health prevention program. Our program, which focused on screening and preventing cardiovascular diseases, was started in Bács-Kiskun County involving 4,462 patients of 40 primary care practices. Between 2006 and 2009, participants were recruited from three different sites; the city of Kecskemét (county seat), and from smaller towns and villages of the neighbouring area.

### 2.2. Inclusion Criteria

General criteria: persons without any known cardiovascular disease and without any medication were applicable for both methods.

Pre-screened patients were selected from the following groups:

- Patients who have not visited their general practitioners for more than two years and whose medical history contained at least one of the following:
  - male over 55 years of age,
  - female over 65 years of age,
  - cardiovascular event (acute myocardial infarction or stroke) in the family medical history,
  - smoker,
  - body mass index (BMI) > 25 kg/m<sup>2</sup> (measured during previous encounters).

Family doctors were authorized to involve randomly selected patients without any known cardiovascular disease and who did not meet the other specific criteria mentioned above.

### 2.3 Exclusion Criteria

- under 18 years of age,
- pregnancy.

Patients who met the inclusion criteria were called in by mail.

### 2.4 Screening Procedures

A data sheet was filled in with the following data:

- personal medical history coded according to the International Classification of Diseases 10th version (ICD-10) (6),
- cardiovascular diseases and/or diabetes mellitus in the family medical history,
- questions about the patient's lifestyle: smoking, alcohol consumption, amount of physical activity,
- anthropometric measurements (body height and weight, calculation of BMI, waist circumference),
- laboratory tests (fasting blood glucose, triglyceride, total-cholesterol, high and low density lipoproteins, high sensitivity C-reactive protein (hs-CRP) level).

Special questions were focused on the eating habits of patients, applicable for the Hungarian circumstances.

Patients were asked to sign the Informed Consent Form.

### 2.5 Intervention

The intervention depended on patients' cardiovascular risk status, and it consisted of the following points:

- if any cardiovascular disease or diabetes mellitus was diagnosed, the patient's family doctor started treating it on the basis of national guidelines,
- high risk patients were initiated follow-ups based on the guidelines of the 5th Hungarian Cardiovascular Consensus Conference (7),
- each patient received personal information about a healthy life style.

The patients' follow-ups were tailored by the above mentioned guidelines.

### 2.6 Mortality Data

After finishing the program, the benefits of screening for the local population were estimated by the comparison of the mortality data of participating family practices and the regional and national mortality trends based on the data of the national census of 2011 (1).

### 2.7 Informatics Support Available for the Program

An electronic medical sheet and a questionnaire about eating habits were integrated into general practitioners' computer program. Program users could download patients' laboratory results from the server of the central laboratory. SCORE points were calculated and recommended changes in lifestyle were generated by software for each patient, and a follow-up plan was established for medical teams on the basis of two data sources and current protocols.

### 2.8 Statistics

Before statistical data processing, the database was checked accurately. The questionable data were revised based on the participating general practitioners' databases, and were corrected or deleted. The outcome of the groups was compared with the Student's t-test, which required p values of less than 0.05.

Besides the crude mortality ratio (death / 1000 people), standardized mortality ratios were calculated with regards to the number of observed deaths as opposed to the expected number of deaths in the given population. For calculating the expected number of deaths, we used Hungarian age- and gender-specific mortality data. The basic year was 2011.

### 2.9 Ethics

The study was previously approved by the Regional Ethical Committee.

## 3 RESULTS

### 3.1 Results of Cardiovascular Screening Program

#### 3.1.1 Characteristics of Population

Altogether 4,462 patients were screened, 1,977 men and 2,485 women. The average age in total was 47.4 years (median: 49 years), 47.9 for men and 47.1 for women.

Table 1 shows the distribution of the study population by gender, age, family medical history, BMI, presence of metabolic syndrome (8), alcohol consumption, regular physical activity and smoking. The anthropometric characteristics of the sample and the results of laboratory tests are presented in Table 2.

**Table 1.** Distribution of the study population by gender, age, family medical history, BMI, metabolic syndrome, alcohol consumption, regular physical activity and smoking.

|                                    | Men   |      | Women |      |
|------------------------------------|-------|------|-------|------|
|                                    | N     | [%]  | N     | [%]  |
| Gender                             | 1,977 | 44.3 | 2,485 | 56.7 |
| Distribution of age-groups         |       |      |       |      |
| w18-19 [year]                      | 9     | 0.5  | 19    | 0.8  |
| 20-29                              | 121   | 6.1  | 205   | 8.3  |
| 30-39                              | 259   | 13.1 | 337   | 13.6 |
| 40-49                              | 653   | 33.1 | 771   | 31.1 |
| 50-59                              | 666   | 33.7 | 813   | 32.8 |
| 60-69                              | 266   | 13.5 | 335   | 13.5 |
| 70-80                              | 2     | 0.1  | 2     | 0.8  |
| Family medical history             |       |      |       |      |
| Acute myocardial infarction        | 17    | 0.8  | 24    | 0.9  |
| Stroke                             | 5     | 0.2  | 7     | 0.2  |
| BMI categories[kg/m <sup>2</sup> ] |       |      |       |      |
| underweight<br>(BMI<18.5)          | 9     | 0.5  | 47    | 1.9  |
| normal<br>(BMI:18.5-24.9)          | 481   | 24.3 | 987   | 39.8 |
| overweight<br>(BMI: 25-29.9)       | 904   | 45.8 | 863   | 34.8 |
| obese<br>(BMI:30-39.9)             | 534   | 27.0 | 522   | 21.0 |
| severe obese<br>(BMI>40)           | 48    | 2.4  | 63    | 2.5  |
| Metabolic syndrome                 | 389   | 19.7 | 467   | 18.8 |
| Alcohol consumption*               | 895   | 45   | 253   | 10   |
| Regular physical activity **       | 648   | 32   | 730   | 29   |
| Smokers                            | 395   | 20   | 266   | 10.7 |

\*women: more than 2 dl beer or 1 dl wine or 3 cl spirits/day, men: more than 5 dl beer or 2 dl wine or 3 cl spirits/day

\*\*weekly at least 3x 30 min. dynamic sport activity

**Table 2.** Results of anthropometric measurements and laboratory tests.

| Anthropometric and laboratory data | Men   |      | Women |      | All   |      |
|------------------------------------|-------|------|-------|------|-------|------|
|                                    | avg   | SD   | avg   | SD   | avg   | SD   |
| Diastolic Blood pressure [Hgmm]    | 83.1  | 19.5 | 81.4  | 28.3 | 82.2  | 24.8 |
| Systolic Blood pressure [Hgmm]     | 133.8 | 16.4 | 128.4 | 16.4 | 130.8 | 16.6 |
| Total serum cholesterol [mmol/l]   | 5.5   | 1.3  | 5.5   | 2.1  | 5.5   | 1.8  |
| High density lipoprotein [mmol/l]  | 1.5   | 0.4  | 1.7   | 4.5  | 1.6   | 3.4  |
| Triglyceride [mmol/l]              | 2.0   | 5.8  | 1.4   | 0.9  | 1.7   | 3.9  |
| Fasting blood glucose [mmol/l]     | 5.4   | 1.3  | 5.1   | 1.0  | 5.2   | 1.2  |
| hs-CRP [mg/l]                      | 4.2   | 7.7  | 4.1   | 0.1  | 4.2   | 7.6  |
| Weight [kg]                        | 85.5  | 16.4 | 71.6  | 15.4 | 77.8  | 17.3 |
| Waist circumference [cm]           | 99.1  | 15.3 | 91.8  | 33.9 | 95.0  | 13.5 |

The appraisal of patients with high cardiovascular risk was based on the criteria of the 5th Hungarian Cardiovascular Consensus Conference (7).

### 3.1.2 SCORE Risk Assessment

Table 3 shows the distribution of the screened patients on the basis of SCORE assessment.

266 patients were classified into high cardiovascular risk group on the basis of SCORE assessment (cardiovascular risk 5% or more). There were more men (252) in the high risk group than women (14).

**Table 3.** Patients' distribution on basis of SCORE assessment.

| SCORE categories | men | %    | women | %    | total | %    |
|------------------|-----|------|-------|------|-------|------|
| <1%              | 493 | 24.9 | 1,556 | 62.7 | 2049  | 46.0 |
| 1%               | 637 | 32.2 | 619   | 24.9 | 1256  | 28.0 |
| 2%               | 269 | 13.6 | 221   | 8.9  | 490   | 11.0 |
| 3-4%             | 326 | 16.5 | 72    | 2.9  | 398   | 8.9  |
| 5-9%             | 227 | 11.5 | 14    | 0.6  | 241   | 5.4  |
| 10-14%           | 21  | 1.1  | 0     | 0    | 21    | 0.5  |
| >15%             | 4   | 0.2  | 0     | 0    | 4     | 0.1  |

A further 78 patients with cardiovascular risk below 5% can be assessed into the high cardiovascular risk group: 3 patients' total cholesterol level was more than 8 mmol/L, one patient's systolic blood pressure was higher than 180 mmHg, 66 patients were seriously obese (BMI>40 kg/m<sup>2</sup>) and 9 patients had early cardiovascular event in their family medical history.

### 3.2 Results of the Modelling to Differentiate the Efficacy of the Two Screening Models (Population Based vs. Pre-Screened)

3,420 patients (1,518 men and 1,902 women) were initiated to the study of the pre-screened group. The second group (1,042 patients) was initiated randomly. Table 4. shows the main characteristics of the two groups.

**Table 4.** Characteristics of the two screening model groups by gender, number, age, anthropometric, and laboratory data.

|                                 | Pre-screened group mean(SD) | Randomly initiated group | p value | Pre-screened group mean(SD) | Randomly initiated group | p value |
|---------------------------------|-----------------------------|--------------------------|---------|-----------------------------|--------------------------|---------|
|                                 | men                         | men                      |         | women                       | women                    |         |
| N                               | 1.528                       | 465                      |         | 1.902                       | 577                      |         |
| age [year]                      | 48.9 (9.8)                  | 40.9 (9.6)               | < 0.001 | 53.6 (11.3)                 | 45.5 (10.2)              | < 0.001 |
| diastolic blood pressure [mmHg] | 83.1(8.9)                   | 83.3(47.9)               | 0.846   | 81.8 (33.7)                 | 81.3 (27.0)              | 0.432   |
| systolic blood pressure [mmHg]  | 135.0 (16.5)                | 126.4 (13.3)             | < 0.001 | 132.0 (17.6)                | 127.5 (15.9)             | < 0.001 |
| cholesterol [mmol/l]            | 5.6 (1.4)                   | 5.1 ( 1.1)               | < 0.001 | 5.7 (1.1)                   | 5.5 (2.3)                | < 0.001 |
| HDL [mmol/l]                    | 1.5 (0.4)                   | 1.5 (0.5)                | 0.34    | 1.6 (0.4)                   | 1.7 (0.5)                | 0.18    |
| triglicerid [mmol/l]            | 2.1(6.2)                    | 1.5 (1.4)                | 0.112   | 1.6 (0.9)                   | 1.4 (0.8)                | 0.088   |
| blood glucose [mmol/l]          | 5.4 (0.7)                   | 5.1 (0.7)                | < 0.001 | 5.2 (0.8)                   | 5.1 (1.0)                | < 0.001 |
| hs-CRP [mg/l]                   | 4.3 (1.3)                   | 3.4 (5.8)                | 0.07    | 4.3 (1.0)                   | 4.1 (1.0)                | 0.173   |
| weight [kg]                     | 87.5 (8.0)                  | 72.5 (15.7)              | < 0.001 | 73.6 (14.6)                 | 71.1 (15.6)              | < 0.001 |
| waist circumference [cm]        | 100.9 (13.0)                | 87.7 (10.7)              | < 0.001 | 94.0 (15.7)                 | 91.2 15.2)               | 0.189   |
| LDL-cholesterol [mmol/l]        | 3.1 (1.22)                  | 2.9 (0.9)                | =0.001  | 3.2 (1.0)                   | 3.0 (1.1)                | < 0.001 |
| BMI [kg/m <sup>2</sup> ]        | 28.9 (4.6)                  | 23.1 (1.6)               | < 0.001 | 28.0 (5.4)                  | 26.5(5.2)                | 0.049   |

The mean SCORE point was 1.82 in the pre-screened group and 0.55 in the random screened group (difference: 1.27, p< 0,001). The distribution of the two groups of patients was different based on SCORE categories. Most of the patients in the randomly screened population belonged

to the low risk categories and only three (0.29%) high risk patients were found. However, there were 274 (8.0%) high risk patients in the pre-screened population. Table 5 shows in details the distribution of the two groups on the basis of SCORE points.

**Table 5.** Distribution of pre-screened and random initiated groups on basis of SCORE categories.

| SCORE categories | Pre-screened group |      |       |      | Random initiated group |      |       |      |
|------------------|--------------------|------|-------|------|------------------------|------|-------|------|
|                  | men                |      | women |      | men                    |      | women |      |
|                  | N                  | %    | N     | %    | N                      | %    | N     | %    |
| <1%              | 295                | 19.4 | 622   | 32.7 | 281                    | 60.4 | 404   | 70.0 |
| 1%               | 496                | 32.7 | 398   | 21.0 | 137                    | 29.5 | 150   | 26.0 |
| 2%               | 218                | 14.4 | 595   | 31.3 | 40                     | 8.6  | 19    | 3.3  |
| 3-4%             | 286                | 18.8 | 236   | 12.4 | 5                      | 1.1  | 3     | 0.5  |
| 5-9%             | 200                | 13.2 | 51    | 2.7  | 2                      | 0.4  | 1     | 0.2  |
| 10-14%           | 19                 | 1.2  | 0     | 0    | 0                      | 0    | 0     | 0    |
| >15%             | 4                  | 0.3  | 0     | 0    | 0                      | 0    | 0     | 0    |

### 3.3 Retrospective Aggregate Mortality Data

Aggregated mortality data were collected from the practices after the program had been completed. The average follow-up was 7.15 years. Data contain all causes of mortality and cardiovascular mortality separately.

We had information on 4,182 patients of the 4,461 screened patients. The total number of deaths: 158, mortality 5.7 %° (national: 12.0), cardiovascular death: 46 patients, 1.3 %° (national: 6.4). Table 6 shows mortality data divided by participating settlements.

**Table 6.** Comparison of the mortality data of participating settlements and participating practices.

|                | General            |         | Participating practices |         | Cardiovascular mortality |         | Participating practices |         |
|----------------|--------------------|---------|-------------------------|---------|--------------------------|---------|-------------------------|---------|
|                | crude (death/1000) | SMR (%) | crude (death/1000)      | SMR (%) | crude (death/1000)       | SMR (%) | crude (death/1000)      | SMR (%) |
| Hungary        | 12.0               | 100.0   | -                       | -       | 6.9                      | 100     | -                       | -       |
| Kecskemet      | 11.0               | 63.9    | 3.4                     | 22.2    | 5.3                      | 47.3    | 1.4                     | 27.0    |
| Lajosmizse     | 15.2               | 94.2    | 3.6                     | 23.3    | 7.7                      | 80.1    | 0.7                     | 14.0    |
| Kiskoros       | 14.0               | 81.4    | 4.5                     | 24.0    | 6.7                      | 76.7    | 1.6                     | 33.4    |
| Szabad-szallas | 17.3               | 100.7   | 3.0                     | 19.4    | 8.6                      | 88.4    | 0.0                     | 0.0     |
| Balló-szög     | 14.9               | 86.6    | 6.9                     | 45.0    | 6.2                      | 36.8    | 2.0                     | 39.4    |
| Harta          | 15.8               | 91.8    | 5.4                     | 35.0    | 7.9                      | 81.6    | 1.5                     | 30.6    |
| Tiszaal-pár    | 19.3               | 112.3   | 13.3                    | 87.2    | 9.8                      | 104.0   | 2.4                     | 47.8    |
| Fülophá-za     | 14.6               | 84.9    | 3.2                     | 25.8    | 6.1                      | 57.1    | 1.6                     | 31.2    |
| Helvécia       | 16.2               | 94.2    | 7.9                     | 50.0    | 3.6                      | 49.7    | 0.0                     | 0.0     |
| All practices  | -                  | -       | 5.7                     | 32      | -                        | -       | 1.3                     | 28.8    |

SMR: standardised mortality ratio. SMR was calculated based on Hungarian sex- and age-specific mortality rates in 2011 (9).

## 4 DISCUSSION

Besides participation in the primary prevention, screening as secondary prevention is an important requirement for primary care services (10-12). Opportunistic screening is usually conducted in the daily practice, while programmes for screening the whole population require comprehensive governmental or public health support, including financial coverage (13).

The Hungarian government decided to launch a program (Managed Care System), in which participating general

practitioners were authorized to follow up their patients at the other two levels of the health care system (outpatient's services, provided by specialists, and inpatient services delivered in hospitals). The description of this wider context of collaboration was beyond the scope of this paper. One of the goals of the managed care system of the NHIFA between 1999 and 2009 was that health case managers were expected to organize public health programs for their patients (14). Within the framework of the Managed Care System we focused on screening for cardiovascular diseases in Kecskemét and its region. Our

main aim was to identify patients who had high risk for a cardiovascular disease without any symptoms. We can say, based on our results, that the basis of an effective cardiovascular prevention should be a well-organized, controlled and sufficiently funded screening programme.

Risk score assessments can help us to identify high risk patients, but we have to conduct numerous examinations with negative results to identify the patients at high risk (15). We compared the outcomes of the pre-screened and randomly screened population in terms of the achieved average risk points. The average scores were significantly higher in the case of the 'pre-screening approach.' We found many more high risk patients in the pre-screened group compared with the randomly screened population (17.4 versus 0.6%), which means that, following the opportunistic screening method, we should screen roughly ten times more people to get similar results.

Mortality was significantly lower in the participating primary care practices than expected on the basis of national mortality data.

#### 4.1 Limitation

Unfortunately, we were unable to assess cardiovascular morbidity and mortality more precisely, because the program budget did not allow a longer follow-up period. The data presented in this paper only predict trends without statistical significance and individual follow up.

We concluded that the screening for cardiovascular diseases can find patients with high risk in an early phase. While screening programs focus on whole populations, only a few individuals will benefit from them, so we should narrow the target population by using pre-screening on the basis of the main risk factors. The tight follow-up of patients can reduce the mortality among the screened population.

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#### CONFLICTS OF INTEREST

The authors declare that no conflicts of interest exist.

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#### ETHICAL APPROVAL

The study was previously approved by the Regional Ethical Committee.

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